

# Chromatographic Enantioseparation by Poly(biphenylacetylene) Derivatives with Memory of Both Axial Chirality and Macromolecular Helicity

**Abstract:** Novel poly(biphenylacetylene) derivatives bearing two acetyloxy groups at the 2- and 2'-positions and an alkoxycarbonyl group at the 4'-position of the biphenyl pendants (poly-**Ac**'s) were synthesized by the polymerization of the corresponding biphenylacetylenes using a rhodium catalyst. The obtained stereoregular (*cis-transoidal*) poly-**Ac**'s folded into a predominantly one-handed helical conformation accompanied by a preferred-handed axially twisted conformation of the biphenyl pendants through noncovalent interactions with a chiral alcohol and both the induced main-chain helicity and the pendant axial chirality were maintained, that is memorized, after complete removal

of the chiral alcohol. The stability of the helicity memory of the poly-**Ac**'s in a solution was lower than that of the analogous poly(biphenylacetylene)s bearing two methoxymethoxy groups at the 2- and 2'-positions of the biphenyl pendants (poly-**MOM**'s). In the solid state, however, the helicity memory of the poly-**Ac**'s was much more stable and showed a better chiral recognition ability toward several racemates than that of the previously reported poly-**MOM** when used as a chiral stationary phase for HPLC. In particular, the poly-**Ac**-based CSP with a helicity memory efficiently separated racemic benzoin derivatives into enantiomers.

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**Keywords:** helicity induction; memory; polyacetylene; biphenyl; high-performance liquid chromatography; chiral stationary phase; enantioseparation

## Introduction

Most biologically and pharmacologically active compounds including drugs, cosmetics, agrochemicals and food additives are chiral, and their physiological properties, such as pharmacodynamics, pharmacokinetics, and toxic and metabolic activities, are often different between enantiomers.<sup>1-4</sup> Therefore, the careful investigation of the biological activities of individual enantiomers has become requisite to avoid serious chemical antagonisms. Therefore, in many fields of science and technology related to chiral compounds, the precise analysis of the enantiomeric compositions and the preparation of both enantiopure isomers have become increasingly important. It is well-known that the direct resolution of enantiomers by high-performance liquid chromatography (HPLC) using chiral stationary phases (CSPs) is one of the most useful methods for both analytical and preparative purposes, and a large number of CSPs for HPLC has been developed so far.<sup>5-12</sup> Particularly, since the discovery of one-handed helical poly(triphenylmethyl methacrylate) (PTrMA)<sup>13-17</sup> and polysaccharide derivatives,<sup>18-21</sup> showing an excellent resolution ability as CSPs, a variety of helical polymers have been prepared for using them as CSPs.<sup>12,22-24</sup>

We recently discovered a quite unique helical polymer, a poly(biphenylacetylene) derivative (poly-**MOM-a**) bearing methoxymethoxy (MOM) groups at the 2- and 2'-positions and a *n*-dodecyloxy group at the 4'-position of the biphenyl pendant, that folds into a preferred-handed helical conformation through noncovalent weak interactions with (*R*)- or (*S*)-1-phenylethanol ((*R*)- or (*S*)-**1**) in the solid state as well as in solution, through which the axial chirality of the biphenyl pendants is also biased.<sup>25</sup> The induced macromolecular helicity and the axial chirality of the biphenyl pendants could be memorized even after complete removal of the optically active alcohol. This unique feature of

poly-**MOM-a** allowed us to develop an unprecedented CSP for HPLC, whose helical chirality as well as the axial chirality was directly switched in the column by sequential treatment with an eluent containing (*R*)- or (*S*)-**1**, leading to the reversible switching of the elution order of the enantiomers. However, the chiral recognition ability of the poly-**MOM-a**-based CSP was rather poor due to the lack of effective interaction sites with the enantiomers. In addition, we previously found that the introduction of the methoxy groups or *n*-propoxy groups at the 2- and 2'-positions of the biphenyl pendants instead of the MOM groups resulted in complete disappearance of the helicity memory or no helicity induction, respectively, indicating that the alkoxymethoxy groups at the 2- and 2'-positions play an important role in the helicity induction and its memory.

On the other hand, we recently reported that an analogous poly(biphenylacetylene) poly-**MOM-b** bearing a butoxycarbonyl

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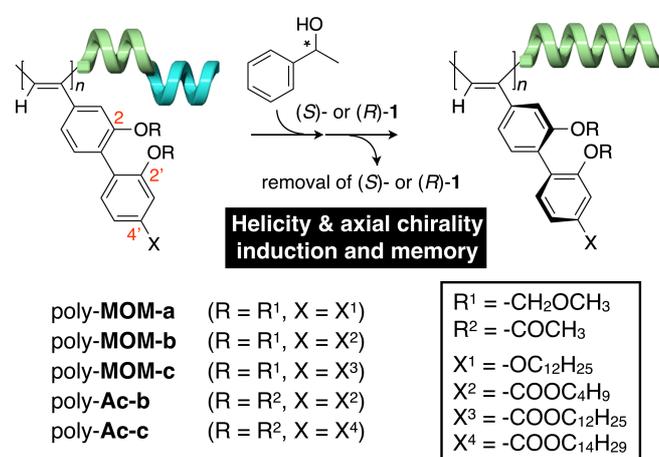
Received: ((will be filled in by the editorial staff))

Revised: ((will be filled in by the editorial staff))

Published online: ((will be filled in by the editorial staff))

ester group at the 4'-position of the biphenyl pendant also showed a similar helicity induction and memory effect and the macromolecular helicity memory of poly-MOM-b was more stably maintained compared with that of poly-MOM-a.<sup>26</sup> Moreover, the poly-MOM-b-based CSP with a helicity memory efficiently resolved several racemic compounds such as chiral binaphthyl compounds and metal tris(acetylacetonato)s. These results suggest that the introduction of a butoxycarbonyl ester group onto the biphenyl pendant can contribute to both the stabilization of the helicity memory and improvement of the chiral recognition ability.

In this study, we synthesized two novel poly(biphenylacetylene)s (poly-Ac-b and poly-Ac-c) bearing two ester (acetyloxy) groups at the 2- and 2'-positions instead of two MOM groups in addition to an ester (alkoxycarbonyl) group at the 4'-position of the biphenyl pendant and investigated the effects of the ester groups at the 2- and 2'-positions on the helicity induction and memory effects along with their chiral recognition abilities as CSPs for HPLC (Scheme 1).



**Scheme 1.** Structures of poly(biphenylacetylene) derivatives bearing various substituents at the 2-, 2'- and 4'-positions of the biphenyl pendant groups. Schematic representation of a preferred-handed macromolecular helicity and axial chirality induction in poly(biphenylacetylene)s through noncovalent interaction with a chiral alcohol ((S)- or (R)-1) and subsequent memory of the helicity and axial chirality after complete removal of the chiral alcohol.

## Materials and Methods

### Instrument

Melting point measurements were performed using a Yanako melting point apparatus and were uncorrected. NMR spectra were measured using a JNM-ECA 500 (JEOL, Tokyo, Japan) spectrometer operating at 500 MHz for <sup>1</sup>H and 125 MHz for <sup>13</sup>C in CDCl<sub>3</sub> using tetramethylsilane (TMS) as the internal standard. IR spectra were recorded with a JASCO (Hachioji, Japan) Fourier Transform IR-460 spectrophotometer. The molecular weights of the polymers were measured by size exclusion chromatography (SEC) on a JASCO PU-2080 liquid chromatograph equipped with a Shodex (Tokyo, Japan) KF-805L (30 cm) column and a photodiode array detector (JASCO MD-2018) at 40 °C using THF as the eluent at a flow rate of 1.0 mL/min. Polystyrene standards (Tosoh, Tokyo, Japan) were used for obtaining the molecular weight calibration curves. Absorption and CD spectra were measured in a 1.0 mm quartz

cell on a JASCO V-570 spectrophotometer and a JASCO J-725 spectropolarimeter, respectively. The temperature was controlled with a JASCO ETC-505T (absorption spectroscopy) and a JASCO PTC-348WI apparatus (CD spectroscopy). The chromatographic enantioseparation experiments were performed using a JASCO PU-2080 liquid chromatograph equipped with a multi-wavelength detector (JASCO MD-2018) and a CD detector (JASCO CD-2095) at ca. 10 °C. TGA was conducted on a SEIKO EXSTAR6000 TG/DTA 6200 (Seiko Instruments Inc., Chiba, Japan) under a heating rate of 30 °C/min. VCD spectra were measured in a 0.50 mm BaF<sub>2</sub> cell with a JASCO JV-2001YS spectrometer equipped with a temperature controller (EYELA NCB-1200) (EYELA, Tokyo, Japan). The concentration was 12 mg/mL in methylcyclohexane (MCH) and temperature was ca. -10 °C. All spectra were collected for ca. 4 h at a resolution of 4 cm<sup>-1</sup>. Elemental analyses were done at the Research Institute for Instrumental Analysis of Advanced Science Research Center, Kanazawa University, Kanazawa, Japan.

### Materials

Anhydrous THF, diethyl ether and dichloromethane were obtained from Kanto Kagaku (Tokyo, Japan). Triethylamine (Et<sub>3</sub>N) was dried over KOH pellets and distilled onto KOH under nitrogen. Acetic anhydride, hydrochloric acid and *N,N*-dimethyl-4-aminopyridine (DMAP) were purchased from Wako Pure Chemical Industries (Osaka, Japan). 1-Dodecanol, 1-tetradecanol, MCH and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC) were from Tokyo Kasei (TCI, Tokyo, Japan). (*R*)- and (*S*)-1 were obtained from Kanto Kagaku. Pyridine, [(norbornadiene)rhodium(I) chloride]<sub>2</sub> [Rh(nbd)Cl<sub>2</sub>] and sodium hydroxide were available from Sigma-Aldrich (St. Louis, MO, USA). The porous spherical silica gel (Daiso gel SP-1000-7) with a mean particle size of 7 μm and a mean pore diameter of 100 nm was kindly provided by Osaka Soda (Osaka, Japan). (2,2'-Bis(methoxymethoxy)-4'-dodecyloxy-4-biphenyl)acetylene (MOM-a)<sup>25</sup> and (2,2'-bis(methoxymethoxy)-4'-butoxycarbonyl-4-biphenyl)acetylene (MOM-b)<sup>26</sup> were prepared according to the previously reported methods.

### Synthesis

(2,2'-Diacetyloxy-4'-butoxycarbonyl-4-biphenyl)acetylene (Ac-b) and (2,2'-diacetyloxy-4'-*n*-tetradecyloxy-4-biphenyl)acetylene (Ac-c) were prepared according to the route shown in Scheme S1.

**Preparation of (2,2'-Dihydroxy-4'-butoxycarbonyl-4-biphenyl)acetylene.** To a solution of compound MOM-b (800 mg, 2.01 mmol) in THF/methanol (1/1, v/v) (270 mL) was slowly added conc. HCl (2.24 mL). After stirring at room temperature for 48 h, the solvent was removed under reduced pressure. The residue was diluted with ethyl acetate and the solution was washed with water and brine, and then dried over Na<sub>2</sub>SO<sub>4</sub>. After filtration, the solvent was removed by evaporation and the crude product was purified by silica gel chromatography using *n*-hexane—ethyl acetate (5/1, v/v) as the eluent to give the desired product as a white solid (616 mg, 99% yield). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, rt): δ 7.76 (d, J = 1.4 Hz, 1H, Ar-H), 7.74-7.71 (dd, J = 1.4, 6.4 Hz, 1H, Ar-H), 7.36 (d, J = 7.8 Hz, 1H, Ar-H), 7.25-7.18 (m,

3H, Ar-H), 6.40-6.05 (broad, 2H, Ar-OH), 4.35 (t,  $J = 6.9$  Hz, 2H, COCH<sub>2</sub>), 3.14 (s, 1H, C≡C-H), 1.77 (quint,  $J = 6.4$  Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>), 1.49 (sex,  $J = 7.8$  Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>), 0.99 (t,  $J = 7.3$  Hz, 3H, CH<sub>2</sub>CH<sub>3</sub>).

**Preparation of Ac-b.** To a solution of (2,2'-dihydroxy-4'-butoxycarbonyl-4-biphenyl)acetylene (168 mg, 0.541 mmol) in anhydrous diethyl ether (5.4 mL) was added pyridine (219  $\mu$ L, 2.70 mmol) and acetic anhydride (255  $\mu$ L, 2.70 mmol). After stirring at room temperature for 12 h, the mixture was diluted with diethyl ether and the solution was washed with 1 N HCl aqueous solution and water. The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub> before evaporating the solvent. The residue was then purified by chromatography on silica gel with *n*-hexane—ethyl acetate (5/1, v/v) as the eluent to give the desired product as a white solid (208 mg, 98% yield). Mp: 95.1-95.7 °C. IR (KBr):  $\nu = 3253$  ( $\equiv$ CH), 2104 (C≡C), 1771, 1710 (C=O) cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, rt):  $\delta$  7.99-7.96 (dd,  $J = 1.8, 6.4$  Hz, 1H, Ar-H), 7.82 (d,  $J = 1.4$  Hz, 1H, Ar-H), 7.45-7.42 (dd,  $J = 1.7, 6.3$  Hz, 1H, Ar-H), 7.37 (d,  $J = 8.0$  Hz, 1H, Ar-H), 7.31 (d,  $J = 1.7$  Hz, 1H, Ar-H), 7.26 (d,  $J = 8.0$  Hz, 1H, Ar-H), 4.35 (t,  $J = 6.4$  Hz, 2H, COCH<sub>2</sub>), 3.16 (s, 1H, C≡C-H), 2.06 (d,  $J = 10.5$  Hz, 6H, 2COCH<sub>3</sub>), 1.77 (quint,  $J = 6.9$  Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>), 1.48 (sex,  $J = 7.8$  Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>), 0.99 (t,  $J = 7.3$  Hz, 3H, CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>, rt):  $\delta$  169.02, 168.86, 165.50, 147.92, 147.59, 134.55, 131.70, 131.12, 130.96, 130.52, 129.79, 127.11, 126.37, 123.87, 123.45, 99.89, 82.23, 78.80, 65.26, 30.71, 20.70, 19.25, 13.77. Anal. Calcd for C<sub>23</sub>H<sub>22</sub>O<sub>6</sub>: C, 70.04; H, 5.62. Found: C, 69.75; H, 5.40.

**Preparation of (2,2'-Bis(methoxymethoxy)-4'-carboxyl-4-biphenyl)acetylene.** To a solution of MOM-b (2.40 g, 6.02 mmol) in THF/methanol (2/1, v/v) (6.0 mL) was added sodium hydroxide (0.36 g, 9.03 mmol). After stirring at 0 °C for 2 h and then at room temperature for 12 h, the mixture was diluted with ethyl acetate and the solution was washed with 1 N HCl aqueous solution and water. After filtration, the solvent was removed by evaporation to give the desired product as a white solid (2.04 g, 99% yield). This was used for the next reaction without further purification. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, rt):  $\delta$  7.92 (d,  $J = 1.7$  Hz, 1H, Ar-H), 7.85-7.81 (dd,  $J = 1.1, 6.8$  Hz, 1H, Ar-H), 7.38 (s, 1H, Ar-H), 7.34 (d,  $J = 8.0$  Hz, 1H, Ar-H), 7.24-7.19 (m, 2H, Ar-H), 5.12 (d,  $J = 29.2$  Hz, 4H, 2OCH<sub>2</sub>O), 3.36 (d,  $J = 4.0$  Hz, 6H, 2OCH<sub>3</sub>), 3.11 (s, 1H, C≡C-H).

**Preparation of (2,2'-Bis(methoxymethoxy)-4'-*n*-tetradecyloxycarbonyl-4-biphenyl)acetylene.** To a solution of (2,2'-Bis(methoxymethoxy)-4'-carboxyl-4-biphenyl)acetylene (100 mg, 0.292 mmol), 1-tetradecanol (81.8 mg, 0.382 mmol), DMAP (46.6 mg, 0.381 mmol) in anhydrous dichloromethane (3.0 mL) was added EDC (89.4 mg, 0.45 mmol) at 0 °C. The mixture was stirred at room temperature for 3 h. After evaporating the solvent, the mixture was diluted with ethyl acetate and the solution was washed with water, and then dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed under reduced pressure and the crude product was purified by silica gel chromatography using *n*-hexane—ethyl acetate (10/1, v/v) as the eluent to give the desired product as a white solid (152 mg, 97% yield). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, rt):  $\delta$  7.85 (d,  $J = 1.2$  Hz, 1H, Ar-H), 7.76-7.74 (dd,  $J = 1.1, 6.3$  Hz, 1H, Ar-H), 7.37 (s, 1H, Ar-H), 7.29 (d,  $J = 8.0$  Hz, 1H, Ar-H), 7.23-7.18 (m, 2H, Ar-H), 5.10 (d,  $J = 24.6$  Hz, 4H, 2OCH<sub>2</sub>O), 4.33 (t,  $J = 6.9$  Hz, 2H, COCH<sub>2</sub>), 3.34 (d,  $J = 4.6$  Hz, 6H, 2OCH<sub>3</sub>), 3.11 (s, 1H, C≡C-H), 1.77 (quint,  $J =$

6.9 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>), 1.44 (quint,  $J = 6.3$  Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>), 1.36-1.22 (m, 20H, CH<sub>2</sub>CH<sub>2</sub>), 0.88 (t,  $J = 6.9$  Hz, 3H, CH<sub>3</sub>).

**Preparation of (2,2'-Dihydroxy-4'-*n*-tetradecyloxycarbonyl-4-biphenyl)acetylene.** To a solution of (2,2'-bis(methoxymethoxy)-4'-*n*-tetradecyloxycarbonyl-4-biphenyl)acetylene (120 mg, 0.22 mmol) in THF/methanol (1/1, v/v) (29.6 mL) was slowly added conc. HCl (246  $\mu$ L). After stirring at room temperature for 30 h, the solvent was removed under reduced pressure. The residue was diluted with ethyl acetate and the solution was washed with water and brine, and then dried over Na<sub>2</sub>SO<sub>4</sub>. After filtration, the solvent was removed by evaporation and the crude product was purified by silica gel chromatography using *n*-hexane—ethyl acetate (3/1, v/v) as the eluent to give the desired product as a white solid (84.7 mg, 84% yield). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, rt):  $\delta$  7.74-7.72 (dd,  $J = 1.7, 6.3$  Hz, 1H, Ar-H), 7.71 (d,  $J = 1.7$  Hz, 1H, Ar-H), 7.35 (d,  $J = 8.0$  Hz, 1H, Ar-H), 7.24-7.16 (m, 3H, Ar-H), 6.0-5.88 (broad, 2H, Ar-OH), 4.33 (t,  $J = 6.9$  Hz, 2H, COCH<sub>2</sub>), 3.14 (s, 1H, C≡C-H), 1.77 (quint,  $J = 6.9$  Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>), 1.44 (quint,  $J = 8.0$  Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>), 1.38-1.20 (m, 20H, CH<sub>2</sub>CH<sub>2</sub>), 0.88 (t,  $J = 6.9$  Hz, 3H, CH<sub>2</sub>CH<sub>3</sub>).

**Preparation of Ac-c.** To a solution of (2,2'-dihydroxy-4'-*n*-tetradecyloxycarbonyl-4-biphenyl)acetylene (70.0 mg, 0.155 mmol) in anhydrous diethyl ether (1.55 mL) was added pyridine (63.0  $\mu$ L, 0.781 mmol) and acetic anhydride (73.3  $\mu$ L, 0.775 mmol). After stirring at room temperature for 12 h, the mixture was diluted with diethyl ether and the solution was washed with 1 N HCl aqueous solution and water. The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub> before evaporating the solvent. The residue was then purified by chromatography on silica gel with *n*-hexane—ethyl acetate (5/1, v/v) as the eluent to give the desired product as a white solid (78.1 mg, 94% yield). Mp: 63.4-64.3 °C. IR (KBr):  $\nu = 3248$  ( $\equiv$ CH), 2104 (C≡C), 1766, 1718 (C=O) cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, rt):  $\delta$  7.98-7.96 (dd,  $J = 1.7, 6.3$  Hz, 1H, Ar-H), 7.82 (d,  $J = 1.7$  Hz, 1H, Ar-H), 7.44-7.42 (dd,  $J = 1.2, 6.3$  Hz, 1H, Ar-H), 7.37 (d,  $J = 8.0$  Hz, 1H, Ar-H), 7.32 (d,  $J = 1.2$  Hz, 1H, Ar-H), 7.26 (d,  $J = 8.0$  Hz, 1H, Ar-H), 4.33 (t,  $J = 6.9$  Hz, 2H, COCH<sub>2</sub>), 3.16 (s, 1H, C≡C-H), 2.06 (d, 6H,  $J = 13.1$  Hz, 2COCH<sub>3</sub>), 1.77 (quint,  $J = 7.4$  Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>), 1.44 (quint,  $J = 6.3$  Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>), 1.36-1.20 (m, 23H, CH<sub>2</sub>CH<sub>2</sub>), 0.88 (t,  $J = 6.8$  Hz, 3H, CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>, rt):  $\delta$  168.99, 168.84, 165.51, 147.95, 147.62, 134.55, 131.73, 131.12, 130.96, 130.55, 129.78, 127.11, 126.38, 123.89, 123.46, 82.24, 78.79, 77.27, 77.02, 76.76, 65.59, 31.92, 29.65, 29.60, 29.53, 29.37, 29.30, 28.68, 26.00, 22.70, 20.69, 20.67, 14.13. Anal. Calcd for C<sub>33</sub>H<sub>42</sub>O<sub>6</sub>: C, 74.13; H, 7.92. Found: C, 73.98; H, 8.00.

**Preparation of (2,2'-Bis(methoxymethoxy)-4'-dodecyloxycarbonyl-4-biphenyl)acetylene (MOM-c).** To a solution of (2,2'-bis(methoxymethoxy)-4'-carboxyl-4-biphenyl)acetylene (150 mg, 0.438 mmol), 1-dodecanol (108  $\mu$ L, 0.580 mmol) and DMAP (70.9 mg, 0.580 mmol) in anhydrous dichloromethane (8.0 mL) was added EDC (128.5 mg, 0.670 mmol) at 0 °C. The mixture was stirred at room temperature for 3 h. After evaporating the solvent, the mixture was diluted with ethyl acetate and the solution was washed with water, and then dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed under reduced pressure and the crude product was purified by silica gel chromatography using *n*-hexane—ethyl acetate (8/1, v/v) as the eluent to give the desired product as a white solid (219 mg, 98% yield). IR (KBr):  $\nu = 3231$  ( $\equiv$ CH), 2105 (C≡C), 1719 (C=O) cm<sup>-1</sup>.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , rt):  $\delta$  7.85 (d,  $J = 1.1$  Hz, 1H, Ar-H), 7.76-7.74 (dd,  $J = 1.1, 6.3$  Hz, 1H, Ar-H), 7.37 (d,  $J = 1.2$  Hz, 1H, Ar-H), 7.30 (d,  $J = 8.0$  Hz, 1H, Ar-H), 7.23-7.18 (m, 2H, Ar-H), 5.10 (d,  $J = 24.0$  Hz, 4H,  $2\text{OCH}_2\text{O}$ ), 4.33 (t,  $J = 6.9$  Hz, 2H,  $\text{COCH}_2$ ), 3.34 (d,  $J = 4.6$  Hz, 6H,  $2\text{OCH}_3$ ), 3.10 (s, 1H,  $\text{C}\equiv\text{C-H}$ ), 1.77 (quint,  $J = 6.9$  Hz, 2H,  $\text{CH}_2\text{CH}_2$ ), 1.47-1.26 (m, 18H,  $\text{CH}_2\text{CH}_2$ ), 0.88 (t,  $J = 6.9$  Hz, 3H,  $\text{CH}_3$ ).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ , rt):  $\delta$  166.43, 154.74, 154.59, 133.21, 131.33, 131.20, 129.24, 125.73, 123.05, 122.87, 118.91, 116.28, 95.22, 95.16, 83.49, 77.54, 77.37, 65.39, 56.19, 56.11, 32.01, 29.76, 29.73, 29.68, 29.66, 29.46, 29.40, 28.84, 26.13, 22.79, 14.23. Anal. Calcd for  $\text{C}_{31}\text{H}_{42}\text{O}_6$ : C, 72.91; H, 8.29. Found: C, 72.78; H, 8.37.

## Polymerization

Polymerizations of **Ac-b**, **Ac-c** and **MOM-c** were conducted with  $[\text{Rh}(\text{nbd})\text{Cl}]_2$  as a catalyst under a dry nitrogen atmosphere according to the method reported previously (Scheme S2)<sup>25</sup> and the results are summarized in Table S1.

Spectroscopic data of poly-**Ac-b**. IR (KBr):  $\nu = 1770, 1720$  ( $\text{C}=\text{O}$ )  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , 55 °C):  $\delta$  7.85-6.50 (br, 6H, Ar-H), 6.20-5.83 (br, 1H,  $\text{C}=\text{CH}$ ), 4.42-4.00 (br, 2H,  $\text{OCH}_2$ ), 2.05-1.20 (br, 6H,  $2\text{COCH}_3$ ), (br, 4H,  $2\text{CH}_2\text{CH}_2$ ), 1.05-0.75 (br, 3H,  $\text{CH}_2\text{CH}_3$ ). Calcd for  $\text{C}_{23}\text{H}_{22}\text{O}_6 \cdot 0.1\text{H}_2\text{O}$ : C, 69.72; H, 5.65. Found: C, 69.49; H, 5.65.

Spectroscopic data of poly-**Ac-c**. IR (KBr):  $\nu = 1772, 1721$  ( $\text{C}=\text{O}$ )  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , 55 °C):  $\delta$  7.85-6.50 (br, 6H, Ar-H), 6.20-5.85 (br, 1H,  $\text{C}=\text{CH}$ ), 4.44-4.00 (br, 2H,  $\text{OCH}_2$ ), 1.90-1.50 (br, 6H,  $2\text{COCH}_3$ ), 1.40-1.15 (m, 24H,  $\text{CH}_2\text{CH}_2$ ), 0.90-0.80 (br, 3H,  $\text{CH}_2\text{CH}_3$ ). Anal. Calcd for  $\text{C}_{33}\text{H}_{42}\text{O}_6 \cdot 0.1\text{H}_2\text{O}$ : C, 73.88; H, 7.93. Found: C, 73.58; H, 7.97.

Spectroscopic data of poly-**MOM-c**. IR (KBr):  $\nu = 1719$  ( $\text{C}=\text{O}$ )  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , 55 °C):  $\delta$  7.77-6.40 (br, 6H, Ar-H), 6.07-5.90 (br, 1H,  $\text{C}=\text{CH}$ ), 4.95-4.55 (br, 4H,  $2\text{OCH}_2\text{O}$ ), 4.33-4.12 (br, 2H,  $\text{OCH}_2$ ), 3.15-2.88 (br, 6H,  $2\text{OCH}_3$ ), 1.78-1.63 (br, 2H,  $\text{CH}_2$ ), 1.45-1.10 (br, 18H,  $\text{CH}_2$ ), 0.90-0.80 (br, 3H,  $\text{CH}_3$ ). Calcd for  $\text{C}_{31}\text{H}_{42}\text{O}_6 \cdot 0.1\text{H}_2\text{O}$ : C, 72.66; H, 8.30. Found: C, 72.45; H, 8.16.

## IR and VCD Calculations

The IR and VCD spectra for a pair of enantiomeric model biphenyl compounds (**M-Ac-c**) of **Ac-c** were calculated using the density functional theory (DFT) method at the B3LYP level and the 6-31G\* basis set in Gaussian 09 program (Gaussian, Inc., Pittsburg, PA) (Fig. S16).<sup>27</sup> The initial dihedral angle between the phenyl groups of the biphenyl units was set to be  $\pm 53.2^\circ$  (right- and left-handed twists (*cisoid*), respectively) on the basis of the crystal structure of **Ac-b** determined by X-ray analysis (Fig. S17) and the *n*-butoxycarbonyl group at the 4'-position of the biphenyl pendant was replaced by a methoxycarbonyl group for simplicity.

## Preparation of HPLC Columns

A solution of poly-**Ac-b** (60 mg) in (*R*)-**1** after standing at 25 °C for 2 h was coated on silica gel (0.39 g) according to the

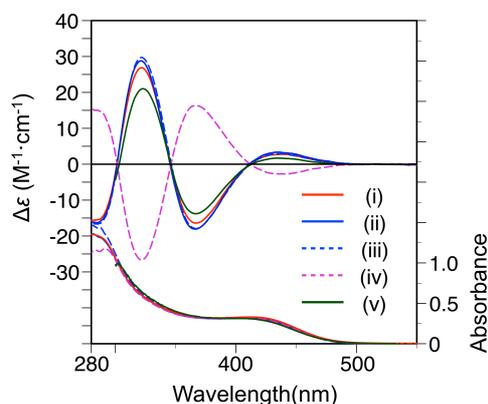
literature method.<sup>28</sup> The poly-**Ac-b** content on the silica gel was estimated to be 13 wt% by thermogravimetric analysis. After fractionating with sieves, the packing material was packed into a stainless-steel column (25  $\times$  0.20 cm (i.d.)) by a slurry method using an ECONO-PACKER MODEL CPP-085 (Chemco).<sup>29</sup> The plate number of the column was estimated for benzene with *n*-hexane/2-propanol (97/3, v/v) as the eluent at a flow rate of 0.2 mL/min at about 10 °C and was 2800. The hold-up time ( $t_0$ ) was estimated using 1,3,5-tri-*tert*-butylbenzene as the non-retained compound.<sup>30</sup>

## Results and Discussion

Two new biphenylacetylene monomers bearing two acetyloxy groups at the 2- and 2'-positions and an *n*-butoxycarbonyl (**Ac-b**) or an *n*-tetradecyloxycarbonyl group (**Ac-c**) at the 4'-position of the biphenyl residue were prepared as outlined in Scheme S1. The polymerizations of **Ac-b** and **Ac-c** were performed in tetrahydrofuran (THF) using a rhodium catalyst ( $[\text{Rh}(\text{nbd})\text{Cl}]_2$ , nbd: norbornadiene) according to a previously reported method,<sup>25</sup> affording the corresponding poly(biphenylacetylene)s, poly-**Ac-b** and poly-**Ac-c**, respectively, in high yields (> 95%) (Scheme S2 and Table S1). The number average molecular weight ( $M_n$ ) and its distribution ( $M_w/M_n$ ) were estimated to be  $5.1 \times 10^5$  and 1.7 (poly-**Ac-b**) and  $6.1 \times 10^5$  and 1.9 (poly-**Ac-c**), respectively, by size exclusion chromatography (SEC) with polystyrene standards in THF. The main-chain stereoregularity of poly-**Ac-b** and poly-**Ac-c** was determined to be highly *cis-transoidal* based on an  $^1\text{H}$  NMR analysis (Fig. S7 and S8).<sup>31,32</sup> Poly-**Ac-c** is soluble even in saturated hydrocarbons, such as *n*-hexane and MCH, whereas poly-**Ac-b** is insoluble in these solvents, but soluble in THF, chloroform and a chiral alcohol **1**. As reported in our previous paper, the stability of the helicity memory of poly-**MOM-a** in solution was largely affected by the solvents; the helicity memory of poly-**MOM-a** was stably maintained in *n*-hexane, while it was quickly lost within a few minutes once dissolved in THF.<sup>25</sup> Therefore, the helicity induction and memory effect were investigated in detail for poly-**Ac-c** in MCH, whereas poly-**Ac-b** with a helicity memory was used to prepare a coated-type CSP for HPLC and its chiral recognition ability was examined under normal phase conditions toward various racemates because poly-**Ac-c** is readily-soluble in eluents under normal phase conditions and its chiral resolving ability as a coated-type CSP could not be evaluated. For comparison, poly-**MOM-c** bearing MOM groups at the 2- and 2'-positions and an *n*-dodecyloxycarbonyl group at the 4'-position of the biphenyl residue, which was soluble in MCH, was also prepared because the previously reported poly-**MOM-b** was insoluble in MCH (Scheme S2 and Table S1).<sup>26</sup>

Poly-**Ac-c** exhibited an intense induced circular dichroism (ICD) in the absorption region of the polyacetylene backbone in the presence of (*S*)- or (*R*)-**1** in MCH at 25 °C (Figs. 1(i) and (iv)), indicating that a preferred-handed helical conformation was induced in poly-**Ac-c** through noncovalent interaction with the chiral alcohol. The ICD intensity gradually increased with time and an increase in the concentration of **1** in MCH and reached a plateau value after standing at 25 °C for 1 h in an MCH/(*R*)-**1** mixture (90:10, v/v) (Fig. S10 and S11). A slight increase in the ICD intensity was also observed at -10 °C (Fig. 1(ii)). Although poly-**Ac-c** exhibited strong ICDs in *n*-hexane and MCH, the ICD intensity significantly decreased in toluene and no detectable ICD signal was observed in THF and chloroform (Fig. S12)

probably due to very weak interactions between the poly-**Ac-c** and the chiral alcohol **1** in these solvents. A similar tendency was also observed for the poly-**MOM**'s.<sup>25,26</sup> Since poly-**Ac-b** is insoluble in MCH and *n*-hexane, but soluble in **1**, we then measured the CD spectrum of poly-**Ac-b** in (*R*)-**1**, which showed intense, but slightly weak Cotton effects (Fig. 1(v)) when compared to those of poly-**Ac-c**, indicating a preferred-handed helix formation of poly-**Ac-b** in (*R*)-**1** whose helix-sense excess may be slightly lower than that of poly-**Ac-c**.



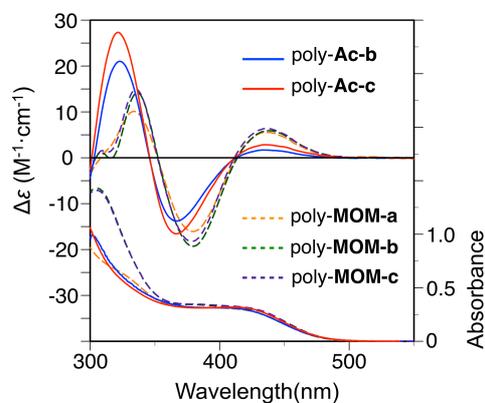
**FIGURE 1.** CD and absorption spectra of poly-**Ac-c** with (*R*)-**1** measured in MCH (MCH/(*R*)-**1** = 90/10, v/v) at 25 °C (i) and –10 °C (ii) after standing at 25 °C for 2 h, and the isolated poly-**Ac-c** in MCH at –10 °C recovered from ii (iii) and those with (*S*)-**1** measured in MCH (MCH/(*S*)-**1** = 90/10, v/v) at 25 °C (iv) and poly-**Ac-b** in (*R*)-**1** at 25 °C (v). [polymer] = 1.0 mM.

It is noteworthy that the Cotton effect patterns of poly-**Ac-b** and poly-**Ac-c** were different from those of poly-**MOM-a**, poly-**MOM-b** and poly-**MOM-c** (Fig. 2). These results suggest that the helical structure induced in the poly-**Ac**'s is slightly different from that of the poly-**MOM**'s probably due to the difference in the bulkiness of the substituents at the 2- and 2'-positions of the biphenyl pendants (MOM and acetyloxy groups), while the substituents introduced at the 4'-position (alkoxy and ester groups) (Scheme 1) hardly affect the main-chain helical structures because they are located far from the polymer backbones.

In our previous report,<sup>25</sup> we demonstrated that the helicity induction in poly-**MOM-a** with nonracemic **1** showed an intense positive nonlinear relationship between the enantiomeric excess (ee) of **1** and the observed ICD intensities ("majority rule").<sup>33</sup> The changes in the ICD intensity of poly-**Ac-c** versus the ee's of **1** in MCH were then measured at 25 and –10 °C to check the effect of the substituents at the 2- and 2'-positions on the chiral amplification behavior. The CD intensities of poly-**Ac-c**, corresponding to the helical sense excesses, were slightly out of proportion to the ee's of **1**, showing a convex deviation from linearity (Fig. S13). However, the nonlinearities observed for poly-**Ac-c** were weaker than those for poly-**MOM-a**,<sup>25</sup> indicating the critical role of the substituents at the 2- and 2'-positions of the biphenyl pendants in achieving a high chiral amplification, resulting from close interactions between the neighboring pendant biphenyl groups along the helical polymer backbone with a high cooperativity.

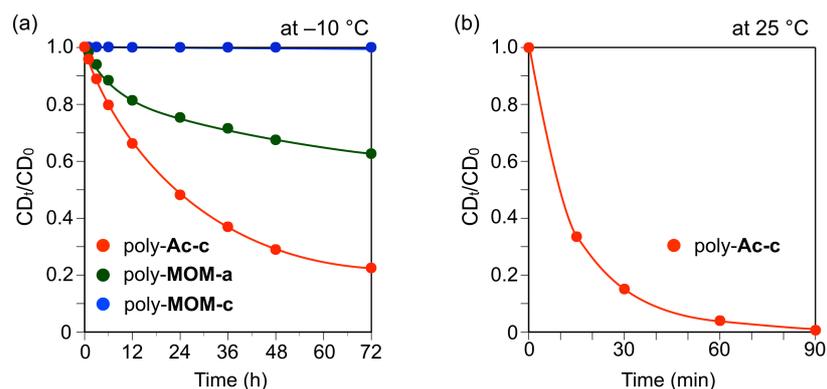
As previously reported, both the macromolecular helicity and the axial chirality can be induced in the poly-**MOM**'s by (*R*)- or (*S*)-**1** in the solid state as well as in solution and further memorized after complete removal of the chiral alcohol **1**.<sup>25,26</sup>

We then investigated if a similar macromolecular helicity and axial chirality memory could be possible for poly-**Ac-c** possessing the acetyloxy groups at the 2- and 2'-positions instead of the MOM groups.



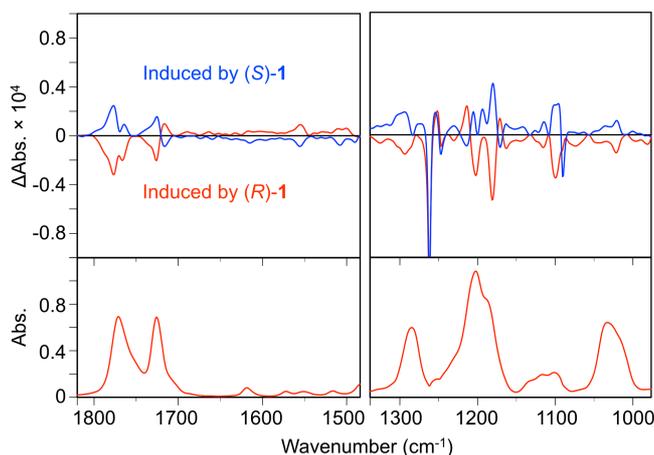
**FIGURE 2.** CD and absorption spectra of poly-**MOM-a** (orange broken lines), poly-**MOM-c** (purple broken lines) and poly-**Ac-c** (red lines) in MCH and poly-**MOM-b** (green broken lines) in toluene in the presence of (*R*)-**1** (toluene/**1** (90/10, v/v)), and poly-**Ac-b** in (*R*)-**1** (blue lines) at 25 °C after standing at 25 °C for 2 h. [polymer] = 1.0 mM.

After helicity induction in poly-**Ac-c** in a mixture of MCH/(*R*)-**1** (90:10, v/v) at 25 °C for 2 h, the polymer was isolated by precipitation into methanol to completely remove (*R*)-**1**, which was confirmed by its <sup>1</sup>H NMR spectrum (Fig. S14). The isolated poly-**Ac-c** dissolved in MCH at –10 °C showed an almost identical CD spectrum to that observed before isolation (Figs. 1(ii) and (iii)). Therefore, it was revealed that a preferred-handed helicity induced in poly-**Ac-c** was retained after complete removal of (*R*)-**1** as is the case for the poly-**MOM**'s.<sup>25,26</sup> The stability of the helicity memory of the poly-**Ac-c** was investigated by following the CD intensity changes in MCH at –10 and 25 °C with time; its half-life periods (*t*<sub>1/2</sub>) were estimated to be approximately 24 h and 10 min, respectively (Fig. 3).<sup>34</sup> By comparing the *t*<sub>1/2</sub> values for poly-**MOM-c** and poly-**MOM-a** (Fig. 3(a)), the stability of the macromolecular helicity memory in MCH at –10 °C decreased in the following order: poly-**MOM-c** > poly-**MOM-a** > poly-**Ac-c**, indicating that the acetyloxy groups introduced at the 2- and 2'-positions of the biphenyl pendants destabilize the helicity memory compared to the MOM groups, while the alkoxycarbonyl (ester) groups at the 4'-position tend to stabilize the helicity memory. In the solid state, however, the poly-**Ac-c** maintained its helicity memory for an extremely long time, at least for 1 month at 25 °C, with no detectable decrease in the ICD intensity (Fig. S15).



**FIGURE 3.** Plots of the ICD intensity ( $\Delta\epsilon_{2nd}$ ) changes ( $CD_t/CD_0$ ) of the isolated poly-Ac-c (●), poly-MOM-a (●) and poly-MOM-c (●) at  $-10\text{ }^\circ\text{C}$  (a) and those of the isolated poly-Ac-c (●) at  $25\text{ }^\circ\text{C}$  (b) in MCH with time.  $CD_0$  represents the initial ICD intensity of the isolated polymers measured in MCH at  $-10$  (a) and  $25\text{ }^\circ\text{C}$  (b) after helicity induction in MCH/(*R*)-1 (90:10, v/v) at  $25\text{ }^\circ\text{C}$  for 2 h (poly-MOM-a and poly-Ac-c) or 48 h (poly-MOM-c). [polymer] = 1.0 mM.

The poly-Ac-c's after treatment with (*R*)-1 and (*S*)-1 and subsequent isolation exhibited mirror image vibrational circular dichroism (VCD) signals in the C=O stretching band region of the two acetyloxy (*ca.*  $1,770\text{ cm}^{-1}$ ) and *n*-tetradecyloxy carbonyl groups (*ca.*  $1,720\text{ cm}^{-1}$ ) (Fig. 4). These results indicated that a preferred-handed axially twisted conformation of the biphenyl pendants is also induced through noncovalent interactions with the chiral alcohol **1**, and the alkoxy carbonyl (ester) groups at the 4'-position appear to be arranged in a preferred-handed helical array along the helical polymer backbone as observed for poly-MOM-b.<sup>26,35</sup> The calculated VCD and IR spectra for a pair of enantiomeric model biphenyl compounds of Ac-c (M-Ac-c) with either a left- or right-handed axially twisted structure are roughly consistent with the observed ones for the isolated poly-Ac-c after helicity induction by (*R*)- and (*S*)-1, respectively (Fig. S16).



**FIGURE 4.** VCD (top) and IR (bottom) spectra of the isolated poly-Ac-c in MCH at  $-10\text{ }^\circ\text{C}$  prepared by the treatment with (*R*)-1 (red lines) and (*S*)-1 (blue lines).

Considering the relationship between the signs of the Cotton effects and the helical sense determined by high-resolution atomic force microscopy observations for the analogous helical poly(phenylacetylene)s<sup>36,37</sup> together with the present VCD results,

the isolated poly-Ac-c with a helicity memory induced by (*R*)-1 showing a negative second Cotton effect at around  $370\text{ nm}$  seems to have a right-handed helical main-chain structure with a left-handed helical array of the pendant biphenyl groups which axially twist into the left-handed direction.

The chiral recognition ability of poly-Ac-b with a macromolecular helicity memory was evaluated as a CSP for HPLC, which had been prepared as follows. Poly-Ac-b dissolved in (*R*)-1 was kept standing at  $25\text{ }^\circ\text{C}$  for 2 h to induce a preferred-handed helical structure (Fig. 1(v)), which was then coated on macroporous silica gel.<sup>28</sup> After the poly-Ac-b-coated silica gel was packed into a stainless-steel column ( $25 \times 0.20\text{ cm}$  (i.d.)),<sup>29</sup> a hexane/2-propanol mixture (97/3, v/v) was thoroughly passed through the column in order to remove (*R*)-1 completely. The results of the resolution of various racemates **2–13** (Fig. 5) are summarized in Table 1. For comparison, the chromatographic resolution results using poly-MOM-b as a coated-type CSP composed of the biphenyl units with the same 4'-butoxycarbonyl substituent, but different 2- and 2'-substituents are also shown in Table 1.<sup>26</sup> Fig. 6 shows the chromatograms for the resolution of **12** on the poly-Ac-b-based CSP. The enantiomers were eluted at the retention times of  $t_1$  and  $t_2$ , showing complete separation. The retention factors,  $k_1 [= (t_1 - t_0)/t_0]$  and  $k_2 [= (t_2 - t_0)/t_0]$ , where the hold-up time ( $t_0$ ) was 3.86 min, were 6.63 and 8.97, respectively, resulting in the separation factor  $\alpha (= k_2/k_1)$  of 1.35.

Poly-Ac-b could not separate racemates **3–6** including the metal tris(acetylacetonato)s (**4–6**), which were separated on poly-MOM-b, while benzoin (**10**) was well resolved on poly-Ac-b, but not resolved on poly-MOM-b. Analogous benzoin derivatives (**11–13**) were also efficiently resolved on poly-Ac-b. The observed difference in the chiral recognition abilities between the two CSPs may be ascribed to the difference in the helical structures between poly-Ac-b and poly-MOM-b as already described as a result of different substituents at the 2- and 2'-positions of the biphenyl groups, which may further induce the helical arrangement of the pendants in a different helical array. We noted that the chiral recognition ability of the poly-Ac-b-based CSP toward racemates **2** and **10** remained unchanged even after one week, indicating that the helicity and axial chirality memory of the poly-Ac-b was quite stable in the solid state.

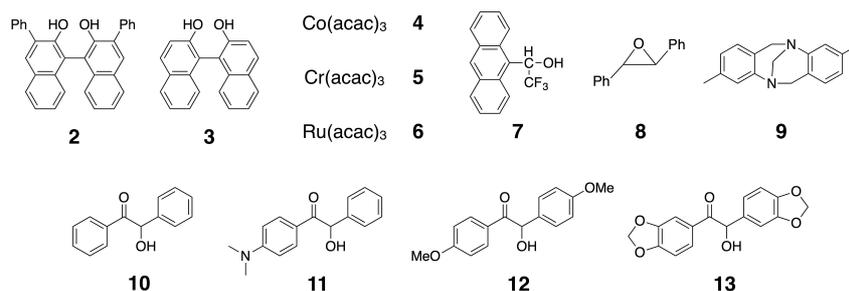


FIGURE 5. Structures of racemates (2–13).

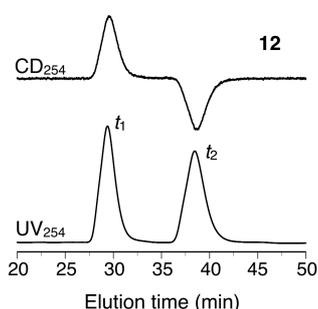


FIGURE 6. HPLC chromatograms for the resolution of **12** on poly-**Ac-b**-based CSP prepared by treatment with (*R*)-**1**. Eluent: hexane–2-propanol (97:3, v/v).

TABLE 1 Chromatographic resolution of racemates (2–13) on poly-**Ac-b**- and poly-**MOM-b**-based CSPs<sup>a</sup>

Racemates	poly- <b>Ac-b</b>		poly- <b>MOM-b</b> <sup>b</sup>	
	$k_1$	$\alpha$	$k_1$	$\alpha$
<b>2</b>	10.3	1.17 (–)	6.80	1.08 (–)
<b>3</b>	6.50	ca.1 (+)	4.50	1.15 (+)
<b>4</b>	1.24	ca.1 (–)	1.21	1.18 (+)
<b>5</b>	1.07	ca.1 (+)	1.01	1.28 (–)
<b>6</b>	1.51	ca.1 (+)	1.41	1.31 (–)
<b>7</b>	3.17	1.0	1.95	1.0
<b>8</b>	0.32	1.0	0.18	ca. 1 (+)
<b>9</b>	0.62	1.0	0.27	ca. 1 (–)
<b>10</b>	1.67	1.18 (–)	1.09	1.0
<b>11</b>	4.95	1.25 (+)	—	—
<b>12</b>	6.63	1.35 (+)	—	—
<b>13</b>	15.8	1.22 (+)	—	—

<sup>a</sup>Column: 25 x 0.20 (i.d.) cm; eluent: hexane–2-propanol (97:3, v/v); Flow rate: 0.2 mL/min; Temperature: 10 °C. The sign of the Cotton effect at 254 nm of the first-eluted enantiomer is shown in parentheses.

<sup>b</sup>Data cited from ref. 26.

## Conclusion

In conclusion, we have prepared two novel poly(biphenylacetylene) derivatives (poly-**Ac**'s) bearing two acetoxy groups at the 2- and 2'-positions and an alkoxy carbonyl group at the 4'-position of the biphenyl pendants.

Both the macromolecular helicity and axial chirality of the biphenyl pendants were induced in the poly-**Ac**'s through noncovalent weak interactions with a chiral alcohol and were almost entirely memorized after complete removal of the chiral alcohol, although the memory of the poly-**Ac**'s in solution was less stable than those of the poly-**MOM**'s composed of the biphenyl units bearing two MOM groups at the 2- and 2'-positions. Poly-**Ac** with a macromolecular helicity memory showed a better chiral recognition ability toward several racemates including the benzoin derivatives than the corresponding poly-**MOM** when used as a CSP for HPLC. The difference in the bulkiness of the substituents introduced at the 2- and 2'-positions of the biphenyl pendants has a significant influence on the induced helical structures, resulting in the difference in their chiral recognition abilities. We believe that these findings will contribute to the development of more practically useful poly(biphenylacetylene)-based CSPs showing a high chiral recognition ability along with a switchable elution order<sup>25</sup> toward diverse racemates.

## Supporting information

Additional supporting information may be found in the online version of this article at the publisher's website.

## Acknowledgement

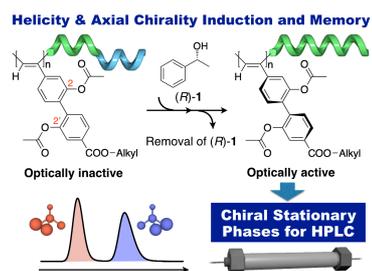
We thank Professor S. Akine (Kanazawa University) for his help in X-ray crystallographic analysis. This work was supported in part by JSPS KAKENHI (Grant-in-Aid for Scientific Research (B), no. 16H04154 (K.M.) and Grant-in-Aid for Scientific Research (S), no. 25220804 (E.Y.).

## REFERENCES AND NOTES

- Ariens E.J. Stereochemistry: A source of problems in medicinal chemistry. *Med. Res. Rev.* 1986;6(4):451–466.
- Kasprzyk-Hordern B. Pharmacologically active compounds in the environment and their chirality. *Chem. Soc. Rev.* 2010;39(11):4466–4503.
- Brooks WH, Guida WC, Daniel KG. The significance of chirality in drug design and development. *Curr. Top. Med. Chem.* 2011;11(7):760–770.

4. Zhou Q, Yu L-S, Zeng S. Stereoselectivity of chiral drug transport: a focus on enantiomer–transporter interaction. *Drug Metab. Rev.* 2014;46(3):283–290.
5. Pirkle WH, Pochapsky TC. Considerations of chiral recognition relevant to the liquid chromatography separation of enantiomers. *Chem. Rev.* 1989;89(2):347–362.
6. Taylor DR, Maher K. Chiral separations by high-performance liquid chromatography. *J. Chromatogr. Sci.* 1992;30(3):67–85.
7. Francotte ER. Enantioselective chromatography as a powerful alternative for the preparation of drug enantiomers. *J. Chromatogr. A* 2001;906(1–2):379–397.
8. Andersson S, Allenmark SG. Preparative chiral chromatographic resolution of enantiomers in drug discovery. *J. Biochem. Biophys. Methods* 2002;54(1–3):11–23.
9. Yamamoto C, Okamoto Y. Optically active polymers for chiral separation. *Bull. Chem. Soc. Jpn.* 2004;77(2):227–257.
10. Okamoto Y, Ikai T. Chiral HPLC for efficient resolution of enantiomers. *Chem. Soc. Rev.* 2008;37(12):2593–2608.
11. Ward TJ, Ward KD. Chiral separations: A review of current topics and trends. *Anal. Chem.* 2012;84(2):626–635.
12. Shen J, Okamoto Y. Efficient separation of enantiomers using stereoregular chiral polymers. *Chem. Rev.* 2016;116(3):1094–1138.
13. Okamoto Y, Suzuki K, Ohta K, Hatada K, Yuki H. Optically active poly(triphenylmethyl methacrylate) with one-handed helical conformation. *J. Am. Chem. Soc.* 1979;101(16):4763–4765.
14. Yuki H, Okamoto Y, Okamoto I. Resolution of racemic compounds by optically active poly(triphenylmethyl methacrylate). *J. Am. Chem. Soc.* 1980;102(20):6356–6358.
15. Okamoto Y, Honda S, Okamoto I, Yuki H, Murata S, Noyori R, Takaya H. Novel packing material for optical resolution: (+)-Poly(triphenylmethyl methacrylate) coated on macroporous silica gel. *J. Am. Chem. Soc.* 1981;103(23):6971–6973.
16. Okamoto Y, Mohri H, Hatada K. Chromatographic optical resolution by optically active poly(diphenyl-2-pyridylmethyl methacrylate) with a highly one-handed helical structure. *Polym. J.* 1989;21(5):439–445.
17. Okamoto Y. Precision synthesis, structure and function of helical polymers. *Proc. Jpn. Acad., Ser. B* 2015;91(6):246–261.
18. Okamoto Y, Yashima E. Polysaccharide derivatives for chromatographic separation of enantiomers. *Angew. Chem., Int. Ed.* 1998;37(8):1021–1043.
19. Yashima E. Polysaccharide-based chiral stationary phases for high-performance liquid chromatographic enantioseparation. *J. Chromatogr. A* 2001;906(1–2):105–125.
20. Ikai T, Okamoto Y. Structure control of polysaccharide derivatives for efficient separation of enantiomers by chromatography. *Chem. Rev.* 2009;109(11):6077–6101.
21. Shen J, Ikai T, Okamoto Y. Synthesis and application of immobilized polysaccharide-based chiral stationary phases for enantioseparation by high-performance liquid chromatography. *J. Chromatogr. A* 2014;1363:51–61.
22. Nakano T. Optically active synthetic polymers as chiral stationary phases in HPLC. *J. Chromatogr. A* 2001;906(1–2):205–225.
23. Yashima E, Maeda K, Iida H, Furusho Y, Nagai K. Helical polymers: Synthesis, structures, and functions. *Chem. Rev.* 2009;109(11):6102–6211.
24. Yashima E, Ousaka N, Taura D, Shimomura K, Ikai T, Maeda K. Supramolecular helical systems: Helical assemblies of small molecules, foldamers, and polymers with chiral amplification and their functions. *Chem. Rev.* 2016; DOI: 10.1021/acs.chemrev.6b00354
25. Shimomura K, Ikai T, Kanoh S, Yashima E, Maeda K. Switchable enantioseparation based on macromolecular memory of a helical polyacetylene in the solid state. *Nat. Chem.* 2014;6(5):429–434.
26. Ishidate R, Shimomura K, Ikai T, Kanoh S, Maeda K. Macromolecular helicity induction and memory in a poly(biphenylacetylene) bearing an ester group and its application to a chiral stationary phase for high-performance liquid chromatography. *Chem. Lett.* 2015;44(7):946–948.
27. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Cossi, M.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09, Revision E.01*; Gaussian, Inc., Wallingford CT, 2009.
28. Okamoto Y, Aburatani R, Hatada K. Chromatographic chiral resolution : XIV. Cellulose tribenzoate derivatives as chiral stationary phases for high-performance liquid chromatography. *J. Chromatogr. A* 1987;389(0):95–102.
29. Okamoto Y, Kawashima M, Hatada K. Chromatographic resolution : XI. Controlled chiral recognition of cellulose triphenylcarbamate derivatives supported on silica gel. *J. Chromatogr. A* 1986;363(2):173–186.
30. Koller H, Rimböck K-H, Mannschreck A. High-pressure liquid chromatography on triacetylcellulose: Characterization of a sorbent for the separation of enantiomers. *J. Chromatogr. A* 1983;282:89–94.
31. Simionescu CI, Percec V, Dumitrescu S. Polymerization of acetylenic derivatives. XXX. Isomers of polyphenylacetylene. *J. Polym. Sci. Pol. Chem. Ed.* 1977;15(10):2497–2509.
32. Kishimoto Y, Eckerle P, Miyatake T, Ikariya T, Noyori R. Living polymerization of phenylacetylenes Initiated by Rh(C≡CC<sub>6</sub>H<sub>5</sub>)(2,5-norbornadiene)[P(C<sub>6</sub>H<sub>5</sub>)<sub>3</sub>]<sub>2</sub>. *J. Am. Chem. Soc.* 1994;116(26):12131–12132.
33. Green MM, Garetz BA, Munoz B, Chang H, Hoke S, Cooks RG. Majority rules in the copolymerization of mirror image isomers. *J. Am. Chem. Soc.* 1995;117(14):4181–4182.
34. The stability of the helicity memory of poly-**Ac-c** was highly dependent on the solvents; once dissolved in THF at –10 °C, the CD quickly disappeared within a few minutes.
35. Shi ZC, Murayama Y, Kaneko T, Teraguchi M, Aoki T. Helix-sense-selective polymerization of 3,5-bis(hydroxymethyl)phenylacetylene connected with a rigid and  $\pi$ -conjugated substituent. *Chem. Lett.* 2013;42(9):1087–1089.
36. Sakurai SI, Okoshi K, Kumaki J, Yashima E. Two-dimensional hierarchical self-assembly of one-handed helical polymers on graphite. *Angew. Chem., Int. Ed.* 2006;45(8):1245–1248.
37. Sakurai SI, Okoshi K, Kumaki J, Yashima E. Two-dimensional surface chirality control by solvent-induced helicity inversion of a helical polyacetylene on graphite. *J. Am. Chem. Soc.* 2006;128(17):5650–5651.

## Graphical Abstract



Poly(biphenylylacetylene)s bearing two acetyloxy groups at the 2- and 2'-positions of the biphenyl pendants formed a preferred-handed helical conformation accompanied by a twist-sense bias of the biphenyl pendants upon interactions with a chiral alcohol, both of which were memorized after complete removal of the chiral alcohol. The polymer with a macromolecular helicity memory showed a good chiral recognition ability toward several racemates when used as a chiral stationary phase for HPLC.