Enzyme-Catalyzed Asymmetric Synthesis; 10.[1] *Pseudomonas cepacia* Lipase Mediated Synthesis of Enantiomerically Pure (2*R*,3*S*)- and (2*S*,3*R*)-2,3-*O*-Cyclohexylideneerythritol Monoacetate from 2,3-*O*-Cyclohexylideneerythritol[2]

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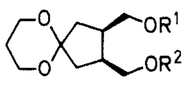
Pseudomonas cepacia lipase catalyzed hydrolysis of 2,3-*O*-cyclohexylideneerythritol diacetate in an emulsion of water and diisopropyl ether gives (2*S*,3*R*)-2,3-*O*-cyclohexylideneerythritol monoacetate [(2*S*,3*R*)-1-acetoxy-2,3-cyclohexylidenedioxy-4-hydroxybutane] with ≥ 99 % ee in 91 % yield by a preferential attack at the *R*-center CH_2OAc group. The enantiomeric (2*R*,3*S*)-2,3-*O*-cyclohexylideneerythritol monoacetate is obtained by acetylation of 2,3-*O*-cyclohexylideneerythritol with vinyl acetate catalyzed by the same enzyme with ≥ 99 % ee in 78 % yield by a combined enantiotopos and enantiomer differentiation through a preferential attack at the *R*-center CH_2OH groups.

Lipases[3,4] are a unique class of hydrolases for asymmetric synthesis[5] because of their high catalytic activity at the liquid-liquid interface formed by water and the insoluble substrate or an organic solvent, and in nearly anhydrous organic solvents. Generally through acetylation of a prochiral diol in an organic solvent and hydrolysis of its diacetate in water access to both enantiomers of the corresponding monoacetate[6,7] with just one enzyme is provided.[8] This is because of the same enantiotopic group recognition by the enzyme in both reactions, and favorable opposite equilibria.

In the case of the 4-position functionalized *meso*-cyclopentane-1,2-dimethanol diacetates and their parent diols, e.g., **1** and **2**, we have studied the enantioselectivity of various lipases in water, in two phase systems formed by water and an organic solvent, and in organic solvents of low water content.[7,9–11] This led among others to the attainment of the enantiomerically pure monoacetates **3** and *ent*-**3**, which are useful chiral building blocks for the synthesis of biologically active isocarbacyclins,[12] on a multigram scale.[9]

We now describe the hydrolysis and acetylation of the isomers of **1** and **2**, i.e., **6** and **7**, by *Pseudomonas cepacia* lipase (PCL) leading to an efficient synthesis of both enantiomers of 2,3-*O*-cyclohexylideneerythritol monoacetate, **8** and *ent*-**8**, in enantiomerically pure form.[9,13]



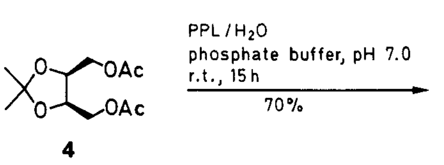
1 $R^1 = R^2 = Ac$
2 $R^1 = R^2 = H$
3 $R^1 = Ac$, $R^2 = H$

Erythritol derivatives such as **8** and *ent*-**8** should serve as useful chiral educts, complementary to D- and L-tartaric acid derived threitol derivatives,[14] since not only, e.g., *erythro*-1,2-glycols but also via epimerization of the corresponding D- and L-ribose derivatives[15] *threo*-1,2-glycols may be obtained. *erythro*- and *threo*-1,2-Diol structural units are found in numerous naturally occuring chiral compounds such as macrolides,[16] pheromones,[17] and eicosanoids.[18,19]

Erythritol derivatives of type **8** and *ent*-**8** were previously synthesized from D-glucose,[20,21] or D-isoascorbic acid,[21,22] from (*E*)-butene-1,4-diol monobenzyl ether by applying the Katsuki–Sharpless asymmetric epoxidation[23] and most recently from 2,3-bis(methoxymethyl)-erythritol through pig pancreas lipase (PPL) catalyzed asymmetric acylation.[24] In the latter case, however, the corresponding monoacylated diol was not obtained enantiomerically pure and the synthesis of, e.g., *threo*-1,2-glycols therefore requires additional steps as compared to the heterocyclic monoacetates **8** and *ent*-**8**. Despite the merits of the above syntheses we felt that there is still a need for a route whereby both enantiomers can be obtained practically from one achiral precursor, and which is amendable to large-scale.[25]

The substrates used for the lipase catalyzed reactions, the diol **7**, and the diacetates **4**[26] and **6** are easily prepared in two and three steps, respectively, from commercially available *meso*-tartaric acid by standard procedures[26,27] in high overall yield.

PPL-catalyzed hydrolysis of the isopropylidene diacetate **4** proceeds only with very low enantioselectivity to give the monoacetate **5** with 13 % ee (Table 1). Expectations as to enhance the enantioselectivity by synthetically tolerable structure modifications[7,9] were met with little success. Thus the cyclohexylidene diacetate **6** was hydrolyzed by PPL only with a slightly higher enantioselectivity to the monoacetate **8** showing an ee value of 41 %.

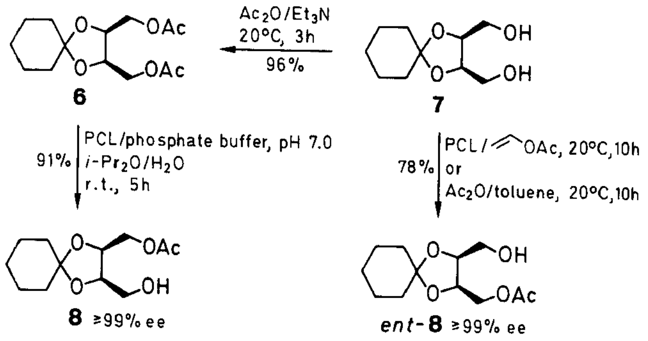


Yet another reason why lipases have turned out to be highly valuable hydrolases for asymmetric synthesis is that various types from fungi, bacteria and mammalians are commercially available. The bacterial lipase from *Pseudomonas cepacia* (PCL)[28] catalyzes the hydrolysis of the diacetate **6** with a much higher enantioselectivity, giving the monoacetate **8** with an ee value of 81 %.[29] As we,[9,10] and others,[30] have observed previously, lipase-catalyzed hydrolyses very often proceed with higher enantio- as well as chemoselectivity, and within a shorter reaction time if by addition of an immiscible organic solvent, such as diethyl ether, *tert*-butyl methyl ether, diisopropyl ether or hexane, a liquid-liquid interface is formed. Thus PCL-catalyzed hydrolysis of the diacetate **6**

Table 1. Lipase-Catalyzed Hydrolyses of *meso*-Diacetates **4** and **6**

Substrate	Product	Lipase	Reaction Medium	Yield (%)	ee (%)
4	**5**	PPL	H_2O	70	13
6	**8**	PPL	H_2O	73	41
6	**8**	PCL	H_2O	85	81
6	**8**	PCL	$H_2O/i\text{-}Pr_2O$	91	≥99

in an emulsion of water and diisopropyl ether gave in 91% yield the monoacetate **8** with an ee value ≥99% (Scheme, Table 1) by a preferential attack on the *R*-center CH_2OAc group. Enantiomeric excess enhancements in lipase-catalyzed hydrolysis through addition of water soluble organic solvents have also been reported.[31] Hydrolysis of **6** in the presence of various water miscible and immiscible organic solvents showed however that as in the case of **1**[10] the interfacial effect is more important.[32] The notion that the interfacial activation of the water-soluble lipases may be due to a conformational change of the enzyme[3] seems to be supported by X-ray structural work[4] which revealed an almost inaccessible active site in the crystal.



Scheme

PPL-catalyzed acetylation of the diol **7** with vinyl acetate as acetyl donor,[33] which also served as solvent, gave the enantiomeric monoacetate *ent*-**8** with an ee value of 77% (Table 2). Interestingly, PPL-catalyzed acylation of acylic 2,3-bis(methoxymethyl)erythritol with trichloroethyl decanoate also occurs preferentially at the *R*-center CH_2OH group, delivering the monoacylated diol with 95% ee.[24] Determination of the kinetic constants $E_1 = k_3/k_1 + k_2$, $E_2 = k_4/k_1 + k_2$ and $\alpha = k_1/k_2$[34] (Figure) for the acetylation of the diol **7**, and the monoaceates **8**/*ent*-**8** gave values of 0.072, 0.139 and 7.7,[9,13] respectively. This indicated that an enhancement of the ee value of the monoacetate *ent*-**8** by an enantiomer differentiating acetylation would not be feasible in this case. Indeed, when the PPL-catalyzed acetylation of diol **7** to the monoacetates *ent*-**8**/**8** was carried further to the extent that the diacetate **6** was formed in 70% yield the monoacetate *ent*-**8** was isolated with a higher but synthetically still insufficient ee value of 88% (Figure) in 30% yield. Here, too, using PCL instead of PPL allowed for the synthesis of the enantiomerically pure monoacetate *ent*-**8**. PCL-catalyzed acetylation of the diol **7** with anhydrous vinyl acetate, which was also used as solvent, gave *ent*-**8** in 93% yield with an ee value of 96% (Table 2) by a preferential attack at the *R*-center CH_2OH group. Determination of the kinetic constants gave in this case for α a value of 50. Thus, partial acetylation of *ent*-**8**/**8** raised through enantiomer differentiation the ee value of *ent*-**8** to ≥99% while decreasing the yield to a still acceptable 78%. The only byproduct was the *meso*-diacetate **6** which can be converted to diol **7**.

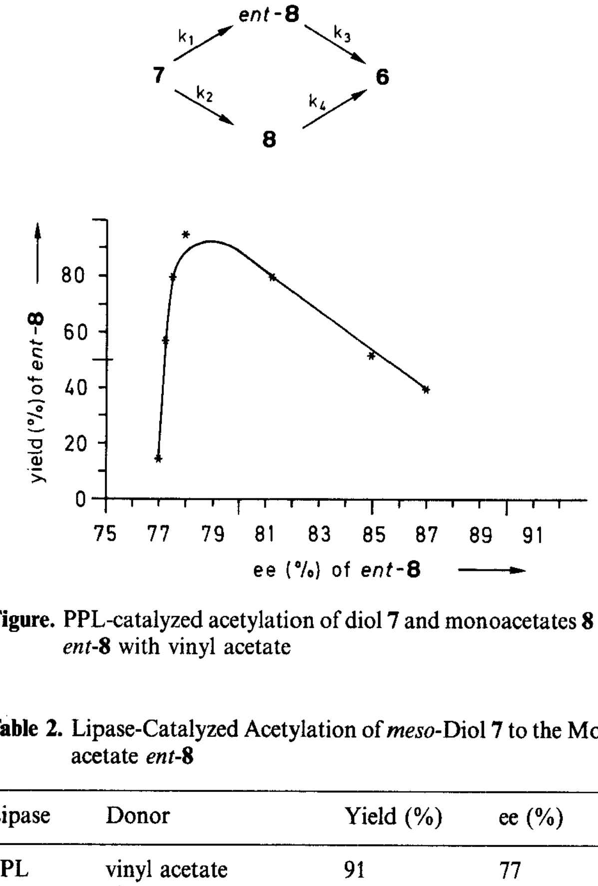


Figure. PPL-catalyzed acetylation of diol **7** and monoacetates **8** and *ent*-**8** with vinyl acetate

Table 2. Lipase-Catalyzed Acetylation of *meso*-Diol **7** to the Monoacetate *ent*-**8**

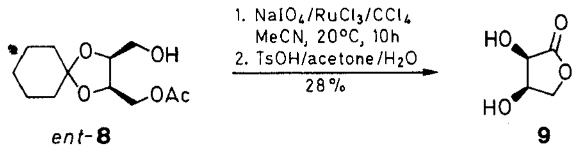
Lipase	Donor	Yield (%)	ee (%)
PPL	vinyl acetate	91	77
PPL	vinyl acetate	31[a]	88
PCL	vinyl acetate	93	96
PCL	vinyl acetate	78[a]	≥99
PCL	acetic anhydride	91	94

[a] Same conditions but with increased reaction time. Decreased yield is due to diacetate formation.

PCL-catalyzed acetylation of the diol **7** with acetic anhydride in toluene[35] at room temperature proceeded with the highest rate of all the acetylations investigated and gave the monoacetate *ent*-**8** in 91% yield with 94% ee. Without PCL no acetylation of **7** occured under the conditions used even after a prolonged time. From the acetylation reactions the lipases were easily recovered by filtration and could be reused with almost no activity loss.

The ee values of **8** and *ent*-**8** were determined by their conversion to the corresponding *Mosher* esters [α-methoxy-α-(trifluoromethyl)phenylacetic acid esters][36] and their analysis by 400 MHz ^{1}H NMR spectroscopy using the baseline separated acetyl signals at $\delta = 2.04$ and 2.06.

Determination of the absolute configuration of *ent*-**8** and hence **8** was done by conversion of the former to D-erythronolactone (2,3-dihydroxy-4-butanolide, **9**).[37]



In summary, through PCL-catalyzed optimized hydrolysis and acetylation of *meso*-diol **7** and *meso*-diacetate **6**, respectively, an easy access to the enantiomerically pure erythritol derivatives **8** and *ent*-**8** is provided. In the light of the results with **3** and *ent*-**3**[9] large-scale synthesis of **8** and *ent*-**8** should pose no problem. As observed with **1** and **2**, PPL and PCL catalyzed reactions of **6** and **7** are fastest at the *R*-center CH_2OAc and CH_2OH groups, respectively.

Gas chromatographic analyses were carried out on a Carlo-Erba 5300 mega instrument equipped with a FID detector and fused-silica capillary column OV 1701. [α] Values were measured at 20°C with a Perkin-Elmer P 141 polarimeter. ^1H NMR spectra were recorded on a Bruker WM 250, WM 300 and AM 400 spectrometer and ^{13}C NMR spectra on a Bruker WP 80 and WM 300 spectrometer. IR spectra were recorded on a Perkin-Elmer 297 spectrometer. The electron impact (EI) mass spectra were run on a Varian-MAT 312 spectrometer at 70 eV. Elemental microanalyses were performed with a Perkin-Elmer 240 A-C instrument at the Institute of Organic Chemistry and Biochemistry of the University of Freiburg. TLC was done on Merck silica gel 60 F_{254} sheets and column chromatography with merck silica gel 60 (0.040–0.063 mm). All enzymic hydrolyses were run and monitored by using a Metrohm pH-stat apparatus consisting of a pH-Meter 620 with an Electrode EA 121, a Dosimat 655 and an Impulsomat 614. For Kugelrohr distillations, oven temperature is given.

meso-Tartaric acid and Celite (hyflo super cel) were purchased from Fluka Feinchemikalien GmbH, D-7910 Neu-Ulm, Germany, and vinyl acetate was obtained from Wacker-Chemie GmbH, D-8000 München 22, Germany. Lipase from pig pancreas (PPL) (E. C. 3.1.1.3; Typ II; crude; steapsin) was purchased from Sigma Chemie GmbH, D-8024 Deisenhofen, Germany, and lipase from *Pseudomonas cepacia* (PCL) (E. C. 3.1.1.3; lipase PS, Amano Pharmaceutical Co., Ltg. Nagoya, Japan) was obtained from Mitsubishi Int. GmbH, D-4000 Düsseldorf, Germany. For acetylations PCL and PPL were dried over P_2O_5 for 4 d at 0.001 Torr and 25°C to a residual H_2O content of $\leq 1\%$. PPL was immobilized for acetylations on Celite according to Wisdom et al.,[38] and the solid material obtained dried for 4 d at 20°C and 0.001 Torr to a residual water content of $\leq 1\%$.

2,3-*O*-Cyclohexylideneerythritol Diacetate (6);Typical Procedure:
To a solution of diol **7** (3.0 g, 14.9 mmol) and Et_3N (4.2 g, 44.7 mmol) was added dropwise under stirring at 20°C Ac_2O (4.6 g, 45.0 mmol). After stirring at this temperature for 3 h the mixture was partitioned between EtOAc (100 mL) and H_2O (100 mL). The layers were shaken, separated and the aqueous phase was extracted with EtOAc (2 x 50 mL). The combined organic layers were washed with brine (50 mL), dried ($MgSO_4$) and concentrated in vacuo. The residue was filtrated with EtOAc through silica gel (10 g). The filtrate was concentrated in vacuo and the residue Kugelrohr distilled to give the diacetate **6** as colorless oil; yield: 4.09 g (96%); bp 124°C/0.001 Torr.

$C_{14}H_{22}O_6$	calc.	C 58.73	H 7.74
(286.3)	found	58.60	7.62

IR (film): ν = 3055 (w), 2995 (m), 2950 (s), 2925 (m), 1750 (s), 1650 (m), 1585 (ss), 1480 (m), 1450 (m), 1385 (m), 1280 (ss), 1240 (ss), 1180 (ss) cm^{-1}.

MS (EI): *m/z* (%) = 286 (7, M^+), 257 (10), 243 (44), 141 (11), 129 (13), 115 (19), 69 (43), 55 (52), 43 (1009.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.25–1.71 (m, 10 H), 2.03 (s, 6 H), 3.99–4.36 (m, 6 H).

2,3-*O*-Isopropylideneerythritol Diacetate (5):
Following the procedure for the synthesis of the diacetate **6** there was obtained from 2,3-*O*-isopropylideneerythritol (6.5 g, 35 mmol) diacetate **5** as colorless oil; yield 8.0 g (94%); bp 85°C/0.001 Torr (Kugelrohr).

$C_{11}H_{18}O_6$	calc.	C 53.64	H 7.37
(246.3)	found	53.46	7.27

IR (film): ν = 2995 (m), 2930 (w), 2900 (w), 1740 (s), 1440 (m), 1370 (s), 1220 (ss), 1175 (m), 1090 (m), 1050 (s) cm^{-1}.

MS (EI): *m/z* = 231 (18), 173 (2), 129 (6), 115 (27), 69 (13), 43 (100).

MS (FI): *m/z* = 231 (M^+ − 15).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.39 (s, 3 H), 1.50 (s, 3 H), 2.09 (s, 6 H), 4.06–4.13 (m, 2 H), 4.27 (dd, J_{gem} = 11.6 Hz, J_{vic} = 4.5 Hz, 2 H), 4.36–4.42 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.80 (q), 25.30 (q), 27.72 (q), 62.43 (t), 74.54 (d), 109.53 (s), 170.53 (s).

(2*S*,3*R*)-2,3-*O*-Isopropylideneerythritol Monoacetate (5):
With PPL in H_2O: PPL (20 g) was added to a rapidly stirred suspension of the diacetate **4** (5.10 g, 20 mmol) in 0.5 M phosphate buffer (250 mL) of pH 7.0. The pH was maintained at 7.0 by pH-stat-controlled addition of 0.2 N aq NaOH. The reaction was allowed to proceed until 1 equiv. of base had been consumed (15 h). The mixture was continuously extracted for 48 h with Et_2O. After separation of the aqueous phase the organic phase was dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed on silica gel (500 g) with EtOAc, giving besides the diacetate **4** (200 mg, 4%) and 2,3-*O*-isopropylideneerythritol (300 mg, 9%) the monoacetate **5** as colorless oil; yield 2.90 g (70%); $[\alpha]_D$ −4.0° (*c* = 0.78, CH_2Cl_2); $[\alpha]_{365}$ −11.3° (*c* = 0.78, CH_2Cl_2); ee = 13% by ^1H NMR shift experiment (400 MHz, $CDCl_3$) with 15 mol% $Eu(tfc)_3$ by using the base line separated acetyl signals.

$C_9H_{16}O_5$	calc.	C 52.93	H 7.90
(204.2)	found	52.60	7.90

IR (film): ν = 3450 (s, br), 2990 (m), 2930 (m), 1740 (s), 1370 (s), 1240 (ss), 1160 (m), 1045 (s), 995 (w) cm^{-1}.

MS (EI): *m/z* (%) = 189 (10), 169 (10), 153 (11), 136 (9), 131 (8), 115 (29), 89 (14), 77 (31), 9 (18), 59 (33), 51 (14), 43 (100).

MS (FI): *m/z* = 205 (M^+ + 1), 189 (M^+ − 15).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.38 (s, 3 H), 1.49 (s, 3 H), 2.09 (s, 3 H), 2.52 (br t, 1 H, OH), 3.65–3.78 (m, 2 H, CH_2OH), 4.09–4.41 (m, 4 H, 2-H, 3-H, CH_2OAc).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.86 (q), 25.15 (q), 27.68 (q), 60.87 (t), 63.10 (t), 74.68 (d), 77.07 (d), 109.06 (s), 170.80 (s).

(2*S*,3*R*)-2,3-*O*-Cycloheylideneerythritol Monoacetate (8):
With PPL in H_2O: PPL (20 g) was added to a rapidly stirred suspension of the diacetate **6** (2.80 g, 9.8 mmol) in 0.5 M phosphate buffer (250 mL) of pH 7.0. The pH was maintained at 7.0 by pH stat controlled addition of 0.3 N NaOH. The reaction was allowed to proceed until 1 equiv of base had been consumed (5 h). The mixture was continuously extracted for 48 h with Et_2O. After separation of the aqueous phase the organic phase was dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed on silica gel (300 g) with EtOAc, giving besides the diacetate **6** (250 mg, 9%) and the diol **7** (140 mg, 7%) the monoacetate **8** as colorless oil; yield 1.75 g (73%); $[\alpha]_D$ −4.3° (*c* = 0.87, CH_2Cl_2); $[\alpha]_{365}$ −14.8° (*c* = 0.87, CH_2Cl_2); ee = 41% by ^1H NMR spectroscopy (400 MHz, $CDCl_3$) of the corresponding *Mosher* esters.

$C_{12}H_{20}O_5$	calc.	C 59.00	H 8.25
(244.3)	found	59.22	8.22

IR (film): ν = 3500 (ss, br), 2945 (ss), 2850 (m), 1740 (ss), 1440 (m), 1385 (s), 1335 (w), 1240 (ss), 1155 (m), 1105 (ss), 1040 (ss), 980 (w) cm^{-1}.

MS (EI): m/z (%) = 244 (12, M^+), 215 (9), 201 (32), 141 (36), 129 (55), 114 (27), 99 (17), 81 (16), 69 (94), 55 (71), 43 (100).

^1H NMR (250 MHz, $CDCl_3$): δ = 1.36–1.79 (m, 10 H), 1.93 (t, J = 6.5 Hz, 1 H, OH), 2.05 (s, 3 H, $OCOCH_3$), 3.65–3.81 (m, 2 H, CH_2OH), 4.19–4.41 (m, 4 H, CH_2OCOCH_3, 2-H, 3-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.98, (q), 22.63 (t), 22.99 (t), 24.04 (t), 33.56 (t), 36.52 (t), 60.05 (t), 62.02 (t), 73.13 (d), 75.60 (d), 108.63 (s), 169.65 (s).

With PCL in H_2O: PCL (2 g) was added to a rapidly stirred suspension of the diacetate **6** (4.87 g, 17.0 mmol) in 0.5 M phosphate buffer (250 mL) of pH 7.0. The pH was maintained at 7.0 by pH stat controlled addition of 0.3 N aq NaOH. The reaction was allowed to proceed until 1 equiv of base had been consumed (5 h). The mixture was continuously extracted for 48 h with Et_2O. After separation of the aqueous phase the organic phase was dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed on silica gel (500 g) with EtOAc, giving besides the diacetate **6** (190 mg, 4 %) and the diol **7** (210 mg, 6 %) the monoacetate **8** as colorless oil; yield 3.52 g (85 %); $[\alpha]_D$ – 8.6° (c = 0.78, CH_2Cl_2); $[\alpha]_{365}$ – 29.3° (c = 0.78, CH_2Cl_2); ee = 81 % by ^1H NMR spectroscopy (400 MHz, $CDCl_3$) of the corresponding *Mosher* esters.

$C_{12}H_{20}O_5$	calc.	C 59.00	H 8.25
(244.3)	found	59.22	8.22

With PCL in a $H_2O/i\text{-}Pr_2O$ emulsion: PCL (2 g) was added to a rapidly stirred emulsion of the diacetate **6** (2.80 g, 9.8 mmol) in 0.5 M phosphate buffer (250 mL) of pH 7.0 and $i\text{-}Pr_2O$ (50 mL). The pH was maintained at 7.0 by pH stat controlled addition of 0.3 N aq NaOH. The reaction was allowed to proceed until 1 equiv of base had been consumed (5 h). The mixture was continuously extracted for 48 h with Et_2O. After separation of the aqueous phase the organic phase was dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed on silica gel (300 g) with EtOAc, giving besides the diacetate **6** (50 mg, 2 %) and the diol **7** (60 mg, 3 %) the monoacetate **8** as colorless oil; yield 2.18 g (91 %); $[\alpha]_D$ – 10.6° (c = 1.26, CH_2Cl_2); $[\alpha]_{365}$ – 36.2° (c = 1.26, CH_2Cl_2); ee ≥ 99 % by ^1H NMR spectroscopy (400 MHz, $CDCl_3$) of the corresponding *Mosher* esters.

(2*R*,2*S*)-2,3-*O*-Cyclohexylideneerythritol Monoacetate (*ent*-8):

A. *With immobilized PPL in vinyl acetate:* To a rapidly stirred suspension of PPL on Celite (20 g) in anhydrous vinyl acetate (200 mL) was added at 20 °C diol **7** (2.00 g, 9.9 mmol). After 6 h the mixture was filtered, the solid washed with vinyl acetate (2 × 30 mL), and the filtrate concentrated in vacuo. The residue was chromatographed on silica gel (200 g) with EtOAc, giving besides the diacetate **6** (57 mg, 2 %) the monoacetate *ent*-**8** as colorless oil; yield 2.20 g (91 %); bp 95℃/0.001 Torr (Kugelrohr).

B. *With PCL in vinyl acetate and a reaction time of 2 h:* To a rapidly stirred suspension of PCL (20 g) in anhydrous vinyl acetate (200 mL) was added at 20℃ diol **7** (2.06 g, 10.2 mmol). After 2 h the mixture was filtered, the enzyme washed with vinyl acetate (2 × 30 mL), and the filtrate concentrated in vacuo. The residue was chromatographed on silica gel (200 g) with EtOAc, giving besides diol **7** (20 mg, 1 %) and diacetate **6** (30 mg, 1 %) the monoacetate *ent*-**8**; yield: 2.31 g (93 %); $[\alpha]_D$ + 10.2° (c = 1.10, CH_2Cl_2); $[\alpha]_{365}$ + 34.7° (c = 1.10, CH_2Cl_2); ee = 96 % by ^1H NMR spectroscopy (400 MHz, $CDCl_3$) of the *Mosher* ester.

C. *With PCL in vinyl acetate and a reaction time of 10 h:* By continuing the above acetylation further for 8 h and workup as described there was obtained besides diacetate **6** (290 mg, 10 %) the monoacetate *ent*-**8**: yield 1.94 g (78 %); $[\alpha]_D$ + 10.6° (c = 1.10, CH_2Cl_2); $[\alpha]_{365}$ + 36.2° (c = 1.10, CH_2Cl_2); ee ≥.99 % by ^1H NMR spectroscopy (400 MHz, $CDCl_3$) of the *Mosher* esters.

D. *With PCL and Ac_2O in toluene:* To a rapidly stirred suspension of PCL (20 g) in anhydrous toluene (200 mL) was added at 20 °C diol **7** (2.17 g, 10.7 mmol) and Ac_2O (2.18 g, 21.4 mmol). After 7 h the mixture was filtrated, the enzyme washed with toluene (2 × 50 mL), and the filtrate concentrated in vacuo. The residue was chromatographed on silica gel (200 g) with EtOAc, giving besides diol **7** (50 mg, 2 %) and diacetate **6** (30 mg, 1 %) the monoacetate *ent*-**8**; yield 2.38 g (93 %); $[\alpha]_D$ + 10.1° (c = 0.77, CH_2Cl_2); $[\alpha]_{365}$ + 34.1° (c = 0.77, CH_2Cl_2); ee = 94 % by ^1H NMR spectroscopy (400 MHz, $CDCl_3$) of the *Mosher* esters. Under the same conditions without PCL no acetylation of diol **7** was observed after 14 h.

D-Erythronolactone (2,3-Dihydroxy-4-butenolide, 9):

To a mixture of CCl_4 (2 mL), MeCN (2 mL) and H_2O (3 mL) were succesively added $NaIO_4$ (400 mg, 2.8 mmol), monoacetate *ent*-**8** (510 mg, 2.09 mmol), and $RuCl_3$ (10 mg, 12.6mol%).[39] After stirring the heterogeneous mixture for 10 h at 20 °C, CH_2Cl_2 (50 mL) was added, the phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. The residue was dissolved in a mixture of acetone (10 mL) and H_2O (1 mL), and TsOH (50 mg) was added. After stirring for 48 h at 20 °C, the solution was concentrated in vacuo and the residue chromatographed on silica gel (20 g) with EtOAc, giving the lactone **9** as colorless crystals; 70 mg (28 %); mp 98 °C; $[\alpha]_D$ – 72.7° (c = 0.56, H_2O).[40]

$C_4H_6O_4$	calc.	C 40.68	H 5.09
(118.1)	found	40.69	5.10

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(40) Note added in proof: After submission of the final draft of the manuscript we learned from a paper by Pottie, M.; Van der Eycken, J.; Vandewalle, M. *Tetrahedron: Asymmetry* **1991**, *2*, 329, describing the lipase (Lipase SAM II Amano) catalyzed synthesis of (2*R*,3*S*)-2,3-*O*-isopropylideneerythritol monopropionate from 2,3-*O*-isopropylideneerythritol and 2,3-*O*-isopropylideneerythritol dipropionate, respectively.

Errata:

– Gais, H.-J.; Hemmerle, H.; Kossek, S. *Synthesis* **1992**, 169.

On page 169, line 31, it should read erythrose instead of ribose

On page 173, Ref. 40 it should read (2*R*,3*S*)-2,3-*O*-isopropylideneerythrol Monoacetate from 2,3-*O*-isopropylideneerythrol and (2*S*,3*R*)-2,3-*O*-isopropylideneerythrol Monobutylrate from 2,3-*O*-isopropylideneerythrol dibutyrate.