Preparation of Optically Active Diol Derivatives by the Enzymatic Hydrolysis of Cyclic Carbonates

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A simple enzymatic method for the preparation of optically active 1,2- and 1,3-diol derivatives is disclosed. In the screening of enzymes, racemic 4-[(2-benzyloxy)ethyl]-1,3-dioxolan-2-one (**1a**) was enantioselectively hydrolyzed by porcine pancreas lipase (PPL) to give optically active (*R*)-**1a** and (*S*)-4-(benzyloxy)butane-1,2-diol (**2a**). The addition of 10% *i*-Pr_2O to the reaction system dramatically improved the reactivity to afford optically pure (*R*)-**1a** in 31% yield. PPL also catalyzed the hydrolysis of several five-membered cyclic carbonates with high enatioselectivity. It is noteworthy that the increment of the carbon number of the substituents reflects the drastic increase in enantioselectivity. On the other hand, the hydrolyses of six- and seven-membered cyclic carbonates were also catalyzed by PPL. In particular, the reaction of a six-membered substrate enantioselectively proceeded. This reaction afforded optically active 1,3-diol derivatives which could not be directly prepared by hitherto known methods using hydrolytic enzymes.

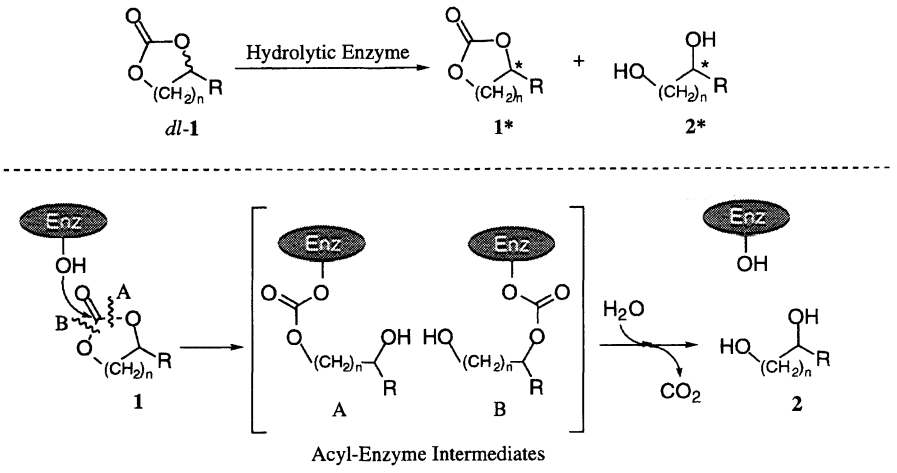
In the synthesis of natural products and biologically active compounds, optically active diols play significant roles as synthons, and therefore, a number of synthetic methods for optically active diol derivatives has been developed. The use of enzymes in the preparation of such optically active compounds is especially attractive due to the remarkable stereoselectivity of the reaction.[1] In particular, the procedure using hydrolytic enzymes is advantageous because of its simplicity of operation. The representative methods are kinetic resolution by the hydrolysis of diacetates in water[2] and esterification of diols in an organic solvent.[3] By using these methods, a variety of optically active 1,2-diol derivatives were prepared. These hitherto known reactions, however, usually gave a mixture of four compounds (diol, diacetate, and monoacetates) which were not easily separable, and hence the product yield were low. In addition, the enantioselectivities of the reactions using primary acetates or alcohols were extremely low in many cases, because the substrate reaction sites were very distant from the asymmetric centers. On the other hand, optically active cyclic carbonates also attracted our attention as challenging targets for protected diol derivatives. For example, cyclic carbonates were important intermediates as masked diols in the synthesis of natural products, such as taxol[4] and mycalamide A.[5] We have noticed that cyclic carbonate is merely a kind of ester, and can be a substrate for hydrolytic enzymes. We report herein on a new entry for the preparation of optically active diols and cyclic carbonates via the enzymatic hydrolysis of cyclic carbonates.[6]

Scheme 1 shows the mechanistic concept of the enzymatic hydrolysis of cyclic carbonates. During the first step, the enzyme attacks the carbonyl group of the substrate to give two kinds of acyl-enzyme intermediates. When a disruption of the C–O bond occurs at site A, a type-A intermediate is produced. On the other hand, a type-B form is afforded when the disruption occurs at site B. During the second step, water molecules attack the acyl-enzyme intermediates. By way of both intermediates, the same diol would be obtained. The second step is not reversible because the acyl moiety of the substrate leaves the reaction system as carbon dioxide. When the enzyme recognizes the stereochemistry of the substrate during the first attack at the carbonyl, optically active, unreacted cyclic carbonate, and resulting diol would be obtained. These compounds could be easily separated. In this concept, the enantioselectivity of the reaction would not be directly affected by the structure of the acyl-enzyme intermediates and/or the ring size of the substrate.

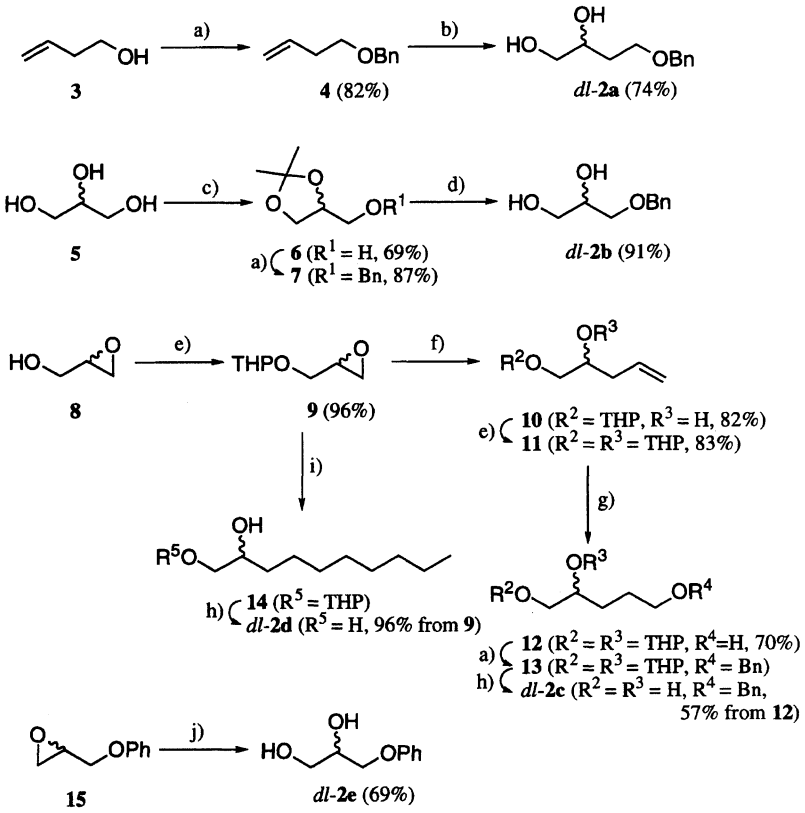
Results and Discussion

Screening of the Enzyme System. Racemic diols, which are precursors of cyclic carbonates, were readily synthesized, as shown in Schemes 2 and 3. Successive treatments of the diols with pyridine and triphosgene (bis(trichloromethyl)carbonate)[7] resulted in the corresponding racemic substrates (Scheme 4).

We selected 4-[(2-benzyloxy)ethyl]-1,3-dioxolan-2-one (*dl*-**1a**, R = $-(CH_2)_2OBn$) as the screening substrate. In the first screening test, 23 commercially available hydrolytic enzymes were used. The selection of enzymes was carried out on the basis of the hydrolytic activity without paying attention to the enantioselectivity. The assay was performed by checking the production of 4-(benzyloxy)butane-1,2-diol (**2a**) using thin-layer chromatography (TLC). As a result (Table 1), only porcine pancreas lipase (EC 3.1.1.3), purchased from Sigma (PPL Type II), hydrolyzed **1a** to give **2a**, while the other enzymes could not hydrolyze **1a**. We

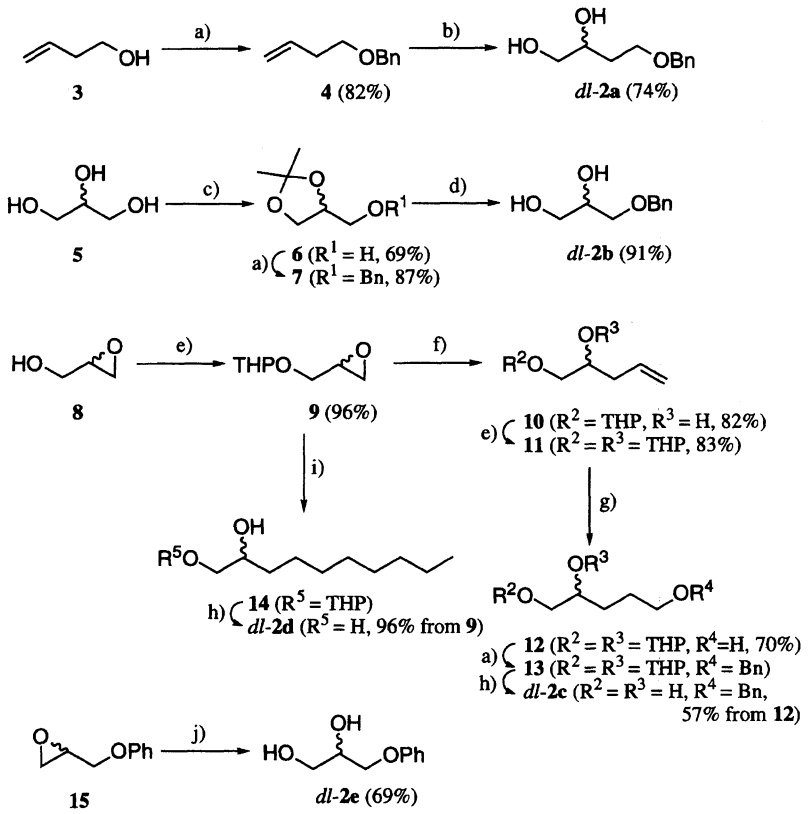


Scheme 1.

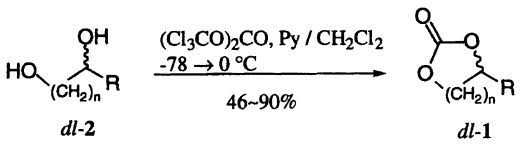


Scheme 2. a) BnBr, NaH/THF, r.t., b) $KMnO_4$/Acetone–H_2O. 0 °C, c) cat. *p*-TsOH/Acetone, r.t., d) 2 M ad HCl/THF, r.t., e) cat. *p*-TsOH, DHP/CH_2Cl_2, r.t., f) CH_2=CHMgBr, cat. CuBr/THF, −10 °C, g) BH_3·THF/THF, 0 °C, then H_2O_2–2 M aq NaOH, r.t., h) cat. *p*-TsOH/MeOH, r.t., i) $CH_3(CH_2)_6MgBr$, cat. CuBr/THF, −10 °C, j) 1 M aq H_2SO_4, r.t.

then performed a detailed analysis of the reaction using PPL. Ninety mg (10 mM) of *dl*-**1a** and 200 mg of PPL were added to 40 ml of a 0.1 M sodium phosphate buffer (pH 6.5), which was then incubated at 30 °C for 24 h. As expected, the reaction proceeded with good enantioselectivity to afford optically active (*R*)-**1a** in 44% ee and (*S*)-**2a** in 82% ee (Table 2, Entry 1). Under these reaction conditions, the conversion[8] and *E* value[8] were 0.35 and 15, respectively. The ee of diol (*S*)-**2a** was determined by the ^{1}H NMR spectrum of the corresponding bis-(+)-MTPA ester (*S*)-**19a** (Scheme 5). A similar analysis of (*R*)-**2a** derived from (*R*)-**1a** with K_2CO_3 was also performed. The absolute configurations of these compounds were determined by comparing the optical-rotation values of **2a** with the reported one, $[\alpha]_D^{27}$ −15.6° (*c* 5.88, MeOH).[9] The active-site model proposed by Jones for the PPL-catalyzed hydrolysis of a primary ester[10] could predict these absolute configurations when the 2-(benzyloxy)ethyl group would locate at the hydrophobic L_H-site, with hydrogen in the H-site, with oxygen in the polar S_P-pocket, and with CH_2OCO in the Acyl-site (Scheme 6).



Scheme 3. a) $NaIO_4$/THF–H_2O, r.t., b) CH_2=CHMgBr/THF, 0 °C, c) BH_3·THF/THF, 0 °C, then H_2O_2–2 M aq NaOH, r.t., d) CH_2=$CHCH_2$MgBr/THF, 0 °C.



Scheme 4.

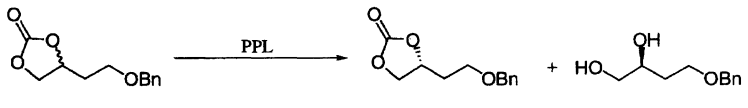
Enantioselective Hydrolysis of Cyclic Carbonate *dl*-1a. Next, our effort focused on optimizing of the reaction conditions in order to produce (*R*)-**1a** with high optical purity. However, changing the amount of enzyme (Table 2, Entry 2) and the reaction time (Entry 3) did not remarkably improve the conversion percent. We then examined the co-solvents. In all cases, the substrate dissolved in the co-solvent. The addition of a 10% water-miscible organic solvent, such as *t*-BuOH (Entry 4), DMSO (Entry 5), or acetone (Entry 6), did not improve the reactivity. Even worse, toluene (Entry 7), a nonpolar solvent, significantly reduced the reactivity. After several trials, the addition of *i*-Pr_2O was found to give the best results. Under the conditions of 30 °C for 12 h, the reaction smoothly proceeded to afford optically pure (*R*)-**1a** in 31% isolated yield (Entry 8). Interestingly, it was also found that the enantioselectivity was somewhat improved at

Table 1. Screening of the Enzyme System[a)]

	Hydrolytic activity		Hydrolytic activity
Trypsin	–	Lipase N	–
α-Chymotrypsin	–	Lipase D	–
Protease N	–	Lipase G	–
Prozyme 6	–	Lipase R	–
Lipase AP	–	Lipase OF	–
Lipase A	–	Lipase LP	–
Lipase CE	–	Lipase (Nagase)	–
Lipase L	–	Lipoprotein lipase	–
Lipase PGE	–	Amino acylase	–
Lipase PS	–	Pig liver esterase	–
Lipase F-AP	–	Porcine pancreas lipase (PPL)	+
Lipase M-AP	–		

a) Incubation was performed using 10 mM of *dl*-**1a** in 0.1 M phosphate buffer (pH 6.5).

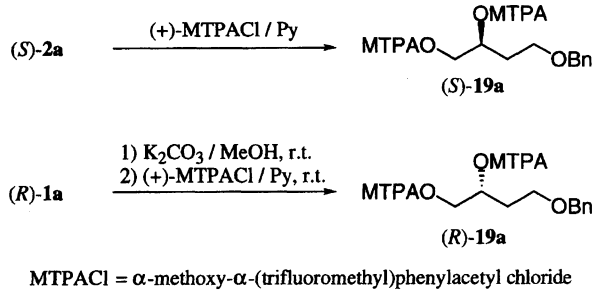
Table 2. Enantioselective Hydrolysis of Cyclic Carbonate *dl*-**1a** with PPL[a)]



dl-**1a** (*R*)-**1a** (*S*)-**2a**

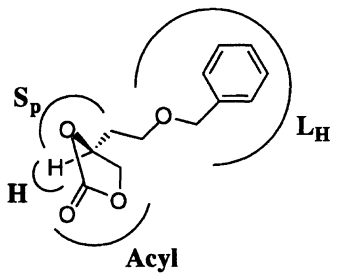
Entry	Co-solv.	PPL mg	Temp °C	Time h	(*R*)-**1a** Yield/%	(*R*)-**1a** ee/%	(*S*)-**2a** Yield/%	(*S*)-**2a** ee/%	Conv.	*E* value
1	—	200	30	24	64	44	34	82[c)]	0.35	15
2	—	500	30	12	49	54	36	80	0.40	15
3	—	500	30	48	38	79	53	64	0.55	11
4	*t*-BuOH	500	30	12	46	68	41	71	0.49	12
5	DMSO	500	30	12	55	41	40	80	0.34	13
6	Acetone	500	30	12	63	40	31	75	0.35	10
7	Toluene	500	30	12	91	12	9	80	0.13	10
8	*i*-Pr_2O	500	30	12	31	>95[b)]	65	52	>0.65	12[d)]
9	*i*-Pr_2O	500	10	12	37	94	51	64	0.59	15

a) Incubation was performed using 10 mM of *dl*-**1a** with PPL in 0.1 M phosphate buffer (pH 6.5) containing 10% co-solvent. b)$[\alpha]_D^{19}$ +32.0° (*c* 0.90, $CHCl_3$). C) $[\alpha]_D^{23}$ −17.9° (*c* 0.78, MeOH). d) Calculated at conv. =0.45—0.59.



MTPACl = α-methoxy-α-(trifluoromethyl)phenylacetyl chloride

Scheme 5.

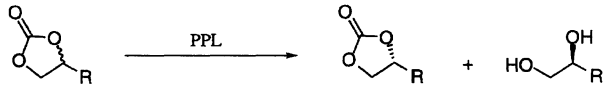


Scheme 6.

a lower reaction temperature (Entry 9). Although the details are not yet clear, this co-solvent effect can be explained in the following manner. Thus, PPL usually works at an interface between water and the organic phase, and increasing the interface area improves the reactivity.[11)] In our case, by adding a water-miscible solvent, the reaction would proceed in a homogeneous system, which is not suitable for PPL. The addition of *i*-Pr_2O, having moderate hydrophilicity and hydrophobicity ($\log P = +1.9$, solvent hydrophobicity values where *P* is the partition coefficient for a given solvent between octan-1-ol and water[12)], would form a fine-particle emulsion, after which the interface area and reactivity increased. On the other hand, toluene and water made a two-phase system which does not form an emulsion; the reaction then proceeded inefficiently.

Application of the Enzymatic Hydrolysis to Various Substrates. We applied this new type of reaction to various other cyclic carbonates. First, we tried to change the substituent in the substrates. Table 3 is a summary of the results using different R groups. It was found that the carbon number of the substituents reflects the enantioselectivity. The reaction of a substrate having a benzyloxymethyl group (**1b**) showed moderate enantioselectivity (Entries 1 and 2, *E* value = 9). Changing the R group to 3-(benzyloxy)propyl (**1c**; longer than **1b**) drastically increased the *E* value up to 22 or 23 (Entries 3 and 4). These results suggest that PPL favors the *S*-form of the five-membered cyclic carbonates with a long side chain, the latter factor of which lipases usually prefer. In order to clarify the characteristics of the reaction, we attempted a reaction of a substrate having a long alkyl chain, i.e., octyl group (**1d**, Scheme 7). In this case, the unreacted substrate was isolated as the corresponding diol after chemical hydrolysis. After detailed analyses, **1d** was found to be hydrolyzed at a higher enantioselectivity than expected (*E* value = 23) to afford optically active diols. In another case of *dl*-**1e** (R = $-CH_2OPh$), the reaction was not suitable for the optimal conditions described above, because *dl*-**1e** is a solid and does not dissolve in a mixture of a buffer and *i*-Pr_2O. In this case, the reaction was carried out in a mixture of a buffer and DMSO (7 : 3) for 12 h at 30 °C (Scheme 8). The reaction also proceeded enantioselectively. Thus, this procedure can be potentially useful for preparing of optically active 3-(aryloxy)propane-1,2-diols, which are pharmaceuticals, intermediates of the β-blocker[13)] and so on, although it is necessary to find more refined conditions. The absolute configurations of the resulting compounds were determined by comparing their optical-rotation signs with those of authentic samples synthesized by the same procedures in Scheme 2 ((*S*)-**1b** derived from D-mannitol,[14)] $[\alpha]_D^{23}$ −11.7° (*c* 0.89, $CHCl_3$); (*S*)-**2c** derived from (*R*)-glycidol, $[\alpha]_D^{21}$ −11.1° (*c* 0.96, MeOH)) or reported ((*S*)-**1d**, $[\alpha]_D^{22}$ −11.9° (*c* 0.43, MeOH);[15)] (*R*)-**1e**,

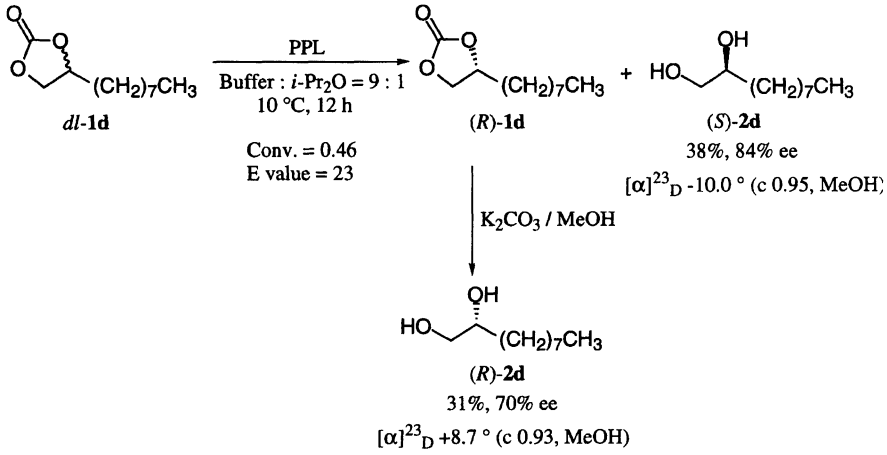
Table 3. Enantioselective Hydrolysis of Cyclic Carbonates *dl*-**1**[a)]



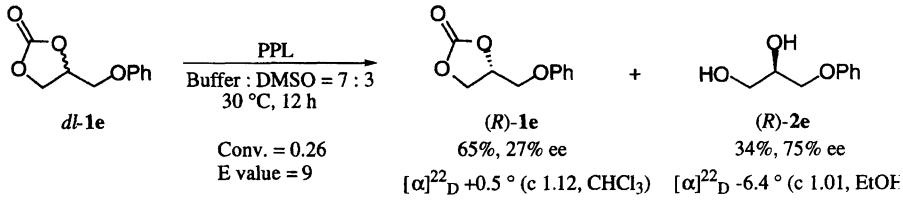
dl-**1** **1*** **2***

Entry	R	Time h	1* Yield/%	1* $[\alpha]_D$/°[b)]	1* ee/%[c)]	2* Yield/%	2* $[\alpha]_D$/°[d)]	2* ee/%[c)]	Conv.	*E* value
1	CH_2OBn (**b**)	12	34		80 (*R*)	49	−1.9[e)]	58 (*R*)	0.58	9
2		24	28	+13.5[f)]	98 (*R*)	61		39 (*R*)	0.72	9
3	$(CH_2)_3OBn$ (**c**)	12	40		78 (*R*)	40	−10.0[g)]	81 (*S*)	0.49	22
4		18	35	+17.9[h)]	96 (*R*)	51		72 (*S*)	0.57	23

a) Incubation was performed using 10 mM of *dl*-**1** with 500 mg of PPL in 0.1 M phosphate buffer (pH 6.5) containing of 10% *i*-Pr_2O at 10°C. b) Measured in MeOH at r.t. c) Determined by HPLC analysis of the corresponding bis-(+)-MTPA esters (**19**). d) Measured in $CHCl_3$ at r.t. e) $c = 0.84$. f) $c = 1.10$. g) $c = 1.22$. h) $c = 0.65$.



Scheme 7.



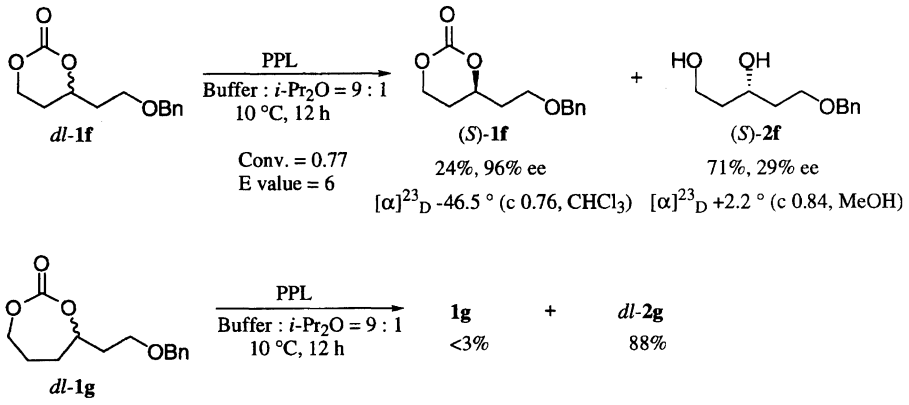
Scheme 8.

$[\alpha]_D^{20} -10.8°$ (*c* 1, EtOH)[16)]).

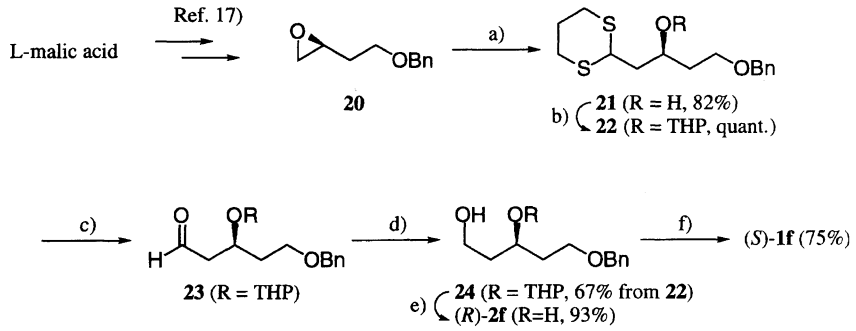
Next, our attention focused on the ring size of the substrate (Scheme 9). Carbonate *dl*-**1f** is a six-membered substrate, and *dl*-**1g** is a seven-membered substrate. Prior to studies of enzymatic reactions using **1f** and **1g**, we examined the chemical stability of these compounds under our standard reaction conditions (solvent, buffer : *i*-$Pr_2O = 9 : 1$; 10 °C, 12 h). In the case of **1f**, chemical hydrolysis did not occur and the corresponding diol (**2f**) was not formed. On the other hand, the seven-membered ring **1g** was slightly unstable in water, and then the diol (**2g**) was recovered in 17% yield. Interestingly, although PPL also accelerated the hydrolysis of **1g**, this reaction proceeded without enantioselectivity. It is noteworthy that the hydrolysis of the six-membered substrate **1f** proceeded selectively. This procedure gave an almost optically pure six-membered cyclic carbonate, which was easily transformed into the corresponding optically active 1,3-diol. The absolute configuration of the produced **2f** was confirmed to be *S* based upon the optical-rotation of an authentic sample (Scheme 10, (*S*)-**1f** derived from L-malic acid, $[\alpha]_D^{23} -46.9°$ (*c* 0.89, $CHCl_3$)). This indicates that PPL preferably hydrolyzed the opposite absolute configuration to that of five-membered substrates. The inversion of the configurations was probably due to a different interaction between the enzyme and the substrates. These details will be reported separately.

Conclusions

A new type of enzymatic reaction of cyclic carbonates has been established, resulting in the formation of a variety of optically active 1,2- and 1,3-diol derivatives. We believed this strategy to be a useful tool for natural-product syntheses. Although the presence of other enzymes, such as esterase, among commercially available PPL, is not negligible in this



Scheme 9.



Scheme 10. a) 1,3-dithiane, *n*-BuLi/THF, −23 °C → r.t., b) cat. *p*-TsOH, DHP/CH_2Cl_2, r.t., c) MeI, $NaHCO_3/CH_3CN$–H_2O, r.t., d) $NaBH_4$/MeOH, 0 °C, e) cat. *p*-TsOH/MeOH, r.t., f) $(Cl_3CO)_2CO$, Py/CH_2Cl_2, −78 → 0 °C.

reaction system, the results of all of the experiments examined suggest that the activity is due, not to the esterases, but to PPL, itself. A further investigation for details is now in progress.

Experimental

General Procedure and Instruments. ^1H (270 MHz) and ^{13}C (67.5 MHz) NMR spectra were measured on a JEOL JNM GX-200 with tetramethylsilane (TMS) as the internal standard. IR spectra were recorded with a JASCO FT/IR-8000 spectrometer. Mass spectra were obtained with a JEOL JMS DX-303 instrument by the EI method, expect for the case of **1e** and **2e**, by the FAB method. Elemental analyses were performed on a Yanaco CHN CORDER. Optical-rotations were measured with a JASCO DIP-181 polarimeter. HPLC data were obtained on a JASCO TRI ROTAR-VI and UVIDEC-100-VI. Kieselgel 60 F_{254} Art. 5715 was used for analytical TLC. Preparative TLC was performed on a Kieselgel 60 F_{254} Art. 5744. Flash column chromatography was performed with a Wakogel C-200. Melting points were obtained on a Yanako melting-point apparatus and were not corrected. Trypsin (EC 3.4.21.4) and α-Chymotrypsin (EC 3.4.21.1) were purchased from E. Merck, Lipase (EC 3.1.21.1) OF from Meito Sangyo Co., Ltd., Lipase LP from Tokyo Jozo Co., Lipase (Nagase) from Nagase Biochemicals, Ltd., Pig Liver Esterase (PLE, EC 3.1.1.1) in $(NH_4)_2SO_4$ suspension and Porcine Pancreas Lipase (PPL) from Sigma Chemical Co., Protease N, Amino acylase (EC 3.5.1.14), Prozyme 6 (EC 3.4.21), Lipoprotein Lipase, and Lipases (A, AP, CE, D, F-AP, G, L, M-AP, N, PGE, PS, and R) from Amano Pharmaceutical Co., Ltd. All other chemicals were also obtained from commercial sources.

Preparation of Racemic 4-(Benzyloxy)butane-1,2-diol (*dl*-2a). Under a nitrogen atmosphere, to a suspension of NaH (60% in oil, 2.9 g, 72.5 mmol) in THF (60 ml) were added a solution of but-3-en-1-ol (**3**, 5.00 g, 69.3 mmol) in THF (20 ml) and a solution of benzyl bromide (12.4 g, 72.5 mmol) in THF (20 ml) at 0 °C. The mixture was stirred for 6 h at room temperature, and the reaction was stopped with a 0.2 M phosphate buffer (pH 6.5) (1 M = 1 mol dm^{-3}). The products were extracted with Et_2O (×4), and the organic layer was washed with brine, and dried over Na_2SO_4. After evaporation under reduced pressure, the residue was purified by flash column chromatography (hexane → hexane/AcOEt=4/1) to give **4** as a colorless oil (9.25 g, 82%); ^1H NMR ($CDCl_3$) δ = 2.38 (ddd, J_1 = 1.5 Hz, J_2 = J_3 = 6.5 Hz, 2H), 3.53 (t, J = 6.5 Hz, 2H), 4.52 (s, 2H), 5.04 (tdd, J_1 = 1.5 Hz, J_2 = 3.5 Hz, J_3 = 10.5 Hz, 1H), 5.10 (ddd, J_1 = 1.5 Hz, J_2 = 3.5 Hz, J_3 = 17.0 Hz, 1H), 5.85 (tdd, J_1 = 6.5 Hz, J_2 = 10.5 Hz, 1H), 7.26 (m, 5H); IR (neat) 2857, 1642, 1455, 1362, 1101, 914, 737, 698 cm^{-1}.

To a solution of **4** (4.20 g, 25.9 mmol) in acetone (140 ml) was added a solution of $KMnO_4$ (6.22 g, 38.9 mmol) in water (120 ml) at 0 °C. The reaction was stopped with sodium disulfite, and the mixture was filtered through a Celite pad and evaporated in vacuo. After the residue was saturated with NaCl, the products were extracted with AcOEt (×4), and the organic layer was dried over Na_2SO_4. After evaporation, the residue was purified by flash column chromatography (AcOHt) to give *dl*-**2a** as a colorless oil (3.76 g, 74%); ^1H NMR ($CDCl_3$) δ = 1.66—1.91 (m, 2H), 2.74 (br.s, 2H), 3.50 (dd, J_1 = 6.0 Hz, J_2 = 11.0 Hz, 1H), 3.59 (m, 2H), 3.62 (dd, J_1 = 4.0 Hz, J_2 = 11.0 Hz, 1H), 3.85—3.98 (m, 1H), 4.52 (s, 2H), 7.19—7.39 (m, 5H); ^{13}C NMR ($CDCl_3$) δ = 32.9, 66.4, 67.4, 70.1, 72.9, 127.6, 128.3, 138.1; IR (neat) 3385, 2926, 2869, 1455,

1366, 1206, 1096, 868, 739, 698 cm^{-1}; MS *m/z* (rel intensity) 196 (M^+; 43), 165 (48), 120 (33), 108 (100), 105 (86), 92 (100), 77 (70).

Other diols were synthesized by the following procedures.

3-(Benzyloxy)propane-1,2-diol (*dl*-2b): To a solution of glycerol (**5**, 31.1 g, 0.338 mol) in acetone (200 ml) was added a catalytic amount of *p*-TsOH, and the mixture was stirred for 6 h at room temperature. The reaction was stopped with sat. $NaHCO_3$ aqueous solution and evaporation. After the residual solution was saturated with NaCl, the products were extracted with AcOEt (×4), and the organic layer was dried over Na_2SO_4. Evaporation followed by distillation gave **6** as a colorless oil (30.7 g, 69%); Bp 99—100 °C/33 mmHg (1 mmHg = 133.322 Pa); ^{1}H NMR ($CDCl_3$) δ = 1.38 (s, 3H), 1.45 (s, 3H), 2.00—2.11 (m, 1H), 3.54—3.67 (m, 1H), 3.67—3.79 (m, 1H), 3.79 (dd, J_1 = 6.5 Hz, J_2 = 8.5 Hz, 1H), 4.04 (dd, J_1 = 6.5 Hz, J_2 = 8.5 Hz, 1H), 4.24 (tdd, J_1 = 4.0 Hz, J_2 = 5.5 Hz, J_3 = 6.5 Hz, 1H); IR (neat) 3443, 2988, 2938, 2884, 1456, 1373, 1213, 1157, 1051, 844 cm^{-1}.

Under a nitrogen atmosphere, to a suspension of NaH (60% in oil, 1.81 g, 45.3 mmol) in THF (20 ml) was added a solution of **6** (4.99 g, 37.8 mmol) in THF (20 ml), followed by the addition of a solution of benzyl bromide (5.0 ml, 41.6 mmol) in THF (20 ml) at 0 °C. After the reaction was quenched with a 0.2 M phosphate buffer (pH 6.5), the products were extracted with Et_2O (×4), and the organic layer was washed with brine and dried over Na_2SO_4. Evaporation followed by purification by flash column chromatography (hexane/AcOEt = 3/1) gave **7** as a colorless oil (7.33 g, 87%); ^{1}H NMR ($CDCl_3$) δ = 1.36 (s, 3H), 1.42 (s, 3H), 3.47 (dd, J_1 = 6.0 Hz, J_2 = 10.0 Hz, 1H). 3.56 (dd, J_1 = 6.0 Hz, J_2 = 10.0 Hz, 1H), 3.74 (dd, J_1 = 6.0 Hz, J_2 = 8.5 Hz, 1H), 4.06 (dd, J_1 = 6.0 Hz, J_2 = 8.5 Hz, 1H), 4.30 (dddd, $J_1 = J_2 = J_3 = J_4$ = 6.0 Hz, 1H), 4.56 (d, J = 12.0 Hz, 1H), 4.56 (d, J = 12.0 Hz, 1H), 7.22—7.42 (m, 5H); IR (neat) 3067, 3032, 2936, 2869, 1497, 1372, 1096, 739 cm^{-1}.

To a solution of **7** (4.84 g, 21.8 mmol) in THF (50 ml) was added 2 M HCl (5.5 ml); the mixture was then stirred overnight. After the mixture was saturated with NaCl, the products were extracted with AcOEt (×4) and the organic layer was dried over Na_2SO_4. After evaporation, the residue was purified by flash column chromatography (AcOEt) to afford *dl*-**2b** as a colorless oil (3.60 g, 91%); ^{1}H NMR ($CDCl_3$) δ = 3.40—3.75 (m, 6H), 3.79—3.89 (m, 1H), 4.50 (s, 2H), 7.21—7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ = 63.8, 70.9, 71.5, 73.3, 127.7, 128.4, 137.8; IR (neat) 3387, 3090, 3065, 3032, 2924, 2869, 1096, 1074, 1046, 741 cm^{-1}; MS *m/z* (rel intensity) 182 (M^+; 39), 164 (4.0), 107 (100), 91 (100), 77 (11).

5-(Benzyloxy)pentane-1,2-diol (*dl*-2c): To a solution of *dl*-glycidol (**8**, 1.02 g, 13.7 mmol) in CH_2Cl_2 (10 ml) was added dihydropyran (6.26 ml, 68.6 mmol) at room temperature. The reaction was stopped with a sat. $NaHCO_3$ aqueous solution. The products were extracted with Et_2O, and the organic layer was washed with brine, and dried over Na_2SO_4. After evaporation, the residue was purified with Kugelrohr distillation (bath temperature, 180 °C/20 mmHg) to afford **9** as a colorless oil (2.06 g, 96%); ^{1}H NMR ($CDCl_3$) δ = 1.44—1.95 (m, 6H), 2.64 (ddd, J_1 = 2.5 Hz, J_2 = 5.0 Hz, J_3 = 24.5 Hz, 1H), 2.82 (td, J_1 = 1.5 Hz, J_2 = 5.0 Hz, 1H), 3.15—3.24 (m, 1H), 3.40 (dd, J_1 = 3.0 Hz, J_2 = 11.5 Hz) and 3.96 (dd, J_1 = 6.5 Hz, J_2 = 11.5 Hz) (1H), 3.45—3.59 (m, 1H), 3.69 (dd, J_1 = 3.5 Hz, J_2 = 11.5 Hz) and 3.73 (dd, J_1 = 5.0 Hz, J_2 = 11.5 Hz) (1H), 3.80—4.00 (m, 1H), 4.65 (t, J=3.5 Hz) and 4.68 (t, J=3.5 Hz) (1H); IR (neat) 3055, 2943, 2872, 1352, 1163, 1123, 1076 cm^{-1}.

Under a nitrogen atmosphere, to a suspension of copper(I) bromide (137 mg, 0.956 mmol) in THF (10 ml) was added vinylmagnesium bromide (1.09 M in THF, 7.0 ml) at −10 °C. After stirring for 10 min, a solution of **9** (1.00 g, 6.33 mmol) in THF (10 ml) was added to the mixture and the stirring was continued for 4 h at −10°C. The mixture was poured into a sat. NH_4Cl aqueous solution and the products were extracted with Et_2O (×3). The organic layer was washed with brine, and dried over Na_2SO_4. Evaporation followed by purification by flash column chromatography (hexane/AcOEt=6/1) gave **10** as a colorless oil (959 mg, 82%); ^{1}H NMR ($CDCl_3$) δ = 1.43—1.67 (m, 4H), 1.67—1.93 (m, 2H). 2.22—2.33 (m, 2H), 3.20 (br.s, 1H), 3.37 (dd, J_1 = 7.0 Hz, J_2 = 10.5 Hz) and 3.57 (d, J = 5.5 Hz) and 3.73 (dd, J_1 = 3.5 Hz, J_2 = 10.5 Hz) (2H), 3.45—3.63 (m, 1H), 3.72—4.02 (m, 2H), 4.54—4.63 (m, 1H). 5.03—5.19 (m, 2H), 5.85 (tdd, J_1 = 7.0 Hz, J_2 = 10.5 Hz, J_3 = 17.0 Hz, 1H); IR (neat) 3424, 2944, 2872, 1642, 1441, 1123, 1074, 1032, 909 cm^{-1}.

To a solution of **10** (820 mg, 4.41 mmol) in CH_2Cl_2 (10 ml) was added dihydropyran (2.01 ml, 22.0 mmol) and a catalytic amount of *p*-TsOH at room temperature; the stirring was continued overnight. The reaction was stopped with sat. $NaHCO_3$ aqueous solution and the products were extracted with Et_2O (×3). The organic layer was washed with brine, and dried over Na_2SO_4. After evaporation, the residue was purified by flash column chromatography (hexane/AcOEt=6/1) to give **11** as a colorless oil (0.99 g, 83%); ^{1}H NMR ($CDCl_3$) δ = 1.36—2.00 (m, 12H), 2.20—2.51 (m, 2H), 3.30—3.64 (m, 4H), 3.64—4.25 (m, 3H), 4.55—4.70 (m, 1H), 4.70—5.05 (m, 1H), 4.98—5.23 (m, 2H), 5.70—6.00 (m, 1H); IR (neat) 2870, 1642, 1441, 1352, 1123, 1076, 990, 911 cm^{-1}.

Under a nitrogen atmosphere, to a solution of **11** (0.99 g, 3.67 mmol) in THF (20 ml) was added BH_3·THF (1.0 M in THF, 7.4 ml) at 0 °C and stirred for 3 h. The reaction was quenched with a drop of water, followed by the addition of a 2 M NaOH aqueous solution (10 ml) and 30% H_2O_2 (10 ml), and the mixture was stirred overnight at room temperature. After the products were extracted with Et_2O (×3), the organic layer was washed with water (×2). The water layer was saturated with NaCl and extracted with Et_2O (×4); the combined organic layer was dried over Na_2SO_4. After evaporation, the residue was purified by flash column chromatography (hexane/AcOEt=1/1) to afford **12** as a colorless oil (743 mg, 70%); ^{1}H NMR ($CDCl_3$) δ = 1.20—2.00 (m, 16H), 3.28—4.20 (m, 10H), 4.50—5.10 (m, 2H); IR (neat) 3405, 2944, 2870, 1352, 1136, 1123, 1076, 1034 cm^{-1}.

Under a nitrogen atmosphere, to a suspention of NaH (60% in oil, 124 mg, 3.10 mmol) in THF (5 ml) was added a solution of **12** (743 mg, 2.58 mmol) in THF (5 ml), benzyl bromide (0.37 ml, 3.10 mmol), and a catalytic amount of *t*-butymmonium iodide at 0 °C. The mixture was stirred overnight under reflex. The products were extracted with Et_2O (×4), and the organic layer was washed with brine, and dried over Na_2SO_4. After evaporation under reduced pressure, **13** was obtained as a colorless oil. This was used in the following reaction without purification. To a solution of **13** in MeOH (5 ml) was added a catalytic amount of *p*-TsOH, and stirred overnight at room temperature. The reaction was stopped with brine, followed by filtration and evaporation. The residue was purified by flash column chromatography (hexane/AcOEt=1/1 → AcOEt) to afford *dl*-**2c** as a colorless oil (310 mg, 57% from **12**); ^{1}H NMR ($CDCl_3$) δ = 1.34—1.85 (m, 4H), 3.37 (dd, J_1 = 7.5 Hz, J_2 = 11.0 Hz, 1H), 3.48 (t, J = 6.0 Hz, 2H), 3.53 (dd, J_1 = 3.0 Hz, J_2 = 11.0 Hz, 1H), 3.57—3.70 (m, 1H), 3.75 (s, 2H), 4.46 (d, J = 16.0 Hz, 1H), 4.49 (d, J = 16.0 Hz, 1H), 7.20—7.42 (m, 5H); ^{13}C NMR ($CDCl_3$) δ = 26.0, 30.1, 66.6, 70.3, 71.9, 72.3, 127.7, 128.0, 128.3, 138.1; IR (neat) 3381, 3088, 3063, 3032, 2936, 2864, 1603, 1495, 1277, 1100, 1073, 739 cm^{-1}; MS *m/z* (rel intensity) 210 (M^+; 56), 192 (5.0), 179 (64), 120 (66), 92 (100), 77 (76).

Decane-1,2-diol (*dl*-2d): Under a nitrogen atmosphere, to

a suspension of copper(I) bromide (150 mg, 1.05 mmol) in THF (10 ml) was added heptylmagnesium bromide (ca. 0.56 M in THF, 22.6 ml) at −10 °C. After stirring for 10 min, a solution of **9** (1.00 g, 6.33 mmol) in THF (10 ml) was added to the mixture and the stirring was continued for 4 h. The mixture was poured into a sat. NH_4Cl aqueous solution and the products were extracted with Et_2O (×4). The organic layer was washed with brine and dried over Na_2SO_4. Evaporation gave crude **14** as a colorless oil. This was used in the following reaction without purification. To a solution of **14** in MeOH (60 ml) was added a catalytic amount of *p*-TsOH, and stirred overnight at room temperature. The reaction was stopped with $NaHCO_3$, followed by filtration and evaporation. The residue was purified by flash column chromatography (hexane/AcOEt=4/1) to afford diol *dl*-**2d** as a solid (970 mg, 96%). This was further recrystalized from hexane; Mp 46.5—48.5 °C; ^{1}H NMR ($CDCl_3$) δ = 0.88 (t, J = 6.5 Hz, 3H), 1.15—1.53 (m, 14H), 1.86—2.03 (m, 1H), 2.03—2.12 (m, 1H), 3.43 (ddd, J_1 = 5.0 Hz, J_2 = 7.5 Hz, J_3 = 10.5 Hz, 2H), 3.59—3.78 (m, 1H); ^{13}C NMR ($CDCl_3$) δ = 14.2, 22.8, 25.8, 29.4, 29.7, 29.9, 32.0, 33.2, 66.9, 72.5; IR (KBr) 3320, 2921, 1468, 1142, 1073, 874 cm^{-1}; MS *m/z* (rel intensity) 173 (M^+−H; 4.5), 157 (12), 143 (100), 43 (100), 31 (100).

3-Phenoxypropane-1,2-diol (*dl*-2e): Racemic 1,2-epoxy-3-phenoxyopropane (**15**, 4.51 ml, 33.3 mmol) was slowly added to 1 M H_2SO_4 (250 ml) at 0 °C, and the mixture was stirred overnight at room temperature. The products were extracted with CH_2Cl_2 (×4), washed with brine, and dried over Na_2SO_4. After evaporation, the residual solid was recrystallized from hexane–CH_2Cl_2 to afford *dl*-**2e** (3.90 g, 69%); Mp 53.5—55 °C; ^{1}H NMR ($CDCl_3$) δ = 2.18—2.31 (m, 1H), 2.74—2.83 (m, 1H), 3.70—3.90 (m, 2H), 4.05 (dd, J_1 = 2.5 Hz, J_2 = 5.0 Hz, 2H), 4.06—4.17 (m, 1H), 6.92 (d, J = 8.5 Hz, 2H), 6.98 (t, J = 7.5 Hz, 1H), 7.30 (td, J_1 = 7.5 Hz, J_2 = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 63.7, 68.9, 70.6, 114.6, 121.2, 129.6, 158.4; IR (KBr) 3301, 1601, 1499, 1250, 1049, 752, 691 cm^{-1}; FABMS (glycerol) *m/z* (rel intensity) 169 (M^++1; 11), 149 (8.8), 133 (2.0), 93 (100), 75 (30). Found: C, 63.72; H, 7.14%. Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.19%.

5-(Benzyloxy)pentane-1,3-diol (*dl*-2f): To a solution of *dl*-**2a** (10.0 g, 51.0 mmol) in THF (175 ml)–water (35 ml) was slowly added sodium periodate (16.7 g, 78.1 mmol) at 0 °C, and the mixture was stirred overnight at room temperature. The mixture was diluted with AcOEt and water, and the products were extracted with AcOEt (×4). The organic layer was washed with a sat. $NaHCO_3$ acueous solution and brine, and dried over Na_2SO_4. After evaporation, the residue was purified by flash column chromatography (hexane/Et_2O=1/1) to afford **16** as a colorless oil (7.98 g, 95%); ^{1}H NMR ($CDCl_3$) δ = 2.70 (td, J_1 = 1.5 Hz, J_2 = 6.0 Hz, 2H), 3.82 (t, J = 6.0 Hz, 2H), 4.53 (s, 2H), 7.28—7.40 (m, 5H), 9.80 (t, J = 1.5 Hz, 1H); IR (neat) 3433, 2865, 1725, 1455, 1364, 1208, 1096, 741, 700 cm^{-1}.

Under a nitrogen atmosphere, to a solution **16** (2.09 g, 12.8 mmol) in THF (20 ml) was added vinylmagnesium bromide (1.09 M in THF, 23.4 ml) at 0 °C. After stirring for 2 h, the mixture was poured into sat. NH_4Cl aqueous solution and the products were extracted with Et_2O (×4). The organic layer was washed with brine and dried over Na_2SO_4. Evaporation followed by purification by flash column chromatography (hexane/AcOEt=4/1) to give **17** as a colorless oil (1.68 g, 69%); ^{1}H NMR ($CDCl_3$) δ = 1.74—1.96 (m, 2H), 2.80 (d, J = 4.0 Hz, 1H), 3.65 (ddd, J_1 = 5.0 Hz, J_2 = 6.5 Hz, J_3 = 16.0 Hz, 1H), 3.70 (ddd, J_1 = 5.0 Hz, J_2 = 9.5 Hz, J_3 = 11.0 Hz, 1H), 4.30—4.41 (m, 1H), 4.52 (s, 2H), 5.11 (ddd, J_1 = J_2 = 1.5 Hz, J_3 = 10.5 Hz, 1H), 5.27 (ddd, J_1 = J_2 = 1.5 Hz, J_3 = 17.0 Hz, 1H), 5.88 (ddd, J_1 = 5.5 Hz, J_2 = 10.5 Hz, J_3 = 17.5 Hz, 1H), 7.24—7.50 (m, 5H); IR (neat) 3405, 2865, 1455, 1366, 1208, 1200, 993, 924, 737, 698 cm^{-1}.

Under a nitrogen atmosphere, to a solution of **17** (1.56 g, 8.13 mmol) in THF (10 ml) was added BH_3·THF (1.0 M in THF, 24.4 ml) at 0 °C and stirred for 2 h. The reaction was quenched with a drop of water, followed by the addition of a 2 M NaOH aqueous solution (24 ml) and 30% H_2O_2 (24 ml); the mixture was then stirred for 5 h at room temperature. After the mixture was saturated with NaCl, the products were extracted with Et_2O (×3) and the combined organic layer was dried over Na_2SO_4. After evaporation, the residue was purified by flash column chromatography (hexane/AcOEt=1/1 → AcOEt) to afford *dl*-**2f** as a colorless oil (1.14 g, 67%); ^{1}H NMR ($CDCl_3$) δ = 1.59—1.95 (m, 4H), 2.86 (br.s, 1H), 3.58 (br.s, 1H), 3.68 (ddd, J_1 = 4.0 Hz, J_2 = 9.5 Hz, J_3 = 17.5 Hz, 1H), 3.72 (ddd, J_1 = 5.0 Hz, J_2 = 9.5 Hz, J_3 = 17.5 Hz, 1H), 3.78—3.90 (m, 2H), 4.03—4.15 (m, 1H), 4.53 (s, 2H), 7.25—7.42 (m, 5H); ^{13}C NMR ($CDCl_3$)=36.7, 38.6, 60.9, 68.6, 70.5, 73.2, 127.69, 127.74, 128.4, 137.9; IR (neat) 3382, 2492, 1455, 1366, 1208, 1096, 741, 698 cm^{-1}; MS *m/z* (rel intensity) 210 (M^+; 15), 192 (13), 120 (6.0), 103 (35), 91 (100), 77 (37).

6-(Benzyloxy)hexane-1,4-diol (*dl*-2g): Under a nitrogen atmosphere, to a solution of **16** (1.08 g, 6.57 mmol) in THF (10 ml) was added allylmagnesium bromide (1.0 M in Et_2O, 13.1 ml) at 0 °C. After stirring for 2 h, the mixture was poured into sat. NH_4Cl aqueous solution and the products were extracted with Et_2O (×3). The organic layer was washed with brine, and dried over Na_2SO_4. Evaporation followed by purification by flash column chromatography (hexane/AcOEt=4/1) gave **18** as a colorless oil (1.09 g, 81%); ^{1}H NMR ($CDCl_3$) δ = 1.63—1.81 (m, 2H), 2.21 (dd, J_1 = J_2 = 6.5 Hz, 2H), 3.04 (br.s, 1H), 3.06 (br.s, 1H), 3.53—3.72 (m, 2H), 3.76—3.88 (m, 1H), 4.47 (s, 2H), 5.00—5.12 (m, 2H), 5.81 (tdd, J_1 = 7.5 Hz, J_2 = 14.0 Hz, J_3 = 16.0 Hz, 1H), 7.19—7.36 (m, 5H); IR (neat) 3420, 2865, 1642, 1455, 1366, 1098, 914, 739, 698 cm^{-1}.

Under a nitrogen atmosphere, to a solution of **18** (1.09 g, 5.29 mmol) in THF (10 ml) was added BH_3·THF (1.0 M in THF, 15.9 ml) at 0°C and stirred for 2 h. The reaction was quenched with a drop of water, followed by the addition of a 2 M NaOH aqueous solution (10 ml) and 30% H_2O_2 (10 ml); the mixture was then stirred overnight at room temperature. The products were extracted with Et_2O (×3), and the organic layer was washed with water (×2). After the mixture became saturated with NaCl, the products were extracted with Et_2O (×3) and the combined organic layer was dried over Na_2SO_4. After evaporation, the residue was purified by flash column chromatography (hexane/AcOEt=1/1) to afford *dl*-**2g** as a colorless oil (950 mg, 80%); ^{1}H NMR ($CDCl_3$) δ = 1.39—1.86 (m, 6H), 3.50—3.72 (m, 4H), 3.72—3.88 (m, 1H), 3.90 (br.s, 2H), 4.46 (d, J = 16.5 Hz, 1H), 4.51 (d, J = 16.5 Hz, 1H), 7.20—7.39 (m, 5H); ^{13}C NMR ($CDCl_3$) δ = 29.0, 34.4, 36.6, 62.5, 68.8, 70.6, 73.2, 127.7, 128.4, 138.0; IR (neat) 3364, 2940, 1455, 1366, 1094, 912, 735, 698 cm^{-1}; MS *m/z* (rel intensity) 225 (M^++1; 71), 206 (52), 118 (11), 107 (59), 91 (100), 77 (90).

Preparation of Racemic Cyclic Carbonates 4-[(2-Benzyloxy)-ethyl]-1,3-dioxolan-2-one (*dl*-1a). Under a nitrogen atmosphere, to a solution of *dl*-**2a** (1.16 g, 5.90 mmol) in CH_2Cl_2 (12 ml) was added pyridine (2.86 ml, 35.4 mmol) at 0 °C, followed by a solution of triphosgene (903 mg, 2.95 mmol) in CH_2Cl_2 (33 ml) at −78 °C; the mixture was then slowly warmed to 0 °C. The reaction was stopped with a sat. NH_4Cl aqueous solution and the products were extracted with CH_2Cl_2 (×3). The organic layer was washed with 1 M HCl (×2), brine, sat. $NaHCO_3$ aqueous solution, and brine,

and dried over Na_2SO_4. After evaporation, the residue was purified by flash column chromatography (hexane/AcOEt=4/1) to give *dl*-**1a** as a colorless oil (1.17 g, 90%). ^{1}H NMR ($CDCl_3$) δ = 1.95—2.17 (m, 2H), 3.62 (ddd, J_1 = 5.0 Hz, J_2 = 10 Hz, J_3 = 9.5 Hz, 1H), 3.64 (ddd, J_1 = 5.0 Hz, J_2 = J_3 = 9.5 Hz, 1H), 4.18 (dd, J_1 = 7.5 Hz, J_2 = 8.5 Hz, 1H), 4.49 (s, 2H), 4.52 (dd, J_1 = 7.5 Hz, J_2 = 8.5 Hz, 1H), 4.88 (dddd, J_1 = J_2 = 7.5 Hz, J_3 = J_4 = 7.0 Hz, 1H), 7.15—7.46 (m, 5H); ^{13}C NMR ($CDCl_3$) δ = 33.9, 65.4, 69.8, 73.2, 75.2, 127.6, 127.8, 128.4, 137.9, 155.0; IR (neat) 3032, 2867, 1794, 1455, 1366, 1173, 1061, 775, 741, 700 cm^{-1}; MS *m/z* (rel intensity) 222 (M^+; 4.7), 160 (39), 131 (6.3), 107 (26), 105 (27), 91 (100).

The other substrates were prepared by the same procedure mentioned above from the corresponding diols.

4-(Benzyloxy)methyl-1,3-dioxolan-2-one (*dl*-1b): 84% from *dl*-**2b**; ^{1}H NMR ($CDCl_3$) δ = 3.59 (dd, J_1 = 4.0 Hz, J_2 = 10.5 Hz, 1H), 3.70 (dd, J_1 = 4.0 Hz, J_2 = 10.5 Hz, 1H), 4.35 (dd, J_1 = 6.0 Hz, J_2 = 8.5 Hz, 1H), 4.45 (dd, J_1 = J_2 = 8.5 Hz, 1H), 4.54 (dd, J = 12.0 Hz, 1H), 4.60 (d, J = 12.0 Hz, 1H), 4.79 (dddd, J_1 = J_2 = 4.0 Hz, J_3 = 6.0 Hz, J_4 = 8.5 Hz, 1H), 7.23—7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ = 66.3, 68.8, 73.7, 75.0, 127.8, 128.1, 128.6, 137.1, 154.9; IR (neat) 3088, 3065, 3032, 2920, 2869, 1796, 1748, 1607, 1497, 1335, 1248, 1173 cm^{-1}; MS *m/z* (rel intensity) 208 (M^+; 18), 181 (3.9), 146 (12), 105 (100), 91 (100), 77 (18).

4-[3-(Benzyloxy)propyl]-1,3-dioxolan-2-one (*dl*-1c): 89% from *dl*-**2c**; ^{1}H NMR ($CDCl_3$) δ = 1.51—1.89 (m, 4H), 3.46 (t, J = 6.0 Hz, 2H), 3.96 (dd, J_1 = 7.5 Hz, J_2 = 8.5 Hz, 1H), 4.40 (dd, J_1 = J_2 = 8.5 Hz, 1H), 4.44 (s, 2H), 4.55—4.62 (m, 1H), 7.20—7.39 (m, 5H); ^{13}C NMR ($CDCl_3$) δ = 24.0, 30.8, 69.2, 69.4, 72.8, 77.0, 127.6, 128.4, 129.5, 138.5, 155.0; IR (neat) 3088, 3063, 2926, 2862, 1813, 1603, 1495, 1103, 1070, 741 cm^{-1}; MS *m/z* (rel intensity) 236 (M^+; 12), 173 (46), 159 (8.0), 145 (3.9), 107 (100), 91 (100), 77 (30).

4-Oxtyl-1,3-dioxolan-2-one (*dl*-1d): 74% from *dl*-**2d**; ^{1}H NMR ($CDCl_3$) δ = 0.88 (t, J = 5.0 Hz, 3H), 1.18—1.55 (m, 12H), 1.61—1.90 (m, 2H), 3.97—4.14 (m, 1H), 4.44—4.51 (m, 1H), 4.51—4.70 (m, 1H); ^{13}C NMR ($CDCl_3$) δ = 14.1, 22.6, 24.4, 29.1, 29.3, 31.8, 33.9, 69.5, 77.2, 155.2; IR (neat) 2928, 1796, 1466, 1385, 1169, 1065 cm^{-1}; MS *m/z* (rel intensity) 201 (M^+ + 1; 24), 138 (100), 67 (52), 55 (100), 43 (100), 31 (31).

4-Phenoxymethyl-1,3-dioxolan-2-one (*dl*-1e): 82% from *dl*-**2e**; 96—98 °C (recrystallized from CH_2Cl_2–hexane); ^{1}H NMR ($CDCl_3$) δ = 4.16 (dd, J_1 = 4.0 Hz, J_2 = 10.5 Hz, 1H), 4.24 (dd, J_1 = 3.5 Hz, J_2 = 10.5 Hz, 1H), 4.55 (dd, J_1 = 6.0 Hz, J_2 = 8.5 Hz, 1H), 4.66 (dd, J_1 = J_2 = 8.5 Hz, 1H), 5.04 (dddd, J_1 = 3.5 Hz, J_2 = 4.0 Hz, J_3 = 6.0 Hz, J_4 = 8.5 Hz, 1H), 6.91 (d, J = 8.0 Hz, 2H), 7.02 (t, J = 7.5 Hz, 1H), 7.30 (td, J_1 = 7.5 Hz, J_2 = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 66.2, 66.9, 74.3, 114.6, 121.9, 129.7, 154.8, 157.8; IR (KBr) 2926, 1804, 1603, 1495, 1397, 1252, 1167, 1092, 760 cm^{-1}; FABMS *m/z* (rel intensity) 195 (M^+ + 1; 2.5), 167 (3.1), 149 (11), 93 (100), 75 (42), Found: C 61.91; H, 5.42%. Calcd for $C_{10}H_{10}O_4$: C, 61.85; H, 5.19%.

4-[2-(Benzyloxy)ethyl]-1,3-dioxan-2-one (*dl*-1f): 70% from *dl*-**2f**; ^{1}H NMR ($CDCl_3$) δ = 1.67—2.10 (m, 4H), 3.61 (ddd, J_1 = 5.0 Hz, J_2 = 10.0 Hz, J_3 = 19.0 Hz, 1H), 3.65 (ddd, J_1 = 5.5 Hz, J_2 = 10.0 Hz, J_3 = 19.0 Hz, 1H), 4.20—4.41 (m, 2H), 4.47 (d, J = 12.0 Hz, 1H), 4.50 (d, J = 12.0 Hz, 1H), 4.58—4.71 (m, 1H), 7.15—7.42 (m, 5H); ^{13}C NMR ($CDCl_3$) δ = 27.1, 35.4, 65.2, 67.1, 73.2, 76.8, 127.6, 127.7, 128.4, 138.0, 148.9; IR (neat) 2867, 1750, 1410, 1250, 1194, 1115, 745, 700 cm^{-1}; MS *m/z* (rel intensity) 236 (M^+; 38), 159 (2.5), 146 (100), 130 (25), 107 (100), 91 (100), 77 (52).

4-[2-(Benzyloxy)ethyl]-1,3-dioxepan-2-one (*dl*-1g): 46% from *dl*-**2g**; ^{1}H NMR ($CDCl_3$) δ = 1.64—2.07 (m, 6H), 3.61 (ddd, J_1 = 5.0 Hz, J_2 = 9.5 Hz, J_3 = 17.0 Hz, 1H), 3.61 (ddd, J_1 = 5.0 Hz, J_2 = 9.5 Hz, J_3 = 17.0 Hz, 1H), 4.03—4.18 (m, 2H), 4.33—4.46 (m, 1H), 4.47 (d, J = 11.5 Hz, 1H), 4.52 (d, J = 11.5 Hz, 1H), 7.20—7.42 (m, 5H); ^{13}C NMR ($CDCl_3$) δ = 26.9, 32.9, 35.9, 65.9, 70.4, 73.1, 79.6, 127.5, 127.6, 128.3, 138.1, 154.7; IR (neat) 2922, 1748, 1455, 1364, 1192, 1086, 938, 739, 700 cm^{-1}; MS *m/z* (rel intensity) 250 (M^+; 50), 188 (64), 159 (100), 145 (38), 107 (100), 91 (100), 77 (100).

Screening of Enzymes. Five μl of *dl*-**1a** and 20—25 mg of commercially available enzyme were incubated in 2.5 ml of 0.1 M phosphate buffer (pH 6.5) for 12 h at 30°C. In the case of PLE, 20 μl of the enzyme was used. The products were extracted with Et_2O and detected by TLC (AcOEt).

Typical Procedure of Enantioselective Hydrolysis of *dl*-1a with PPL. To 200-ml Erlenmeyer flask containing 92.9 mg (0.418 mmol) of *dl*-**1a** was added 4 ml of *i*-Pr_2O following by addition of 36 ml of 0.1 M phosphate buffer (pH 6.5). To the mixture was added 500 mg of PPL and incubated for 12 h at 10 °C. After the mixture was saturated with NaCl, the products were extracted with Et_2O (×4) and dried over Na_2SO_4. Evaporation and purification by flash column chromatography (hexane/AcOEt=2/1 → AcOEt) afforded (*R*)-**1a** (33.9 mg, 37%, >95%ee) and (*S*)-**2a** (42.2 mg, 51%, 52%ee).

Enantioselective hydrolysis of the other cases were carried out by the same procedure. In the case of *dl*-**1e**, a mixed system of 0.1 M phosphate butter (pH 6.5, 28 ml) and DMSO (12 ml) was used as the solvent. All of the spectral data (^{1}H NMR, ^{13}C NMR, IR, and MS) were in full agreement with those of the racemates. The optical-rotations of the obtained optically active compounds are shown in Tables 2 and 3 and Schemes 7, 8, and 9. The ee's of diols **2** were determined by ^{1}H NMR or HPLC (column, Zorbax SIL, 0.46mm×25 cm, Du Point Instruments) analyses of the bis-(+)-MTPA ester **19**, which were converted from **2**, as shown in Scheme 5. The ee's of cyclic carbonates **1** were determined by similar analyses of the corresponding diols **2** derived from **1** with K_2CO_3. The conditions of the analyses are given in below.

2a: ^{1}H NMR (270 MHz, $CDCl_3$) δ = 4.66 (dd, J_1 = 2.5 Hz, J_2 = 12.5 Hz, 1H, MTPAOC**H**$_2$, (*S*)), δ 4.72 (dd, J_1 = 2.5 Hz, J_2 = 12.5 Hz, 1H, MTPAOC**H**$_2$, (*R*)).

2b: HPLC (eluent, hexane/AcOEt = 90/10; flow rate, 0.5 ml min^{-1})(*S*) 41 min, (*R*) 38 min.

2c: HPLC (eluent, hexane/AcOEt = 90/10; flow rate, 0.5 ml min^{-1})(*S*) 46 min, (*R*) 48 min.

2d: HPLC (eluent, hexane/AcOEt = 96/4; flow rate, 0.5 ml min^{-1})(*S*) 54 min, (*R*) 52 min.

2e: HPLC (eluent, hexane/AcOEt = 90/10; flow rate, 0.5 ml min^{-1})(*S*) 28 min, (*R*) 31 min.

2f: HPLC (eluent, hexane/AcOEt = 90/10; flow rate, 0.5 ml min^{-1})(*S*) 50 min, (*R*) 46 min.

The absolute configurations of **2a**, **2b**, and **2e** were determined by comparing their signs of optical rotations with those reported (shown in the text). In other cases, the absolute configurations were determined by comparing the optical-rotations with those of synthesized authentic samples. Authentic (*S*)-**1b** and (*S*)-**2c** were synthesized from optically active starting materials by the same procedure of preparing racemic ones.

Preparation of Authentic (*S*)-1f. Under a nitrogen atmosphere, to a solution of 1,3-dithiane (851 mg, 7.08 mmol) in THF (18 ml) was added *n*-BuLi (1.56 M in hexane, 4.2 ml) at 0 °C and stirred for 45 min. A solution of (*S*)-1,2-epoxy-4-(benzyloxy)butane (**20**)[17] (969 mg, 5.44 mmol) in THF (5 ml) was added to the mixture at −23 °C, and the stirring was continued for 2 h at the

same temperature and for 2 h at room temperature. The reaction was quenched with a sat. NH_4Cl aqueous solution, and the products were extracted with AcOEt (×3), washed with brine, and dried over Na_2SO_4. After evaporation, the residue was purified by flash column chromatography (hexane/AcOEt = 5/1) to give **21** as a colorless oil (1.33 g, 82%); ^{1}H NMR ($CDCl_3$) δ = 1.70—2.03 (m, 5H), 2.03—2.18 (m, 1H), 2.77—3.00 (m, 4H), 3.14 (br.s, 1H), 3.62—3.77 (m, 2H), 4.09—4.20 (m, 1H), 4.29 (dd, J_1 = 5.0 Hz, J_2 = 9.5 Hz, 1H), 4.52 (s, 2H), 7.22—7.39 (m, 5H); IR (neat) 3451, 2903, 1424, 1364, 1275, 1090, 737, 700 cm^{-1}.

To a solution of **21** (1.33 g, 4.48 mmol) in CH_2Cl_2 (20 ml) was added dihydropyran (4.00 ml, 44.8 mmol) and a catalytic amount of *p*-TsOH at room temperature; the stirring was continued overnight. The reaction was stopped with a sat. $NaHCO_3$ aqueous solution and the products were extracted with Et_2O (×3). The organic layer was washed with brine, and dried over Na_2SO_4. After evaporation, the residue was purified by flash column chromatography (hexane/AcOEt = 10/1→4/1) to give **22** as a colorless oil (1.72 g, quant.); ^{1}H NMR ($CDCl_3$) δ = 1.45—2.14 (m, 12H), 2.91—2.79 (m, 4H), 3.45—3.56 (m) and 3.60—3.63 (m) (3H), 3.83—3.96 (m), 4.02—4.13 (m), and 4.23—4.27 (m) (3H), 4.44—4.53 (m, 2H), 4.57—4.60 (m) and 4.69—4.71 (m) (1H), 7.36—7.25 (m, 5H); IR (neat) 2940, 2361, 1455, 1362, 1277, 1076, 1026, 907, 870, 814, 739, 698 cm^{-1}.

Under a nitrogen atmosphere, to a solution of **22** (950 mg, 2.49 mmol) in CH_3CN (24 ml)–water (6 ml) were added methyl iodide (0.917 ml, 24.9 mmol) and $NaHCO_3$ (2.09 g, 24.9 mmol) at 0 °C, and stirred for 4 d at room temperature. The reaction was stopped with a sat. $NaHCO_3$ aqueous solution, and the products were extracted with Et_2O (×4). The combined organic layer was washed with brine and dried over Na_2SO_4. Evaporation afforded crude aldehyde **23**. This was used in the following reaction without purification. To a solution of **23** in MeOH (20 ml) was added $NaBH_4$ (109 mg, 2.88 mmol) at 0 °C, and stirred for 45 min. The reaction was stopped with brine, and the solvent was removed in vacuo. The products were extracted with Et_2O (×4), washed with brine, and dried over Na_2SO_4. Evaporation and purification by flash column chromatography (hexane/AcOEt = 3/1→ 2/1 → 1/1) afford **24** as a colorless oil (492 mg, 67% from **22**); ^{1}H NMR ($CDCl_3$) δ = 1.35—1.95 (m) and 1.97—2.11 (m) (10 H), 3.37—4.14 (m, 8H), 4.40—4.73 (m, 1H), 4.50 (s) and 4.51 (s) (2H), 7.21—7.45 (m, 5H); IR (neat) 3426, 2492, 1455, 1362, 1026, 903, 810, 739, 698 cm^{-1}.

To a solution of **24** in MeOH (20 ml) was added a catalytic amount of *p*-TsOH, and stirred overnight at room temperature. The reaction was quenched with $NaHCO_3$, and the mixture was filtered through a Celite pad and evaporated. The residue was purified by flash column chromatography (hexane/AcOEt = 1/1→ AcOEt) to afford (*R*)-**2f** as a colorless oil (310 mg, 93%). The spectral data (^{1}H NMR, ^{13}C NMR, IR, and MS) of (*R*)-**2f** were in full agreement with those of the sample obtained by an enzymatic reaction.

Under a nitrogen atmosphere, to a solution of (*R*)-**2f** (50.3 mg, 0.240 mmol) in CH_2Cl_2 (10 ml) was added pyridine (0.44 ml, 5.45 mmol) at 0 °C, followed by a solution of triphosgene (43.0 mg, 0.144 mmol) in CH_2Cl_2 (33 ml) at −78 °C; the mixture was then slowly warmed to 0 °C. The reaction was stopped with a sat. NH_4Cl aqueous solution, and the products were extracted with CH_2Cl_2 (×3). The organic layer was washed with 1 M HCl (×2), brine, sat. $NaHCO_3$ aqueous solution, and brine, and dried over Na_2SO_4. After evaporation, the residue was purified by flash column chromatography (hexane/AcOEt = 4/1) to give (*S*)-**1f** as a colorless oil (42.4 mg, 75%). The spectral data (^{1}H NMR, ^{13}C NMR, IR, and MS) of (*S*)-**1f** were in full agreement with those of the sample obtained by enzymatic reaction. The optical-rotation of (*S*)-**1f** was shown in the text.

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