Spectral Assignment of Poly[cyclohexene oxide-*alt*-carbon dioxide]

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Received April 27, 2001; Revised Manuscript Received June 20, 2001

ABSTRACT: Signals of ^{13}C NMR spectra of poly[cyclohexene oxide-*alt*-carbon dioxide] in a carbonyl region split into two parts: 153.7 and 153.3−153.1 ppm. To assign these signals, isotactic and syndiotactic model dimers and tetramers were synthesized. The signals of isotactic oligomers appeared at 153.8 ppm, whereas the signals of syndiotactic isomers appeared at higher field and shifted to higher field (up to 153.1 ppm) on going from dimer to tetramer. These results led to the final assignment of the copolymer: the signal at 153.7 ppm includes isotactic diads, and the ones at 153.3−153.1 ppm include syndiotactic diads.

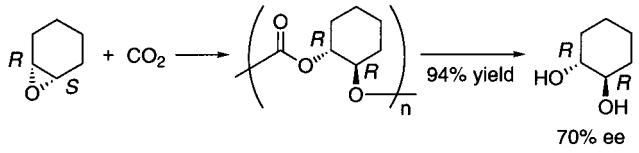
Introduction

Stereochemical information of polymers is conveniently collected by ^{13}C NMR spectroscopy, because signals of ^{13}C NMR spectra of polymers split clearly reflecting configurational sequences. Assignment of the peaks to the corresponding sequences is commonly based on spectroscopic analyses of oligomers with well-defined stereochemical identity. For example, Sato et al. assigned signals of methylenes and *ipso* carbons in polystyrene, referring to signal assignment of all diastereomers of styrene pentamer.[1] Zambelli and Bovey assigned the stereochemistry of methyl carbons in polypropylene through synthesis of model compounds.[2]

Alternating copolymerization of cyclohexene oxide and carbon dioxide has received great interest in recent years because of utilization of carbon dioxide as a raw material.[3] In 1994, Kuran et al. demonstrated that ^{13}C NMR spectroscopy could be applicable to determination of the stereochemistry of the copolymer.[4] They observed two main signals at 153.7 and 153.1 ppm in a carbonate region and attributed them to syndiotactic diad (-*SS*-*RR*-, [r]) and isotactic diad (-*SS*-*SS*- or -*RR*-*RR*-, [m]),[5] in analogy to 2,2′-oxydicyclohexanol, syndiotactic and isotactic dimeric diol models having an ethereal linkage in place of a carbonate functionality.

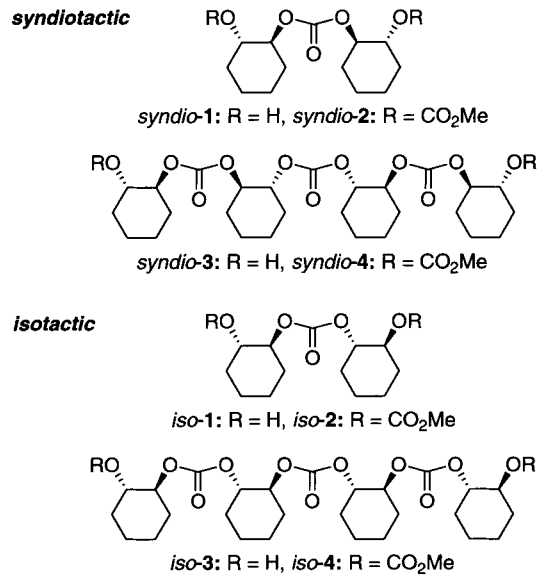
Recently, we[6] and Coates et al.[7] have independently succeeded in the asymmetric alternating copolymerization of cyclohexene oxide and carbon dioxide. The resulting copolymer is easily hydrolyzed into *trans*-1,2-cyclohexanediol and CO_2 by alkali treatment, which enables unambiguous determination of the degree of asymmetric induction. In our study, optically active polycarbonate was obtained, and the enantiomeric excess of the diol was 70%, namely, (*R*,*R*):(*S*,*S*) = 85:15 (Scheme 1). The diol was obtained in 94% yield from the polycarbonate. Thus, even if the remaining 6% of the diol unit might be (*S*,*S*), we can safely estimate that the enantiomeric excess of the diol unit should be at least $\{85 \times 0.94 - (15 \times 0.94 + 6)\}/\{85 \times 0.94 + (15 \times 0.94 + 6)\} = 60\%$, corresponding to (*R*,*R*):(*S*,*S*) = 80:20. Shown in Figure 1 parts a and b are the ^{13}C NMR charts of the copolymers of 3% ee and 70% ee, respectively. As one readily sees from Figure 1b, the intensity

Scheme 1



ratio of signals at 153.7 and 153.1 ppm is roughly 5:1. If Kuran's assignment were correct, syndiotactic diads should be predominant in this copolymer. However, the enantiomeric excess of >60% means that the syndiotactic diads would be less than 40% of all the diads. This contradiction prompted us to reexamine the assignment.

In this report, we describe synthesis of appropriate syndiotactic and isotactic model dimers **1** (R = H) and **2** (R = CO_2Me) as well as tetramers **3** (R = H) and **4** (R = CO_2Me) and present configurational assignment of these oligomers and the copolymer by means of ^{13}C NMR.



Results and Discussions

Our synthetic strategy for model oligomers **1**-**4** is illustrated in Scheme 2. A dimer will be easily prepared

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10.1021/ma010732r CCC: $20.00
Published on Web 08/04/2001

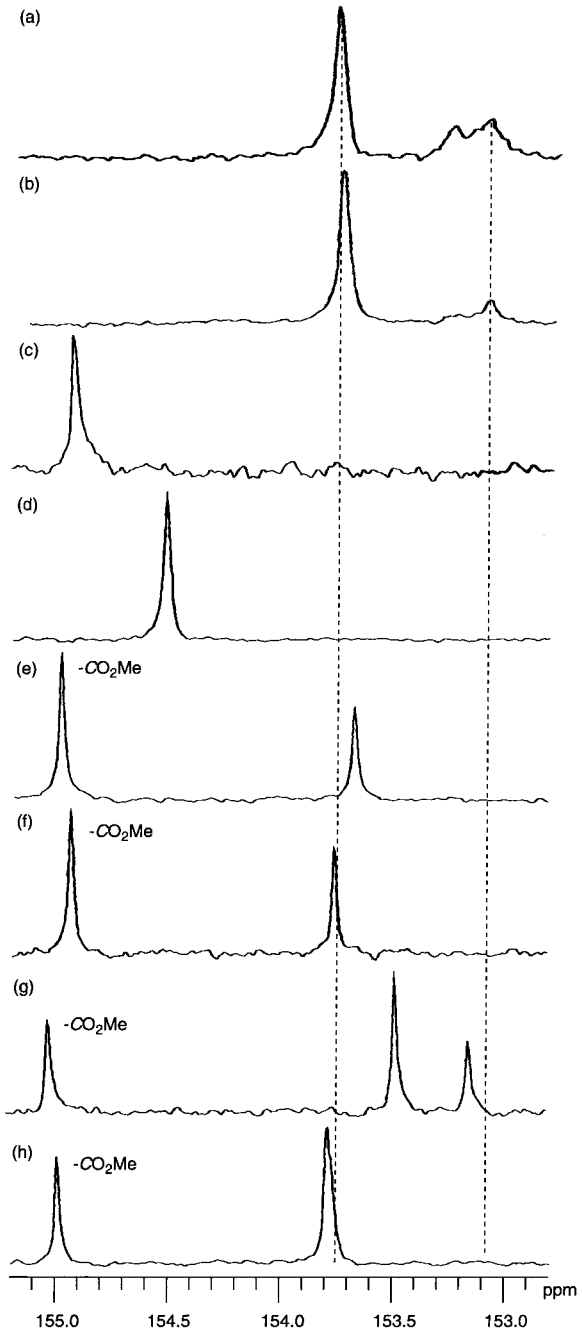


Figure 1. Carbonyl region of ^{13}C NMR spectra of (a) poly[cyclohexene oxide-*alt*-carbon dioxide] of 3% ee, (b) poly[cyclohexene oxide-*alt*-carbon dioxide] of 70% ee, (c) *syndio*-**1**, (d) *iso*-**1**, (e) *syndio*-**2**, (f) *iso*-**2**, (g) *syndio*-**4**, and (h) *iso*-**4**.

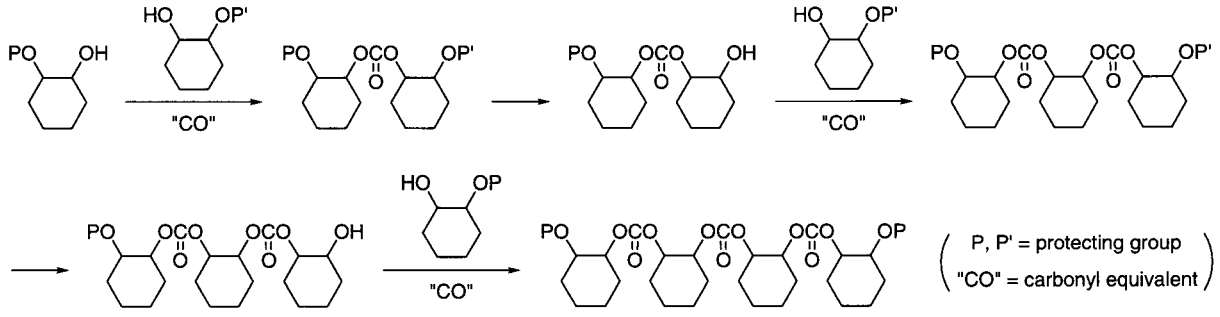
from two differently monoprotected *trans*-1,2-cyclohexanediols (=monomers) and a carbonyl equivalent. Selective deprotection will give a dimer alcohol, which will be then combined with a monomer and a carbonyl equivalent to yield a trimer, and then a tetramer will be produced in a similar manner. One can easily assume that tetramer will be given from two dimers. However, the protocol applied to this transformation resulted in trimer formation owing probably to back biting (vide infra). To realize the strategy in Scheme 2, we used 1,1′-carbonyl diimidazole (Im_2CO) as a carbonyl equivalent and benzyl (Bn) and *tert*-butyldimethylsilyl (TBS) groups as the different hydroxy-protecting groups that allow selective cleavage. Thus, starting with (*S*,*S*)- or (*R*,*R*)-*trans*-1,2-cyclohexanediol **5**, we prepared four monomers [(*S*,*S*)- or (*R*,*R*)-**6**,**7**] in moderate yields as summarized in Scheme 3.

First, we synthesized syndiotactic and isotactic dimer diols (*syndio*-**1** and *iso*-**1)** with a carbonate linkage (Scheme 4). Treatment of (*R*,*R*)-**7** with Im_2CO (1 mol) produced imidazole-1-carboxylic ester, which without isolation was allowed to react with (*S*,*S*)-**6** (1 mol) to provide the dimer *syndio*-**8**. Removal of the silyl group with $BF_3{\cdot}OEt_2$ gave a dimer alcohol, *syndio*-**9**. Finally, *syndio*-**9** was converted into the dimer diol *syndio*-**1** by hydrogenolysis with palladium on carbon. In a similar manner, isotactic dimer diol *iso*-**1** was provided from (*S*,*S*)-**6** and (*S*,*S*)-**7**. Parts c and d of Figure 1 show ^{13}C NMR spectra of *syndio*-**1** and *iso*-**1**, respectively. *Syndio*-**1** showed a signal at 154.9 ppm, a lower field than the 154.5 ppm of *iso*-**1**.

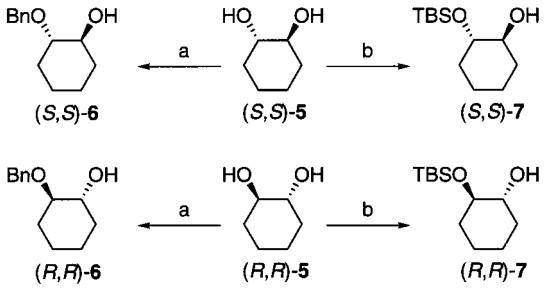
Because dimers *syndio*-**1** and *iso*-**1** have hydroxy groups that do not exist in the main chain of the copolymer, these are not proper model compounds. Thus, we protected the hydroxy groups of *syndio*-**1** and *iso*-**1** with a methoxycarbonyl group and isolated *syndio*-**2** and *iso*-**2**, which more resemble the main chain structure of the copolymer (Scheme 5). Parts e and f of Figure 1 show ^{13}C NMR spectra of *syndio*-**2** and *iso*-**2**. In contrast to the results of *syndio*-**1** and *iso*-**1**, the signal of *iso*-**2** (153.8 ppm) appears at a slightly lower field than that of *syndio*-**2** (153.7 ppm), and these signals have shifted to the chemical shift range of the copolymer.

As the chemical shift difference between *syndio*-**2** and *iso*-**2** is much smaller (0.1 ppm) than the one (0.6 ppm) between the two signals (153.7 and 153.1 ppm) of the copolymer, it seems that the dimers are too short to mimic the diads in the copolymer. In addition, a few more signals observed at 153.3 and 153.2 ppm in the copolymer (Figure 1a,b) indicate possible signal splitting, reflecting longer configurational sequences. Indeed, Coates et al. proposed that ^{13}C NMR spectrum of the copolymer split according to tetrad configurations. By comparing ^{13}C NMR spectrum of the copolymer with the calculated probability of all tetrad configurations on the

Scheme 2. Synthetic Strategy for Model Oligomers: Stepwise Elongation

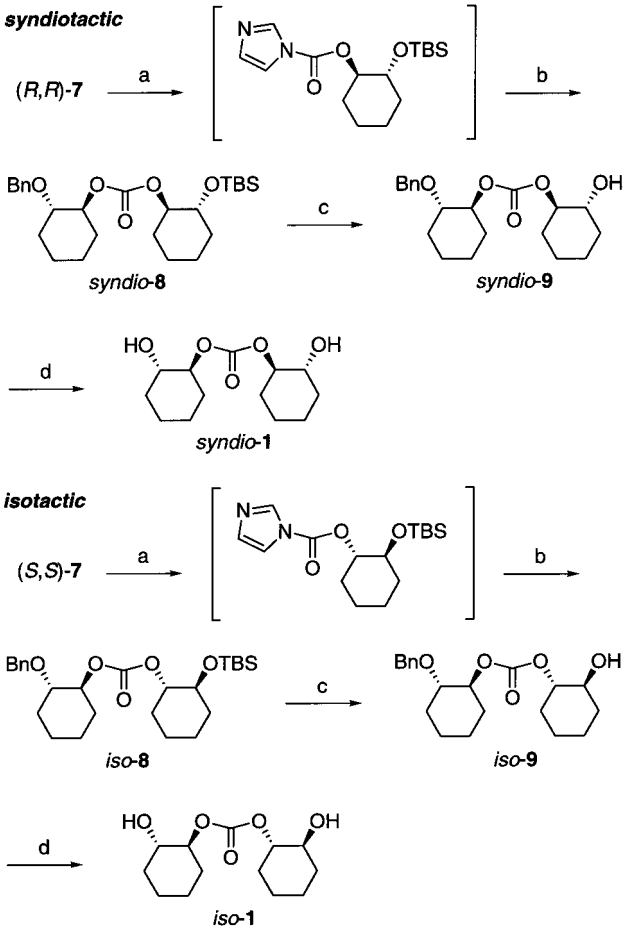


Scheme 3[a]



[a] Key: (a) $BnOC(=NH)CCl_3$, TfOH (0.10 equiv), cyclohexane, CH_2Cl_2, room temperature; (b) TBSOTf (1.1 eq), Et_3N (2.0 equiv), CH_2Cl_2, 0 °C to room temperature.

Scheme 4[a]

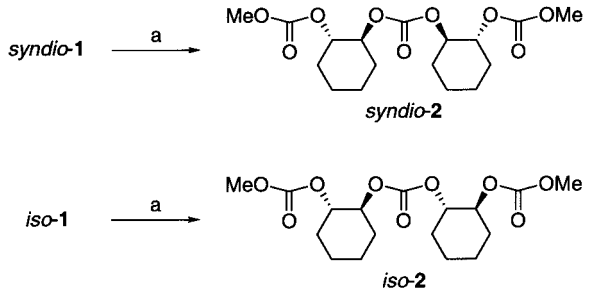


[a] Key: (a) NaH, THF, room temperature, then Im_2CO; (b) (*S*,*S*)-**6**, NaH, reflux; (c) $BF_3{\cdot}OEt_2$, CH_3CN, 0 °C; (d) H_2, Pd/C, EtOH, room temperature.

basis of enantioselectivity, they assayed the spectrum of the copolymer and attributed a large signal at 153.7 ppm to the m-centered tetrad ([mmm], [mmr], [rmr]), small signals at 153.3 and 153.2 ppm to the statistically equivalent [mrm]/[rrr] tetrad, and a signal at 153.1 ppm to the [mrr] tetrad.[7] To further clear the influence of the longer sequence, we synthesized syndiotactic and isotactic tetramers (*syndio*-**4** and *iso*-**4**) and measured ^{13}C NMR focusing on the central carbonate carbon signals.

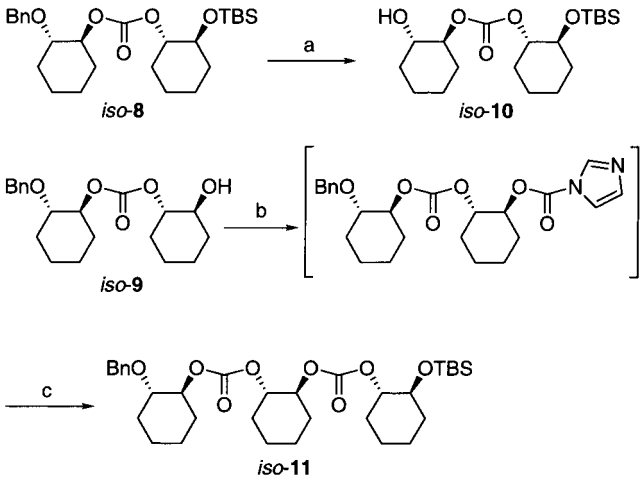
For the preparation of tetramers, we prepared *iso*-**10** by debenzylation of *iso*-**8** and first attempted the coupling with *iso*-**9** through carbonation using Im_2CO in the manner same as for the preparation of **8** (Scheme 6). What was isolated was a complex mixture with the

Scheme 5[a]



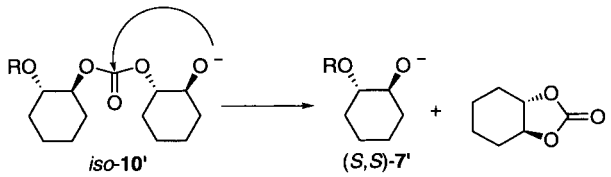
[a] Key: (a) $ClCO_2Me$, DMAP, Py, CH_2Cl_2, 0 °C.

Scheme 6[a]



[a] Key: (a) H_2, Pd/C, EtOH, room temperature; (b) NaH, THF, room temperature, then Im_2CO; (c) *iso*-**10**, NaH, reflux.

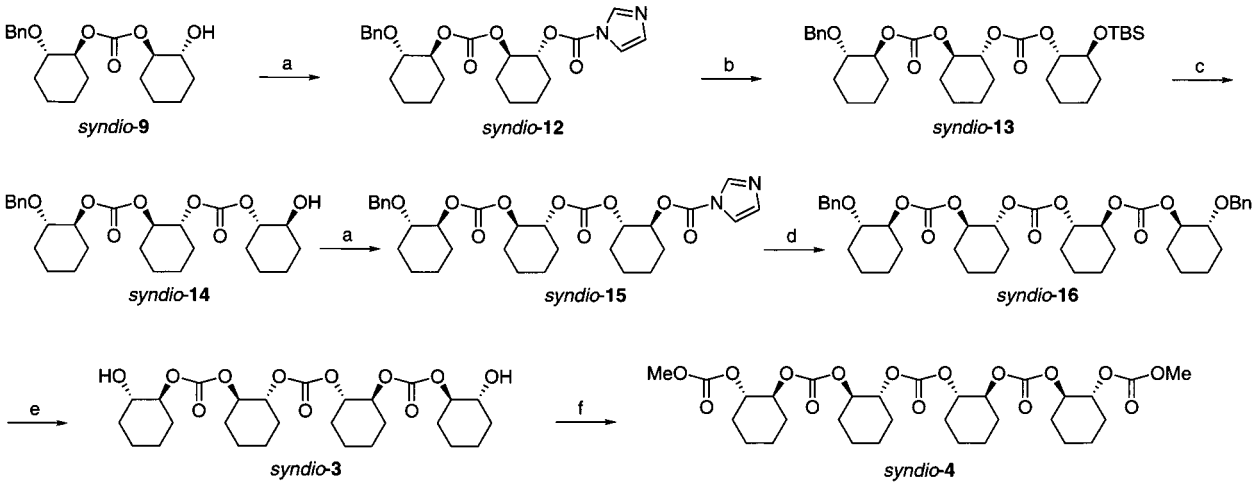
Scheme 7. Back-Biting Reaction



major product being trimer *iso*-**11**. This degradation probably took place through the back biting reaction: an alkoxide moiety attacked the carbonyl group in *iso*-**10′** intramolecularly to yield an alkoxide of monomer (*S*,*S*)-**7′** and a cyclic carbonate (Scheme 7). Thus, strongly basic reagent NaH is not suitable when dimer alcohol participates in the reaction. Although DBU in a catalytic amount was effective for the acylation of a dimer alcohol with Im_2CO to give an imidazole-1-carboxylic ester, it turned out to be ineffective for carbonate formation from imidazole-1-carboxylic ester.

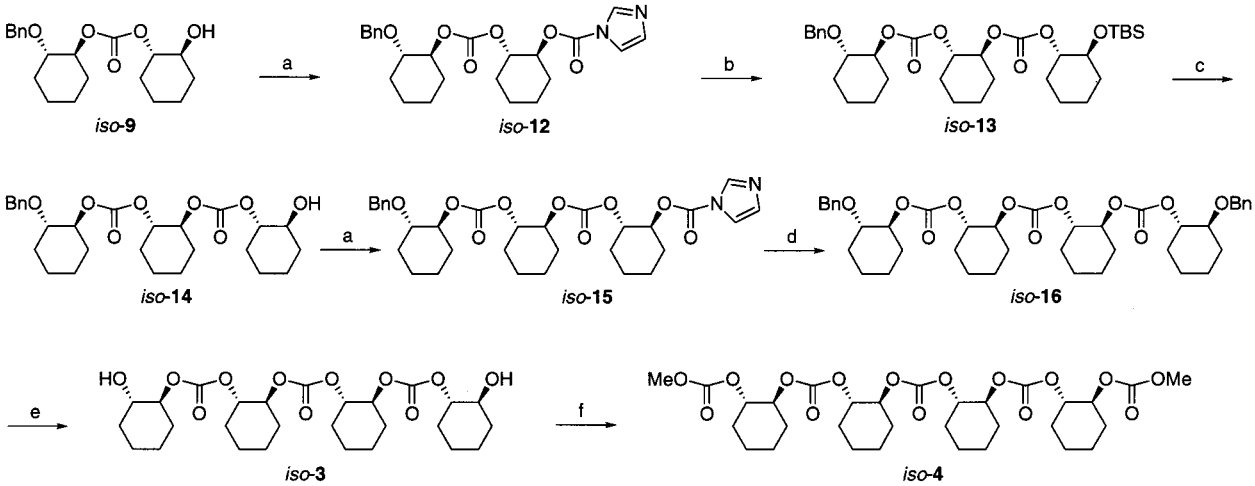
With the negative results of the dimer coupling in head, we next examined stepwise elongation as shown in Scheme 8. An equimolar reaction of Im_2CO with *syndio*-**9** in the presence of DBU gave imidazole-1-carboxylic ester *syndio*-**12** which was treated with sodium salt of (*S*,*S*)-**7** to give trimer *syndio*-**13**. Desilylation gave *syndio*-**14**, which was combined with Im_2CO to give imidazole-1-carboxylic ester *syndio*-**15**. Esterification of *syndio*-**15** with (*R*,*R*)-**6** provided tetramer *syndio*-**16**. Debenzylation of *syndio*-**16** followed by methoxycarbonylation using methyl chloroformate and pyridine furnished tetramer *syndio*-**4** in 71% overall yield. In the last step, the amount of pyridine was critical: pyridine in excess caused degradation to shorter oligo-

Scheme 8. Synthesis of Syndiotactic Tetramer[a]



[a] Key: (a) Im_2CO, DBU, CH_2Cl_2, room temperature; (b) (*S*,*S*)-**7**, NaH, THF, 50 °C; (c) BF_3·OEt_2, CH_3CN, 0 °C;. (d) (*R*,*R*)-**6**, NaH, THF, 50 °C; (e) H_2, Pd/C, EtOH, room temperature; (f) $ClCO_2Me$, Py, CH_2Cl_2, room temperature.

Scheme 9. Synthesis of Isotactic Tetramer[a]



[a] Key: (a) Im_2CO, DBU, CH_2Cl_2, room temperature; (b) (*S*,*S*)-**7**, NaH, THF, 50 °C; (c) BF_3·OEt_2, CH_3CN, 0 °C; (d) (*S*,*S*)-**6**, NaH, THF, 50 °C; (e) H_2, Pd/C, EtOH, room temperature; (f) $ClCO_2Me$, Py, CH_2Cl_2, room temperature;

mers. Similarly, isotactic tetramer *iso*-**4** was prepared starting with dimer alcohol *iso*-**9**, monomer (*S*,*S*)-**6**, and (*S*,*S*)-**7** (Scheme 9). ^{13}C NMR Spectra of *syndio*-**4** and *iso*-**4** are shown in Figure 1-(g), (h), respectively. Chemical shift of *iso*-**4** (153.8 ppm) is almost identical with that of dimer *iso*-**2**,[8] whereas the central carbonyl carbon signal of *syndio*-**4** appeared at 153.1 ppm, 0.6 ppm higher field than that of *syndio*-**2** (153.7 ppm). The difference is of significance. These results clearly suggest that the copolymer should show a m-diad peak at around 153.7 ppm and a r-diad peak at a field higher than the m-diad peak. Accordingly, we can safely conclude that (1) the signal at 153.7 ppm of the copolymer corresponds to signals of central carbonyl carbons of m-centered tetrads and (2) signals of central carbonyl carbons of r-centered tetrads locate outside the signal at 153.7 ppm region, probably at a higher field.

Conclusion

We have synthesized *syndio*- and *iso*-diad model carbonates, assigned ^{13}C NMR signals of the alternating copolymer derived from cyclohexene oxide and carbon dioxide, and concluded that the signal splitting of the copolymer reflects tetrad configuration. The signal at 153.7 ppm of the copolymer is attributed to the central carbonyl carbons of m-centered tetrad; the signals at higher field (153.3−153.1 ppm) of the copolymer are assigned to the central carbonyl carbons of r-centered tetrads. The conclusion agrees well with Coates' assignment that is based on the probability calculation of all the tetrad configurations.

Experimental Section

General Methods. Melting points were determined on a Yanaco MP-500D melting point apparatus. Optical rotation was measured on a JASCO DIP-360 spectrometer using a 1-dm cell. IR spectra were recorded on a JASCO IR-810 spectrometer or a SHIMADZU FTIR-8100A spectrometer. Nuclear magnetic resonance spectra were recorded in deuteriochloroform on a Varian Mercury 200 (^1H 200 MHz; ^{13}C 50 MHz) spectrometer. Chemical shifts are reported in ppm from an internal standard: tetramethylsilane (0 ppm) for ^1H and deuteriochloroform (77.0 ppm) for ^{13}C. Most of reagents were purchased from Aldrich or Wako Pure Chemical Industries Ltd. All the solvents used for reactions were distilled under argon after drying over an appropriate drying reagent. For silica gel column chromatography, Wako-gel C-200 was used.

(1*S*,2*S*)-2-Benzyloxy-1-cyclohexanol [(*S*,*S*)-6].[9] To a solution of (1*S*,2*S*)-1,2-cyclohexanediol (0.58 g, 5.0 mmol) and benzyl trichloroacetimidate (1.0 mL, 5.5 mmol) in a mixture

of dichloromethane (30 mL) and cyclohexane (15 mL) in a dry 80 mL Schlenk tube was added trifluoromethanesulfonic acid (44 μL, 0.50 mmol). The mixture was stirred at room temperature for 20 h and then poured into diethyl ether (80 mL). The resulting organic layer was washed with saturated aqueous $NaHCO_3$ (30 mL × 2) and with brine (30 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated by rotary evaporation. Addition of hexane (20 mL) to the residue afforded insoluble trichloroacetamide, which was removed by filtration. The filtrate was concentrated in vacuo; the residue was purified by silica gel column chromatography to afford (*S*,*S*)-**6** (0.57 g, 57% yield) as a colorless oil, R_f 0.34 (hexanes−ethyl acetate = 4:1). ^{1}H NMR ($CDCl_3$): δ 7.40−7.22 (m, 5H), 4.69 (d, 1H), 4.47 (d, 1H), 3.60−3.06 (m, 2H), 2.62 (br, 1H), 2.24−1.88 (m, 2H), 1.84−1.56 (m, 2H), 1.46−1.08, (m,4H).

(1*S*,2*S*)-2-*t*-Butyldimethylsiloxy-1-cyclohexanol [(*S*,*S*)-7].[10] To an ice-cold solution of (1*S*,2*S*)-1,2-cyclohexanediol (0.51 g, 4.4 mmol) and triethylamine (1.23 mL, 8.8 mmol) in dichloromethane (15 mL) placed in a dry 80 mL Schlenk tube was added slowly a solution of *tert*-butyldimethylsilyl triflate (1.10 mL, 4.8 mmol) in dichloromethane (5.0 mL). The reaction mixture was stirred at 0 °C for 2 h and then poured into diethyl ether (100 mL). The solution was washed with saturated aqueous $NaHCO_3$ (30 mL × 2) and then with brine (30 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. Purification of the residue by silica gel column chromatography gave (*S*,*S*)-**7** (0.66 g, 62% yield) as a colorless oil, R_f 0.40 (hexanes−ethyl acetate = 7:1). ^{1}H NMR ($CDCl_3$): δ 3.45−3.25 (m, 2H), 2.46 (br, 1H), 2.14−1.50 (m, 8H), 0.90 (s, 9H), 0.10, (s, 3H), 0.09 (s, 3H).

Synthesis of Syndiotactic Model Compounds. (1*S*,2*S*)-1-Benzyloxy-2-{[(1*R*,2*R*)-2-(*tert*-butyldimethylsiloxy)-1-cyclohexyloxy]carbonyloxy}cyclohexane (*syndio*-8). In a dry 20 mL Schlenk tube, sodium hydride (60% oil suspension, 8.0 mg, 0.20 mmol) was placed and washed with dry hexane (1.0 mL × 2). Then, a solution of (*R*,*R*)-**7** (0.46 g, 2.0 mmol) in THF (4.0 mL) was added. The resulting mixture was stirred at room temperature for 30 min and added to a solution of 1,1′-carbonyldiimidazole (0.32 g, 2.0 mmol) in THF (2.0 mL) placed in a 100 mL Schlenk tube. The resulting mixture was stirred at room temperature for 3 h. To this reaction mixture was added a mixture of sodium hydride (60% oil suspension, 8.0 mg, 0.20 mmol) and (*S*,*S*)-**6** (0.41 g, 2.0 mmol) in THF (4.0 mL) generated in a manner as described above. The whole mixture was heated to reflux for 12 h before concentration under reduced pressure. The residue was dissolved by diethyl ether (30 mL), washed with 1 M aqueous HCl (15 mL × 2); the aqueous layer was extracted with diethyl ether (30 mL × 2). The combined organic layer was washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by silica gel column chromatography gave *syndio*-**8** (0.58 g, 62% yield) as a colorless viscous oil, R_f 0.21 (hexane: ethyl acetate = 20:1). $[\alpha]_D^{22}$ −11.3° (*c* 1.0, $CHCl_3$). IR (neat): 1735 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.37−7.22 (m, 5H), 4.74−4.43 (m, 4H), 3.71−3.57 (m, 1H), 3.52−3.39 (m, 1H), 2.16−1.14, (m, 16H), 0.84 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 154.27, 138.78, 128.17, 127.36, 127.29, 79.73, 78.27, 77.79, 71.37, 71.27, 32.91, 29.36, 29.19, 28.86, 25.65, 22.89, 22.74, 22.63, 17.89, −4.83, −4.88. Anal. Calcd for $C_{26}H_{42}O_5Si$: C, 67.49; H, 9.15. Found: C, 67.40; H, 9.21.

(1*R*,2*R*)-2-{[(1*S*,2*S*)-2-Benzyloxy-1-cyclohexyloxy]carbonyloxy}-1-cyclohexanol (*syndio*-9). To an ice-cold solution of *syndio*-**8** (0.56 mg, 1.21 mmol) in acetonitrile (8.0 mL) in a dry 20 mL Schlenk tube was added slowly a solution of BF_3·OEt_2 (0.30 mL, 2.4 mmol) in acetonitrile (3.0 mL). The mixture was stirred at 0 °C for 3.5 h, and the solvent was removed under reduced pressure. The residue dissolved in diethyl ether (30 mL) was washed with saturated aqueous $NaHCO_3$ (30 mL × 2); the aqueous layer was extracted with ethyl acetate (50 mL). The combined organic layer was washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Silica gel column chromatography of the residue gave syndio-**9** (0.66 g, 91% yield) as a colorless viscous oil, R_f 0.34 (hexanes−ethyl acetate = 2:1). $[\alpha]_D^{22}$ −3.4° (*c* 1.85, $CHCl_3$). IR (neat): 1740 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.37−7.20 (m, 5H), 4.78−4.52 (m, 3H), 4.50−4.34 (m, 1H), 3.66−3.36 (m, 2H), 2.46 (br s, 1H), 2.18−1.94, (m, 4H), 1.80−1.60 (m, 4H), 1.55−1.10 (m, 8H). ^{13}C NMR ($CDCl_3$): δ 154.54, 138.59, 128.18, 127.34, 127.27, 81.68, 78.93, 78.67, 72.22, 71.18, 32.53, 29.67, 29.61, 29.58, 23.67, 23.52, 23.06, 22.99. Anal. Calcd for $C_{20}H_{28}O_5$: C, 68.94; H, 8.10. Found: C, 68.64; H, 8.38.

(1*R*,2*R*)-2-{[(1*S*,2*S*)-2-Hydroxy-1-cyclohexyloxy]carbonyloxy}-1-cyclohexanol (*syndio*-1). In a 20 mL Schlenk tube were placed *syndio*-**9** (72 mg, 0.21 mmol), Pd/C (10 wt %, 31 mg) and ethanol (4.0 mL). The mixture was stirred under a hydrogen atmosphere (1 atm) at room temperature for 43 h, filtered, and concentrated in vacuo. Purification of the residue by silica gel column chromatography (hexanes−ethyl acetate = 1:2) gave *syndio*-**1** (51 mg, 94% yield) as a colorless solid, mp 92−94 °C. $[\alpha]_D^{22}$ 0° (*c* 0.50, $CHCl_3$). IR ($CHCl_3$): 1740 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 4.55−4.35 (m, 2H), 3.66−3.44 (m, 2H), 3.33 (br s, 2H), 2.18−1.58, (m, 8H), 1.50−1.14 (m, 8H). ^{13}C NMR ($CDCl_3$): δ 154.92, 81.69, 72.50, 32.84, 30.12, 23.87. Anal. Calcd for $C_{13}H_{22}O_5$: C, 60.45; H, 8.58. Found: C, 60.18; H, 8.41.

(1*R*,2*R*)-1-(Methoxycarbonyloxy)-2-[{(1*S*,2*S*)-2-(methoxycarbonyloxy)-1-cyclohexyloxy}carbonyloxy}cyclohexane (*syndio*-2). In a dry 20 mL Schlenk tube were placed *syndio*-**1** (29 mg, 0.11 mmol) dissolved in dichloromethane (2.0 mL), pyridine (1.0 mL), and DMAP (2.4 mg, 0.02 mmol). To the mixturewas slowly added methyl chloroformate (0.34 mL, 4.40 mmol) in dichloromethane (2.0 mL) at 0 °C. The resulting mixture was stirred at 0 °C for 4 h, diluted with diethyl ether (20 mL), washed with 1 M aqueous HCl (10 mL × 2) and brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by silica gel column chromatography (hexanes−ethyl acetate = 2:1) gave *syndio*-**2** (39 mg, 95% yield) as a colorless solid, mp 113−115 °C. $[\alpha]_D^{22}$ −0.1° (*c* 0.55, $CHCl_3$). IR ($CHCl_3$): 1750 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 4.72−4.60 (m, 4H), 3.78 (s, 6H), 2.24−1.98 (m, 4H), 1.90−1.18 (m, 12H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 154.97, 153.65, 77.14, 77.04, 54.66, 29.62, 22.97. Anal. Calcd for $C_{17}H_{26}O_9$: C, 54.54; H, 7.00. Found: C, 54.26; H, 7.23.

(1*R*,2*R*)-2-{[(1*S*,2*S*)-2-Benzyloxy-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyl imidazole-1-carboxylate (*syndio*-12). In a dry 20 mL Schlenk tube were placed 1,1′-carbonyldiimidazole (0.28 g, 1.70 mmol) and *syndio*-**9** (0.30 g, 0.85 mmol) dissolved in dichloromethane (5.0 mL) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 25 μL, 0.17 mmol) in this order. The mixture was stirred at room temperature for 1 h, washed with water (15 mL × 3), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by silica gel column chromatography gave *syndio*-**12** (0.35 g, 92% yield) as a colorless viscous oil, R_f 0.16 (hexanes−ethyl acetate = 2:1). $[\alpha]_D^{22}$ −38.0° (*c* 1.10, $CHCl_3$). IR (neat): 1740, 1760 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 8.01 (s, 1H), 7.33−7.15 (m, 6H), 6.92 (s, 1H), 5.06−4.76 (m, 2H), 4.72−4.56 (m, 1H), 4.42 (s, 2H), 3.37−3.22 (m, 1H), 2.36−1.08 (m, 16H). ^{13}C NMR ($CDCl_3$): δ 154.06, 147.87, 138.53, 137.00, 130.42, 128.11, 127.20, 126.94, 116.88, 79.29, 78.36, 77.76, 76.44, 70.64, 29.96, 29.74, 29.47, 29.33, 23.12, 22.95, 22.82. Anal. Calcd for $C_{24}H_{30}N_2O_6$: C, 65.14; H, 6.83. Found: C, 64.92; H, 6.72.

(1*S*,2*S*)-1-Benzyloxy-2-{[(1*R*,2*R*)-2-{[(1*S*,2*S*)-2-(*tert*-butyldimethylsilyloxy)-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyloxy]carbonyloxy}cyclohexane (*syndio*-13). In a dry 20 mL Schlenk tube, sodium hydride (60% oil suspension, 30 mg, 0.75 mmol) was placed and washed with dry hexane (1.0 mL × 2). To this was added a solution of (*S*,*S*)-**7** in THF (4.0 mL). The mixture was stirred for 1 h at room temperature before treatment with a solution of *syndio*-**12** in THF (4.0 mL). The resulting mixture was stirred at 50 °C for 2 h before concentration under reduced pressure. The residue was dissolved by diethyl ether (20 mL), washed with 1 M aqueous HCl (20 mL × 2), and the aqueous layer was extracted with diethyl ether (20 mL × 2). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under

reduced pressure. Silica gel column chromatography of the residue gave *syndio*-**13** (0.16 g, 34% yield) as a colorless viscous oil, R_f 0.08 (hexanes−ethyl acetate = 20:1). $[\alpha]_D^{22}$ 4.8° (*c* 1.00, $CHCl_3$). IR (neat) 1740, 1750 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.37−7.21 (m, 5H), 4.76−4.63 (m, 3H), 4.60 (s, 2H), 4.51−4.38 (m, 1H), 3.64−3.52 (m, 1H), 3.50−3.37 (m, 1H), 2.20−1.10 (m, 24H), 0.85 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 153.82, 153.74, 138.64, 128.23, 127.45, 127.36, 79.80, 78.37, 77.66, 76.14, 75.87, 71.29, 71.11, 32.63, 29.14, 28.96, 28.62, 25.64, 22.69, 22.61, 22.54, 22.42, 17.91, −4.89, −4.94. Anal. Calcd for $C_{33}H_{52}O_8Si$: C, 65.53; H, 8.67. Found: C, 65.38; H, 8.54.

(1*S*,2*S*)-2-{[(1*R*,2*R*)-2-{[(1*S*,2*S*)-2-Benzyloxy-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyloxy]carbonyloxy}-1-cyclohexanol (*syndio*-14). To an ice-cold solution of *syndio*-**13** (0.24 mg, 0.40 mmol) in acetonitrile (5.0 mL) in a dry 20 mL Schlenk tube was added slowly a solution of $BF_3{\cdot}OEt_2$ (0.10 mL, 0.80 mmol) in acetonitrile (5.0 mL). The mixture was stirred at 0 °C for 2 h, and the solvent was removed under reduced pressure. Workup and purification by silica gel column chromatography gave *syndio*-**14** (0.15 g, 78% yield) as a colorless viscous oil, R_f 0.36 (hexanes−ethyl acetate = 2:1). $[\alpha]_D^{22}$ 14.1° (*c* 0.50, $CHCl_3$); IR ($CHCl_3$) 1740 cm^{-1};^1H NMR (200 MHz, $CDCl_3$) δ 7.41−7.23 (m, 5H), 4.80−4.52 (m, 5H), 4.34−4.15 (m, 1H), 3.52−3.18 (m, 2H), 2.51 (br s, 1H), 2.24−1.00 (m, 24H). ^{13}C NMR ($CDCl_3$) δ 154.41, 154.08, 138.59, 128.33, 127.80, 127.47, 81.94, 79.30, 78.96, 77.31, 71.98, 71.34, 32.64, 29.93, 29.76, 23.67, 23.34, 23.23. Anal. Calcd for $C_{27}H_{38}0_8$: C, 66.10; H, 7.81. Found: C, 66.08; H, 8.07.

(1*S*,2*S*)-2-{[(1*R*,2*R*)-2-{[(1*S*,2*S*)-2-Benzyloxy-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyl imidazole-1-carboxylate (*syndio*-15). Into a dry 20 mL Schlenk tube were placed 1,1′-carbonyldiimidazole (94 mg, 0.58 mmol) and *syndio*-**14** (0.140 g, 0.29 mmol) dissolved in dichloromethane (5.0 mL), and DBU (8.8 μL, 0.058 mmol) were placed in this order. After stirred for 30 min at room temperature, workup and purification by silica gel column chromatography (hexanes−ethyl acetate = 2:1) gave *syndio*-**15** (0.145 g, 86% yield) as a colorless solid, mp 35−37 °C. $[\alpha]_D^{22}$ 32.0° (*c* 1.00, $CHCl_3$). IR ($CHCl_3$): 1760 cm^{-1}. ^1H NMR ($CDCl_3$): δ 8.11 (s, 1H), 7.42−7.20 (m, 6H), 7.05 (s, 1H), 4.82−4.45 (m, 7H), 3.41−3.24 (m, 1H), 2.30−1.13 (m, 24H). ^{13}C NMR ($CDCl_3$) δ 153.88, 153.76, 147.80, 138.76, 137.19, 130.53, 128.22, 127.46, 127.26, 117.13, 79.18, 78.76, 78.15, 77.14, 76.38, 71.54, 29.80, 29.64, 29.61, 29.37, 23.13, 22.88, 22.76, 22.71. Anal. Calcd for $C_{31}H_{40}N_2O_9$: C, 63.68; H, 6.90. Found: C, 63.59; H, 7.10.

(1*R*,2*R*)-1-Benzyloxy-2-{[(1S,2S)-2-{[(1*R*,2*R*)-2-{[(1*S*,2*S*)-2-benzyloxy-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyloxy]carbonyl-oxy}cyclohexane (*syndio*-16). In a dry 20 mL Schlenk tube was placed sodium hydride (60% oil suspension, 9.6 mg, 0.24 mmol), which was washed with dry hexane (1.0 mL × 2). To this was added a solution of (*R*,*R*)-**6** (50 mg, 0.24 mmol) in THF (4.0 mL). The mixture was stirred for 1 h at room temperature, followed by addition of a solution of *syndio*-**15** (0.138 g, 0.24 mmol) in THF (4.0 mL). After the resulting mixture was stirred at 50 °C for 6 h, workup and purification by silica gel column chromatography (hexanes−ethyl acetate = 10:1) gave *syndio*-**16** (55 mg, 32% yield) as a colorless amorphous solid. $[\alpha]_D^{22}$ 0.0° (*c* 0.50, $CHCl_3$). IR ($CHCl_3$): 1740 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.37−7.21 (m, 10H), 4.73−4.50 (m, 10H), 3.49−3.33 (m, 2H), 2.19−1.90 (m, 8H), 1.77−1.12 (m, 24H). ^{13}C NMR ($CDCl_3$): δ 153.77, 153.33, 138.80, 128.24, 27.58, 127.35, 79.04, 78.26, 76.36, 76.03, 71.60, 29.65, 29.45, 28.87, 22.95, 22.36. Anal. Calcd for $C_{41}H_{54}O_{11}$: C, 68.12; H, 7.53. Found: C, 68.23; H, 7.75.

(1*R*,2*R*)-2-{[(1*S*,2*S*)-2-{[(1*R*,2*R*)-2-{[(1*S*,2*S*)-2-Hydroxy-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyloxy]carbonyloxy}-1-cyclohexanol (*syndio*-3). In a 20 mL Schlenk tube were placed *syndio*-**16** (23 mg, 0.032 mmol), Pd/C (10 wt %, 26 mg), and ethanol (5.0 mL). The mixture was stirred under a hydrogen atmosphere (1 atm) at room temperature for 35 h, filtered, and concentrated in vacuo. Purification of the residue by silica gel column chromatography (hexanes−ethyl acetate = 1:1) gave *syndio*-**3** (16 mg, 94% yield) as a colorless solid, mp 156−159 °C. $[\alpha]_D^{22}$ 0.3° (*c* 0.50, $CHCl_3$). IR ($CHCl_3$): 1740 cm^{-1}. ^1H NMR ($CDCl_3$): δ 4.76−4.47 (m, 6H), 3.70−3.48 (m, 4H), 2.20−1.94 (m, 8H), 1.84−1.64 (m, 8H), 1.58−1.16 (m, 16H). ^{13}C NMR ($CDCl_3$): δ 154.48, 154.42, 82.45, 78.05, 77.76, 72.04, 32.35, 30.33, 30.24, 29.98, 23.98, 23.86, 23.45, 23.41. Anal. Calcd for $C_{27}H_{42}O_{11}$: C, 59.76; H, 7.80. Found: C, 59.99; H, 8.04.

(1*R*,2*R*)-1-(Methoxycarbonyloxy)-2-{[(1*S*,2*S*)-2-{[(1*R*,2*R*)-2-{[(1*S*,2*S*)-2-(methoxycarbonyloxy)-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyloxy]carbonyloxy}cyclohexane (*syndio*-4). To a solution of *syndio*-**3** (34 mg, 0.062 mmol), dissolved in dichloromethane (2.0 mL) and placed in a dry 20 mL Schlenk tube, were added methyl chloroformate (0.48 mL, 6.20 mmol) and then pyridine (0.10 mL, 1.24 mmol) drop by drop at room temperature. The mixture was stirred at room temperature for 4 h (the reaction was monitored by TLC) before additional methyl chloroformate (0.20 mL, 2.59 mmol) and pyridine (50 μL, 0.60 mmol) were added. After another 4 h, more methyl chloroformate (0.20 mL, 2.59 mmol) and pyridine (50 μL, 0.60 mmol) were added, and the mixture was stirred for 14 h. All volatile materials were removed under reduced pressure; the residue was dissolved in ethyl acetate (30 mL). The organic layer was washed with water (10 mLx2), brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated by rotary evaporation. Purification of the residue by silica gel column chromatography (hexanes−ethyl acetate = 2:1) gave *syndio*-**4** (31 mg, 76% yield) as a colorless amorphous solid. $[\alpha]_D^{22}$ 0.2° (*c* 0.74, $CHCl_3$). IR ($CHCl_3$): 1750 cm^{-1}. ^1H NMR ($CDCl_3$) δ 4.75−4.60 (br, 8H), 3.77 (s, 6H), 2.20−2.00 (m, 8H), 1.82−1.20 (m, 24H). ^{13}C NMR ($CDCl_3$): δ 155.01, 153.47, 153.14, 77.17, 76.93, 76.51, 54.75, 29.63, 29.61, 28.94, 22.96, 22.44. Anal. Calcd for $C_{31}H_{46}O_{15}$: C, 56.53; H, 7.04. Found: C, 56.72; H, 6.94.

Synthesis of Isotactic Model Compounds. (1*S*,2*S*)-1-Benzyloxy-2-{[(1*S*,2*S*)-2-(*tert*-butyldimethylsiloxy)-1-cyclohexyloxy]carbonyloxy}cyclohexane (*iso*-8). In a dry 20 mL Schlenk tube was placed sodium hydride (60% oil suspension, 6.8 mg, 0.17 mmol), which was washed with dry hexane (1.0 mL × 2). Then, a solution of (*S*,*S*)-**7** (0.38 g, 1.65 mmol) in THF (7.0 mL) was added. The resulting mixture was stirred at room temperature for 1 h and added to a solution of 1,1′-carbonyldiimidazole (0.28 g, 1.70 mmol) in THF (5.0 mL) placed in a 100 mL Schlenk tube. The resulting mixture was stirred at room temperature for 3.5 h. To this reaction mixture was added a mixture of sodium hydride (60% oil suspension, 6.8 mg, 0.17 mmol) and (*S*,*S*)-**6** (0.34 g, 1.66 mmol) in THF (7.0 mL) generated in a manner as described above. The whole mixture was heated to reflux for 18 h. Workup and purification by silica gel column chromatography (hexanes−ethyl acetate = 20:1) gave *iso*-**8** (0.59 g, 75% yield) as a colorless solid, mp 61−63 °C. $[\alpha]_D^{22}$ 24.1° (*c* 1.0, $CHCl_3$). IR ($CHCl_3$): 1735 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.38−7.20 (m, 5H), 4.76−4.46 (m, 4H), 3.66−3.54 (m, 1H), 3.50−3.36 (m, 1H), 2.12−1.15 (m, 16H), 0.87 (s, 9H), 0.06 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 154.0, 138.83, 128.14, 127.29, 80.08, 78.90, 78.50, 72.23, 71.30, 33.54, 29.77, 29.55, 25.70, 23.32, 23.20, 17.95, −4.68, −4.89. Anal. Calcd for $C_{26}H_{42}O_5Si$: C, 67.49; H, 9.15. Found: C, 67.33; H, 9.31.

(1*S*,2*S*)-2-{[(1*S*,2*S*)-2-Benzyloxy-1-cyclohexyloxy]carbonyloxy}-1-cyclohexanol (*iso*-9). To an ice-cold solution of *iso*-**8** (0.56 mg, 1.21 mmol) dissolved in acetonitrile (7.0 mL) and placed in a dry 100 mL Schlenk tube was added slowly a solution of $BF_3{\cdot}OEt_2$ (0.10 mL, 0.80 mmol) in acetonitrile (7.0 mL), and then the resulting mixture was stirred at 0 °C for 1.5 h. Workup and purification by silica gel column chromatography (hexanes−ethyl acetate = 1:1) gave *iso*-**9** (0.14 g, 98% yield) as a colorless solid, mp 67−69 °C. $[\alpha]_D^{22}$ 28.7° (*c* 1.0, $CHCl_3$). IR ($CHCl_3$): 1740 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.40−7.20 (m, 5H), 4.77−4.53 (m, 3H), 4.47−4.35 (m,1H), 3.62−3.53 (m, 1H), 3.45−3.34 (m, 1H), 2.71 (br s, 1H), 2.20−1.95 (m, 4H), 1.80−1.60 (m, 4H), 1.52−1.15 (m, 8H). ^{13}C NMR ($CDCl_3$): δ 154.42, 138.47, 128.08, 127.27, 81.72, 79.16, 79.11, 72.21, 71.17, 32.54, 29.82, 29.74, 29.67, 23.67, 23.56, 23.23, 23.16. Anal. Calcd for $C_{20}H_{28}O_5$: C, 68.94; H, 8.10. Found: C, 68.73; H, 8.25.

(1*S*,2*S*,1′*S*,2′*S*)-2,2′-Carbonyldioxydicyclohexanol (*iso*-1). In a 20 mL Schlenk tube were placed *iso*-**9** (96 mg, 0.28 mmol), Pd/C (10 wt %, 68 mg) and ethanol (5.0 mL). The mixture was stirred under a hydrogen atmosphere (1 atm) at room temperature for 21 h, filtered, and concentrated in vacuo. Purification of the residue by silica gel column chromatography gave *iso*-**1** (70 mg, 96% yield) as a colorless oil, R_f 0.39 (hexanes−ethyl acetate = 1:2). $[\alpha]_D^{22}$ 47.3° (*c* 0.71, $CHCl_3$). IR (neat): 1740 cm^{-1}. ^1H NMR ($CDCl_3$): δ 4.50−4.34 (m, 2H), 3.68−3.50 (m, 2H), 3.08 (br s, 2H), 2.20−1.92 (m, 4H), 1.86−1.54 (m, 4H), 1.50−1.12 (m, 8H). ^{13}C NMR ($CDCl_3$): δ 154.50, 82.19, 72.45, 32.75, 29.83, 23.80, 23.68. Anal. Calcd for $C_{13}H_{22}O_5$: C, 60.45; H, 8.58. Found: C, 60.46; H, 8.83.

(1*S*,2*S*)-1-(Methoxycarbonyloxy)-2-[{(1*S*,2*S*)-2-(methoxycarbonyloxy)-1-cyclohexyloxy}carbonyloxy}cyclohexane (*iso*-2). In a dry 20 mL Schlenk tube were placed *iso*-**1** (37 mg, 0.14 mmol) dissolved in dichloromethane (4.0 mL), pyridine (1.0 mL), and DMAP (3.4 mg, 0.028 mmol). To this mixture was slowly added methyl chloroformate (0.43 mL, 5.60 mmol) in dichloromethane (2.0 mL) at 0 °C, and then the resulting mixture was stirred at 0 °C for 5 h. Workup and purification by silica gel column chromatography (hexanes−ethyl acetate = 7:1) gave *iso*-**2** (32 mg, 62% yield) as a colorless solid, mp 108−110 °C. $[\alpha]_D^{22}$ 21.0° (*c* 1.1, $CHCl_3$): IR ($CHCl_3$): 1750 cm^{-1}. ^1H NMR ($CDCl_3$): δ 4.72−4.60 (m, 4H), 3.77 (s, 6H), 2.24−2.15 (m, 4H), 1.82−1.25 (m, 12H). ^{13}C NMR ($CDCl_3$): δ 154.92, 153.75, 77.28, 77.03, 54.63, 29.69, 29.60, 23.00. Anal. Calcd for $C_{17}H_{26}O_9$: C, 54.54; H, 7.00. Found: C, 54.53; H, 7.18.

(1*S*,2*S*)-1-(Methoxycarbonyloxy)-2-[{(1*S*,2*S*)-2-(methoxycarbonyloxy)-1-cyclohexyloxy}carbonyloxy}cyclohexane (*iso*-12). Into a dry 20 mL Schlenk tube, 1,1′-carbonyldiimidazole (0.39 g, 2.40 mmol) and *iso*-**9** (0.41 g, 1.16 mmol) dissolved in dichloromethane (8.0 mL) and DBU (25 μL, 0.17 mmol) were placed in this order. After the mixture was stirred at room temperature for 30 min, workup and purification by silica gel column chromatography (hexanes−ethyl acetate = 2:1) gave *iso*-**12** (0.51 g, 96% yield) as a colorless solid, mp 90−92 °C. $[\alpha]_D^{22}$ 63.8° (*c* 0.50, $CHCl_3$). IR ($CHCl_3$): 1765, 1735 cm^{-1}. ^1H NMR ($CDCl_3$): δ 8.12 (s, 1H), 7.45−7.22 (m, 6H), 7.05 (s,1H), 5.02−4.80 (m, 2H), 4.72−4.48 (m, 1H), 3.44−3.28 (m, 1H), 2.40−1.10 (m,16H). ^{13}C NMR ($CDCl_3$): δ 154.20, 147.86, 138.62, 137.06, 130.48, 128.11, 127.28, 127.23, 117.02, 79.55, 79.00, 78.77, 76.33, 71.22, 30.02, 29.77, 29.57, 23.18. Anal. Calcd for $C_{24}H_{30}N_2O_6$: C, 65.14; H, 6.83. Found: C, 65.11; H, 6.82.

(1*S*,2*S*)-1-Benzyloxy-2-{[(1*S*,2*S*)-2-{[(1*S*,2*S*)-2-(*tert*-butyldimethylsilyloxy)-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyloxy]carbonyloxy}cyclohexane (*iso*-13). In a dry 20 mL Schlenk tube, sodium hydride (60% oil suspension, 38 mg, 0.95 mmol) was placed and washed with dry hexane (1.0 mL × 2). To this was added a solution of (*S*,*S*)-**7** (0.22 g, 0.95 mmol) in THF (4.0 mL). The mixture was stirred for 1 h at room temperature before treatment with a solution of *iso*-**12** (0.42 g, 0.95 mmol) in THF (4.0 mL). The resulting mixture was stirred at 50 °C for 3 h. Workup and purification by silica gel column chromatography gave *iso*-**13** (0.24 g, 42% yield) as a colorless viscous oil, R_f 0.05 (hexanes−ethyl acetate = 20:1). $[\alpha]_D^{22}$ 28.9° (*c* 0.64, $CHCl_3$). IR (neat): 1750, 1740 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.34−7.24 (m, 5H), 4.76−4.42 (m, 6H), 3.64−3.50 (m, 1H), 3.47−3.34 (m, 1H), 2.20−1.10 (m, 24H), 0.86 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 154.20, 154.13, 138.77, 128.17, 127.32, 80.38, 79.03, 76.88, 76.55, 72.19, 71.36, 33.60, 29.83, 29.71, 29.63, 29.55, 25.70, 23.34, 23.23, 23.01, 22.97, 17.94, −4.69, −4.87. Anal. Calcd for $C_{33}H_{52}O_8Si$: C, 65.53; H, 8.67. Found: C, 65.40; H, 8.87.

(1*S*,2*S*)-2-{[(1*S*,2*S*)-2-{[(1*S*,2*S*)-2-Benzyloxy-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyloxy]carbonyloxy}-1-cyclohexanol (*iso*-14). To an ice-cold solution of *iso*-**13** (0.23 g, 0.38 mmol) in acetonitrile (8.0 mL) in a dry 50 mL Schlenk tube was added slowly a solution of $BF_3{\cdot}OEt_2$ (96 μL, 0.76 mmol) in acetonitrile (7.0 mL). The mixture was stirred at 0 °C for 5 h, and then workup and purification by silica gel column chromatography gave *iso*-**14** (0.18 g, 97% yield) as a colorless viscous oil, R_f 0.21 (hexanes−ethyl acetate = 2:1). $[\alpha]_D^{22}$ 29.5° (*c* 1.0, $CHCl_3$). IR ($CHCl_3$): 1740 cm^{-1}. ^1H NMR ($CDCl_3$): δ7.35−7.24 (m, 5H), 4.76−4.52 (m, 5H), 4.47−4.33 (m, 1H), 3.65−3.50 (m, 1H), 3.47−3.34 (m, 1H), 2.37 (br s, 1H), 2.24−1.98 (m, 6H), 1.80−1.16 (m, 18H). ^{13}C NMR ($CDCl_3$): δ154.17, 154.06, 138.65, 128.10, 127.23, 81.96, 79.07, 78.93, 77.26, 76.89, 72.24, 71.24, 32.60, 29.73, 29.68, 23.70, 23.60, 23.17, 23.14, 23.02, 22.98. Anal. Calcd for $C_{27}H_{38}O_8$: C, 66.10; H, 7.81. Found: C, 65.95; H, 8.11.

(1*S*,2*S*)-2-{[(1*S*,2*S*)-2-{[(1*S*,2*S*)-2-Benzyloxy-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyl imidazole-1-carboxylate (*iso*-15). In a dry 20 mL Schlenk tube, 1,1′-carbonyldiimidazole (0.12 g, 0.72 mmol) and *iso*-**14** (0.18 g, 0.36 mmol) dissolved in dichloromethane (5.0 mL) and DBU (11 μL, 0.072 mmol) were placed in this order. After stirred for 1 h at room temperature, workup and purification by silica gel column chromatography (hexanes−ethyl acetate = 2:1) gave *iso*-**15** (0.18 g, 87% yield) as a colorless solid, mp 40−42 °C. $[\alpha]_D^{22}$ 49.5° (*c* 1.0, $CHCl_3$). IR ($CHCl_3$): 1760, 1740 cm^{-1}. ^1H NMR ($CDCl_3$): δ 8.19 (s, 1H), 7.40 (s, 1H), 7.34−7.23 (m, 5H), 7.05 (s, 1H), 4.98−4.79 (m, 2H), 4.75−4.50 (m, 5H), 3.46−3.33 (m, 1H), 2.38−1.15 (m, 24H). ^{13}C NMR ($CDCl_3$): δ 153.98, 153.92, 147.79, 138.65, 137.05, 130.50, 128.11, 127.27, 127.23, 117.05, 79.08, 78.95, 78.72, 77.48, 76.70, 76.53, 71.22, 29.98, 29.77, 29.61, 29.30, 23.20, 23.16, 22.88. Anal. Calcd for $C_{31}H_{40}N_2O_9$: C, 63.68; H, 6.90. Found: C, 63.86; H, 6.99.

(1*S*,2*S*)-1-Benzyloxy-2-{[(1S,2S)-2-{[(1*S*,2*S*)-2-benzyloxy-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyloxy]carbonyl-oxy}cyclohexane (*iso*-16). In a dry 20 mL Schlenk tube was placed sodium hydride (60% oil suspension, 12 mg, 0.29 mmol), which was washed with dry hexane (1.0 mL × 2). To this was added a solution of (*S*,*S*)-**6** (60 mg, 0.29 mmol) in THF (4.0 mL). The mixture was stirred for 1 h at room temperature, followed by addition of a solution of *iso*-**15** (0.17 g, 0.29 mmol) in THF (4.0 mL), and then the resulting mixture was stirred at 50 °C for 4 h. Workup and purification by silica gel column chromatography (hexanes−ethyl acetate = 10:1) gave *iso*-**16** (89 mg, 41% yield) as a colorless amorphous solid. $[\alpha]_D^{22}$ 22.6° (*c* 0.78, $CHCl_3$). IR ($CHCl_3$): 1740 cm^{-1}. ^1H NMR ($CDCl_3$): δ7.35−7.23 (m, 10H), 4.72−4.54 (m, 10H), 3.46−3.33 (m, 2H), 2.20−1.98 (m, 8H), 1.82−1.60 (m, 8H), 1.52−1.16 (m, 16H). ^{13}C NMR ($CDCl_3$): δ 154.06, 153.84, 138.74, 128.14, 127.28, 79.05, 78.98, 77.04, 76.81, 71.29, 29.76, 29.64, 23.22, 23.00. Anal. Calcd for $C_{41}H_{54}O_{11}$: C, 68.12; H, 7.53. Found: C, 68.07; H, 7.64.

(1*S*,2*S*)-2-{[(1*S*,2*S*)-2-{[(1*S*,2*S*)-2-{[(1*S*,2*S*)-2-hydroxy-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyloxy]carbonyloxy}-1-cyclohexanol (*iso*-3). In a 20 mL Schlenk tube were placed *iso*-**16** (33 mg, 0.046 mmol), Pd/C (10 wt %, 41 mg) and ethanol (5.0 mL). The mixture was stirred under a hydrogen atmosphere (1 atm) at room temperature for 40 h, filtered, and concentrated in vacuo. Purification of the residue by silica gel column chromatography (hexanes−ethyl acetate = 1:1) gave *iso*-**3** (24 mg, 98% yield) as a colorless solid, mp 69−71 °C; $[\alpha]_D^{22}$ 43.3° (*c* 0.40, $CHCl_3$). IR ($CHCl_3$): 1740 cm^{-1}. ^1H NMR ($CDCl_3$): δ 4.77−4.54 (m, 4H), 4.46−4.34 (m, 2H), 3.68−3.47 (m, 2H), 2.60−1.16 (br s + m, 34H). ^{13}C NMR ($CDCl_3$): δ 154.20, 153.79, 82.11, 77.29, 77.23, 72.39, 32.68, 29.77, 29.68, 23.79, 23.69, 23.04. Anal. Calcd for $C_{27}H_{42}O_{11}$: C, 59.76; H, 7.80. Found: C, 59.54; H, 8.04.

(1*S*,2*S*)-1-(Methoxycarbonyloxy)-2-{[(1*S*,2*S*)-2-{[(1*S*,2*S*)-2-{[(1*S*,2*S*)-2-(methoxycarbonyloxy)-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyloxy]carbonyloxy}-1-cyclohexyloxy]carbonyloxy}cyclohexane (*iso*-4). To a solution of *iso*-**3** (16 mg, 0.029 mmol) dissolved in dichloromethane (2.0 mL) and placed in a dry 10 mL Schlenk tube were added methyl chloroformate (0.22 mL, 2.90 mmol) and then pyridine (24 μL, 0.29 mmol) drop by drop at room temperature. The mixture was stirred at room temperature for 3 h (the reaction was monitored by TLC) before additional methyl chloroformate (0.10 mL, 1.29 mmol) and pyridine (24 μL, 0.29 mmol) were added, and the mixture was stirred for 3.5 h. Workup and purification by silica gel column chromatography (hexane: ethyl acetate = 1:1) gave *iso*-**4** (16 mg, 85% yield) as a colorless

amorphous solid. $[\alpha]_D^{22}$ 25.5° (*c* 0.61, $CHCl_3$). IR ($CHCl_3$): 1750 cm^{-1}. ^1H NMR ($CDCl_3$): δ 4.74−4.54 (br, 8H), 3.76 (s, 6H), 2.30−2.00 (m, 8H), 1.86−1.18 (m, 24H). ^{13}C NMR ($CDCl_3$): δ 154.98, 153.79, 77.32, 77.17, 77.10, 54.68, 29.71, 29.62, 23.05. Anal. Calcd for $C_{31}H_{46}O_{15}$: C, 56.53; H, 7.04. Found: C, 56.69; H, 7.11.

Acknowledgment. We are grateful to Prof. T. Kitayama (Osaka University) for helpful discussions. This work was partially supported by the Grant-in-Aids for COE Research on Elements Science, No. 12CE2005 from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

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MA010732R