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Enantioselective microbial hydrolysis of dissymmetrical cyclic carbonates with disubstitution

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Abstract—Enantioselective microbial hydrolysis of C_1 and C_2 dissymmetrical cyclic carbonates with disubstitution (methyl and another groups) has been developed. *Pseudomonas diminuta* (FU0090), a bacterium, efficiently catalyzes the hydrolysis of five-membered cyclic carbonates. While the trans-substrates are hydrolyzed with low enantioselectivities and/or reactivities, the microbe hydrolyzes the cis-substrates with very high enantioselectivities to afford the corresponding almost optically pure *anti*-(2*R*,3*S*)-diols. On the other hand, six-membered *trans*-cyclic carbonates are enantioselectively hydrolyzed to afford the corresponding optically active *syn*-(2*R*,4*R*)-diols, although the hydrolysis of the cis-substrates gives racemic compounds. In all cases, the enzyme prefers the (*R*)-enantiomer for the carbon atom bearing a methyl group.

1. Introduction

Optically active diols are important intermediates for the synthesis of natural products, and many synthetic procedures for such compounds have been developed. Although the asymmetric dihydroxylation of olefins is one of the most popular ways to prepare chiral 1,2-diols,[1] this method does not always satisfactorily work in terms of the enantioselectivity in some cases. For example, the oxidation of (*Z*)-disubstituted olefins is not a suitable tool for the preparation of optically active *anti*-1,2-diols.[2] On the other hand, optically active 1,3-diols are not easily synthesized by direct preparation methods.

The use of enzymes in the preparation of such optically active compounds is especially attractive due to the remarkable stereoselectivity and its benign effect on the environment. Enzymatic hydrolysis of diacetates and esterification of diols are the representative biochemical methods to prepare such compounds.[3] The reactions, however, produce a mixture of more than two compounds (diol, diacetate, and two monoacetates), which causes difficulty with the purification, and the almost examples have been limited to the reaction of *meso*- and C_2-symmetrical compounds. Recently, the kinetic resolution of cyclic carbonates with hydrolytic enzymes is one of the attractive methods for preparing optically active diols.[4] We have already reported the enzyme-mediated hydrolysis of cyclic carbonates, and have accomplished the efficient preparation of various kinds of optically active diols.[5,6] Commercially available porcine pancreas lipase (PPL, Type II from Sigma) catalyzes the hydrolysis of monosubstituted cyclic carbonates to afford the corresponding optically active 1,2- and 1,3-diols.[5] On the other hand, *Pseudomonas diminuta* (FU0090), which is a bacterium isolated from the soil and classified by NCIMB Japan Co. Ltd, hydrolyzes the C_2-symmetrical five- and six-membered cyclic carbonates with a dimethyl group, and then optically active 2,3-butanediol and 2,4-pentanediol were obtained.[6a] This type of reaction proceeds irreversibly because the acyl moiety of the substrate leaves the reaction system as carbon dioxide. The enzyme, however, has a high substrate specificity for the side chain of the substrate, and the reaction of the substrate bearing a diethyl group was not hydrolyzed at all. During our studies on this microbial reaction, we observed that even C_1- and C_2-dissymmetrical disubstituted substrates could be enantioselectively hydrolyzed when one of the substituent was a methyl group. Herein, we reported the application of the microbial hydrolysis to various five- and six-membered cyclic carbonates bearing methyl and another groups, and then prepared the corresponding optically active 1,2- and 1,3-diols with two chiral centers

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Keywords: Cyclic carbonates; Enantioselective hydrolysis; Enzymes; Microbial reaction; Optically active diols.

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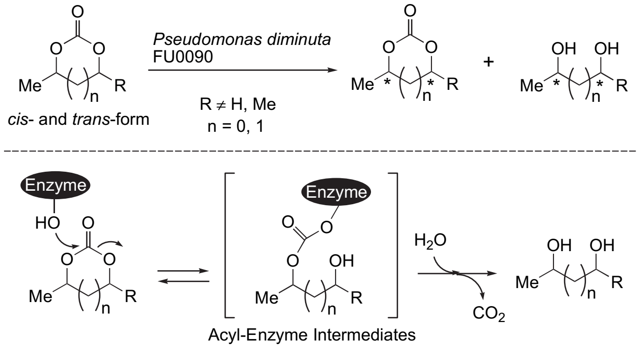
(Scheme 1). In particular, the optically pure *anti*-1,2-diols were obtained from the five-membered *cis*-substrates with high enantioselectivities.[6b]



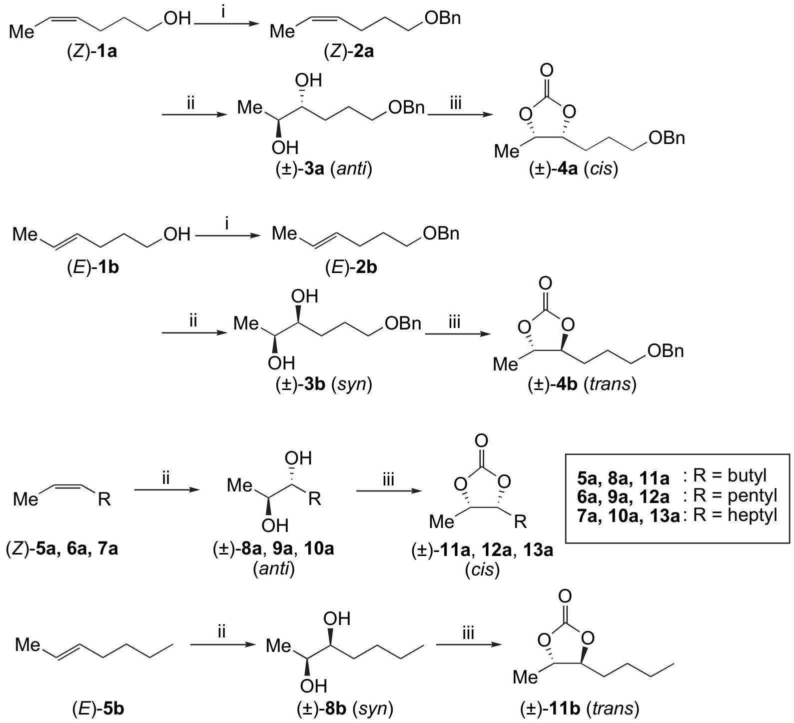
Scheme 1.

2. Results and discussion

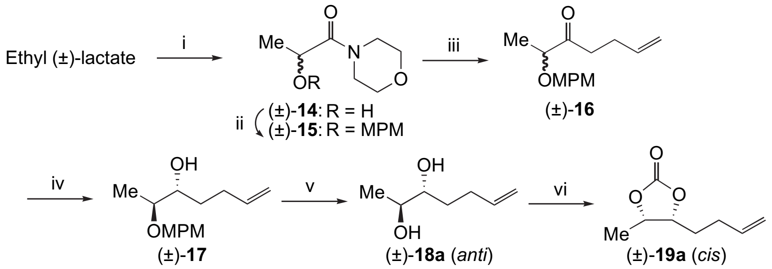
The diastereomeric *anti*- and *syn*-racemic diols, which were the precursors of cyclic carbonates, were readily synthesized. The compounds 1,2-diols are selectively prepared starting from (*Z*)- and (*E*)-olefins, respectively, as shown in Schemes 2 and 3. On the other hand, selective reduction of β-hydroxy ketones followed by separation with column chromatography on silica gel afforded *anti*- and *syn*-1,3-diols (Scheme 4). In all cases, successive treatment of the diols with pyridine and bis(trichloromethyl)carbonate (triphosgene) resulted in the corresponding racemic substrates.

First, we selected the racemic five-membered cyclic carbonates, diastereomers of the *cis*- and *trans*-4-(3-benzyloxy)propyl-5-methyl-1,3-dioxolan-2-ones ((±)-**4a** and **4b**, respectively) as the representative substrates. After the reaction of (±)-**4** (ca. 84 mg, 10 mM) with *P. diminuta* in 50 mL of glucose medium at 30 °C, the bacterium catalyzed the hydrolysis of both substrates, and the corresponding *anti*- and *syn*-6-benzyloxy-2,3-diols (**3a** and **3b**, respectively) were obtained, as expected (Scheme 5). The trans-form substrate ((±)-**4b**) was enantioselectively hydrolyzed to give the optically active (2*R*,3*R*)-**3b** ($[\alpha]_D^{22}$ +11.5 (*c* 0.72, MeOH), 75% ee) in 23% yield and the remaining (4*S*,5*S*)-**4b** ($[\alpha]_D^{22}$ −10.0 (*c* 0.35, MeOH), 54% ee) in 44% yield. In this case, the enzyme preferentially hydrolyzed the (4*R*,5*R*)-form in the same stereoselective manner as in the case of the C_2-symmetrical (±)-*trans*-4,5-dimethyl-1,3-dioxolan-2-one (**38b**) bearing a dimethyl group.[6a] The hydrolysis, however, proceeded with moderate enantioselectivity, and the conversion and *E* value of the reaction for 48 h were 0.42 and 12, respectively,[7] while **38b** was hydrolyzed with high enantioselectivity (*E* value=70). To determine the stereochemistry of the resulting (2*R*,3*R*)-**3b**, the sign of the optical rotation was compared with that of the authentic sample (2*S*,3*S*)-**3b** ($[\alpha]_D^{27}$ −13.8 (*c* 1.16, MeOH), 77% ee), which was transformed from (*E*)-**2b** by the asymmetric dihydroxylation method with AD-mix-α and $CH_3SO_2NH_2$ in *t*-BuOH/H_2O (Scheme 6).[1]

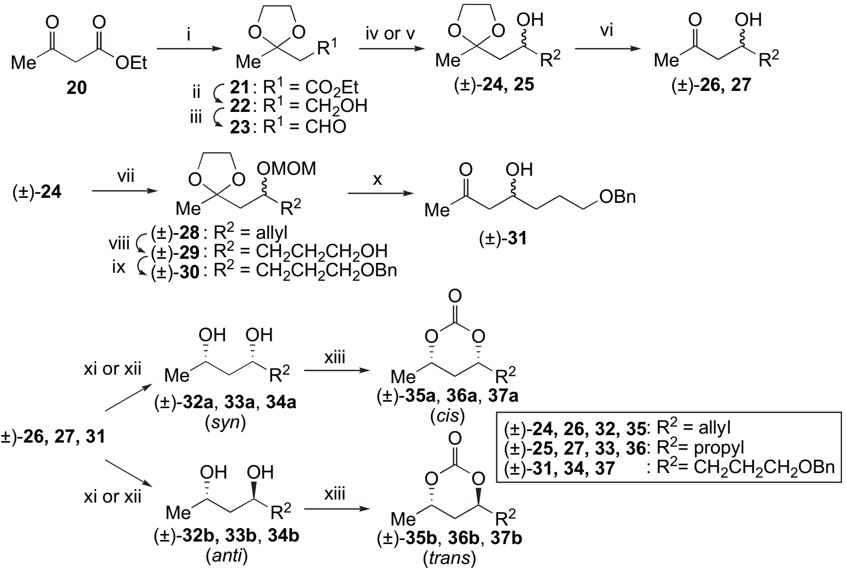
On the other hand, the enantioselectivity of the hydrolysis of the *cis*-substrate ((±)-**4a**) was almost perfect. The reaction of (±)-**4a** for 48 h produced the remaining cyclic carbonate (4*R*,5*S*)-**4a** ($[\alpha]_D^{26}$ +10.9 (*c* 1.68, MeOH), 97% ee) in 43% yield and the resulting optically pure diol (2*R*,3*S*)-**3a** ($[\alpha]_D^{25}$ −14.0 (*c* 2.54, MeOH)) in 40% yield (conv.=0.49, *E* value[3]=>200). Although, we have already reported the hydrolysis of *cis*-4,5-dimethyl-1,3-dioxolan-2-one (**38a**; the *meso*-cyclic carbonate bearing a dimethyl group) as the C_1-symmetrical substrate,[6a] this is the first



Scheme 2. (i) BnBr, NaH/THF, reflux ((*E*)-**2b**, 98%); (ii) cat. OsO_4, NMO/acetone/H_2O, rt (**3a**, 86% from **1a**; **3b**, 63%; **8a**, 49%; **8b**, 87%; **9a**, 82%; **10a**, 55%); (iii) triphosgene, Py/CH_2Cl_2, $-78\rightarrow0$ °C (**4a**, 92%; **4b**, 96%; **11a**, 78%; **11b**, 85%; **12a**, 60%; **13a**, 97%).

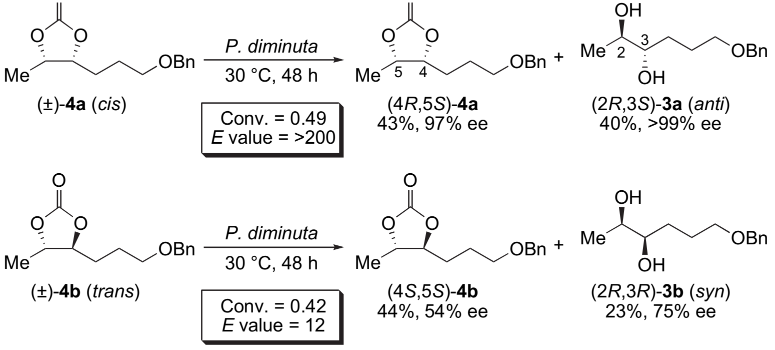


Scheme 3. (i) Morpholine, reflux (69%); (ii) MPMCl, NaH/THF, rt (87%); (iii) $CH_2{=}CHCH_2CH_2MgBr$/THF, rt (74%); (iv) $ZnBH_4/Et_2O$ (48%); (v) cat. *p*-TsOH/MeOH (76%); (vi) triphosgene, Py/CH_2Cl_2, −78→0 °C (51%).

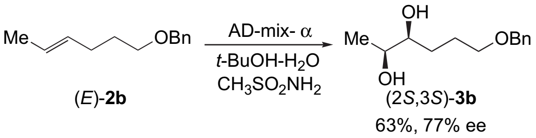


Scheme 4. (i) cat. *p*-TsOH, ethylene glycol/benzene, reflux (73%); (ii) $LiAlH_4$/THF, rt (91%); (iii) $(COCl)_2$, DMSO, Et_3N/CH_2Cl_2, −78 °C→rt (75%); (iv) $CH_2{=}CHCH_2MgBr$/THF, rt (**24**, 88%); (v) propylmagnesium bromide/THF, rt (**25**, 76%); (vi) 2 M HCl aq/THF (**26**, 71%; **27**, 79%); (vii) MOMCl, *i*-Pr_2NH/CH_2Cl_2 (89%); (viii) $BH_3\cdot$THF/THF then 2 M NaOH aq, H_2O_2 (90%); (ix) BnBr, NaH/THF (88%); (x) 2 M HCl aq/THF (71%); (xi) *Procedure A*, $NaBH_4$/MeOH (**32a** (56%)+**32b** (28%); **33a** (64%)+**33b** (32%); **34a** (50%)+**34b** (34%)); (xii) *Procedure B*, $MeNB(OAc)_3H$/AcOH/CH_3CN (**32a** (24%)+**32b** (73%); **33a** (16%)+**33b** (78%); **34a** (37%)+**34b** (56%)); (xiii) triphosgene, Py/CH_2Cl_2, −78 °C→rt (**35a**, 78%; **35b**, 55%; **36a**, 30%; **36b**, 42%; **37a**, 79%; **37b**, 76%).

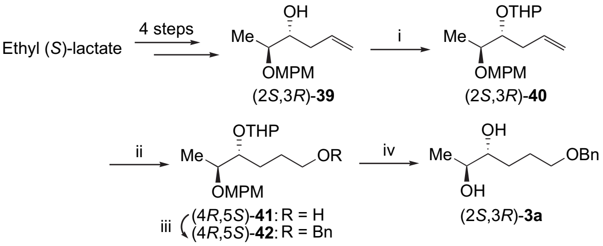
example of the enantioselective hydrolysis of the *cis*-disubstituted carbonates. The absolute configuration of the *anti*-diol was determined by comparing the optical rotation with that of the optically active authentic (2*S*,3*R*)-**3a** ($[\alpha]_D^{25}$ +12.9 (*c* 1.34, MeOH)), which was prepared from ethyl (*S*)-lactate in seven steps (Scheme 7). In the case of *anti*-1,2-diol, the asymmetric dihydroxylation of (*Z*)-**2a** with AD-mix-α proceeded with very low enantioselectivity to give (2*R*,3*S*)-**3a** in only 18% ee. These show that the microbial hydrolysis apparently has some advantage for the preparation of optically active *anti*-1,2-diol with high ee.



Scheme 5.

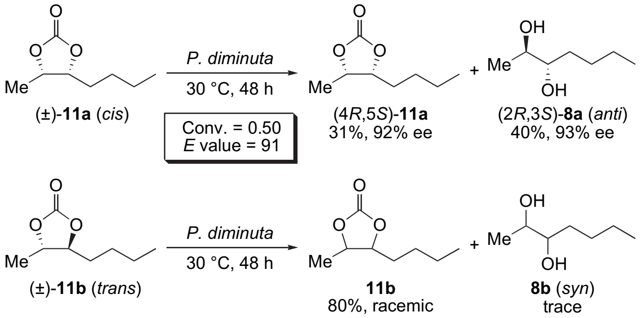


Scheme 6.



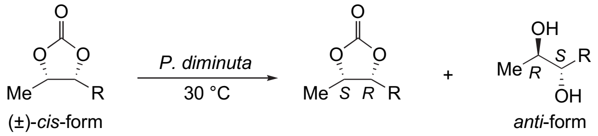
Scheme 7. (i) DHP, *p*-TsOH/CH_2Cl_2 (64%); (ii) $BH_3\cdot THF$/THF then 2 M NaOH aq, H_2O_2 (62%); (iii) BnBr, NaH/THF (81%); (iv) *p*-TsOH/MeOH (38%).

The difference in the reactivity between the diastereomers is noticeably observed during the hydrolysis of the substrates bearing a butyl group ((±)-**11a** and **11b**) as a substituent (Scheme 8). The hydrolysis of the *cis*-substrate (±)-**11a** smoothly proceeded to give optically active compounds, (4*R*,5*S*)-**11a** (92% ee, $[\alpha]_D^{22}$ +14.6 (*c* 1.04, MeOH)) in 31% yield and (2*R*,3*S*)-**8a** (93% ee, $[\alpha]_D^{23}$ −22.0 (*c* 0.82, MeOH)) in 40% yields (reaction for 48 h; conv.=0.50, *E* value=91). Interestingly, in the case of the *trans*-isomer (±)-**11b**, the enzyme scarcely catalyzed the substrate at all.



Scheme 8.

Then, we applied the microbial reaction to several five-membered *cis*-cyclic carbonates (Scheme 9, Table 1). As expected, all the substrates were hydrolyzed with high enantioselectivity. The reaction of the substrate bearing an unsaturated substituent (R=3-butenyl, (±)-**19a**, entry 3) gave a result similar to that of (±)-**11a**, which has the corresponding saturated group. The bacterium smoothly catalyzed the hydrolysis of (±)-**19a** for 48 h to give the optically active (4*R*,5*S*)-**19a** (63% ee) and (2*R*,3*S*)-**18a** (95% ee) in 46 and 42% yields, respectively (conv.=0.40, *E* value=75). The optically active **18a** is an important precursor for the synthesis of a biologically active deoxysugar, D-amicetose.[8] On the other hand, the substrates bearing a longer chain, (±)-**12a** (R=pentyl, entry 1) and **13a** (R=heptyl, entry 2) showed excellent enantioselectivities, although the reactivities were low. For the reactions going for 96 h, the resulting (2*R*,3*S*)-**9a** and **10a** were obtained in their optically pure forms, and the *E* values were over 200.



Scheme 9.

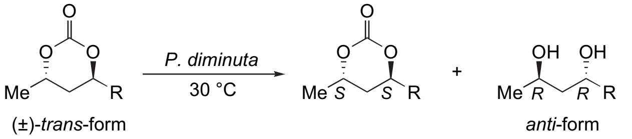
Next, our attention focused on the ring size of the substrate, and we tried the reaction of racemic six-membered cyclic carbonates (Scheme 10, Table 2). As expected, *P. diminuta* catalyzed the hydrolysis of all the substrates examined to afford the corresponding 1,3-diols. The stereoselective manner, however, was quite different from that of the five-membered substrates. In the case of the *trans*-substrate bearing an allyl group (**35b**, entry 1), the substrate was smoothly hydrolyzed with good enantioselectivity to give the optically active remaining (4*S*,6*S*)-**35b** (72% ee) in 39% yield and the resulting (2*R*,4*R*)-**32b** (84% ee, $[\alpha]_D^{21}$ −29.7 (*c* 0.66, $CHCl_3$)) in 26% yield (reaction for 48 h; conv.=0.46, *E* value=25). The absolute configuration of the diol **32b** was determined by comparing the optical rotation with that reported; (2*R*,4*R*)-**32b** (96% ee), lit.[9] $[\alpha]_D^{23}$ −34.1 (*c* 1.13, $CHCl_3$). The reaction for 72 h (entry 2) gave optically pure (4*S*,6*S*)-**35b** in 27% yield. It is noteworthy that the enzyme preferentially catalyzes the hydrolysis of (*R*)-enantiomer at the asymmetric center bearing a methyl group as

Table 1. Microbial hydrolysis of several five-membered (±)-*cis*-cyclic carbonates[a]

Entry	R	Time (h)	Carbonate			Diol			Conv.[b]	*E*[c]
				Yield (%)	ee (%)		Yield (%)	ee (%)		
1	Pentyl	96	**12a**	77	18[d]	**9a**	14	>99[e]	0.15	>200
2	Heptyl	96	**13a**	84	13[f]	**10a**	11	>99[g]	0.12	>200
3	3-Butenyl	48	**19a**	46	63[h]	**18a**	42	95[i]	0.40	75

[a] The reaction was performed using 10 mM of the substrate.
[b] Calculated by ee(carbonate)/[ee(carbonate)+ee(diol)].
[c] Calculated by ln[(1−conv.)(1−ee(carbonate))]/ln[(1−conv.)(1+ee(carbonate))].
[d] $[\alpha]_D^{28}$ +6.10 (*c* 1.08, MeOH).
[e] $[\alpha]_D^{28}$ −20.4 (*c* 0.89, MeOH).
[f] $[\alpha]_D^{29}$ +3.58 (*c* 0.79, MeOH).
[g] $[\alpha]_D^{24}$ −10.1 (*c* 0.39, MeOH).
[h] $[\alpha]_D^{23}$ +7.93 (*c* 1.20, MeOH).
[i] $[\alpha]_D^{23}$ −19.1 (*c* 1.31, MeOH).

well as that in the case of the five-membered substrates. Changing the substituent from allyl to propyl (**36b**, entry 3) and 3-benzyloxypropyl (**37b**, entry 4) decreased the reactivity and the enantioselectivity. For example, the reaction of **36b** for 48 h gave the optically active (2*R*,4*R*)-**33b** in 84% ee, but the conversion and *E* value were only 0.10 and 13, respectively. The longer reaction time scarcely improved the conversion at all. Interestingly, although the enzyme accelerated the hydrolysis of the cis-substrates and the reactions for 48 h gave the remaining carbonates (**35a**, 37%; **36a**, 48%; **37a**, 47%) and the corresponding diols (**32a**, 31%; **33a**, 28%; **34a**, 18%), all of the products were almost racemates.



Scheme 10.

Based on all of our observations, we can formulate an empirical rule for predicting the enantioselectivity in this microbial reaction.[10] For the rigid five-membered substrates, the active site model is illustrated in Figure 1. First, a methyl group at C-5 position of the substrates is necessary for the enantioselective reaction because we have also found that monosubstituted cyclic carbonates (R^1=H), such as 4-methyl-1,3-dioxolan-2-one (**43**) and 4-(2-benzyloxy)ethyl-1,3-dioxolan-2-one (**44**) in Figure 2, are smoothly hydrolyzed without enantioselectivity. Second, the enzyme prefers (5*R*)-substrates in all cases. These results indicate that the enzyme apparently distinguishes the stereochemistry at the asymmetric center substituted with a methyl group and the *cis*-(5*R*)-substrate is most suitable for the active site of the enzyme (R^1=Me, R^2=alkyl, R^3=H). In the case of the fast reactive enantiomer, the methyl group would locate at the *S* (small)-pocket, with hydrogen in *H*-site, and with R^2 group in *L* (large)-pocket. In the reaction of *trans*-substrates, the elongation of the substituent (R^3) at the C-4 position decreases both the reactivity and the enantioselectivity. Because the introduction of a benzyloxy group on the side chain could improve the reactivity, the oxygen atom of the substrates could play an important role for the interaction between the substrates and the enzyme.

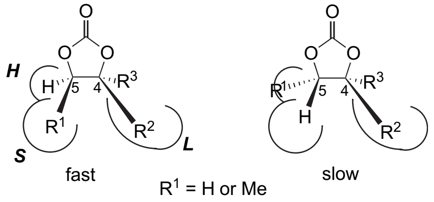
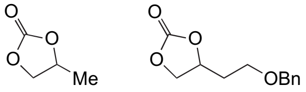


Figure 1.



43 **44**

Figure 2.

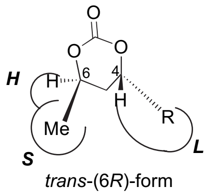


Figure 3.

On the other hand, for the six-membered *trans*-cyclic carbonates, R group at the pseudo-equatorial position could turn to *L*-pocket when the pseudo-axial methyl group locates at the *S*-pocket (Fig. 3). This indicates that the *trans*-(6*R*)-substrate might be a most preferable isomer. But, it is difficult to understand the stereoselective mode because the six-membered ring is very flexible in comparison with the five-membered ring. Consequently, the enantio- and diastereoselectivity of the hydrolysis was lower than those in the case of the five-membered substrates.

3. Conclusion

In this paper, we have established the microbial enantioselective hydrolysis of five- and six-membered cyclic carbonates bearing two substituents, which are methyl and another groups, as a new route to optically active diols. In particular, this is the first report for the enantioselective hydrolysis of five-membered *cis*-cyclic carbonates, which are favorably hydrolyzed with high enantioselectivity to give the corresponding optically pure *anti*-1,2-diols. Furthermore, we can postulate the active site model for the hydrolase through the microbial reaction for various substrates.

Table 2. Microbial hydrolysis of several six-membered (±)-*trans*-cyclic carbonates[a]

Entry	R	Time (h)	Carbonate			Diol			Conv.[b]	*E*[c]
				Yield (%)	ee (%)		Yield (%)	ee (%)		
1	Allyl	48	**35b**	39	72	**32b**	26	84	0.46	25
2	Allyl	72	**35b**	27	>99[d]	**32b**	29	61	0.62	>20
3	Propyl	48	**36b**	80	10	**33b**	16	84[e]	0.10	13
4	$-(CH_2)_3OBn$	48	**37b**	71	6	**34b**	7	84	0.07	12

[a] The reaction was performed using 10 mM of the substrate.

[b] Calculated by ee(carbonate)/[ee(carbonate)+ee(diol)].

[c] Calculated by ln[(1−conv.)(1−ee(carbonate))]/ln[(1−conv.)(1+ee(carbonate))].

[d] $[\alpha]_D^{20}$ −75.7 (*c* 1.00, $CHCl_3$).

[e] $[\alpha]_D^{22}$ −8.91 (*c* 0.63, $CHCl_3$).

4. Experimental

4.1. General

^{1}H (300 or 500 MHz) and ^{13}C (75 or 125 MHz) NMR spectra were measured on a JEOL JNM AL-300 and α-500 with tetramethylsilane (TMS) as the internal standard. IR spectra were recorded with Shimadzu FTIR-8300 and IR Prestige-21 spectrometers. Mass spectra were obtained with a JEOL EI/FAB mate BU25 Instrument by the EI method. Optical rotations were measured with a Jasco DIP-1000 polarimeter. HPLC data were obtained on Shimadzu LC-10AD$_{VP}$, SPD-10A$_{VP}$, and sic 480II data station (System Instruments Inc.). GLC data were taken on GL Sciences GC 353B and sic 480II data station (System Instruments Inc.). E. Merck Kieselgel 60 F$_{254}$ Art. 5715 was used for analytical TLC. Preparative TLC was performed on E. Merck Kieselgel 60 F$_{254}$ Art. 5744. Column chromatography was performed with Silica Gel 60N (63–210 mm, Kanto Chemical Co. Inc.). Melting points were obtained on a Yanako melting point apparatus and were not corrected. All other chemicals were also obtained from commercial sources.

4.2. Preparation of 1,2-diols

4.2.1. (2*RS*,3*SR*)-(6-Benzyloxy)hexane-2,3-diol ((±)-3a (*anti*)). Under an argon atmosphere, to a suspension of NaH (60% in oil, 900 mg, 22 mmol) in THF (10 mL) was added a solution of (*Z*)-4-hexen-1-ol (**1a**, 2.0 g, 20 mmol) in THF (15 mL) and benzyl bromide (2.9 mL, 24 mmol) at 0 °C. The mixture was stirred for 6 h under reflux, and the reaction was quenched with 0.1 M phosphate buffer (pH 6.5). The products were extracted with AcOEt (×3), 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 on silica gel (hexane/AcOEt=2/1) to give (*Z*)-(6-benzyloxy)-2-hexene (**2a**) as a colorless oil (3.7 g).

To a solution of (*Z*)-**2a** (3.7 g, 19.6 mmol) in acetone (7 mL) and H_2O (3 mL) were added 4-methylmorpholine *N*-oxide (10.0 g, 80 mmol), *t*-BuOH (0.3 mL), and a catalytic amount of OsO_4, and the mixture was stirred for 2 h at room temperature. After addition of NaS_2O_4, stirring for 30 min, and filtration through a Celite pad, the products were extracted with AcOEt (×3), 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 on silica gel (hexane/AcOEt=1/1) to give (±)-**3a** as a colorless oil (3.9 g, 86% from **1a**); IR (neat) 3399, 2930, 1714, 1454, 1277, 1099, 714 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ=1.15 (d, J=6.5 Hz, 3H), 1.41–1.85 (m, 4H), 3.50–3.82 (m, 4H), 4.53 (s, 2H), 7.28–7.38 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ=17.0, 26.5, 28.9, 70.3, 70.5, 73.1, 74.7, 127.7, 128.4, 129.5, 137.9; MS *m/z* (rel intensities) 224 (M$^+$, 5.6%), 206 (2.5), 107 (100), 91 (100); HRMS *m/z* 224.1419 (224.1413 calcd for $C_{13}H_{20}O_3$, M$^+$).

4.2.2. (2*RS*,3*RS*)-(6-Benzyloxy)hexane-2,3-diol ((±)-3b (*syn*)). According to the procedure for the preparation method described above, (*E*)-4-hexen-1-ol (**1b**, 1.02 g, 10.2 mmol) was converted to (*E*)-(6-benzyloxy)-2-hexene (**2b**, 1.90 g, 98%) as a colorless oil. Then, (*E*)-**2b** (56.5 mg, 0.30 mmol) was converted to (±)-**3b** as a colorless oil (41.7 mg, 63%); IR (neat) 3399, 2926, 2857, 1454, 1098, 1072, 737, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ=1.18 (d, J=6.0 Hz, 3H), 1.45–1.52 (m, 1H), 1.62 (br s, 2H), 1.64–1.72 (m, 1H), 1.79 (td, J_1=J_2=6.0 Hz, 1H), 3.34 (ddd, J_1=3.0 Hz, J_2=6.5 Hz, J_3=9.5 Hz, 1H), 3.54 (t, J=6.0 Hz, 2H), 3.56–3.62 (m, 1H), 4.23 (s, 2H), 7.26–7.38 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=19.3, 26.0, 30.9, 70.5, 70.9, 73.2, 75.8, 127.8, 128.5, 137.9; MS *m/z* (rel intensities) 224 (M$^+$, 1.7%), 206 (0.6), 107 (34), 91 (100); HRMS *m/z* 224.1412 (224.1413 calcd for $C_6H_{14}O_2$, M$^+$).

4.2.3. (2*RS*,3*SR*)-Heptane-2,3-diol ((±)-8a (*anti*)). According to the procedure for the preparation of **3a** described above, (*Z*)-2-heptene (**5a**, 564 mg, 5.75 mmol) was converted to (±)-**8a** as a colorless oil (375 mg, 49%); IR (neat) 3379, 2932, 1462, 1379, 1055, 984, 737 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ=0.92 (t, J=7.0 Hz, 3H), 1.14 (d, J=6.5 Hz, 3H), 1.24–1.43 (m, 5H), 1.43–1.53 (m, 1H), 2.39 (br s, 2H), 3.54–3.65 (m, 1H), 3.79 (qd, J_1=3.0 Hz, J_2=6.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=14.0, 16.5, 22.7, 28.2, 31.4, 70.4, 74.9; MS *m/z* (rel intensities) 132 (M$^+$, 5.6%), 113 (37), 104 (28), 83 (46), 71 (90), 57 (100); HRMS *m/z* 132.1137 (132.1150 calcd for $C_7H_{16}O_2$, M$^+$).

4.2.4. (2*RS*,3*RS*)-Heptane-2,3-diol ((±)-8b (*syn*)). According to the procedure for the preparation of **3a** described above, (*E*)-2-heptene (**5b**, 1.01 g, 10.4 mmol) was converted to ((±)-**8b** as a colorless oil (1.18 g, 87%); IR (neat) 3370, 2957, 2934, 2872, 1458, 1375, 1057 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ=0.92 (t, J=7.0 Hz, 3H), 1.20 (d, J=6.0 Hz, 3H), 1.33–1.52 (m, 6H), 2.29 (br s, 2H), 3.31–3.36 (m, 1H), 3.60 (qd, J_1=J_2=6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=14.0, 19.5, 22.7, 27.7, 33.1, 70.9, 76.2; MS *m/z* (rel intensities) 132 (M$^+$, 12%), 114 (11), 107 (31), 91 (100), 71 (51); HRMS *m/z* 132.1151 (132.1150 calcd for $C_7H_{16}O_2$, M$^+$).

4.2.5. (2*RS*,3*SR*)-Octane-2,3-diol ((±)-9a (*anti*)). According to the procedure for the preparation of **3a** described above, (*Z*)-2-octene (**6a**, 2.02 g, 18.1 mmol) was converted to (±)-**9a** as a colorless oil (2.15 g, 82%); IR (neat) 3285, 2955, 2940, 2916, 2857, 1485, 1069, 1055 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ=0.90 (t, J=7.0 Hz, 3H), 1.15 (d, J=6.5 Hz, 3H), 1.25–1.36 (m, 5H), 1.37–1.43 (m, 2H), 1.46–1.55 (m, 1H), 1.70 (br s, 1H), 1.98 (br s, 1H), 3.61–3.64 (m, 1H), 3.77–3.83 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ=14.0, 16.6, 22.6, 25.7, 31.7, 31.9, 70.4, 74.9; MS *m/z* (rel intensities) 146 (M$^+$, 6.9%), 128 (18), 110 (16), 101 (100), 99 (42), 85 (39); HRMS *m/z* 146.1361 (146.1307 calcd for $C_8H_{18}O_2$, M$^+$).

4.2.6. (2*RS*,3*SR*)-Decane-2,3-diol ((±)-10a (*anti*)). According to the procedure for the preparation of **3a** described above, (*Z*)-2-decene (**7a**, 656 mg, 4.68 mmol) was converted to (±)-**10a** as a colorless oil (446 mg, 55%); IR (neat) 3293, 2955, 2916, 2853, 1487, 1468, 1069 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ=0.88 (t, J=7.0 Hz, 3H), 1.15 (d, J=6.5 Hz, 3H), 1.21–1.51 (m, 12H), 1.82 (br s, 2H), 3.59–3.64 (m, 1H), 3.76–3.83 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ=14.1, 16.6, 22.6, 26.0, 29.2, 29.6, 31.8, 70.4, 74.9; MS *m/z* (rel intensities) 174 (M^+, 7.6%), 156 (4.8), 138 (6.3), 129 (100), 113 (14), 99 (15); HRMS *m/z* 174.1625 (174.1620 calcd for $C_{10}H_{22}O_2$, M^+).

4.2.7. (2*RS*,3*SR*)-6-Heptene-2,3-diol ((±)-18a (*anti*)). To ethyl (±)-lactate (10.0 g, 0.08 mol) was added morpholine (14.8 g, 0.17 mol), and the mixture was stirred overnight under reflux. After removal of the excess morpholine in vacuo, the residue was purified by distillation under reduced pressure to afford (±)-2-hydroxy-1-morpholinopropan-1-one (**14**) as a colorless oil (9.35 g, 69%); bp 109–110 °C/3 mmHg; IR (neat) 3420, 2858, 2341, 1643, 1439, 1273, 1115, 845, 571 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ=1.33 (d, J=6.5 Hz, 3H), 3.38–3.76 (m, 8H), 3.87 (br s, 1H), 4.45 (q, J=6.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=21.1, 42.6, 45.2, 63.9, 66.2, 66.6, 173.6.

Under an argon atmosphere, to a suspension of NaH (553 mg, 13.8 mmol, 60% in oil) in THF (20 mL) was added a solution of (±)-**14** (2.0 g, 12.6 mmol) in THF (10 mL) and *p*-methoxybenzyl chloride (1.9 mL, 2.2 g, 13.8 mmol) at 0 °C. After the mixture was stirred for 24 h at room temperature, the reaction was stopped with 0.2 M phosphate buffer (pH 6.5). The products were extracted with AcOEt (×3), 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 on silica gel (hexane/AcOEt=1/1) to give (±)-2-(4-methoxybenzyloxy)-1-morpholinopropan-1-one (**15**) as a colorless oil (3.06 g, 87%); IR (neat) 2961, 2903, 2857, 1647, 1514, 1464, 1437, 1248 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ=1.43 (d, J=7.0 Hz, 3H), 3.60–3.67 (m, 8H), 3.80 (s, 3H), 4.30 (q, J=7.0 Hz, 1H), 4.40 (d, J=11.5 Hz, 1H), 4.52 (d, J=11.5 Hz, 1H), 6.88 (d, J=8.5 Hz, 2H), 7.25 (dd, J_1=2.5 Hz, J_2=8.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=17.8, 42.4, 45.6, 55.2, 66.7, 67.0, 70.8, 75.0, 113.8, 129.4, 129.5, 159.4, 170.7.

Under an argon atmosphere, to a solution of (±)-**15** (4.6 g, 16.5 mmol) in THF (40 mL) was added 3-butenylmagnesium bromide (90 mL, 2.2 M in THF) at 0 °C and stirred for 24 h at room temperature. After the reaction was stopped with satd NH_4Cl aqueous solution, the products were extracted with AcOEt (×3), 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 on silica gel (hexane/AcOEt=10/1) to give (±)-2-(4-methoxybenzyloxy)-6-hepten-3-one (**16**) as a colorless oil (3.03 g, 74%); IR (neat) 2978, 2936, 2837, 1717, 1514, 1250, 1111 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ=1.32 (d, J=7.0 Hz, 3H), 2.28–2.35 (m, 2H), 2.63 (td, J_1=7.5 Hz, J_2=17.5 Hz, 1H), 2.67 (td, J_1=7.5 Hz, J_2=17.5 Hz, 1H), 3.80 (s, 3H), 3.91 (q, J=6.5 Hz, 1H), 4.44 (d, J=11.5 Hz, 1H), 4.47 (d, J=11.5 Hz, 1H), 4.91–5.07 (m, 2H), 5.81 (tdd, J_1=6.5 Hz, J_2=10.5 Hz, J_3=17.0 Hz, 1H), 6.86–6.91 (m, 2H), 7.23–7.29 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=17.4, 27.2, 36.5, 55.3, 71.6, 80.3, 113.9, 115.2, 129.4, 129.6, 137.2, 159.4, 212.2.

Under an argon atmosphere, to a solution of (±)-**16** (2.0 g, 8.06 mmol) in Et_2O (30 mL) was slowly added $Zn(BH_4)_2$ (120 mL, ca. 0.13 M in Et_2O) at −30 °C, and the mixture was stirred for 24 h. The reaction was quenched with 0.2 M phosphate buffer (pH 6.5). The products were extracted with AcOEt (×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 on silica gel (hexane/AcOEt=10/1) to give (2*RS*,3*SR*)-2-(4-methoxybenzyloxy)-6-hepten-3-one ((±)-**17**) as a colorless oil (962 mg, 48%). The diastereoselectivity was not determined, but the amount of the minor isomer was very small; IR (neat) 3447, 2928, 2855, 1613, 1514, 1248, 1080, 1036 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ=1.15 (d, J=6.5 Hz, 3H), 1.41–1.59 (m, 2H), 1.63 (br s, 1H), 2.03–2.18 (m, 1H), 2.20–2.34 (m, 1H), 3.49 (dq, J_1=3.5 Hz, J_2=6.5 Hz, 1H), 3.69–3.78 (m, 1H), 3.80 (s, 3H), 4.44 (d, J=11.5 Hz, 1H), 4.53 (d, J=11.5 Hz, 1H), 4.94–5.07 (m, 2H), 5.83 (tdd, J_1=6.5 Hz, J_2=10.5 Hz, J_3=17.0 Hz, 1H), 6.85–6.90 (m, 2H), 7.23–7.28 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=14.2, 22.6, 31.6, 55.3, 60.4, 70.3, 72.4, 113.8, 114.8, 129.2, 138.4, 157.8.

To a solution of (±)-**17** (195 mg, 0.78 mmol) in MeOH (30 mL) was added a catalytic amount of *p*-TsOH at room temperature, and stirred overnight. The reaction was stopped with satd $NaHCO_3$ aqueous solution, and the products were extracted with AcOEt (×3), and dried over Na_2SO_4. After evaporation under reduced pressure, the residue was purified by flash column chromatography on silica gel (hexane/AcOEt=5/1) to give (±)-**18a** (*anti*) as a colorless oil (77.4 mg, 76%); IR (neat) 3377, 3077, 2974, 2926, 2855, 1641, 1449, 1065, 910 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ=1.16 (d, J=6.5 Hz, 3H), 1.52 (dt, J_1=6.5 Hz, J_2=7.5 Hz, 2H), 1.96 (br s, 2H), 2.04–2.30 (m, 2H), 3.64 (dt, J_1=3.5 Hz, J_2=6.5 Hz, 1H), 3.81 (qd, J_1=3.5 Hz, J_2=6.5 Hz, 1H), 5.07 (tdd, J_1=J_2=1.5 Hz, J_3=17.0 Hz, 2H), 5.85 (tdd, J_1=6.5 Hz, J_2=10.5 Hz, J_3=17.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=16.7, 30.2, 30.7, 70.4, 74.4, 115.1, 138.3; MS *m/z* (rel intensities) 130 (M^+, 2.0%), 112 (6.1), 94 (4.4), 85 (8.4), 83 (15), 73 (13); HRMS *m/z* 130.0946 (130.0994 calcd for $C_7H_{14}O_2$, M^+).

4.3. Preparation of 1,3-diols

4.3.1. (2*RS*,4*SR*)- and (2*RS*,4*RS*)-6-Heptene-2,4-diol ((±)-32a (*syn*) and (±)-32b (*anti*)). To a solution of ethyl 3-oxobutanoate (**20**, 30.0 g, 231 mmol) in benzene (60 mL) were added a solution of ethylene glycol (42.9 g, 691.6 mmol) in benzene (60 mL) and a catalytic amount of *p*-TsOH at room temperature. After the mixture was stirred for 20 h under reflux, the reaction was stopped with satd $NaHCO_3$ aqueous solution at 0 °C. The organic layer was washed with satd $NaHCO_3$ aqueous solution (×3) and brine, and dried over Na_2SO_4. After evaporation under reduced pressure, the residue was purified by distillation to give ethyl (2-methyl-1,3-dioxolan-2-yl)acetate (**21**) as a colorless oil (29.4 g, 73%); bp 90–120 °C (23 mmHg); IR (neat) 3468, 2889, 1744, 1377, 1225, 1049 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=1.27 (t, J=7.0 Hz, 2H), 1.51 (s, 3H), 2.67 (s, 2H), 3.99 (s, 4H), 4.16 (q, J=7.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=14.2, 24.5, 44.2, 60.5, 64.8, 107.6.

Under an argon atmosphere, to a suspension of $LiAlH_4$ (15.0 g, 86.2 mmol) in THF (150 mL) was added a solution of **21** (3.30 g, 86.2 mmol) in THF (90 mL) at 0 °C. The mixture was stirred for 1 h. The reaction was quenched slowly with H_2O (3.3 mL), 15% NaOH (3.3 mL), H_2O (6.6 mL) at 0 °C, and the mixture was stirred for 24 h. After filtration through a Celite pad and evaporation under reduced pressure, the residue was purified by distillation to give 2-(2-methyl-1,3-dioxolan-2-yl)ethanol (**22**) as a colorless oil (10.3 g, 91%); bp 100–114 °C (24 mmHg); IR (neat) 3383, 1651, 1381, 1150, 1016 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=1.37 (s, 3H), 1.95 (t, J=5.5 Hz, 2H), 2.94 (t, J=5.5 Hz, 1H), 3.76 (dt, J_1=J_2=5.5 Hz, 2H), 4.0 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=23.8, 40.3, 59.0, 64.5, 110.0.

Under an argon atmosphere, to a solution of oxalyl chloride (5.77 g, 45.5 mmol) in CH_2Cl_2 (30 mL) was added a solution of DMSO (7.09 g, 90.1 mmol) in CH_2Cl_2 (30 mL) at −78 °C. After 5 min, a solution of **22** (5.01 g, 37.9 mmol) in THF (40 mL) was added to the mixture at −78 °C, and the mixture was stirred for 10 min. After an addition of triethylamine (13.8 g, 136.4 mmol) to the solution at −78 °C, the mixture was warmed up to 0 °C. The reaction was stopped with 0.1 M phosphate buffer (pH 6.5). The products were extracted with AcOEt (×3), 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 on silica gel (hexane/AcOEt=6/1→5/1→3/1) to give 3-(1,3-dioxolan-2-yl)-butanal (**23**) as a colorless oil (3.71 g, 75%); IR (neat) 1715, 1418, 1385, 1360, 1132, 1047 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ=1.43 (s, 3H), 2.72 (d, J=3.0 Hz, 2H), 3.93–4.07 (m, 4H), 9.76 (t, J=3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=25.0, 52.5, 64.8, 107.6, 200.2.

Under an argon atmosphere, to a solution of **23** (610 mg, 4.69 mmol) in THF (80 mL) was added a solution of allylmagnesium bromide (9.38 mL, 1.0 M THF solution) at 0 °C. After the mixture was stirred for 1 h, the reaction was stopped with satd NH_4Cl aqueous solution at 0 °C. The products were extracted with AcOEt (×3), 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 on silica gel (hexane/AcOEt=5/1) to give (±)-2-methyl-2-(2-hydroxy-4-penten)-1,3-dioxolane (**24**) as a colorless oil (700 mg, 88%); IR (neat) 2982, 1641, 1217, 1107, 1045 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ=1.37 (s, 3H), 1.70–1.95 (m, 2H), 2.10–2.35 (m, 2H), 3.57 (s, 1H), 3.92–4.03 (m, 1H), 3.98–4.03 (s, 4H), 5.02–5.18 (m, 2H), 5.85 (tdd, J_1=7.0 Hz, J_2=10 Hz, J_3=17 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=24.1, 41.7, 44.2, 64.3, 64.7, 67.5, 110.4, 117.3, 134.8.

To a solution of (±)-**24** (1.00 g, 5.83 mmol) in THF (20 mL) was added a solution of 2 M HCl aq (20 mL) at 0 °C. The mixture was stirred for 6 h and the reaction was stopped with H_2O at 0 °C. The products were extracted with AcOEt (×3), 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 on silica gel (hexane/AcOEt=5/1) to give (±)-4-hydroxy-6-hepten-2-one (**26**) as a colorless oil (530 mg, 71%); IR (neat) 3429, 2924, 1709, 1420, 1167, 997 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ=2.18 (s, 3H), 2.20–2.33 (m, 2H), 2.58 (dd, J_1=8.5 Hz, J_2=17.5 Hz, 1H), 2.63 (dd, J_1=4.0 Hz, J_2=17.5 Hz, 1H), 3.13 (br s, 1H), 4.05–4.20 (m, 1H), 5.02–5.20 (m, 2H), 5.70–5.90 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=30.7, 40.8, 49.1, 66.9, 118.0, 134.1, 209.6.

Procedure A: to a solution of (±)-**26** (810 mg, 6.33 mmol) in MeOH (40 mL) was added sodium borohydride (479 mg, 12.7 mmol) at 0 °C. After the mixture was stirred for 2 h at room temperature, the reaction was stopped with brine at 0 °C. The products were extracted with AcOEt (×3), 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 on silica gel (hexane/AcOEt=3/1) to give (±)-**32a** (*syn*) and (±)-**32b** (*anti*) as colorless oils (**32a**, 446 mg, 56%; **32b**, 223 mg, 28%).

Procedure B: under an argon atmosphere, to Me_4NBH_4 (1.07 g, 12.0 mol) were slowly added AcOH (4 mL) at 0 °C and CH_3CN (11 mL) at room temperature, and the mixture was stirred for 30 min. After the addition of (±)-**26** (699 mg, 5.46 mmol) in CH_3CN (10 mL) at 0 °C and stirring for 3 h, the reaction was quenched with 0.5 M $C_4H_4KNaO_6$ aqueous solution (10 mL). The products were extracted with AcOEt (×3), and the organic layer was washed with satd $NaHCO_3$ aqueous solution, brine, and dried over Na_2SO_4. After evaporation under reduced pressure, the residue was purified by flash column chromatography on silica gel (hexane/AcOEt=3/1) to give (±)-**32a** (*syn*) and (±)-**32b** (*anti*) as colorless oils (**32a**, 172 mg, 24%; **32b**, 516 mg, 73%).

Compound (±)-**32a** (*syn*): IR (neat) 3339, 3077, 2969, 2932, 1641, 1418, 1375, 1325 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=1.21 (d, J=6.0 Hz, 3H), 1.51 (td, J_1=10.0 Hz, J_2=14.5 Hz, 1H), 1.61 (td, J_1=2.5 Hz, J_2=14.0 Hz, 1H), 2.17–2.25 (m, 2H), 3.10 (br s, 1H), 3.29 (br s, 1H), 3.83–3.97 (m, 1H), 3.98–4.17 (m, 1H), 5.10–5.20 (m, 2H), 5.76–5.88 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=24.0, 42.6, 44.1, 68.9, 71.8, 118.3, 134.2; MS *m/z* (rel intensities) 131 (M^++H, 11%), 112 (36), 94 (41), 89 (100), 87 (69), 73 (28); HRMS *m/z* 131.1060 (131.1072 calcd for $C_7H_{15}O_2$, M^++H).

Compound (±)-**32b** (*anti*): IR (neat) 3368, 3077, 2970, 2932, 1641, 1412, 1375, 1350 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=1.24 (d, J=6.0 Hz, 3H), 1.62 (dd, J_1=J_2=6.0 Hz, 2H), 2.18–2.32 (m, 2H), 2.64 (br s, 2H), 4.00 (tt, J_1=J_2=6.0 Hz, 1H), 4.16 (tq, J_1=J_2=6.0 Hz, 1H), 5.05–5.20 (m, 2H), 5.74–5.90 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=23.5, 41.9, 43.5, 65.4, 68.1, 118.3, 134.6; MS *m/z* (rel intensities) 130 (M^+, 5.5%), 112 (20), 94 (13), 89 (11), 85 (54), 71 (95); HRMS *m/z* 130.0995 (130.0994 calcd for $C_7H_{14}O_2$, M^+).

4.3.2. (2*RS*,4*SR*)- and (2*RS*,4*RS*)-heptane-2,4-diol ((±)-33a (*syn*) and (±)-33b (*anti*)). According to the procedure for the preparation of **24** described above, the aldehyde **23** (1.15 g, 8.82 mmol) was converted to (±)-1-(2-methyl-1,3-dioxolan-2-yl)-2-pentanol (**25**) as a colorless oil (1.17 g, 76%); IR (neat) 3526, 2957, 2934, 2874, 1377, 1256, 1219, 1044 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, J=7.0 Hz, 3H), 1.22–1.60 (m, 4H), 1.37 (s, 3H), 1.76 (dd, J_1=9.0 Hz, J_2=14.5 Hz, 1H), 1.82 (dd, J_1=2.0 Hz, J_2=14.5 Hz, 1H), 3.56 (s, 1H), 3.85–3.95 (m, 1H), 3.95–4.06 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=14.1, 18.6, 24.1, 39.5, 44.8, 64.2, 64.7, 67.7, 110.4.

According to the procedure for the preparation of **26** described above, **25** (602 mg, 3.46 mmol) was converted to (±)-4-hydroxy-2-heptanone (**27**) as a colorless oil (356 mg, 79%); IR (neat) 3441, 2959, 2932, 2874, 1713, 1418, 1362, 1167 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ=0.93 (t, J=7.0 Hz, 3H), 1.20–1.57 (m, 4H), 2.18 (s, 3H), 2.54 (dd, J_1=9.0 Hz, J_2=17.5 Hz, 1H), 2.61 (dd, J_1=3.0 Hz, J_2=17.5 Hz, 1H), 2.97 (br s, 1H), 3.90–4.10 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=13.9, 18.6, 30.7, 38.5, 49.9, 67.3, 210.0.

Procedure A: according to the procedure for the preparation of **32** described above, (±)-**27** (645 mg, 4.96 mmol) was converted to (±)-**33a** (*syn*) and (±)-**33b** (*anti*) as colorless oils (**33a**, 420 mg, 64%; **33b**, 210 mg, 32%).

Procedure B: according to the procedure for the preparation of **32** described above, (±)-**27** (566 mg, 4.35 mmol) was converted to (±)-**33a** (*syn*) and (±)-**33b** (*anti*) as colorless oils (**33a**, 89.0 mg, 16%; **33b**, 445 mg, 78%).

Compound **33a** (*syn*): IR (neat) 3349, 2961, 2932, 2872, 1418, 1375, 1323 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ=0.93 (t, J=7.0 Hz, 3H), 1.21 (d, J=6.5 Hz, 3H), 1.29–1.62 (m, 6H), 2.97 (br s, 2H), 3.86–3.88 (m, 1H), 4.01–4.10 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ=14.0, 18.4, 24.2, 40.4, 44.6, 69.2, 72.8; MS *m/z* (rel intensities) 132 (M^+, 6.1%), 114 (100), 101 (6.7), 96 (41), 87 (20), 71 (100); HRMS *m/z* 132.1119 (132.1150 calcd for $C_7H_{16}O_2$, M^+).

Compound **33b** (*anti*): IR (neat) 3348, 2961, 2932, 2872, 1456, 1418, 1377, 1325 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ=0.94 (t, J=7.0 Hz, 3H), 1.24 (d, J=6.0 Hz, 3H), 1.10–1.81 (m, 4H), 1.61 (dd, J_1=5.0 Hz, J_2=6.0 Hz, 2H), 2.50 (br s, 2H), 3.90–4.01 (m, 1H), 4.08–4.25 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=14.0, 18.9, 23.5, 39.5, 43.9, 65.5, 69.1; MS *m/z* (rel intensities) 132 (M^+, 2.0%), 114 (28), 101 (17), 96 (25), 87 (13), 71 (90); HRMS *m/z* 132.1141 (132.1150 calcd for $C_7H_{16}O_2$, M^+).

4.3.3. (*2RS*,*4SR*)- and (*2RS*,*4RS*)-7-benzyloxyheptane-2,4-diol ((±)-34a (*syn*) and (±)-34b (*anti*)). Under an argon atmosphere, to a solution of (±)-**24** (2.00 g, 11.6 mmol) in CH_2Cl_2 (30 mL) was added a solution of diisopropylamine (6.1 mL, 34.9 mmol) and chloromethylmethylether (1.8 mL, 23.3 mmol). The mixture was stirred for 17 h at room temperature and the reaction was stopped with 0.1 M phosphate buffer (pH 6.5) at 0 °C. The products were extracted with AcOEt (×3), 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 on silica gel (hexane/AcOEt=10/1→7/1→4/1) to give (±)-2-(2-methoxymethoxypent-4-enyl)-2-methyl-1,3-dioxolane (**28**) as a colorless oil (2.2 g, 89%); IR (neat) 2934, 1639, 1377, 1146, 1040 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ=1.36 (s, 3H), 1.86 (dd, J_1=5.0 Hz, J_2=14.5 Hz, 1H), 1.91 (dd, J_1=6.0 Hz, J_2=14.5 Hz, 1H), 2.25–2.48 (m, 2H), 3.39 (s, 3H), 3.79–3.87 (m, 1H), 3.89–3.98 (m, 4H), 4.67 (d, J=7.0 Hz, 1H), 4.68 (d, J=7.0 Hz, 1H), 5.02–5.14 (m, 2H), 5.84 (tdd, J_1=7.0 Hz, J_2=10.0 Hz, J_3=17.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=24.3, 40.1, 43.1, 55.7, 64.3, 64.4, 73.6, 95.6, 109.0, 117.3, 134.7.

Under an argon atmosphere, to a solution of (±)-**28** (1.00 g, 4.63 mol) in THF (15 mL) was added $BH_3 \cdot THF$ (9.3 mL, 9.26 mol) at 0 °C. The mixture was stirred for 40 min and the reaction was quenched with 2 M NaOH (9.3 mL) and H_2O_2 (9.3 mL). After 1 h, the products were extracted with Et_2O (×3), 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 on silica gel (hexane/AcOEt=1/1) to give (±)-4-methoxymethoxy-5-(2-methyl-1,3-dioxolan-2-yl)-1-pentanol (**29**) as a colorless oil (900 mg, 90%); IR (neat) 3476, 2886, 1036 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ=1.35 (s, 3H), 1.55–2.05 (m, 7H), 3.40 (s, 3H), 3.66 (t, J=7.0 Hz, 2H), 3.75–3.85 (m, 1H), 3.86–4.01 (m, 4H), 4.63 (d, J=7.0 Hz, 1H), 4.72 (d, J=7.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=24.3, 28.1, 32.0, 43.5, 55.7, 62.9, 64.3, 64.5, 73.9, 95.5, 108.9.

Under an argon atmosphere, to a solution of NaH (890 mg, 22.2 mmol) in THF (30 mL) was added a solution of (±)-**29** (2.59 g, 11.1 mmol) in THF (25 mL) and benzyl bromide (1.3 mL, 11.1 mmol) at 0 °C. The mixture was stirred for 48 h under reflux and the reaction was stopped with 0.1 M phosphate buffer (pH 6.5) at 0 °C. The products were extracted with AcOEt (×3), 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 on silica gel (hexane/AcOEt=10/1) to give (±)-2-(5-benzyloxy-2-methoxymethoxypentyl)-2-methyl-1,3-dioxolane (**30**) as a colorless oil (3.2 g, 88%); IR (neat) 2932, 2880, 1454, 1375, 1038, 947, 916, 737, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ=1.35 (s, 3H), 1.50–2.05 (m, 6H), 3.37 (s, 3H), 3.49 (t, J=6.0 Hz, 2H), 3.70–3.81 (m, 1H), 3.82–4.00 (m, 4H), 4.50 (s, 2H), 4.62 (d, J=7.0 Hz, 1H), 4.70 (d, J=7.0 Hz, 1H), 7.20–7.40 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=24.3, 25.1, 32.2, 43.6, 55.7, 64.3, 64.4, 70.3, 72.8, 73.8, 95.4, 108.9, 127.4, 127.5, 128.3, 138.6.

To a solution of (±)-**30** (1.00 g, 3.09 mmol) in THF (50 mL) was added a solution of 2 M HCl aq (20 mL) at 0 °C. The mixture was stirred for 24 h and the reaction was stopped with 0.2 M phosphate buffer (pH 6.5) at 0 °C. The products were extracted with Et_2O (×3), 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 on silica gel (hexane/AcOEt=5/1) to give (±)-7-benzyloxy-4-hydroxy-heptan-2-one (**31**) as a colorless oil (510 mg, 71%); IR (neat) 3433, 2926, 2859, 1711, 1454, 1362, 1099, 739, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ=1.45–1.85 (m, 4H), 2.17 (s, 3H), 2.53–2.63 (m, 2H), 3.29 (br s, 1H), 3.51 (t, J=6.0 Hz, 2H), 4.00–4.10 (m, 1H), 4.51 (s, 2H), 7.27–7.35 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ=25.9, 30.8, 33.5, 50.1, 67.4, 70.2, 73.0, 127.6, 127.7, 128.4, 138.3, 209.7.

Procedure A: according to the procedure for the preparation of **32** described above, (±)-**31** (500 mg, 2.12 mmol) was converted to (±)-**34a** (*syn*) and (±)-**34b** (*anti*) as colorless oils (**34a**, 252 mg, 50%; **34b**, 168 mg, 34%).

Procedure B: according to the procedure for the preparation of **32** described above, (±)-**31** (315 mg, 1.34 mmol) was converted to (±)-**34a** (*syn*) and (±)-**34b** (*anti*) as colorless oils (**34a**, 118 mg, 37%; **34b**, 177 mg, 56%).

Compound **34a** (*syn*): IR (neat) 3383, 2928, 2857, 1454, 1406, 1323, 1099, 737, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ=1.18 (d, J=6.0 Hz, 3H), 1.43–1.80 (m, 6H), 3.52 (t, J=6.0 Hz, 2H), 3.66 (br s, 2H), 3.80–3.92 (m, 1H), 3.97–4.09 (m, 1H), 4.53 (s, 2H), 7.22–7.39 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=23.0, 25.2, 33.8, 44.8, 68.9, 70.0, 72.3, 72.8, 127.6, 127.8, 128.3, 138.5; MS *m/z* (rel intensities) 238 (M^+, 4.9%), 179 (9.2), 149 (100), 107 (66), 99 (43), 91 (100); HRMS *m/z* 238.1570 (238.1569 calcd for $C_{14}H_{22}O_3$, M^+).

Compound **34b** (*anti*): IR (neat) 3377, 2928, 2857, 1454, 1408, 1312, 1099, 737, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ=1.22 (d, J=6.0 Hz, 3H), 1.50–1.82 (m, 6H), 2.80 (br s, 1H), 3.42 (br s, 1H), 3.46–3.59 (m, 2H), 3.90–4.00 (m, 1H), 4.08–4.21 (m, 1H), 4.53 (s, 2H), 7.24–7.39 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ=23.4, 26.5, 34.9, 44.0, 65.4, 69.2, 70.5, 73.1, 127.7, 127.8, 128.4, 137.9; MS *m/z* (rel intensities) 238 (M^+, 7.7%), 179 (79), 147 (21), 131 (77), 107 (100), 91 (100); HRMS *m/z* 238.1572 (238.1569 calcd for $C_{14}H_{22}O_3$, M^+).

4.4. Preparation of five-membered cyclic carbonates

4.4.1. (4*RS*,5*SR*)-4-(3-Benzyloxy)propyl-5-methyl-1,3-dioxolan-2-one ((±)-4a (*cis*)). Under an argon atmosphere, pyridine (7.9 g, 0.10 mmol) was added to a solution of (±)-**3a** (3.9 g, 17.2 mmol) in CH_2Cl_2 (30 mL) at 0 °C, followed by addition of a solution of triphosgene (3.1 g, 10.3 mmol) in CH_2Cl_2 (15 mL) at −78 °C. The mixture was then slowly warmed to 0 °C and stirred for 1 h. The reaction was stopped with a satd 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, satd $NaHCO_3$ aqueous solution, and brine, and dried over Na_2SO_4. After evaporation, the residue was purified by column chromatography on silica gel (hexane/AcOEt=1/1) to give (±)-**4a** as a colorless oil (3.96 g, 92%); IR (neat) 2938, 2859, 1798, 1717, 1452, 1368, 1184, 1074, 743 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ=1.36 (d, J=7.0 Hz, 3H), 1.66–1.90 (m, 4H), 3.48–3.53 (m, 1H), 3.53–3.60 (m, 1H), 4.51 (s, 2H), 4.65 (ddd, J_1=4.0 Hz, J_2=5.5 Hz, J_3=7.0 Hz, 1H), 4.82 (dq, J_1=J_2=7.0 Hz, 1H), 7.28–7.38 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=14.5, 25.9, 69.1, 72.9, 75.9, 79.7, 127.6, 127.7, 128.4, 138.2, 154.6; MS *m/z* (rel intensities) 250 (M^+, 18%), 173 (15), 107 (56), 91 (100); HRMS *m/z* 250.1187 (250.1205 calcd for $C_{14}H_{18}O_4$, M^+).

4.4.2. (4*RS*,5*RS*)-4-(3-Benzyloxy)propyl-5-methyl-1,3-dioxolan-2-one ((±)-4b (*trans*)). According to the procedure for the preparation of **4a** described above, (±)-**3b** (445 mg, 1.99 mmol) was converted to (±)-**4b** (*trans*) as a colorless oil (478 mg, 96%); IR (neat) 2934, 2859, 1798, 1454, 1373, 1186, 1074 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ=1.43 (d, J=6.5 Hz, 3H), 1.59–1.87 (m, 4H), 3.45–3.60 (m, 2H), 4.22 (ddd, J_1=2.0 Hz, J_2=6.5 Hz, J_3=12.0 Hz, 1H), 4.38 (dq, J_1=J_2=6.5 Hz, 1H), 4.50 (s, 2H), 7.27–7.38 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ=19.5, 25.1, 30.2, 69.1, 73.0, 78.4, 83.3, 127.6, 127.7, 128.4, 138.1, 154.5; MS *m/z* (rel intensities) 250 (M^+, 28%), 173 (19), 71 (22), 43 (100); HRMS *m/z* 250.1200 (250.1205 calcd for $C_7H_{12}O_3$, M^+).

4.4.3. (4*RS*,5*SR*)-4-Butyl-5-methyl-1,3-dioxolan-2-one ((±)-11a (*cis*)). According to the procedure for the preparation of **4a** described above, (±)-**8a** (375 mg, 2.84 mmol) was converted to (±)-**11a** (*cis*) as a colorless oil (350 mg, 78%); IR (neat) 2959, 1788, 1462, 1371, 1190, 1070, 777 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ=0.93 (t, J=7.0 Hz, 3H), 1.30–1.42 (m, 3H), 1.36 (d, J=6.5 Hz, 3H), 1.49–1.60 (m, 2H), 1.67–1.78 (m, 1H), 4.64 (ddd, J_1=3.5 Hz, J_2=7.0 Hz, J_3=10.0 Hz, 1H), 4.84 (qd, J_1=J_2=7.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=13.8, 14.5, 22.3, 28.4, 75.9, 79.9, 154.7; MS *m/z* (rel intensities) 159 (M^++H, 4.5%), 101 (46), 85 (100), 72 (100), 57 (100); HRMS *m/z* 159.1046 (159.1021 calcd for $C_8H_{15}O_3$, M^++H).

4.4.4. (4*RS*,5*RS*)-4-Butyl-5-methyl-1,3-dioxolan-2-one ((±)-11b (*trans*)). According to the procedure for the preparation of **4a** described above, (±)-**8b** (1.07 g, 8.10 mmol) was converted to (±)-**11b** (*trans*) as a colorless oil (1.09 g, 85%); IR (neat) 2959, 2934, 2872, 1798, 1454, 1377, 1188, 775 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ=0.93 (t, J=6.5 Hz, 3H), 1.31–1.55 (m, 4H), 1.46 (d, J=6.5 Hz, 3H), 1.60–1.83 (m, 2H), 4.19 (dt, J_1=5.0 Hz, J_2=6.5 Hz, 1H), 4.38 (dq, J_1=J_2=6.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ=13.8, 19.1, 22.3, 26.7, 32.8, 78.4, 83.5, 154.6; MS *m/z* (rel intensities) 159 (M^++H, 2.0%), 101 (17), 85 (36), 71 (61), 57 (100); HRMS *m/z* 159.0966 (159.1021 calcd for $C_8H_{15}O_3$, M^++H).

4.4.5. (4*RS*,5*SR*)-4-Methyl-5-pentyl-1,3-dioxolan-2-one ((±)-12a (*cis*)). According to the procedure for the preparation of **4a** described above, (±)-**9a** (2.08 g, 18.6 mmol) was converted to (±)-**12a** (*cis*) as a colorless oil (1.63 g, 60%); IR (neat) 2957, 2932, 2860, 1798, 1466, 1370, 1186, 1071 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ=0.91 (t, J=7.0 Hz, 3H), 1.23–1.45 (m, 5H), 1.36 (d, J=6.5 Hz, 3H), 1.45–1.64 (m, 2H), 1.64–1.80 (m, 1H), 4.63 (ddd, J_1=3.5 Hz, J_2=7.0 Hz, J_3=10.0 Hz, 1H), 4.82 (dq, J_1=J_2=7.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=13.9, 14.5, 22.4, 25.2, 28.8, 31.4, 75.9, 79.9, 154.6; MS *m/z* (rel intensities) 173 (M^++H, 3.9%), 157 (4.8), 129 (13), 110 (21), 99 (78), 85 (68); HRMS *m/z* 173.1174 (173.1178 calcd for $C_9H_{17}O_3$, M^++H).

4.4.6. (4*RS*,5*SR*)-4-Heptyl-5-methyl-1,3-dioxolan-2-one ((±)-13a (*cis*)). According to the procedure for the preparation of **4a** described above, (±)-**10a** (418 mg, 2.01 mmol) was converted to (±)-**13a** (*cis*) as a colorless oil (405 mg, 97%); IR (neat) 2953, 2928, 2857, 1798, 1370, 1180, 1072 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ=0.89 (t, J=6.0 Hz, 3H), 1.24–1.44 (m, 9H), 1.36 (d, J=6.5 Hz, 3H), 1.45–1.64 (m, 2H), 1.64–1.81 (m, 1H), 4.63 (ddd, J_1=3.5 Hz, J_2=6.5 Hz, J_3=10.0 Hz, 1H), 4.82 (dq, J_1=J_2=6.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=14.0, 14.5, 22.6, 25.6, 28.8, 29.0, 29.2, 31.7, 75.9, 79.9, 154.7; MS *m/z* (rel intensities) 201 (M^++H, 2.1%), 156 (1.9), 138

(29), 127 (33), 113 (17), 99 (11); HRMS *m/z* 201.1490 (201.1491 calcd for $C_{11}H_{21}O_3$, M^++H).

4.4.7. (4*RS*,5*SR*)-4-(3-Butenyl)-5-methyl-1,3-dioxolan-2-one ((±)-19a (*cis*)). According to the procedure for the preparation of **4a** described above, (±)-**18a** (325 mg, 2.50 mmol) was converted to (±)-**19a** (*cis*) as a colorless oil (200 mg, 51%); IR (neat) 2982, 2926, 2853, 1798, 1370, 1186, 1074, 916 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=1.37 (d, J=6.5 Hz, 3H), 1.55–1.69 (m, 1H), 1.75–1.93 (m, 1H), 2.07–2.24 (m, 1H), 2.24–2.75 (m, 1H), 4.61–4.73 (m, 1H), 4.84 (dq, J_1=J_2=6.5 Hz, 1H), 5.00–5.18 (m, 2H), 5.80 (tdd, J_1=6.5 Hz, J_2=10.5 Hz, J_3=17.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ=14.5, 28.1, 29.5, 75.8, 78.9, 116.4, 136.2, 154.5; MS *m/z* (rel intensities) 156 (M^+, 13%), 114 (16), 112 (6.8), 97 (39), 85 (12), 84 (51); HRMS *m/z* 156.0736 (156.0787 calcd for $C_8H_{12}O_3$, M^+).

4.5. Preparation of six-membered cyclic carbonates

4.5.1. (4*RS*,6*SR*)-4-Allyl-6-methyl-1,3-dioxan-2-one ((±)-35a (*cis*)). According to the procedure for the preparation of **4a** described above, (±)-**32a** (100 mg, 0.77 mmol) was converted to (±)-**35a** (*cis*) as a colorless oil (93.2 mg, 78%); IR (neat) 2980, 2936, 1748, 1643, 1400, 1248, 1229, 1117 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=1.42 (d, J=6.0 Hz, 3H), 1.64 (td, J_1=12.0 Hz, J_2=14.0 Hz, 1H), 2.07 (td, J_1=3.0 Hz, J_2=14.0 Hz, 1H), 2.38–2.45 (m, 1H), 2.49–2.56 (m, 1H), 4.48 (ddt, J_1=3.0 Hz, J_2=J_3=6.0 Hz, 1H), 4.56 (ddq, J_1=3.0 Hz, J_2=6.0 Hz, J_3=11.5 Hz, 1H), 5.12–5.22 (m, 2H), 5.76–5.84 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=21.1, 33.9, 75.1, 77.9, 119.4, 131.2, 149.1; MS *m/z* (rel intensities) 157 (M^++H, 3.7%), 141 (3.2), 129 (4.4), 112 (5.0), 97 (15), 87 (8.8); HRMS *m/z* 157.0864 (157.0865 calcd for $C_8H_{13}O_3$, M^++H).

4.5.2. (4*RS*,6*RS*)-4-Allyl-6-methyl-1,3-dioxan-2-one ((±)-35b (*anti*)). According to the procedure for the preparation of **4a** described above, (±)-**32b** (403 mg, 3.10 mmol) was converted to (±)-**35b** (*anti*) as a colorless oil (265 mg, 55%); IR (neat) 2980, 2938, 1746, 1643, 1387, 1254, 1202, 1119 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=1.45 (d, J=6.0 Hz, 3H), 1.90 (ddd, J_1=4.5 Hz, J_2=6.0 Hz, J_3=9.0 Hz, 1H), 2.03 (ddd, J_1=4.5 Hz, J_2=7.0 Hz, J_3=14.0 Hz, 1H), 2.38–2.44 (m, 1H), 2.57–2.63 (m, 1H), 4.56–4.61 (m, 1H), 4.68–4.74 (m, 1H), 5.16–5.23 (m, 2H), 5.75–5.84 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=20.8, 31.5, 39.0, 77.0, 77.3, 119.5, 131.5, 149.2; MS *m/z* (rel intensities) 157 (M^++H, 30%), 141 (2.1), 129 (4.4), 112 (11), 97 (26), 84 (13); HRMS *m/z* 157.0873 (157.0865 calcd for $C_8H_{13}O_3$, M^++H).

4.5.3. (4*RS*,6*SR*)-4-Methyl-6-propyl-1,3-dioxan-2-one ((±)-36a (*cis*)). According to the procedure for the preparation of **4a** described above, (±)-**33a** (383 mg, 2.9 mmol) was converted to (±)-**36a** (*cis*) as a colorless oil (139 mg, 30%); IR (neat) 2961, 2936, 2874, 1744, 1400, 1248, 1198, 1115 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ=0.96 (t, J=7.0 Hz, 3H), 1.35–1.83 (m, 6H), 1.42 (d, J=6.0 Hz, 3H), 4.30–4.49 (m, 1H), 4.49–4.70 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=13.7, 17.7, 21.2, 34.8, 37.3, 75.1, 78.6, 149.4; MS *m/z* (rel intensities) 159 (M^++H, 34%), 143 (2.7), 130 (42), 114 (43), 86 (77), 72 (100); HRMS *m/z* 159.1022 (159.1021 calcd for $C_8H_{15}O_3$, M^++H).

4.5.4. (4*RS*,6*RS*)-4-Methyl-6-propyl-1,3-dioxan-2-one ((±)-36b (*anti*)). According to the procedure for the preparation of **4a** described above, (±)-**33b** (650 mg, 4.93 mmol) was converted to (±)-**36b** (*anti*) as a colorless oil (323 mg, 42%); IR (neat) 2961, 2938, 2874, 1746, 1387, 1252, 1204, 1134 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ=0.96 (t, J=7.5 Hz, 3H), 1.41 (d, J=6.5 Hz, 3H), 1.42–1.79 (m, 6H), 4.39–4.49 (m, 1H), 4.49–4.61 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=13.7, 18.2, 20.8, 32.4, 36.9, 72.7, 75.9, 149.4; MS *m/z* (rel intensities) 159 (M^++H, 51%), 129 (6.1), 115 (12), 99 (6.1), 86 (7.1), 71 (100); HRMS *m/z* 159.1047 (159.1021 calcd for $C_8H_{15}O_3$, M^++H).

4.5.5. (4*RS*,6*SR*)-4-(3-Benzyloxypropyl)-6-methyl-1,3-dioxan-2-one ((±)-37a (*syn*)). According to the procedure for the preparation of **4a** described above, (±)-**34a** (100 mg, 0.42 mmol) was converted to (±)-**37a** (*syn*) as a colorless oil (87.8 mg, 79%); IR (neat) 2932, 2857, 1746, 1042, 1244, 1194, 1113, 737, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ=1.39 (d, J=6.0 Hz, 3H), 1.50–1.90 (m, 4H), 1.98–2.10 (m, 2H), 3.44–3.58 (m, 2H), 4.38–4.58 (m, 2H), 4.50 (s, 2H), 7.24–7.40 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=21.2, 24.7, 32.3, 34.7, 69.4, 72.9, 75.1, 78.6, 127.6, 128.4, 138.3, 149.1; MS *m/z* (rel intensities) 264 (M^+, 4.2%), 221 (5.8), 160 (100), 130 (15), 107 (96), 91 (100); HRMS *m/z* 264.1373 (264.1362 calcd for $C_{15}H_{20}O_4$, M^+).

4.5.6. (4*RS*,6*RS*)-4-(3-Benzyloxy-propyl)-6-methyl-1,3-dioxan-2-one ((±)-37b (*anti*)). According to the procedure for the preparation of **4a** described above, (±)-**34b** (520 mg, 2.19 mmol) was converted to (±)-**37b** (*anti*) as a colorless oil (437 mg, 76%); IR (neat) 2934, 2859, 1746, 1387, 1252, 1207, 1115, 737, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ=1.40 (d, J=6.5 Hz, 3H), 1.65–2.10 (m, 6H), 3.44–3.60 (m, 2H), 4.44–4.60 (m, 1H), 4.50 (s, 2H), 4.62–4.74 (m, 1H), 7.24–7.42 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=20.7, 25.2, 31.9, 32.4, 69.3, 72.7, 72.9, 75.9, 127.6, 128.4, 138.2, 149.3; MS *m/z* (rel intensities) 264 (M^+, 6.9%), 173 (6.5), 159 (4.6), 107 (46), 91 (100), 71 (100); HRMS *m/z* 264.1336 (264.1362 calcd for $C_{15}H_{20}O_4$, M^+).

4.6. Typical procedure for the hydrolysis of cyclic carbonates with *P. diminuta*

The basal medium for the microbial reaction consists of glucose (10 g), polypeptone (7 g), and yeast extract (5 g) in 1 L of 0.1 M phosphate buffer (pH 6.5). A 500-mL Erlenmeyer flask each containing 100 mL of sterilized basal medium was inoculated with a loopful of *P. diminuta*, and incubated for 48 h at 30 °C. To the broth was added 80 μL (84 mg) of (±)-**4a** (*cis*) and the cultivation was continued. After 50 mL of acetone was added to the mixture followed by saturation with NaCl and filtration through a Celite pad, the products were extracted with AcOEt, and the organic layer was dried over Na_2SO_4. After evaporation, the residue was purified by column chromatography on silica gel (hexane/AcOEt=5/1) to afford (4*R*,5*S*)-**4a** (36.1 mg, 43%; 97% ee) and (2*R*,3*S*)-**3a** (30.1 mg, 40%; >99% ee) as colorless oils. The ee of (2*R*,3*S*)-**3a** was determined by HPLC analysis of the corresponding bis-(+)-MTPA ester. Conditions of the HPLC analysis: column, Zorbax-Sil (0.46 mm×25 cm, DuPont Instruments); eluent, hexane/AcOEt=90/10; flow rate, 0.5 mL/min; retention time, 30 (2*R*,3*S*) and 32 (2*S*,3*R*) min. To determine the ee of (4*R*,5*S*)-**4a**, the cyclic carbonate was hydrolyzed with K_2CO_3 to afford the corresponding (2*S*,3*R*)-**3a**. The absolute configuration was confirmed by comparing its optical rotation sign with that of the authentic sample (2*S*,3*R*)-**3a**, and the preparation method is described in the following section.

Enantioselective reactions of the other substrates were carried out by the same procedure. The results were shown in the text. All the spectral data (^{1}H and ^{13}C NMR, IR, and MS) were in full agreement with those of the racemates. The ee's of diols were determined by HPLC or ^{1}H NMR analysis. The ee's of cyclic carbonates were determined by similar analyses of the corresponding diols derived from the carbonates with K_2CO_3. The methods and the conditions are given below:

Compound **3b**: HPLC analysis of the corresponding bis-(+)-MTPA ester. Conditions of the HPLC analysis: column, Zorbax-Sil (0.46 mm×25 cm, Agilent Technologies); eluent, hexane/AcOEt=90/10; flow rate, 0.5 mL/min; retention time, 36 (2*S*,3*S*) and 39 (2*R*,3*R*) min.

Compound **8a**: ^{1}H NMR (500 MHz) analysis of the corresponding bis-(+)-MTPA ester. Signals at δ 3.42 (d, J=1.0 Hz)+3.50 (d, J=1.0 Hz) ($CH_3O\times2$, (2*S*,3*R*)) and 3.46 (t, J=1.0 Hz) ($CH_3O\times2$, (2*R*,3*S*)).

Compound **9a**: ^{1}H NMR (500 MHz) analysis of the corresponding bis-(+)-MTPA ester. Signals at δ 3.42 (s)+3.50 (d, J=1.0 Hz) ($CH_3O\times2$, (2*S*,3*R*)) and 3.45 (s)+3.46 (s) ($CH_3O\times2$, (2*R*,3*S*)). The absolute configuration was confirmed by comparing its optical rotation sign with that reported; (2*S*,3*R*)-**9a**, lit.[11] $[\alpha]_D^{18}$ +22.73 (*c* 1.10, MeOH).

Compound **10a**: ^{1}H NMR analysis of the corresponding bis-(+)-MTPA ester. Signals at δ 3.42 (d, J=1.0 Hz)+3.50 (s) ($CH_3O\times2$, (2*S*,3*R*)) and 3.45 (d, J=1.0 Hz)+3.46 (s) ($CH_3O\times2$, (2*R*,3*S*)).

Compound **18a**: ^{1}H NMR analysis of the corresponding bis-(+)-MTPA ester. Signals at δ 3.42 (s)+3.49 (s) ($CH_3O\times2$, (2*S*,3*R*)) and 3.45 (s)+3.46 (s) ($CH_3O\times2$, (2*R*,3*S*)).

Compound **32a**: HPLC analysis of the corresponding bis-(+)-MTPA ester. Conditions of the HPLC analysis: column, Zorbax-Sil (0.46 mm×25 cm); eluent, hexane/AcOEt=90/10; flow rate, 0.5 mL/min; retention time, 16 and 17 min.

Compound **32b**: HPLC analysis of the corresponding bis-(+)-MTPA ester. Conditions of the HPLC analysis: column, Zorbax-Sil (0.46 mm×25 cm); eluent, hexane/AcOEt=90/10; flow rate, 0.5 mL/min; retention time, 14 (2*R*,4*R*) and 16 (2*S*,4*S*) min.

Compound **33a**: HPLC analysis of the corresponding bis-(+)-MTPA ester. Conditions of the HPLC analysis: column, Zorbax-Sil (0.46 mm×25 cm); eluent, hexane/AcOEt=90/10; flow rate, 0.5 mL/min; retention time, 13.6 and 14.4 min.

Compound **33b**: HPLC analysis of the corresponding bis-(+)-MTPA ester. Conditions of the HPLC analysis: column, Zorbax-Sil (0.46 mm×25 cm); eluent, hexane/AcOEt=90/10; flow rate, 0.5 mL/min; retention time, 13 (2*R*,4*R*) and 14 (2*S*,4*S*) min.

Compound **34a**: HPLC analysis of the corresponding bis-(+)-MTPA ester. Conditions of the HPLC analysis: column, Zorbax-Sil (0.46 mm×25 cm); eluent, hexane/AcOEt=90/10; flow rate, 0.5 mL/min; retention time, 30 and 32 min.

Compound **34b**: HPLC analysis of the corresponding bis-(+)-MTPA ester. Conditions of the HPLC analysis: column, Zorbax-Sil (0.46 mm×25 cm); eluent, hexane/AcOEt=90/10; flow rate, 0.5 mL/min; retention time, 26 (2*R*,4*R*) and 32 (2*S*,4*S*) min.

4.7. Preparation of the authentic sample (2*S*,3*R*)-3a

According to the procedure described above for the preparation of (±)-**17**, (2*S*,3*R*)-2-(4-methoxybenzyloxy)-5-hexen-3-ol (**39**) was prepared from ethyl (*S*)-lactate in four steps.

Under an argon atmosphere, to a solution of (2*S*,3*R*)-**39** (502 mg, 2.13 mmol) in $CHCl_2$ (10 mL) were added 3,4-dihydro-2*H*-pyran (2.0 mL, 1.8 g, 21 mmol) and a catalytic amount of *p*-TsOH at 0 °C, and stirred overnight at room temperature. The reaction was stopped with satd $NaHCO_3$ aqueous solution, and the products were extracted with $CHCl_2$ (×3). 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 on silica gel (hexane/AcOEt=10/1→5/1) to give (4*R*,5*S*)-5-(4-methoxybenzyloxy)-4-tetrahydropyranyloxy-1-hexene (**40**) as a colorless oil (433 mg, 64%). This compound included some impurity, but this was used without further purification.

Under an argon atmosphere, to a solution of (2*S*,3*R*)-**40** (400 mg, 1.25 mmol) in THF (10 mL) was added $BH_3\cdot THF$ (1.25 mL, 2.0 M in THF) at 0 °C and stirred for 4 h at room temperature. The reaction was quenched with a drop of water, followed by the addition of 2 M NaOH aqueous solution (2.5 mL) and 35% H_2O_2 (2.5 mL), and the mixture was stirred overnight at room temperature. After the mixture was saturated with NaCl, products were extracted with Et_2O (×3), and the organic layer was dried over Na_2SO_4. After evaporation under reduced pressure, the residue was purified by flash column chromatography on silica gel (hexane/AcOEt=1/1→AcOEt) to give (4*R*,5*S*)-5-(4-methoxybenzyloxy)-4-tetrahydropyranyloxy-1-hexanol (**41**) as a colorless oil (262 mg, 62%).

According to the procedure for the preparation of (*Z*)-**2a** described above, (4*R*,5*S*)-**41** (329 mg, 0.973 mmol) was converted to (4*R*,5*S*)-1-benzyloxy-5-(4-methoxybenzyloxy)-4-tetrahydropyranyloxyhexane (**42**, 337 mg, 81%) as a colorless oil.

According to the procedure for the preparation of (±)-**18a** described above, (4*R*,5*S*)-**42** (259 mg, 0.605 mmol) was converted to (2*S*,3*R*)-**3a** (51.6 mg, 38%) as a colorless oil; $[\alpha]_D^{25}$ +12.9 (*c* 1.34, MeOH). All the spectral data (^{1}H and

^{13}C NMR, IR, and MS) of (2*S*,3*R*)-**3a** were in full agreement with those of (±)-**3a**.

4.8. Preparation of the authentic sample (2*S*,3*S*)-3b

Under an argon atmosphere, to a solution of (2*S*,3*R*)-**24** (400 mg, 1.25 mmol) in *t*-BuOH (5 mL)/H_2O (5 mL) mixed solvent was added AD-mix-α (1.4 g), and the mixture was stirred at room temperature. After the mixture changed to a biphasic clear solution, to the solution were added $CH_3SO_2NH_2$ (95 mg) and (*E*)-**2b** (190 mg, 1.0 mmol) at 0 °C, and stirred overnight at room temperature. After addition of NaS_2O_4 and stirring for 30 min, the products were extracted with AcOEt (×4), and the organic layer was washed with 2 M NaOH aqueous solution (×2). After the organic layer was dried over Na_2SO_4 and evaporated under reduced pressure, the residue was purified by flash column chromatography on silica gel (hexane/AcOEt=1/1) to give (2*S*,3*S*)-**3b** as a colorless oil (148 mg, 66%); $[\alpha]_D^{27}$ −13.8 (*c* 1.16, MeOH); $[\alpha]_D^{23}$ −8.0 (*c* 1.87, $CHCl_3$). All the spectral data (^{1}H and ^{13}C NMR, IR, and MS) of (2*S*,3*S*)-**3b** were in full agreement with those of (±)-**3b**.

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