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A novel dynamic kinetic resolution accompanied by intramolecular transesterification: asymmetric synthesis of a 4-hydroxymethyl-2-oxazolidinone from serinol derivatives

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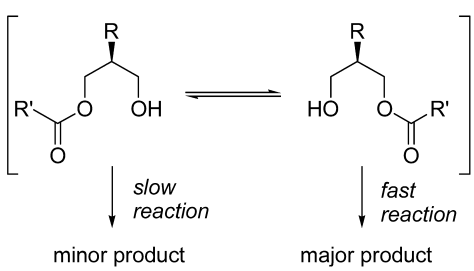
Abstract—Reaction paths of the one-pot reaction of (*R*)-2-(α-methylbenzyl)amino-1,3-propanediol (**1**) and 2-chloroethyl chloroformate with DBU giving (4*S*,α*R*)-4-hydroxymethyl-3-(α-methylbenzyl)-2-oxazolidinone [(4*S*)-**2**] (94% de) were investigated. Intermediates of this reaction, 2-chloroethyl (2*S*)- and 2-chloroethyl (2*R*)-3-hydroxy-2-[(α*R*)-α-methylbenzyl]aminopropyl carbonates [(2*S*)-**4** and (2*R*)-**4**], were synthesized individually. After the addition of DBU to the respective solution of the carbonate (2*S*)-**4** and that of (2*R*)-**4** in dichloromethane, the intramolecular transesterification between (2*S*)-**4** and (2*R*)-**4** and the diastereoselective intramolecular cyclization proceeded to afford (4*S*)-**2** in high diastereomeric excess. Therefore, two monocarbonates (2*S*)-**4** and (2*R*)-**4** were kinetically resolved by this cyclization during the intramolecular transesterification between (2*S*)-**4** and (2*R*)-**4**. We found that this process involved dynamic kinetic resolution accompanied by intramolecular transesterification.

1. Introduction

Dynamic kinetic resolution (DKR) is a powerful method for the preparation of optically active compounds,[1] and the reaction mechanisms of some kinds of DKR have been studied in detail.[2] Racemic and epimeric mixtures are resolved kinetically with racemization and epimerization to give optically active compounds by DKR. Kinetic resolution also prepares optically active compounds from the racemate; however, their maximum yields are limited to 50%, because less reactive substrates remain in the reaction mixture. DKR includes two reactions. The first is kinetic resolution, and the other is equilibrium between two racemic or epimeric intermediates. Because of the rapid equilibrium, all substrates including less reactive substrates are consumed, and the theoretical yields are up to 100%. α-Substituted carbonyl compounds such as ketones, esters, amides, and hydantoins are frequently used for the substrates in DKR,[1a,b,d,f,h–j] and other types of compounds (cyanohydrins, alkyl lithiums, alkyl zinc chlorides, Grignard reagents, vinyl esters, etc.) also have been investigated as substrates for DKR.[1b,c,e–j]

On the other hand, migration of functional groups also creates equilibrium. For example, acyl groups of some monoacyl 1,3-propanediols migrate to create an equilibration (intramolecular transesterification).[3] If the reactivities of two monoesters were different enough to be resolved, a mixture of the monoesters would be a suitable substrate for DKR (Scheme 1). However, DKR involving the intramolecular transesterification has not been well studied.

We are investigating the asymmetric desymmetrization of 2-substituted propane derivatives.[4] In the preceding communication, we disclosed a one-pot reaction of (*R*)-2-(α-methylbenzyl)amino-1,3-propanediol (**1**) and 2-chloroethyl chloroformate with DBU to give optically active (4*S*,α*R*)-4-hydroxymethyl-3-(α-methylbenzyl)-2-oxazolidinone [(4*S*)-**2**] in high diastereomeric excess (94% de) (Fig. 1).[4a] In the reaction mixture of **1** and 2-chloroethyl chloroformate before the addition of DBU, the monocarbonates (2*S*)-**4** and (2*R*)-**4** (1:1, 40%) as intermediates and a dicarbonate **3** (5%) are obtained after work-up and



Scheme 1. Possibility of DKR of 1,3-propanediol monoester derivatives.

Keywords: dynamic kinetic resolution; transesterification; oxazolidinone; serinol.

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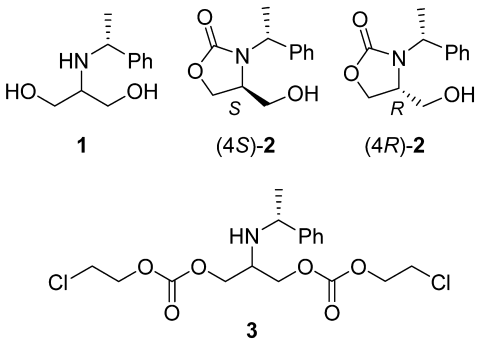
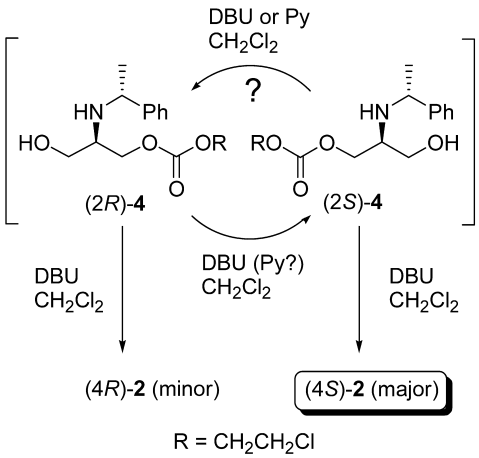


Figure 1.



Scheme 2. Possible paths to afford (4*S*)-**2**.

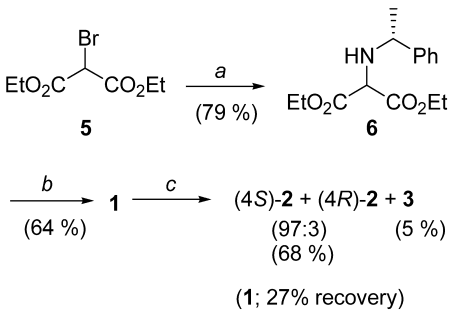
purification with silica gel column chromatography. The oxazolidinone (4*S*)-**2** is obtained in 94% de from the equimolar mixture of (2*S*)-**4** and (2*R*)-**4** quantitatively by treatment of DBU (Scheme 2).[4a] We have proposed the possible paths indicating that (i) monocarbonates (2*S*)-**4** and (2*R*)-**4** exist as an equimolar mixture before the addition of DBU, and (ii) at least the monocarbonate (2*R*)-**4** is converted to (2*S*)-**4** via intramolecular transesterification after the addition of DBU, after which the cyclization of (2*S*)-**4** proceeds to give (4*S*)-**2**.[4a]

Herein, we report the details of reaction pathways from the serinol **1** to (4*S*)-**2** including the transesterification between the monocarbonates (2*R*)-**4** and (2*S*)-**4**.

2. Results and discussion

2.1. Preparation of the oxazolidinones (4*S*)-2 and (4*R*)-2

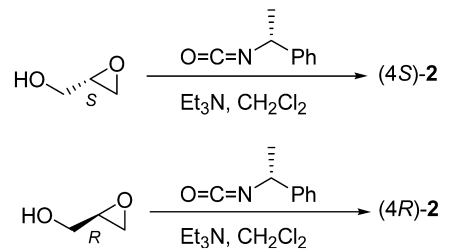
The oxazolidinone (4*S*)-**2**[4a] was prepared by a three-step synthesis from diethyl bromomalonate (**5**). Amination of **5** with (*R*)-α-methylbenzylamine (**6**) gave diethyl (*R*)-(α-methyl-benzyl)aminomalonate. The ester groups were reduced with sodium borohydride by Soai's method[5] to give **1** (Scheme 3). To a mixture of the serinol **1** and pyridine in dichloromethane was added 2-chloroethyl chloroformate by one-shot with gentle warming. After the mixture was stirred for 15 h, it was cooled with an ice bath, and DBU was added to the mixture. The resulting mixture



Scheme 3. *Reagents and conditions*: (a) (*S*)-α-methylbenzylamine, Et_3N, CH_3CN, rt; (b) $NaBH_4$, MeOH, THF; (c) 2-chloroethyl chloroformate, Py, CH_2Cl_2, then DBU, 1°C to rt.

was stirred for 4 h to afford (4*R*)-**2** (94% de, 68% yield). We have already reported that 2-chloroethyl chloroformate is the best chloroformate for this reaction among other chloroformates, including methyl, ethyl, benzyl, phenyl, 2,2,2-trichloroethyl, and 1,2,2,2-tetrachloroethyl chloroformates.[4a]

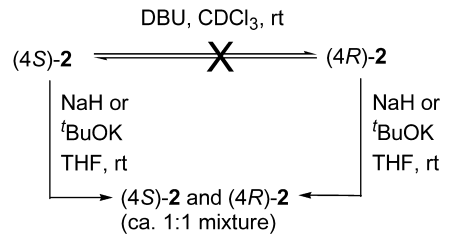
The absolute configurations of (4*S*)-**2** and (4*R*)-**2** were determined by comparison with the spectral data of the samples obtained from (*R*)-α-methylbenzyl isocyanate and (*S*)-glycidol and from the isocyanate and (*R*)-glycidol, respectively (Scheme 4).[6] The spectrum data of (4*S*)-**2** were also in agreement with those of the reported data[7] of an antipode of (4*S*)-**2**.



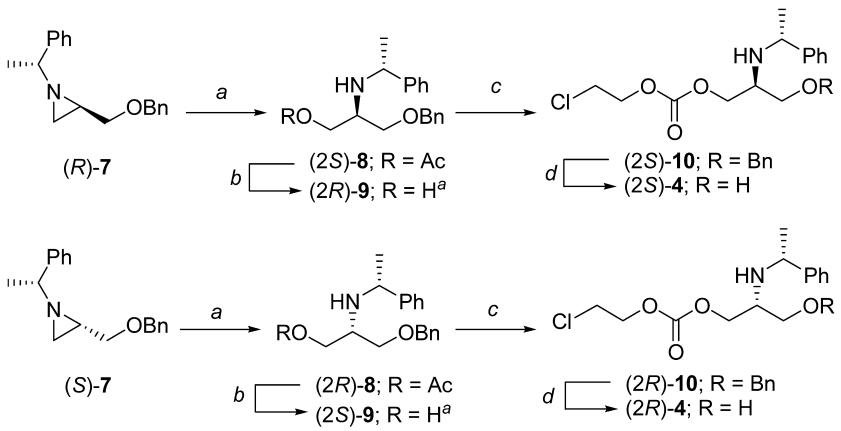
Scheme 4. Preparation of the oxazolidinones from glycidols.

2.2. Stability of (4*S*)-2 and (4*R*)-2 in the basic reaction conditions

It might be expected that the two oxazolidinones (4*S*)-**2** and (4*R*)-**2** would epimerize by acyl transfer[6,8] in the basic reaction conditions. Therefore, we studied the stability of (4*S*)-**2** and (4*R*)-**2** in the reaction mixtures. Respective solutions of (4*S*)-**2** and (4*R*)-**2** in $CDCl_3$ (0.04 mol/L) were treated with three equivalents of DBU at room temperature for 24 h; however, ^1H NMR analyses of both reaction mixtures showed no reactions, and each oxazolidinone was recovered quantitatively (Scheme 5). Thus, (4*S*)-**2** and



Scheme 5. Acyl transfer of the oxazolidinones.



Scheme 6. *Reagents and conditions*: (a) AcOH, $CHCl_3$, reflux, 6 h; (b) KOH, EtOH, reflux, 30 min; (c) $ClCO_2CH_2CH_2Cl$, Py, CH_2Cl_2, rt, 15 h; (d) $BF_3{\cdot}OEt_2$, Me_2S, CH_2Cl_2, rt, 3 h. [a]Ref. 7.

(4*R*)-**2** were stable in the reaction mixture. On the other hand, (4*S*)-**2** and (4*R*)-**2** converted independently to their approximate equimolar diastereomixtures by sodium hydride or potassium *tert*-butoxide in THF at room temperature for 24 h.

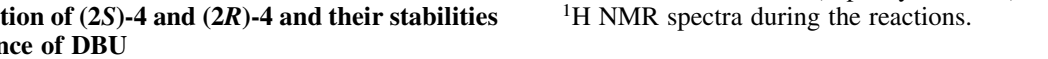
2.3. Preparation of (2*S*)-4 and (2*R*)-4 and their stabilities in the presence of DBU

To investigate the intramolecular transesterification between monocarbonates (2*S*)-**4** and (2*R*)-**4** and their intramolecular cyclization, we prepared diastereomerically pure monocarbonates (2*S*)-**4** and (2*R*)-**4** individually. Mono-*O*-benzylserinol (2*R*)-**9**, which was derived from an optically active aziridine (*R*)-**7** according to the reported procedure,[7] was treated with 2-chloroethyl chloroformate to give carbonate (2*S*)-**10** (Scheme 6). Although we tried to remove the benzyl group of (2*S*)-**10** with catalytic hydrogenation using Pd/C and Pt_2O in an atmosphere of hydrogen, complex mixtures were obtained. This benzyl group was removed with a boron trifluoride diethyl ether complex and dimethylsulfide in dichloromethane[9] to afford monocarbonate (2*S*)-**4**. Monocarbonate (2*R*)-**4** was also prepared from (*S*)-**7** by an analogous procedure.

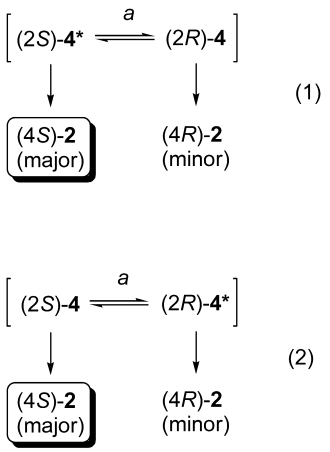
Respective $CDCl_3$ solutions (0.04 mol/L) of the monocarbonates (2*R*)-**4** and (2*S*)-**4** were treated with pyridine-d_5 (1 equiv.) at room temperature for 12 h. No transesterification occurred, and the monocarbonates were recovered in diastereomerically pure forms in each case (Scheme 7). Therefore, the intramolecular transesterification between (2*S*)-**4** and (2*R*)-**4** did not proceed before the addition of DBU.

2.4. Treatment of (2*S*)-4 and (2*R*)-4 with DBU

To confirm the intramolecular transesterification between the monocarbonates (2*S*)-**4** and (2*R*)-**4** in the presence of DBU (Scheme 2), we treated a $CDCl_3$ solution (0.04 mol/L) of (2*S*)-**4**, which is a direct precursor of the major oxazolidinone (4*S*)-**2**, and pyridine-d_5 (1 equiv.) with DBU (3 equiv.) (Scheme 8, Eq. 1). The reaction was carried out in a spinning NMR tube at 26°C, and each process was monitored by ^{1}H NMR analysis (Fig. 2). The yields were determined from the integration of the materials compared to an internal standard (triphenylmethane) in the 400 MHz ^{1}H NMR spectra during the reactions.



Scheme 7.



Scheme 8. Treatment of (2*S*)-**4** and (2*R*)-**4** with DBU (*: starting material). *Reaction conditions*: (a) DBU, Py-d_5, $CDCl_3$, room temp. 24 h.

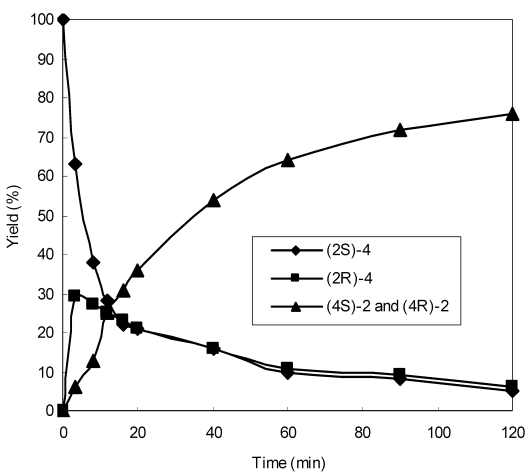


Figure 2. Progress of the reaction starting from (2*S*)-**4**.

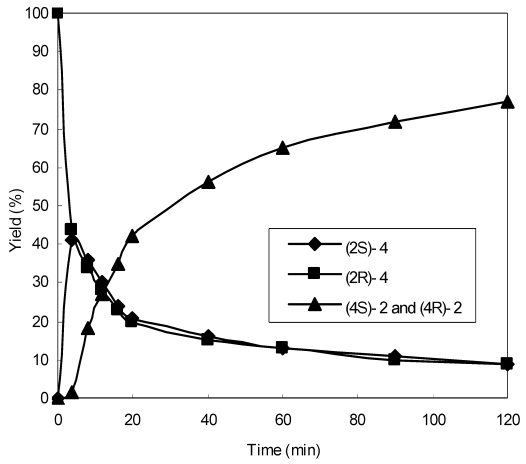
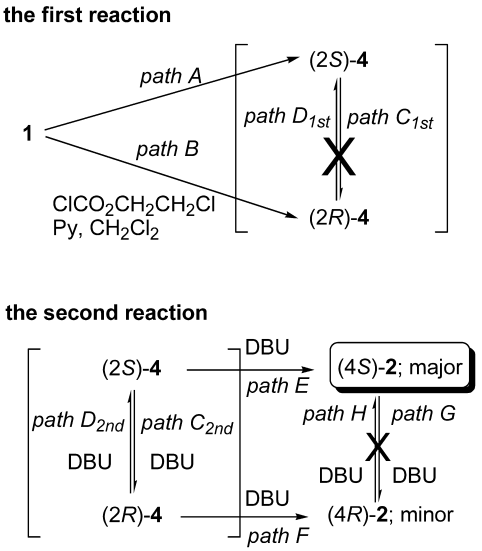


Figure 3. Progress of the reaction starting from (2*R*)-**4**.

As shown in Figure 2, the monocarbonate (2*S*)-**4** began to be converted to (2*R*)-**4** immediately after the addition of DBU, and the ratio of (2*S*)-**4** and (2*R*)-**4** became 1:1 within 16 min. The oxazolidinones **2** also began to form immediately, and the yield increased according to the decrease in the equimolar mixture of the monocarbonates (2*S*)-**4** and (2*R*)-**4**. Thus, the intramolecular transesterification from (2*S*)-**4** to (2*R*)-**4** proceeded in the reaction mixture to afford the equimolar mixture of the monocarbonates (2*S*)-**4** and (2*R*)-**4**. The NMR analysis continued for 2 h. After the analysis, the mixture was further allowed to stand for 22 h at room temperature. After work-up, the oxazolidinone (4*S*)-**2** was obtained quantitatively in 92% de.

Next, we examined the reactions from (2*R*)-**4** (Scheme 8, Eq. 2). The starting material, monocarbonate (2*R*)-**4**, is a direct precursor of the minor oxazolidinone (4*R*)-**2**. As shown in Figure 3, the monocarbonate (2*R*)-**4** was also converted to (2*S*)-**4** immediately after the addition of DBU, and (2*R*)-**4** became a 1:1 mixture of (2*R*)-**4** and (2*S*)-**4** within 4 min. This period giving the 1:1 mixture of monocarbonates from (2*R*)-**4** was shorter than that from (2*S*)-**4** (within 16 min). The yields of oxazolidinones (4*S*)-**2** and (4*R*)-**2** increased according to the decrease in the equimolar mixture of (2*S*)-**4** and (2*R*)-**4**. After the ^{1}H NMR was analyzed for 2 h, the mixture was further allowed to stand for 22 h at room temperature, and the oxazolidinone (4*S*)-**2** was obtained quantitatively in 91% de.

In the presence of DBU, the ratio of the oxazolidinones (4*S*)-**2**/(4*R*)-**2** could not be estimated by ^{1}H NMR analysis because of an overlap of the signals of (4*S*)-**2**, (4*R*)-**2**, and DBU in $CDCl_3$. Therefore, we treated the 1:1 mixture of monocarbonates (2*S*)-**4** and (2*R*)-**4** with DBU (3 equiv.) in dichloromethane (0.04 mol/L) at room temperature. After the reaction mixture was stirred for 4, 8, 16, 32, 48, and 64 min, a small amount of the reaction mixture was analyzed with HPLC after work-up. The ratio of the oxazolidinones (4*S*)-**2**/(4*R*)-**2** (96:4) was kept constant during the reaction. The diastereomeric excess (92% de) of (4*S*)-**2** from the 1:1 mixture of the monocarbonates (2*S*)-**4** and (2*R*)-**4**[4a] was identical to the diastereomeric excess of (4*S*)-**2** from the two pure starting materials, (2*S*)-**4** and (2*R*)-**4** (Figs. 2 and 3). Therefore, in the case of the reactions



Scheme 9. Pathways from **1** to (4*S*)-**4** and (4*R*)-**4**.

from (2*S*)-**4** and (2*R*)-**4**, (4*S*)-**2** would be given diastereoselectively (about 92% de) during the reaction.

3. Conclusions

The one-pot reaction of the serinol **1** with 2-chloroethyl chloroformate in dichloromethane affords the oxazolidinone (4*S*)-**2** in excellent diastereoselectivity. This one-pot reaction involves two reactions (Scheme 9); the first reaction is from the serinol **1** to the monocarbonates (2*S*)-**4** and (2*R*)-**4** with no selectivity (paths *A* and *B*), and the second reaction is the intramolecular cyclization (paths *E* and *F*) accompanied by the intramolecular transesterification of the monocarbonates (2*S*)-**4** and (2*R*)-**4** (paths C_{2nd} and D_{2nd}). The monocarbonates (2*S*)-**4** and (2*R*)-**4** are stable under the first reaction conditions; the intramolecular transesterification between (2*S*)-**4** and (2*R*)-**4** (paths C_{1st} and D_{1st}) and the intramolecular cyclization of the monocarbonates are not observed. After addition of DBU, intramolecular transesterification of the monocarbonates (paths C_{2nd} and D_{2nd}) occurred rapidly and reached equilibrium, and oxazolidinones (4*S*)-**2** and (4*R*)-**2** began to form (paths *E* and *F*). With respect to the intramolecular cyclization of the monocarbonates to give the oxazolidinones, (2*S*)-**4** is more reactive than (2*R*)-**4**, affording (4*S*)-**2** predominantly. Therefore, oxazolidinone (4*S*)-**2** is obtained diastereoselectively from the mixture of monocarbonates (2*S*)-**4** and (2*R*)-**4** in excellent yield. This one-pot reaction is the first example of a dynamic kinetic resolution accompanied by intramolecular transesterification.

4. Experimental

4.1. General

Melting porints were measured with Yanaco MP-3 apparatus and are uncorrected. Optical rotations were determined on a JASCO DIP-140 polarimeter. IR spectra were recorded

on a Hitachi 215 spectrophotometer. NMR spectra were obtained with a JEOL JNM-LA500 (^{1}H NMR: 500 MHz), a JEOL JNM-GSX400 (^{1}H NMR: 400 MHz and ^{13}C NMR: 100 MHz), and a JEOL JNM-AL300 (^{1}H NMR: 300 MHz) spectrometers using tetramethylsilane as an internal standard. MS and high-resolution MS (HR-MS) were taken on a JEOL JMS-DX302 spectrometer. Column chromatography was performed with Merck silica gel 60 (230–400 mesh). Analytical TLC was performed on plates pre-coated with 0.25 mm layer of silica gel 60 F_{254} (Merck).

4.2. Synthesis of the oxazolidinones (4*S*)-2 and (4*R*)-2

4.2.1. Diethyl (*R*)-(α-methylbenzyl)aminomalonate (6). A mixture of triethylamine (23.9 g, 236 mmol) and (*R*)-α-methylbenzylamine (28.5 g, 235 mmol) was added to a mixture of diethyl bromomalonate (**5**) (92% purity, Aldrich, 61.1 g, 321 mmol as 92% purity) in acetonitrile (235 mL) at room temperature and the resulting mixture was stirred for 9 h at room temperature. After the reaction mixture was concentrated in vacuo, the residue was diluted with diethyl ether (100 mL) and extracted with 10% hydrochloric acid (100 mL×2). The extracts were combined, washed with diethyl ether (100 mL×2), alkalified (pH; ca. 10) with 20% sodium hydroxide aqueous solution (ca. 100 mL), and extracted with diethyl ether (150 mL×3 and 50 mL×1). The extracts were combined, washed with water (100 mL, three times), dried with magnesium sulfate, and concentrated in vacuo to give **6** (65.8 g, 79%) as a brown liquid. This material was used at the next reaction without any other purification. A small amount of **6** was distilled (Kugelrohr, ~165°C/0.18 Torr) for analysis. Colorless liquid. $[\alpha]_D^{22}$=+61.6° (*c* 1.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.22–7.32 (5H, m, Ar), 4.24 (2H, q, *J*=7.1 Hz, C*H*$_2$Me), 4.15 (1H, dq, *J*=10.7, 7.1 Hz, C*H*HMe), 4.13 (1H, dq, *J*=10.7, 7.1 Hz, CH*H*Me), 3.89 (1H, s, C*H*N), 3.80 (1H, q, *J*=6.6 Hz, PhC*H*Me), 1.39 (3H, d, *J*=6.6 Hz, PhCH*Me*), 1.27 (3H, t, *J*=7.1 Hz, CH$_2$*Me*), 1.22 (3H, t, *J*=7.1 Hz, CH$_2$*Me*). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.9, 168.1, 143.7, 128.4 (×2), 127.2, 126.8 (×2), 63.0, 61.7 (×2), 56.5, 24.6, 14.3, 14.1. IR (film) cm^{-1}: 1730, 1750. MS (EI) *m*/*z*: 279 (M^+, 0.25%), 264 (6.7), 206 (27), 120 (20), 105 (100), 77 (0.1). Anal. Calcd for $C_{15}H_{21}NO_4$: C, 64.50; H, 7.58; N, 5.01. Found: C, 64.31; H, 7.68; N, 4.95.

4.2.2. (*R*)-2-(α-Methylbenzyl)amino-1,3-propanediol (1). Methanol (142 mL) was added dropwise[5] for 2 h to a mixture of **6** (49.4 g, 177 mmol) and sodium borohydride (16.7 g, 441 mmol) in THF (354 mL) with stirring without cooling. This reaction was exothermic reaction, and the maximum internal temperature was 56°C. After being stirred for 15 h with allowing cooling to room temperature, the reaction mixture was concentrated in vacuo. The residue was diluted with ethyl acetate (100 mL) and extracted with 10% hydrochloric acid (250 mL). The extract was washed with ethyl acetate (200 mL×2 and 100 mL×1), alkalified (ca. pH 11) with 20% aqueous sodium hydroxide (180 mL), and extracted with ethyl acetate (100 mL×2 and 50 mL×5). The extracts were combined, washed with water (100 mL), dried with magnesium sulfate, filtered, and concentrated in vacuo to give a crude **1**. This crude material was recrystallized with ethyl acetate/methanol (40:1, 974 mL) to give a pure **1** (19.4 g). A solid given from the filtrate was also recrystallized to afford a pure **1** (2.6 g, total 22.0 g, 64%). Colorless plates, mp 117–118°C (ethyl acetate/methanol, 40:1). $[\alpha]_D^{21}$=+57.1° (*c* 1.0, MeOH). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.30–7.35 (5H, m, Ar), 7.23–7.25 (1H, m, Ar), 3.91 (1H, q, *J*=6.6 Hz, PhC*H*), 3.73 (1H, dd, *J*=11.0, 4.6 Hz, OC*H*H), 3.53 (1H, dd, *J*=11.0, 4.0 Hz, OCH*H*), 3.52 (2H, d, *J*=5.2 Hz, OCH_2), 2.64 (1H, quintet-like m, NC*H*CH$_2$O), 1.39 (3H, d, *J*=6.6 Hz, Me). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.2, 128.5 (×2), 127.0, 126.3 (×2), 63.6, 61.9, 56.9, 55.7, 24.9. IR (KBr) cm^{-1}: 3320, 3220, 1050, 955. MS (positive FAB) *m*/*z*: 196 [$(M+1)^+$]. Anal. Calcd for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.78; N, 7.17. Found: C, 67.49; H, 8.75; N, 7.08.

4.2.3. (4*S*)-2 from the serinol 1 (Scheme 3). The serinol **1** (5.00 g, 25.6 mmol) was dissolved in methylene chloride (640 mL, 0.04 mol/L) at 40°C (bath temperature). Pyridine (2.16 g, 25.6 mmol) was added, and then 2-chloroethyl chloroformate (3.66 g, 25.6 mmol) was added by one-shot to the mixture at room temperature. After being stirred for 24 h at room temperature, the mixture was cooled to 1°C (internal temperature) using an ice bath and treated with DBU (11.9 g, 76.8 mmol). The resulting mixture was stirred for 4 h with warming to room temperature. The reaction mixture was washed twice with 5% hydrochloric acid (60 mL) and once with water (60 mL). The mixture was then dried, filtered and concentrated in vacuo to give a yellow oil (5.92 g) which was chromatographed on silica gel (hexane/ethyl acetate, 1:2, column 7 cm φ×22 cm) to afford the dicarbonate **3** (503 mg, 5%) as a colorless oil and a mixture of oxazolidinones (4*S*)-**2** and (4*R*)-**2** (3.85 g, 68% yield, 97:3, 94% de) as colorless crystals. The crystals (3.84 g) were recrystallized from *tert*-butyl methyl ether (30 mL) to give pure (4*S*)-**2** as colorless plates (2.19 g).

To recover the starting material **1**, the 5% hydrochloric acid layers to be given after washing the reaction mixture were combined, alkalified (pH; ca. 11) with sodium hydroxide, and extracted with ethyl acetate (200 mL×1 and 100 mL×7). The extracts were combined, washed with water, dried with magnesium sulfate, filtered, and concentrated in vacuo. The residue was filtered through a short silica gel column and filtrate was concentrated in vacuo to give a crude **1** (1.94 g), which was recrystallized with ethyl acetate (30 mL) to give a pure **1** (1.36 g, 27% recovery).

4.2.4. (4*S*)-2 from (*S*)-(−)-glycidol (Scheme 4). (*R*)-(+)-α-Methylbenzyl isocyanate (2.48 g, 16.9 mmol) was added to a mixture of (*S*)-(−)-glycidol (1.25 g, 16.9 mmol) and triethylamine (3.5 mL) in dichloromethane (12 mL) at room temperature, and this mixture was refluxed for 36 h.[6] After being cooled to room temperature, the reaction mixture was poured into saturated aqueous ammonium chloride and extracted with dichloromethane. The extracts were combined, dried with magnesium sulfate, filtered, and concentrated in vacuo to give brown viscous oil. The oil was chromatographed on silica gel (hexane/ethyl acetate, 1:4) to give a mixture of (4*S*)-**2** and (4*R*)-**2** (94:6) as a white solid (1.59 g, 42% yield). The solid was recrystallized from (*tert*-butyl methyl ether/THF 7:1, 11.4 mL) to give pure (4*S*)-**2** as colorless plates (1.16 g, 31% yield from the glycidol).

4.2.5. (4*R*)-2 from (*R*)-(+)-glycidol (Scheme 4). According to the procedure described for the preparation of (4*S*)-**2** from (*R*)-(+)-glycidol, a mixture of (4*R*)-**2** and (4*S*)-**2** (94:6) was obtained from (*R*)-(+)-glycidol (1.25 g, 16.9 mol) and (*R*)-(+)-α-methylbenzyl isocyanate (2.48 g, 16.9 mmol) as a white solid (1.46 g, 39% yield). This mixture was recrystallized from hexane/ethyl acetate (1:1, 10 mL) to give colorless plates (1.08 g, 29% yield from the glycidol).

4.2.6. (4*S*, α*R*)-4-Hydroxymethyl-3-(α-methylbenzyl)-2-oxazolidinone [(4*S*)-2]. Colorless plates, mp 88–89°C (*tert*-butyl methyl ether/THF 7:1). $[\alpha]_D^{20}$=+102.1° (*c* 1.0, $CHCl_3$) [for (4*R*, α*S*)-enantiomer, ref.,[7] $[\alpha]_D^{27}$=−93.0° (*c* 1.0, $CHCl_3$)]. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.31–7.49 (5H, m, Ar), 5.31 (1H, q, *J*=7.1 Hz, PhC*H*), 4.32 (1H, dd, *J*=9.3, 8.5 Hz, CO_2CHH), 4.21 (1H, dd, *J*=8.5, 6.3 Hz, CO_2CHH), 3.95 (1H, m, $NCHCH_2$), 3.22 (1H, dt, *J*=12.2, 4.8 Hz, HOC*H*H), 3.13 (1H, ddd, *J*=12.2, 8.4, 2.8 Hz, HOCH*H*), 1.69 (3H, d, *J*=7.1 Hz, Me), 0.93 (1H, dd, *J*=8.4, 4.8 Hz, OH); (400 MHz, $CDCl_3$ and D_2O) δ: 7.37–7.53 (5H, m, Ar), 5.30 (1H, q, *J*=7.3 Hz, PhC*H*), 4.32 (1H, t, *J*=8.5 Hz, CO_2CHH), 4.21 (1H, dd, *J*=8.5, 6.3 Hz, CO_2CHH), 3.95 (1H, m, $NCHCH_2$), 3.21 (1H, dt, *J*=12.2, 4.8 Hz, HOC*H*H), 3.13 (1H, dd, *J*=12.2, 2.7 Hz, HOCH*H*), 1.69 (3H, d, *J*=7.3, Me). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 158.6, 141.2, 128.8 (×2), 128.0, 126.6 (×2), 64.6, 61.2, 54.8, 51.0, 15.6. IR ($CHCl_3$) cm^{-1}: 1715. MS (EI) *m*/*z*: 221 (M^+, 16%), 190 (24), 105 (100), 77 (8). Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.21; H, 6.80; N, 6.52.

4.2.7. (4*R*,α*R*)-4-Hydroxymethyl-3-(α-methylbenzyl)-2-oxazolidinone [(4*R*)-2]. Colorless plates, mp 85–86°C (hexane/ethyl acetate, 1:1). $[\alpha]_D^{20}$=+40.7° (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.38 (4H, m, Ar), 7.33 (1H, m, Ar), 5.15 (1H, q, *J*=7.3 Hz, PhC*H*), 4.22 (2H, d, *J*=7.3 Hz, CO_2CH_2), 3.66 (1H, dt, *J*=6.3, 4.9 Hz, HOC*H*H), 3.58 (1H, m, HOCH*H*), 3.54 (1H, m, $NCHCH_2$), 1.69 (3H, d, *J*=7.3 Hz, Me), 1.65 (1H, dd, *J*=6.8, 4.6 Hz, OH); (400 MHz, $CDCl_3$ and D_2O) δ: 7.38 (4H, m, Ar), 7.33 (1H, m, Ar), 5.15 (1H, q, *J*=7.1 Hz, PhC*H*), 4.22 (2H, d, *J*=7.6 Hz, CO_2CH_2), 3.65 (1H, dd, *J*=11.2, 5.1 Hz, HOC*H*H), 3.56 (1H, m, HOCH*H*), 3.52 (1H, m, $NCHCH_2$), 1.69 (3H, d, *J*=7.1 Hz, Me). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 158.4, 139.1, 128.7 (×2), 127.9, 127.1 (×2), 65.0, 62.6, 55.6, 53.0, 18.7. IR ($CHCl_3$) cm^{-1}: 1715. MS (EI) *m*/*z*: 221 (M^+, 17%), 190 (25), 105 (100), 77 (8). Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.17; H, 6.84; N, 6.35.

4.2.8. (*R*)-2-(α-Methylbenzyl)amino-1,3-propanediol di(2-chloroethyl)carbonate (3). A colorless oil. $[\alpha]_D^{21}$=+1.9° (*c* 1.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.21–7.36 (5H, m, Ar), 4.38 (2H, t, *J*=5.7 Hz, $ClCH_2CH_2$), 4.34 (2H, t, *J*=5.7 Hz, $ClCH_2CH_2$), 4.25 (1H, dd, *J*=11.1, 5.5 Hz, CO_2CHH), 4.20 (1H, dd, *J*=11.1, 4.3 Hz, CO_2CHH), 4.11 (1H, dd, *J*=10.9, 5.5 Hz, CO_2CHH), 4.08 (1H, dd, *J*=10.9, 5.7 Hz, CO_2CHH), 3.96 (1H, q, *J*=6.6 Hz, PhC*H*), 3.71 (2H, t, *J*=5.7 Hz, $ClCH_2$), 3.68 (2H, t, *J*=5.7 Hz, $ClCH_2$), 2.95 (1H, m $NCHCH_2O$), 1.33 (3H, d, *J*=6.6 Hz, Me). IR (film) cm^{-1}: 1750. MS (positive FAB) *m*/*z*: 408 [(M+1)$^+$]. HRMS-FAB *m*/*z*: [(M+1)$^+$] calcd for $C_{17}H_{24}NO_6Cl_2$, 408.0982; found, 408.0982.

4.3. Treatment of the oxazolidinones (4*S*)-2 and (4*R*)-2 with bases (Scheme 5)

4.3.1. With DBU. A mixture of (4*S*)-**2** (4.3 mg, 19 μmol) and DBU (8.9 mg, 58 μmol) in $CDCl_3$ (0.49 mL) in a NMR tube was allowed to stand for 48 h at room temperature. Another oxazolidinone (4*R*)-**2** (4.3 mg) was also examined by this method; however, no reaction occurred in each case (checked with ^{1}H NMR).

4.3.2. With sodium hydride. A mixture of (4*S*)-**2** (15 mg, 69 μmol) and sodium hydride (ca. 60% oil suspension, 2.8 mg) in THF was stirred for 17 h at room temperature. The reaction was quenched with saturated aqueous ammonium chloride, and the mixture was extracted with ethyl acetate. The organic extracts were combined, dried with magnesium sulfate, filtered, and concentrated in vacuo to give a mixture of the oxazolidinones (4*S*)-**2** and (4*R*)-**2** (49:51 mixture, 10.4 mg, 69% yield). Another oxazolidinone (4*R*)-**2** (15 mg) was also examined by this method, and the mixture of (4*S*)-**2** and (4*R*)-**2** (43:57 mixture, 11.1 mg, 74% yield) was given.

4.3.3. With potassium *tert*-butoxide. A mixture of (4*S*)-**2** (9.8 mg, 44 μmol) and potassium *tert*-butoxide (4.1 mg) in THF (0.44 mL) was stirred for 24 h at room temperature. The reaction was quenched with saturated aqueous ammonium chloride, and the mixture was extracted with ethyl acetate. The organic extracts were combined, dried with magnesium sulfate, filtered, and concentrated in vacuo to give a mixture of the oxazolidinones (4*S*)-**2** and (4*R*)-**2** (1:1 mixture, 9.2 mg, 94% yield). Another oxazolidinone (4*R*)-**2** (9.8 mg) was also examined by this method, and the mixture of (4*S*)-**2** and (4*R*)-**2** (1:1 mixture, 9.3 mg, 95% yield) was given.

4.4. Asymmetric synthesis of monocarbonates (2*S*)-4 and (2*R*)-4 (Scheme 6)

4.4.1. (2*R*,α*R*)-1-[(α-Methylbenzyl)aziridin-2-yl]methyl benzyl ether [(2*R*)-7]. According to the reported procedure,[7] we prepared (2*R*)-**7**. A colorless oil. $[\alpha]_D^{26}$=+56.2° (*c* 1.0, $CHCl_3$) [for (2*S*,α*S*)-enantiomer, ref.,[7] $[\alpha]_D^{26}$=−58.4° (*c* 1.0, $CHCl_3$)]. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.23–7.38 (10H, m, Ar), 4.66 (1H, d, *J*=12.0 Hz, PhC*H*HO), 4.57 (1H, d, *J*=12.0 Hz, PhCH*H*O), 3.55 (1H, dd, *J*=10.5, 5.4 Hz, BnOC*H*H), 3.51 (1H, dd, *J*=10.5, 6.6 Hz, BnOCH*H*), 2.48 (1H, q, *J*=6.6 Hz, PhC*H*N), 1.58 (1H, d, *J*=3.4 Hz, NC*H*H), 1.83 (1H, m, $NCHCH_2O$), 1.48 (3H, d, *J*=6.6 Hz, Me), 1.34 (1H, d, *J*=6.3 Hz, NCH*H*). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.2, 138.3, 128.4 (×4), 127.3 (×3), 126.7, 126.6 (×2), 72.9, 72.6, 69.6, 39.1, 31.2, 23.3. IR (film) cm^{-1}: 2975, 2860, 1505, 1465. MS (EI) *m*/*z*: 267 (M^+, 0.4%), 146 (100), 105 (31), 91 (53). HRMS-EI *m*/*z*: (M^+) calcd for $C_{18}H_{21}NO$, 267.1624; found, 267.1619.

4.4.2. (2*S*,α*R*)-1-[(α-Methylbenzyl)aziridin-2-yl]methyl benzyl ether [(2*S*)-7]. According to the reported procedure,[7] we prepared (2*S*)-**7**. A colorless oil. $[\alpha]_D^{26}$=+17.0° (*c* 1.3, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.38–7.40 (2H, m, Ar), 7.21–7.33 (6H, m, Ar), 7.16–7.18 (2H, m, Ar), 4.34 (1H, d, *J*=12.2 Hz, PhC*H*HO), 4.31 (1H, d, *J*=12.2 Hz, PhCH*H*O), 3.43 (1H, dd, *J*=10.7, 5.9 Hz, BnOC*H*H), 3.40

(1H, dd, *J*=10.7, 5.5 Hz, BnOCH*H*), 2.49 (1H, q, *J*=6.6 Hz, PhC*H*N), 1.82 (1H, d, *J*=3.4 Hz, NC*H*H), 1.74 (1H, ddd, *J*=12.0, 5.7, 3.4 Hz, NC*H*CH_2O), 1.49 (1H, d, *J*=6.6 Hz, NCH*H*), 1.43 (3H, d, *J*=6.6 Hz, Me). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.8, 137.7, 127.6 (×2), 127.5 (×2), 126.8 (×2), 126.7 (×2), 126.3, 126.2 (×2), 72.0, 71.7, 69.1, 37.4, 31.3, 22.8. IR (film) cm^{-1}: 2980, 2870, 1503, 1465. MS (EI) *m*/*z*: 267 (M^+, 0.4%), 146 (100), 105 (31), 91 (53). HRMS-EI *m*/*z*: (M^+) calcd for $C_{18}H_{21}NO$, 267.1624; found, 267.1626.

4.4.3. (2*S*,α*R*)-3-Benzyloxy-2-(α-methylbenzyl)aminopropyl acetate [(2*S*)-8]. According to the reported procedure,[7] we prepared (2*S*)-**8** from (2*R*)-**7**. A colorless oil. $[\alpha]_D^{25}$=+47.2° (*c* 1.0, $CHCl_3$) [for (2*R*,α*S*)-enantiomer, ref.,[7] $[\alpha]_D^{25}$=−49.0° (*c* 1.0, $CHCl_3$)]. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.37–7.21 (10H, m, Ar), 4.53 (1H, d, *J*=12.2 Hz, PhC*H*H), 4.49 (1H, d, *J*=12.2 Hz, PhCH*H*), 4.02 (2H, d, *J*=5.9 Hz, AcOCH_2), 3.88 (1H, q, *J*=6.3 Hz, PhC*H*Me), 3.52 (1H, dd, *J*=9.5, 5.4 Hz, BnOC*H*H), 3.44 (1H, dd, *J*=9.5, 4.3 Hz, BnOCH*H*), 2.82 (1H, m, NC*H*CH_2O), 1.97 (3H, s, Ac), 1.31 (3H, d, *J*=6.3 Hz, PhCH*Me*). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.4, 145.4, 137.9, 128.2 (×4), 127.43, 127.40 (×2), 126.7, 126.4 (×2), 73.1, 68.5, 65.0, 58.1, 55.6, 25.0, 20.9. IR (film) cm^{-1}: 1740 (C=O). MS (EI) *m*/*z*: 327 (M^+, 1.0%), 206 (65), 146 (23), 105 (100), 102 (22), 91 (39). HRMS-EI *m*/*z*: calcd for $C_{20}H_{25}NO_3$, 327.1830; found, 327.1836.

4.4.4. (2*R*,α*R*)-3-Benzyloxy-2-(α-methylbenzyl)aminopropyl acetate [(2*R*)-8]. According to the reported procedure,[7] we prepared (2*R*)-**8** from (2*S*)-**7**. A colorless oil. $[\alpha]_D^{29}$=+27.9° (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35–7.21 (10H, m, Ar), 4.42 (s, 2H, PhCH_2), 4.13 (2H, d, *J*=5.1 Hz, AcOCH_2), 3.94 (1H, q, *J*=6.6 Hz, PhC*H*Me), 3.40 (2H, d, *J*=5.6 Hz, BnCH_2O), 2.86 (1H, m, NC*H*CH_2O), 2.02 (3H, s, Ac), 1.32 (3H, d, *J*=6.6 Hz, PhCH*Me*). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.5, 145.2, 137.9, 128.2 (×2), 128.0 (×2), 127.35, 127.29 (×2), 126.7, 126.4, 72.9, 70.3, 63.5, 55.4, 53.4, 53.2, 24.9, 20.9. IR (film) cm^{-1}: 1740 (C=O). MS (EI) *m*/*z*: 327 (M^+, 1.2%), 206 (67), 146 (9), 105 (100), 102 (24), 91 (36). HRMS-EI *m*/*z*: (M^+) calcd for $C_{20}H_{25}NO_3$, 327.1832; found, 327.1836.

4.4.5. (2*R*,α*R*)-3-Benzyloxy-2-(α-methylbenzyl)aminopropanol [(2*R*)-9]. According to the reported procedure,[7] we prepared (2*R*)-**9** from (2*S*)-**8**. A colorless oil. $[\alpha]_D^{24}$=+80.3° (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.38–7.20 (10H, m, Ar), 4.54 (1H, d, *J*=12.1 Hz, PhC*H*HO), 4.50 (1H, d, *J*=12.1 Hz, PhCH*H*O), 3.87 (1H, q, *J*=6.4 Hz, PhC*H*), 3.58 (1H, dd, *J*=9.5, 4.9 Hz, BnOC*H*H), 3.43 (1 h, dd, *J*=9.5, 4.6 Hz, BnOCH*H*), 3.42 (2H, d, *J*=5.4 Hz, HOCH_2), 2.72 (1H, m, NC*H*CH_2), 1.34 (3H, d, *J*=6.4 Hz, Me). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.2, 137.8, 128.3 (×2), 128.2 (×2), 127.5, 127.4 (×2), 126.8, 126.4, 73.2, 69.4, 62.8, 55.9, 55.4, 25.0. IR (film) cm^{-1}: 3400, 2850, 1455, 1110. MS (EI) *m*/*z*: 285 (M^+, 1.1%), 254 (27), 164 (65), 105 (100), 91 (45). HRMS-EI *m*/*z*: (M^+) calcd for $C_{18}H_{23}NO_2$, 285.1730; found, 285.1732.

4.4.6. (2*S*,α*R*)-3-Benzyloxy-2-(α-methylbenzyl)aminopropanol [(2*S*)-9]. According to the reported procedure,[7] we prepared (2*S*)-**9** from (2*R*)-**8**. A colorless oil. $[\alpha]_D^{28}$=−2.1° (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.22–7.36 (10H, m. Ar), 4.43 (1H, d, *J*=12.7 Hz, PhC*H*HO), 4.39 (1H, d, *J*=12.7 Hz, PhCH*H*O), 3.88 (1H, q, *J*=6.6 Hz, PhC*H*), 3.67 (1H, dd, *J*=11.0, 4.4 Hz, BnOC*H*H), 3.47 (1H, dd, *J*=9.5, 6.1 Hz, HOC*H*H), 3.43 (1H, dd, *J*=11.0, 3.9 Hz, BnOCH*H*), 3.42 (1H, dd, *J*=9.5, 4.9 Hz, HOCH*H*), 2.78 (1H, m, NC*H*CH_2), 1.36 (3H, d, *J*=6.6 Hz, Me). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.3, 137.9, 128.3 (×2), 128.1 (×2), 127.4, 127.3 (×2), 126.8, 126.3, 126.2, 73.0, 71.1, 61.1, 55.2, 55.1, 24.7. IR (film) cm^{-1}: 3400, 2960, 1455, 1105. MS (EI) *m*/*z*: 285 (M^+, 1.2%), 254 (34), 164 (76), 105 (100), 91 (43). HRMS-EI *m*/*z*: (M^+) calcd for $C_{18}H_{23}NO_2$, 285.1730; found, 285.1733.

4.4.7. (2*S*,α*R*)-3-Benzyloxy-2-(α-methylbenzyl)aminopropyl 2-chloroethyl carbonate [(2*S*)-10]. To a mixture of (2*S*)-**9** (738 mg, 2.58 mmol) and pyridine (0.44 g, 5.2 mmol) in dichloromethane (6.5 mL) was added 2-chloroethyl chloroformate (0.74 g, 5.2 mmol) at room temperature. After being stirred for 15 h, the reaction mixture was poured into water and extracted with dichloromethane. The extracts were combined, dried with magnesium sulfate, filtered, and concentrated in vacuo. The residue was chromatographed on silica gel (hexane/dichloromethane/ethyl acetate, 5:2:1) to afford (2*S*)-**10** as a colorless oil (972 mg, 83%). $[\alpha]_D^{25}$=+37.2° (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.37–7.20 (10H, m, Ar), 4.53 (1H, d, *J*=12.2 Hz, PhC*H*HO), 4.49 (1H, d, *J*=12.2 Hz, PhCH*H*O), 4.31 (2H, t, *J*=5.9 Hz, ClCH_2CH_2O), 4.10 (2H, dd, *J*=5.9, 2.0 Hz, OCO$_2$CH_2CHN), 3.87 (1H, q, *J*=6.6 Hz, PhC*H*), 3.66 (2H, t, *J*=5.9 Hz, ClCH_2), 3.55 (1H, dd, *J*=9.5, 5.1 Hz, BnOC*H*H), 3.46 (1H, dd, *J*=9.5, 4.2 Hz, BnOCH*H*), 2.86 (1H, m, NC*H*CH_2O), 1.31 (3H, d, *J*=6.6 Hz, Me). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.3, 145.2, 137.8, 128.14 (×2), 128.09 (×2), 127.4, 127.3 (×2), 126.7, 126.4 (×2), 73.0, 68.5, 68.1, 67.0, 55.5, 53.5, 25.0. IR (film) cm^{-1}: 1755. MS (EI) *m*/*z*: 391 (M^+, 1.2%), 272 (19), 270 (58), 166 (19), 146 (29), 105 (100), 91 (40). HRMS-EI *m*/*z*: (M^+) calcd for $C_{21}H_{26}NO_4Cl$, 391.1558; found, 391.1549.

4.4.8. (2*R*,α*R*)-3-Benzyloxy-2-(α-methylbenzyl)aminopropyl 2-chloroethyl carbonate [(2*S*)-10]. According to the synthetic procedure for (2*S*)-**10**, we prepared (2*R*)-**10** (771 mg, 70%) from (2*S*)-**9** (800 mg). A colorless oil. $[\alpha]_D^{26}$=+29.0 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34–7.21 (10H, m, Ar), 4.41 (2H, s, PhCH_2O), 4.35 (2H, t, *J*=5.9 Hz, ClCH_2CH_2O), 4.22 (2H, d, *J*=5.1 Hz, OCO$_2$-CH_2CHN), 3.94 (1H, q, *J*=6.6 Hz, PhC*H*), 3.69 (2H, t, *J*=5.9 Hz, ClCH_2), 3.42 (2H, d, *J*=5.4 Hz, BnOCH_2), 2.90 (1H, m, NC*H*CH_2O), 1.33 (3H, d, *J*=6.4 Hz, Me). ^{13}C (100 MHz, $CDCl_3$) δ: 154.5, 145.1, 137.8, 128.4 (×2), 128.2 (×2), 127.3, 127.2 (×2), 126.7, 126.3 (×2), 72.9, 70.0, 67.2, 67.0, 55.4, 53.2, 41.1, 24.9. IR (film) cm^{-1}: 1740. MS (EI) *m*/*z*: 391 (M^+, 1.4%), 272 (17), 270 (49), 166 (15), 146 (69), 105 (100), 91 (64). HRMS-EI *m*/*z*: (M^+) calcd for $C_{21}H_{26}NO_4Cl$, 391.1558; found, 391.1551.

4.4.9. 2-Chloroethyl (2*S*,α*R*)-3-hydroxy-2-(α-methylbenzyl)aminopropyl carbonate [(2*S*)-4]. Dimethyl sulfide (0.10 mL) was added to the mixture of (2*S*)-**10** (20 mg, 51 μmol) and boron trifluoride etherate (72 mg, 0.51 mmol) in dichloromethane (0.3 mL) at 0°C.[9] After being stirred for

3.5 h with allowing warming to room temperature, the reaction mixture was poured into 5% aqueous sodium hydrogen carbonate, and extracted with ethyl acetate. The extracts were combined, washed with water twice, dried with magnesium sulfate, filtered, and concentrated in vacuo to afford (2*S*)-**7** as an yellowish oil (9.0 mg, 58%). $[\alpha]_D^{27}$=+5.9° (*c* 0.6, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.16–7.28 (5H, m, Ar), 4.28 (2H, t, *J*=5.7 Hz, $ClCH_2CH_2O$), 4.06 (1H, dd, *J*=10.5, 5.6 Hz, $OCO_2CHHCHN$), 4.00 (1H, dd, *J*=11.0, 6.1 Hz, $OCO_2CHHCHN$), 3.83 (1H, q, *J*=6.6 Hz, PhC*H*), 3.62 (3H, m, $ClCH_2$ and HOC*H*H), 3.38 (1H, dd, *J*=11.1, 4.3 Hz, HOCH*H*), 2.78 (1H, m, $NCHCH_2O$), 1.30 (3H, d, *J*=6.6 Hz, Me). IR (film) cm^{-1}: 1760. MS (positive FAB) *m*/*z*: 302 [(M+1)$^+$]. HRMS-FAB *m*/*z*: [(M+1)$^+$] calcd for $C_{14}H_{21}NO_4Cl$, 302.1160; found, 302.1165.

4.4.10. 2-Chloroethyl (2*R*,α*R*)-3-hydroxy-2-(α-methylbenzyl)aminopropyl carbonate [(2*R*)-4]. According to the synthetic procedure of (2*S*)-**4**, we prepared (2*R*)-**4** (138 mg, 52%) from (2*R*)-**10** (347 mg). An yellowish oil $[\alpha]_D^{26}$=+71.9° (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.32–7.33 (4H, m, Ar), 7.26 (1H, m, Ar), 4.40 (2H, t, *J*=5.6 Hz, $ClCH_2CH_2O$), 4.28 (1H, dd, *J*=11.2, 5.4 Hz, $OCO_2CHHCHN$), 4.16 (1H, dd, *J*=11.2, 4.4 Hz, $OCO_2CHHCHN$), 3.97 (1H, q, *J*=6.6 Hz, PhC*H*), 3.72 (2H, t, *J*=5.6 Hz, $ClCH_2$), 3.46 (1H, dd, *J*=11.0, 4.9 Hz, HOC*H*H), 3.40 (1H, dd, *J*=11.0, 6.3 Hz, HOCH*H*), 2.80 (1H, m, $NCHCH_2O$), 1.37 (3H, d, *J*=6.6 Hz, Me). IR (film) cm^{-1}: 1750. MS (positive FAB) *m*/*z*: 302 [(M+1)$^+$]. HRMS-FAB *m*/*z*: [(M+1)$^+$] calcd for $C_{14}H_{21}NO_4Cl$, 302.1160; found, 302.1165.

4.5. The studies of the DKR of the monocarbonates in the presence of DBU

4.5.1. The study using ^{1}H NMR (Figs. 2 and 3). DBU (10 mg, 65 μmol), was added to a mixture of (2*S*)-**4** (6.9 mg, 23 μmol), pyridine-d_5 (1.8 mL, 23 μmol), and triphenylmethane (1.7 mg, 7 μmol) in $CDCl_3$ (0.57 mL) in a NMR tube. After being shaken vigorously for a few seconds, the ^{1}H NMR spectra of the mixture were begun to measure immediately at 26°C. The other carbonate (2*S*)-**4** was also examined by this method.

4.5.2. Diastereomixture of monocarbonates (2*S*)-4 and (2*R*)-4. To a mixture of **1** (100 mg, 0.51 mmol) and pyridine (0.51 mmol) in dichloromethane (13 mL) was added 2-chloroethyl chloroformate (53 μL, 0.51 mmol) at room temperature. After being stirred for 24 h at this temperature, the reaction mixture was poured into saturated aqueous ammonium chloride and extracted with dichloromethane. The extracts were combined, dried with magnesium sulfate, filtered, and concentrated in vacuo. The residue was chromatographed on a silica gel column (hexane/ethyl acetate; 1:4) to give the dicarbonate **3** (9%) and a mixture of (2*S*)-**4** and (2*R*)-**4** (1:1 mixture, 40%). The aqueous layer was alkalified with 10% aqueous sodium hydroxide and extracted with ethyl acetate. The extracts were combined, dried with magnesium sulfate, filtered, and concentrated in vacuo to recover **1** as white crystals (44%).

4.5.3. Treatment of the 1:1 mixture of monocarbonates (2*S*)-4 and (2*R*)-4 with DBU. DBU (11 mg, 74 μmol) was added to a mixture of (2*S*)-**4** and (2*R*)-**4** (1:1, 7.7 mg, 26 μmol) and triphenylmethane (1.3 mg, 5.3 μmol) as an internal standard in dichloromethane (0.5 mL) at room temperature. After being stirred for 15 h, the reaction mixture was poured into saturated aqueous ammonium chloride and extracted with dichloromethane. The extracts were combined, dried with magnesium sulfate, filtered, and concentrated in vacuo to give (4*S*)-**2** (97% yield, 94% de, ^{1}H NMR analysis).[4a]

4.5.4. Analysis of the ratio of the products (4*S*)-2 and (4*R*)-2 from the 1:1 mixture of the carbonates (2*S*)-4 and (2*R*)-4. To a mixture of **1** (100 mg, 0.512 mmol) and pyridine (61 μL, 0.77 mmol) in dichloromethane (13 mL) was added 2-chloroethyl chloroformate (95 mg, 0.67 mmol) at room temperature. After the resulting mixture was stirred for 24 h at room temperature, triphenylmethane (32.3 mg, 0.13 mmol) and DBU (234 mg, 1.54 mmol) was added. In the each experimental time, 500 μL of the reaction mixture was collected and poured into 10% hydrochloric acid (0.5 mL). The mixture was shaken, and the organic layer was used for the HPLC analysis. The yield and the ratio of the products (4*S*)-**2** and (4*R*)-**2** were obtained by the comparison of their HPLC area. HPLC conditions, column; LiChroCART/LiChrospher Si 60 (5 μm, Merck), solvent; hexane/ethyl acetate, 3:7, flow rate; 0.5 mL/min, detection; UV (254 nm), Retention time, (4*S*)-**2**; 35.0 min, (4*R*)-**2**; 33.0 min. The ratio of the HPLC area for (4*S*)-**2** and (4*R*)-**2** was in good agreement with that of the ^{1}H NMR integration.

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