JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Communication
pubs.acs.org/JACS

# *P*-Chiral Phosphine–Sulfonate/Palladium-Catalyzed Asymmetric Copolymerization of Vinyl Acetate with Carbon Monoxide

Akifumi Nakamura, Takeharu Kageyama, Hiroki Goto, Brad P. Carrow, Shingo Ito, and Kyoko Nozaki*

Department of Chemistry and Biotechnology, Graduate School of Engineering, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan

Ⓢ *Supporting Information*

**ABSTRACT:** Utilization of palladium catalysts bearing a *P*-chiral phosphine–sulfonate ligand enabled asymmetric copolymerization of vinyl acetate with carbon monoxide. The obtained γ-polyketones have head-to-tail and isotactic polymer structures. The origin of the regio- and stereoregularities was elucidated by stoichiometric reactions of acylpalladium complexes with vinyl acetate. The present report for the first time demonstrates successful asymmetric coordination–insertion (co)polymerization of vinyl acetate.

Synthesis and application of optically active polymers has been an important subject in polymer science because their chiral nature is essential for many well-defined functions and properties, as exemplified by polypeptide and nucleic acid chemistry.[1,2] Among various artificial polymers, γ-polyketones obtained by the alternating copolymerization of monosubstituted ethenes with carbon monoxide (CO) are endowed with various structural regularities (Figure 1): head-to-tail regioregularity, syndiotactic or isotactic stereoregularity (tacticity), and in the isotactic structure, enantioselectivity to control the absolute stereochemistry.[3] During the last few decades, asymmetric monosubstituted ethenes/CO copolymerization was achieved using nonpolar olefins such as propylene and vinylarenes.[1,4,5] Until now, however, there have been no reports of the regulation of tacticity and enantioselectivity by coordination–insertion polymerization of fundamental polar vinyl monomers such as vinyl acetate and methyl acrylate with carbon monoxide.[6,7] The introduction of polar functional groups into polyketones in a highly controlled manner has been a significant challenge, since it would drastically alter the polymer properties and expand the range of applications. In 2007, we reported the first example of copolymerization of vinyl acetate and carbon monoxide using palladium/phosphine–sulfonate catalysts, but the resulting copolymers showed low regio- and stereoregularities.[8,9] Here we report the synthesis of the first optically active *P*-chiral phosphine–sulfonate ligands[10] and their application to palladium-catalyzed asymmetric copolymerization of vinyl acetate with carbon monoxide.

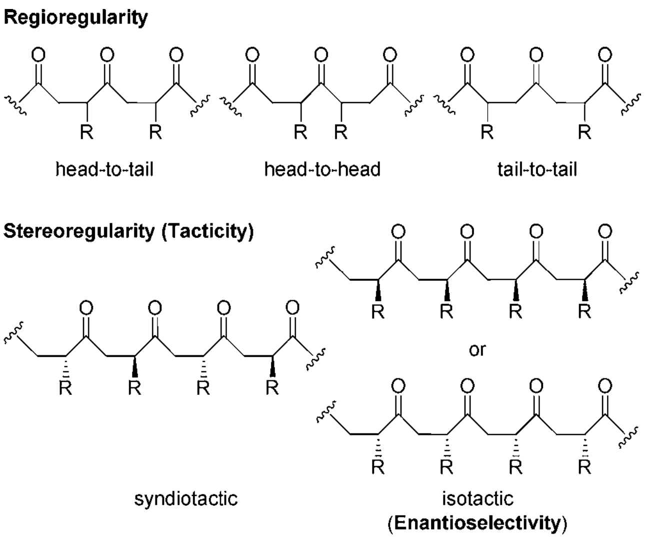


**Figure 1.** Possible structural regularities in monosubstituted ethene/carbon monoxide copolymers.

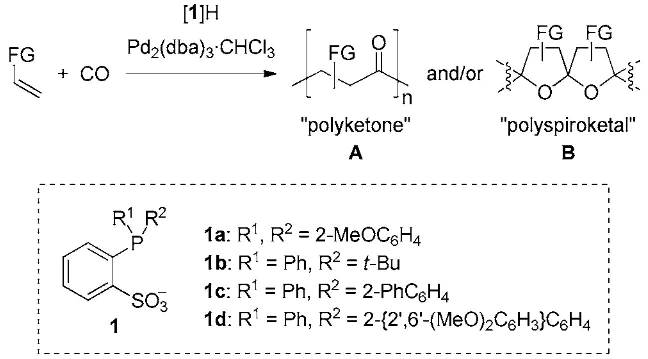
A series of *P*-chiral ligand precursors [**1b**]H–[**1d**]H were prepared according to literature procedures.[10a,c,11] The enantiomerically pure ligands **1b** and **1d** were prepared by HPLC separation of the corresponding racemates with a chiral stationary phase (CHIRALPAK IC). Copolymerization of vinyl acetate with carbon monoxide was performed in the presence of a mixture of $Pd_2(dba)_3{\cdot}CHCl_3$ and [**1**]H (Table 1). The use of achiral ligand **1a** resulted in the formation of polyketone **A** with 71% head-to-tail selectivity (entry 1). The regioselectivity was estimated by the integration ratio of the ketone carbonyl region in $^{13}C$ NMR spectra (Figure 2), assuming that the broad signal at 201.5 ppm corresponds to either head-to-head or tail-to-tail structure and that multiple signals from 202–204 ppm corresponds to all the other regioisomeric structures.[12,13] In entries 2–4, three types of racemic *P*-chiral ligands **1b**–**1d** were employed for the copolymerization. In entries 2 and 3, the copolymerization produced polyspiroketal **B** as a major product instead of polyketone **A**.[3] In contrast, higher chemo-, regio- and stereoselectivities were obtained when using ligand **1d**, bearing phenyl and 2′,6′-dimethoxy(1,1′-biphenyl)-2-yl groups on the phosphorus atom (entry 4), and the ratio of head-to-tail structure was improved to 84%. Furthermore, the resonance at 203.5 ppm became predominant, which suggests higher regio- and stereoregularities.

Encouraged by the result in entry 4, asymmetric copolymerization was examined with enantiomerically pure ligand (*S*)-(−)-**1d** (entry 5). Unexpectedly, the regio- and stereo-

**Received:** May 8, 2012
**Published:** July 23, 2012

dx.doi.org/10.1021/ja3044344 | *J. Am. Chem. Soc.* 2012, 134, 12366–12369

**Table 1. Copolymerization of Polar Vinyl Monomers with Carbon Monoxide**[a]



| entry | ligand | FG | yield (mg) | TOF ($h^{-1}$) | $M_n$ ($\times 10^3$)[b] | $M_w/M_n$[b] | A or B[c] | h-to-t (%)[c] |
|---|---|---|---|---|---|---|---|---|
| 1 | **1a** | OAc | 320 | 14 | 65 | 1.6 | **A** | 71 |
| 2 | (*rac*)-**1b** | OAc | 150 | 6.6 | 14 | 1.5 | **B** | |
| 3 | (*rac*)-**1c** | OAc | 500 | 22 | 44 | 1.5 | 1:5 (**A**:**B**) | |
| 4 | (*rac*)-**1d** | OAc | 230 | 10 | 25 | 1.2 | **A** | 84 |
| 5 | (*S*)-**1d** | OAc | 170 | 7.4 | 20 | 1.8 | **A** | 90 |
| 6 | (*S*)-**1d** | $CO_2Me$ | 106 | 4.7 | 10 | 1.2 | **A** | >99 |
| 7 | (*S*)-**1d** | Ph | 101 | 3.8 | 12 | 1.1 | **A** | >99 |

[a] Conditions: $Pd_2(dba)_3\cdot CHCl_3$ (5 μmol), ligand **1** (12 μmol), and vinyl monomer (2.5 mL) were stirred under carbon monoxide pressure (6.0 MPa) for 20 h at 70 °C in a 50-mL autoclave. [b] Determined by SEC analysis using polystyrene standards. [c] Determined by NMR analysis.

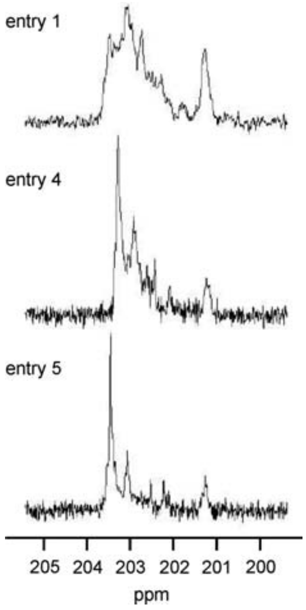


**Figure 2.** Ketone regions in the $^{13}C$ NMR spectra of the polyketones obtained in entries 1, 4, and 5 in Table 1 ($CDCl_3$).

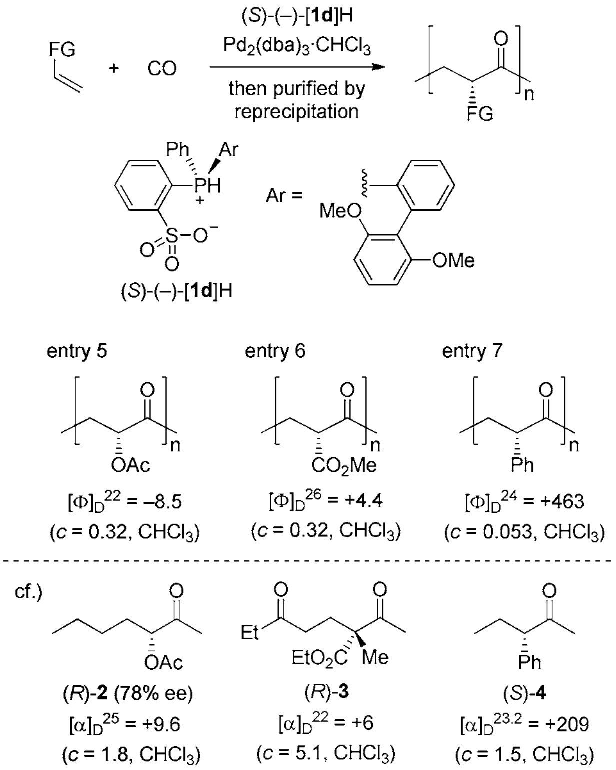
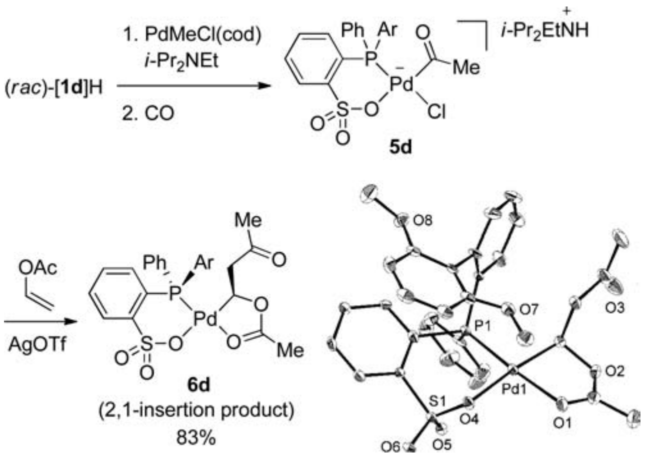


**Figure 3.** Asymmetric copolymerization of vinyl acetate with carbon monoxide using optically active (*S*)-(−)-**1d**/$Pd_2(dba)_3\cdot CHCl_3$. Optical rotation values of analogous model compounds are also shown for comparison.[19]

regularities were improved compared with the results using (*rac*)-**1d** (Figure 2).[14] The solubility of the resulting polymer in entry 5 was lower than that of entry 4 in $CDCl_3$, indicating different higher-order structures.[15,16] Although the reason for the different regio- and stereoregularities between entry 4 and 5 is still unclear, chain transfer between the two enantiomeric palladium complexes may be operating during the polymerization with *rac*-**1d** so that one chain contains segments formed by each enantiomer of the catalyst.[17]

The resulting vinyl acetate/carbon monoxide copolymer in entry 5 exhibited moderate optical rotation ($[\Phi]_D^{22} = -8.5$, $c$ = 0.32, $CHCl_3$), which may correspond to regions of enantioenriched isotactic structure (Figure 3). The absolute configuration of the asymmetric center in the polymer main chain was inferred from the results of the reaction shown in Scheme 1 (vide infra).[18] These data represent the first example of the synthesis of an optically active γ-polyketone having ester substituents directly attached to the main chain. Although the absolute value of the specific optical rotation is not high, it does

**Scheme 1. Synthesis and Molecular Structure of 6d**[a]



[a] Hydrogen atoms and solvent molecules are omitted for clarity. Ar = 2′,6′-dimethoxy(1,1′-biphenyl)-2-yl.

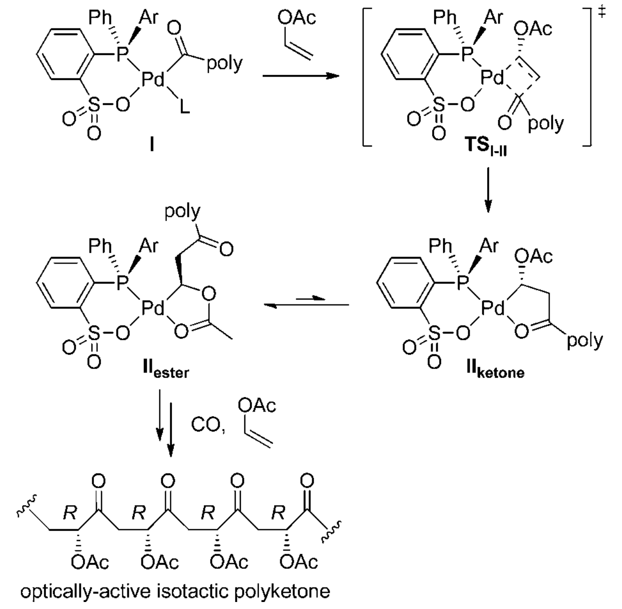
not necessarily indicate low selectivity considering that reported model compounds similar to the repeating unit of the copolymer, such (*S*)-**2**, also exhibit moderate values (Figure 3).[19a]

Copolymerization reactions of other monosubstituted ethenes with carbon monoxide were also investigated. The use of methyl acrylate as a comonomer produced a regiocontrolled alternating copolymer, as confirmed by the observation of a single resonance in the ketone carbonyl region of the $^{13}C$ NMR spectrum (entry 6).[9] The copolymer exhibited an optical rotation value $[\Phi]_D^{26}$ = +4.4 (*c* = 0.32, $CHCl_3$),[20] which is consistent with a small optical rotation value of analogous molecule (*R*)-**3**[19b] as shown in Figure 3. However, epimerization of the asymmetric center may have occurred, since our previous studies revealed that the methine proton in the methyl acrylate/CO copolymer was exchangeable with deuterium by the treatment with MeOD.[9b] In contrast, the styrene/CO copolymer obtained in entry 7 exhibited a large optical rotation value $[\Phi]_D^{24}$ = +463 (*c* = 0.053, $CHCl_3$),[20] which is one of the highest values reported for styrene/CO copolymers.[4,5] These results indicate that the introduction of *P*-chirogenic centers into phosphine−sulfonate ligands is an effective strategy for catalyst-controlled asymmetric polymerization.[11]

The origin of regio- and stereoregularities in the copolymerization of vinyl acetate with carbon monoxide was investigated by the stoichiometric reaction of palladium complexes bearing chiral ligand (*rac*)-**1d** with vinyl acetate (Scheme 1). First, acetylpalladium complex **5d** bearing ligand **1d** was synthesized by the reaction of phosphonium−sulfonate [**1d**]H with PdMeCl(cod) in the presence of Hünig's base followed by treatment with carbon monoxide. Next, reaction of **5d** with an excess amount of vinyl acetate in the presence of AgOTf to afforded 2,1-insertion complex **6d** in 83% yield. NMR and X-ray analyses revealed that the major isomer arises from 2,1-insetion of vinyl acetate, and the ester carbonyl coordinates to the palladium center preferentially over the ketone carbonyl. The highly selective 2,1-insertion in this reaction contrasts the corresponding reaction with ligand **1a** where both 2,1- and 1,2-insertion products were detected.[21] In complex **6d**, the acetylmethyl group lies on the same side of the metal square plane as the 2′,6′-dimethoxy(1,1′-biphenyl)-2-yl moiety of the phosphorus atom.

The relative configuration in **6d** and asymmetric copolymerization can be rationalized by the reaction sequence outlined in Scheme 2. According to density functional theory calculation, vinyl acetate insertion proceeds via coordination of vinyl acetate at the position *cis* to the phosphine moiety followed by migration of the acetyl group.[22] The relative configuration in **6d** can be explained by coordination of vinyl acetate to the metal such that the acetoxy group is located on the same side of the square plane as the smaller phenyl group on the phosphorus atom to avoid steric repulsion with the bulky 2′,6′-dimethoxy(1,1′-biphenyl)-2-yl group (**TS**$_{\mathbf{I-II}}$ in Scheme 2). If this stereoselective insertion of vinyl acetate operates in the copolymerization reaction of entry 5 of Table 1, *R*-configuration of the stereocenter would be generated using (*S*)-**1d**, giving an isotactic-rich copolymer with *R*-configuration in the main chain.

**Scheme 2. Possible Explanation for the Enantioface Selection in Asymmetric Copolymerization of Vinyl Acetate with Carbon Monoxide**[a]



[a] Ar = 2′,6′-dimethoxy(1,1′-biphenyl)-2-yl; poly = polymer chain.

In summary, we have developed asymmetric copolymerization of vinyl acetate, methyl acrylate, or styrene with carbon monoxide using palladium complexes ligated by *P*-chiral phosphine−sulfonates to synthesize optically active polyketones. The utilization of *P*-chiral phosphine−sulfonate ligands enables the microstructure regulation of coordination−insertion polymerization of polar vinyl monomers. Further improvement of the selectivity in this copolymerization and application of these chiral palladium/phosphine−sulfonate catalysts to other reactions will be forthcoming.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

Experimental procedures, supplementary experiments, NMR spectra, and crystal data for (*rac*)-[**1b**]H, (*S*)-(−)-[**1d**]H, and **6d**. This material is available free of charge via the Internet at http://pubs.acs.org.

## AUTHOR INFORMATION

**Corresponding Author**

nozaki@chembio.t.u-tokyo.ac.jp

**Notes**

The authors declare no competing financial interest.

## ACKNOWLEDGMENTS

This work was supported by Funding Program for Next Generation World-Leading Researchers, Green Innovation and the Global COE Program "Chemistry Innovation through Cooperation of Science and Engineering" from Japan Society for the Promotion of Science (JSPS), Japan. A.N. is grateful to the JSPS for a Research Fellowship for Young Scientists.

## REFERENCES

(1) Ito, S.; Nozaki, K. In *Catalytic Asymmetric Synthesis*, 3rd ed.; Ojima, I., Ed.; Wiley: Hoboken, NJ, 2010; Chapter 13, pp 931−985.

(2) (a) Okamoto, Y.; Nakano, T. *Chem. Rev.* **1994**, *94*, 349−372. (b) Yashima, E.; Maeda, K.; Iida, H.; Furusho, Y.; Nagai, K. *Chem. Rev.* **2009**, *109*, 6102−6211 and references therein.

(3) (a) Drent, E.; Budzelaar, P. H. M. *Chem. Rev.* **1996**, *96*, 663−681. (b) Bianchini, C.; Meli, A. *Coord. Chem. Rev.* **2002**, *225*, 35−66. (c) Durand, J.; Milani, B. *Coord. Chem. Rev.* **2006**, *250*, 542−560.

(4) For reviews, see: (a) Nakano, K.; Kosaka, N.; Hiyama, T.; Nozaki, K. *Dalton Trans.* **2003**, 4039−4050. (b) Nozaki, K. *J. Polym. Sci. A: Polym. Chem.* **2004**, *42*, 215−221. (c) Nozaki, K. *Pure Appl. Chem.* **2004**, *76*, 541−546. (d) Nozaki, K. *Polym. J.* **2005**, *37*, 871−876.

(5) For recent examples of the copolymerization of vinylarenes with carbon monoxide since 2005, see: (a) Scarel, A.; Durand, J.; Franchi, D.; Zangrando, E.; Mestroni, G.; Carfagna, C.; Mosca, L.; Seraglia, R.; Consiglio, G.; Milani, B. *Chem.—Eur. J.* **2005**, *11*, 6014−6023. (b) Schatz, A.; Scarel, A.; Zangrando, E.; Mosca, L.; Carfagna, C.; Gissibl, A.; Milani, B.; Reiser, O. *Organometallics* **2006**, *25*, 4065−4068. (c) Bajracharya, G. B.; Koranne, P. S.; Tsujihara, T.; Takizawa, S.; Onitsuka, K.; Sasai, H. *Synlett* **2009**, 310−314. (d) Axet, M. R.; Amoroso, F.; Bottari, G.; D'Amora, A.; Zangrando, E.; Faraone, F.; Drommi, D.; Saporita, M.; Carfagna, C.; Natanti, P.; Seraglia, R.; Milani, B. *Organometallics* **2009**, *28*, 4464−4474.

(6) (a) Nakamura, A.; Ito, S.; Nozaki, K. *Chem. Rev.* **2009**, *109*, 5215−5244. (b) Ito, S.; Nozaki, K. *Chem. Rec.* **2010**, *10*, 315−325.

(7) For asymmetric copolymerization of carbon monoxide with olefins having a functional group at a remote position, see: (a) Kacker, S.; Jiang, Z.; Sen, A. *Macromolecules* **1996**, *29*, 5852−5858. (b) Nozaki, K.; Kawashima, Y.; Nakamoto, K.; Hiyama, T. *Polym. J.* **1999**, *31*, 1057−1060. (c) Murtuza, S.; Harkins, S. B.; Sen, A. *Macromolecules* **1999**, *32*, 8697−8702. (d) Lee, J. T.; Alper, H. *Chem. Commun.* **2000**, 2189−2190. (e) Moineau, C.; Mele, G.; Alper, H. *Can. J. Chem.* **2001**, *79*, 587−592. (f) Nozaki, K.; Shibahara, F.; Elzner, S.; Hiyama, T. *Can. J. Chem.* **2001**, *79*, 593−597. (g) Fujita, T.; Nakano, K.; Yamashita, M.; Nozaki, K. *J. Am. Chem. Soc.* **2006**, *128*, 1968−1975.

(8) (a) Kochi, T.; Nakamura, A.; Ida, H.; Nozaki, K. *J. Am. Chem. Soc.* **2007**, *129*, 7770−7771. See also: (b) Kageyama, T.; Ito, S.; Nozaki, K. *Chem. Asian J.* **2011**, *6*, 690−697.

(9) For copolymerization of methyl acrylate with carbon monoxide by achiral palldium phosphine−sulfonate catalysts: (a) Nakamura, A.; Munakata, K.; Kochi, T.; Nozaki, K. *J. Am. Chem. Soc.* **2008**, *130*, 8128−8129. (b) Nakamura, A.; Munakata, K.; Ito, S.; Kochi, T.; Chung, L. W.; Morokuma, K.; Nozaki, K. *J. Am. Chem. Soc.* **2011**, *133*, 6761−6779.

(10) All the *P*-chiral phosphine−sulfonate ligands ever reported were used only in a racemic form. See: (a) Sundararaju, B.; Tang, Z.; Achard, M.; Sharma, G. V. M.; Toupet, L.; Bruneau, C. *Adv. Synth. Catal.* **2010**, *352*, 3141−3146. (b) Shen, Z. L.; Jordan, R. F. *J. Am. Chem. Soc.* **2010**, *132*, 52−53. (c) Perrotin, P.; McCahill, J. S. J.; Wu, G.; Scott, S. L. *Chem. Commun.* **2011**, *47*, 6948−6950. (d) Anselment, T. M. J.; Anderson, C. E.; Rieger, B.; Boeddinghaus, M. B.; Fässler, T. F. *Dalton Trans.* **2011**, *40*, 8304−8313. (e) Piche, L.; Daigle, J.-C.; Rehse, G.; Claverie, J. P. *Chem.—Eur. J.* **2012**, *18*, 3277−3285.

(11) We have examined other achiral and chiral phosphine−sulfonate ligands. See Supporting Information for details.

(12) See Supporting Information for the method to estimate head-to-tail regioregularity.

(13) For $^{13}$C NMR spectra in the region of the carbonyl group of propylene/CO copolymers, see: (a) Barsacchi, M.; Batistini, A.; Consiglio, G.; Suter, U. W. *Macromolecules* **1992**, *25*, 3604−3606. (b) Jiang, Z.; Sen, A. *J. Am. Chem. Soc.* **1995**, *117*, 4455−4467. (c) Gambs, C.; Chaloupka, S.; Consiglio, G.; Togni, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 2486−2488. For styrene/CO copolymers, see: (d) Bronco, S.; Consiglio, G. *Macromol. Chem. Phys.* **1996**, *197*, 355−365.

(14) In isotactic propylene/CO copolymers in ref 13, the half width of the sharpest ketone signal in the $^{13}$C NMR spectra can be estimated to be within 2−6 Hz. Since the width of the sharpest ketone signal of the vinyl acetate/CO copolymer obtained in entry 5 was found to be 5 Hz, we concluded that the stereoregularity of the vinyl acetate/CO copolymer was controlled to be isotactic.

(15) Differential scanning calorimetry (DSC) analysis revealed that the copolymers obtained using (*S*)-**1d** showed glass transition temperatures ($T_g$s) almost identical to those obtained using achiral **1a**. See Supporting Information for details.

(16) The VAc/CO copolymer obtained using (*S*)-**1d** more easily isomerizes to form polyspiroketal structure **B** than that obtained using **1a**, also suggesting the presence of regio- and stereoregular structures.

(17) Rix, F. C.; Rachita, M. J.; Wagner, M. I.; Brookhart, M.; Milani, B.; Barborak, J. C. *Dalton Trans.* **2009**, 8977−8992.

(18) According to the proposed mechanism (discussed later), the vinyl acetate/CO copolymer, which exhibited a negative optical rotation value, would possess *R*-configuration in the main chain. This is not consistent with the fact that model compound (*R*)-**2** shows a positive optical rotation value. This reverse rotation may be attributed to the presence of higher order structures in the vinyl acetate/CO polyketone.

(19) (a) Scheid, G.; Kuit, W.; Ruijter, E.; Orru, R. V. A.; Henke, E.; Bornscheuer, U.; Wessjohann, L. A. *Eur. J. Org. Chem.* **2004**, 1063−1074. (b) Boeckman, R. K., Jr.; del Rosario Ferreira, M. R.; Mitchell, L. H.; Shao, P.; Neeb, M. J.; Fang, Y. *Tetrahedron* **2011**, *67*, 9787−9808. (c) Genna, D. T.; Posner, G. H. *Org. Lett.* **2011**, *13*, 5358−5361.

(20) The absolute configuration of the asymmetric center was tentatively assigned based on the same facial selection as for vinyl acetate. See refs 8b and 9b.

(21) See Supporting Information for details.

(22) Nakamura, A. Ph.D. Thesis, The University of Tokyo, Tokyo, Japan, 2012. See also ref 9b.