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Lipase-Catalyzed Enantiomer Selective Hydrolysis of 1,2-Diol Diacetates

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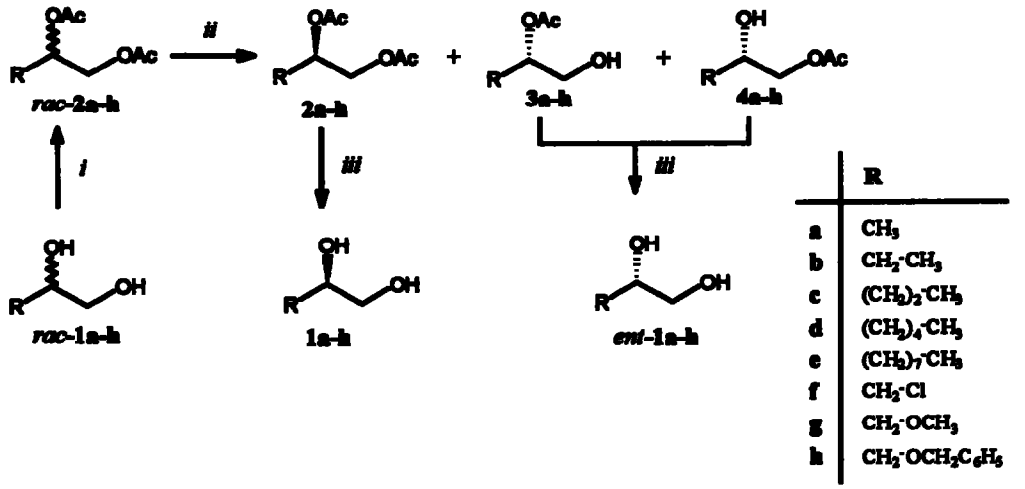
Abstract: Enantiomer selective hydrolysis of racemic 1,2-diol diacetates (*rac*-2a-h) was investigated by using the inexpensive commercial porcine pancreatic lipase. The hydrolysis proceeds with variable regioselectivity but with moderate to good enantioselectivity yielding a mixture of isomeric monoacetates (3a-h and 4a-h) and unchanged diacetate enantiomers (2a-h). Evidence was found that both monoacetates (3a-h and 4a-h) are formed with the same sense of enantiomer selectivity.

1,2-Diols are important structural unit or synthetic building block for a large number of biologically active natural or synthetic compounds. The two enantiomers of such compounds possess different biological activity, e.g. while the active enantiomer of pheromone brevicomin contains 1,2-dioxy-butane subunit with *R* configuration the other isomer shows inhibitory properties[1]. Prostacyclin analogs showing platelet-aggregation inhibitory properties were synthesized from (*S*)-1,2-heptanediol[2] These examples indicate that there is a need for rational method of enantioseparation of racemic 1,2-diols.

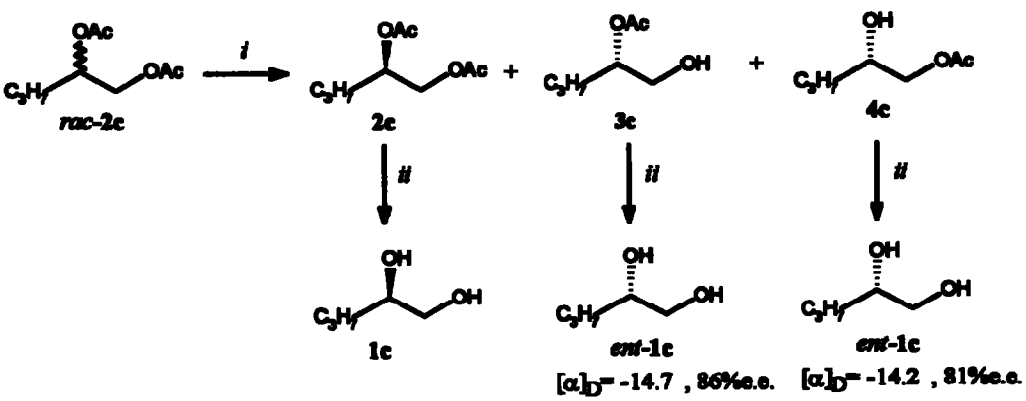
The utility of hydrolases, especially lipases for enantiomer and regioselective transformation of alcohols and related compounds is well known[3]. Recently, lipase catalyzed transformations of 1,2-diol derivatives were studied by several groups. Although hydrolysis[4] or alcoholysis[5] of 1,2-diol diacetates were also investigated, enzymic acylation (transesterification) was chosen as a tool for kinetic resolution of racemic 1,2-diols in the majority of these studies[6-11]. Transesterification methods applying lipase from *Candida cylindracea* (CcL) in aqueous biphasic system consisting tributyrin as ester component[6], porcine pancreatic lipase (PPL) in ethyl acetate or butyrate[7] or methyl propionate[8] matrix, or lipase from *Pseudomonas* sp. (Amano PS) in tetrahydrofurane containing vinyl acetate and triethylamine[9, 10] have been reported. Acylation of diols by acetic- or butyric anhydride catalyzed by PPL in ether or tetrahydrofurane has also been investigated[11]. Generally, high or exclusive regioselectivity preferring the primary hydroxyl groups has been observed by these enzymic acylations parallel with variable degree of enantiomer selectivity. Contrarily, hydrolysis[4] or alcoholysis[5] of 1,2-diol diacetates by using lipases from *Pseudomonas* sp. (*P. aeruginosa* lipase, and Amano PS, respectively) proceeded with moderate regio- and variable enantiomer selectivity.

In the present study our aim was to investigate the hydrolysis of 1,2-diol diacetates catalyzed by the inexpensive PPL (Scheme 1., Table) with respect mainly to the degree of enantiomer selectivity and applicability. Enantiomer selectivity of hydrolysis could be compared to that observed by enzymic acylation of the parent diols[8] with methyl propionate using the same lipase (PPL) in the case of diols *rac*-1a,b,c,e.



Scheme 1. *PPL-catalyzed enantiomer selective hydrolysis of 1,2-diol diacetates*
Reagents: *i.)* Ac_2O, cat. H_2SO_4, reflux, 15 min; *ii.)* PPL, H_2O, pH 7, r.t.; *iii.)* cat. NaOMe, MeOH, r.t.

Although enhanced enantiomer selectivity is often observed by acylation of racemic alcohols in organic media in comparison with the hydrolysis of the ester of the same alcohol by the same enzyme[3], in the case of 1,2-diols the situation is opposite. Enantiomer selectivities of hydrolyses of diacetates *rac*-2a,b,c,e have proved to be superior to those observed by acylation of the corresponding diols *rac*-2a,b,c,e with methyl propionate[8] in each case. Furthermore, our preliminary experiments have shown that the hydrolysis of 1,2-diol diacetate *rac*-2d catalyzed by PPL proceeds at least one magnitude faster than the corresponding transesterification of the parent diol *rac*-1d in ethyl acetate or methyl propionate with the same enzyme.
The ratio of monoacetate regioisomers (3 and 4) obtained by hydrolysis[12] much depends on the constitution of the diacetate *rac*-2 (Table), contrarily to the exclusive acylation of the primary hydroxyl group in the acylation[8]. The monoacetate regioisomers have proven to be separable by simple vacuum-chromatography[24] from the 3+4c,d,e,h mixtures. Analysis of each diol products *ent*-1c obtained from the separated monoacetates 3c and 4c (Scheme 2.) showed that the enantiomer-preferences are the same in the PPL hydrolysis for primary and secondary acetoxy groups.



Scheme 2. *Regioselectivity - enantiomer preference correlation in PPL hydrolysis*
Reagents: *i.)* PPL, H_2O, pH 7, r.t., 30% conversion; *ii.)* cat. NaOMe, MeOH, r.t.

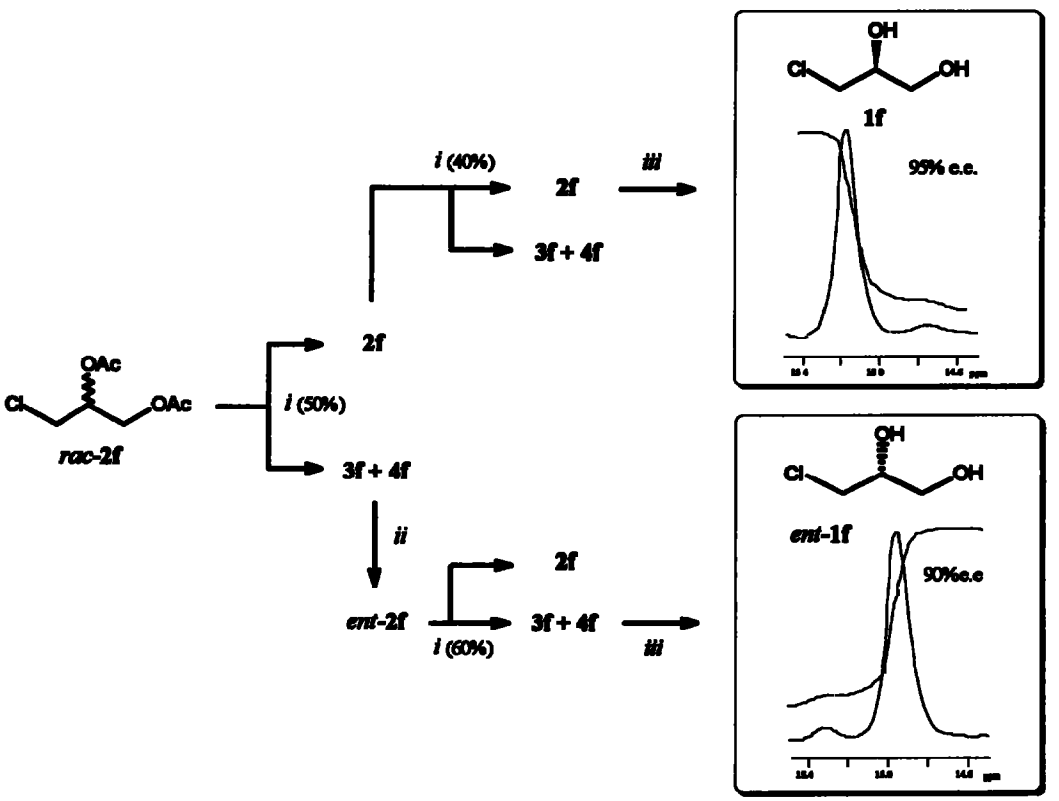
Table: PPL-catalyzed enantiomer selective hydrolysis of 1,2-diol diacetates [a]

Substrate *rac*-2	Conv. %	2, Yield[b] %	$[\alpha]_D$ of 1	e.e. of 1[c], %	Config. of 1	3:4 ratio[d]	3+4, Yield[b], %	$[\alpha]_D$ of *ent*-1	e.e. of *ent*-1[c], %
a	50	75	-4.85 [f]	28	*R*	0.62	64	+4.19 [f]	24
	30					0.45	61	+5.33 [f]	30
	70[e]	49	-9.09 [f]	52	*R*				
b	50	58	+8.9 [g]	72	*R*	1.1	67	-8.8 [g]	69
	30					1.0	86	-10.5 [g]	82
	70[e]	48	+11.6 [g]	91	*R*				
c	50	77	+14.1 [h]	81	*R*	2.2	80	-13.2 [h]	76
	30					2.5	86	-14.5 [h]	85
	70[e]	48	+17.4 [h]	>96	*R*				
d	50	78	+10.9 [i]	72	*R*	0.57	72	-9.4 [i]	56
	30					0.64	80	-11.4 [i]	68
	70[e]	68	+13.4 [i]	80	*R*				
e	50	73	+9.4 [j]	77	*R*	0.75	71	-7.4 [j]	62
	30					0.81	77	-9.3 [j]	78
	70[e]	70	+11.0 [j]	92	*R*				
f	50	81	+4.2 [k]	58	*S*	4.4	75	-4.0 [k]	55
	30					4.0	68	-4.9 [k]	68
	70[e]	57	+6.3 [k]	87	*S*				
g	50	75	+3.2 [l]	54	*S*	4.3	54	-2.9 [l]	49
	30					4.4	50	-4.4 [l]	75
	70[e]	54	+5.4 [l]	92	*S*				
h	50	81	-2.8 [m]	51	*S*	1.7	73	+3.0 [m]	55
	30					1.7	75	+3.1 [m]	57
	70[e]	63	-3.3 [m]	61	*S*				

a: reaction conditions: 5-20 mg PPL/mmol substrate, water, pH 7.5, RT, 0.2-3 h. For details see the Experimental section; *b*: isolated yield after separation in respect to the given conversion; *c*: determined by NMR using Eu-shift reagents[13] and/or comparing the measured optical rotatory power with the corresponding literature data given for each diol below; *d*: Isomeric ratio was estimated from the integration of the CO-CH_3, -CH_2-O, and CH-O signals in the ^{1}H-NMR spectra of 3+4 mixtures; *e*: The diacetate fraction separated after hydrolysis to 30% conversion was further hydrolyzed to a degree which corresponds to 70% conversion of the original substrate; *f*: (neat). Maximum value found[14] for (*S*), $[\alpha]_D$ +17.48° (neat); *g*: (c 2.5, ethanol). The highest values found[15] for the pure enantiomers: (*S*), $[\alpha]^{20}_D$ -12.87 (c 2.5, ethanol), (*R*), $[\alpha]^{20}_D$ +12.4 (c 2.5, ethanol); *h*: (c 12, ethanol). Maximum values found for (*R*), $[\alpha]_D$ +16.2 (c 14, ethanol)[16] and for (*S*), $[\alpha]^{25}_D$ -16.1 (c 3, ethanol)[17]. Since our preparation had higher (+17.4°) rotation value as found in the literature optical purity calculations are based on our own value; *i*: (c 12, ethanol). Literature values found for (*R*), $[\alpha]^{20}_D$ +16.8 (c 12, ethanol)[18,19] and for (*S*), $[\alpha]^{22}_D$ -16.6 (c 11.9, ethanol), 100% e.e.[19]; *j*: (c 1, ethanol). Literature value found[20] for (*S*), $[\alpha]^{22}_D$ -11.9° (c 1, ethanol), >94% e.e.; *k*: (c 5, water). Literature values found[21] for (*R*), $[\alpha]^{22}_D$ +7.1 (c 5, water), >94%e.e. and for (*S*), $[\alpha]^{22}_D$ -6.4 (c 5, water), 88% e.e.; *l*: (c 2, ethanol). The highest values found[22] for (*R*), $[\alpha]^{21}_D$ +5.9 (c 1.7, ethanol) and for (*S*), $[\alpha]^{21}_D$ -5.4 (c 2, ethanol); *m*: (c 10, benzene). Maximum value found[23] for (*S*), $[\alpha]^{20}_D$ +5.45 (c 10, benzene).

It is noteworthy, that quite consistent structure-regioselectivity and structure-enantiomer selectivity equations could be obtained for the PPL hydrolysis of diacetates *rac*-2a-h by minimizing multilinear equation systems using NMR signals (acetate methyl, O-methyne, O-methylene chemical shifts), calculated (MM2) distances, mass of side substituent R, and TLC Rf value of the diacetates as unconditional parameters.

In case of hydrolyses with moderate enantiomer selectivity a cascade procedure can be applied to enhance the enantiomeric purity. This possibility is illustrated by the tandem hydrolysis of *rac*-2f (Scheme 3.).



Scheme 3. *Cascade hydrolysis of 1,2-diacetoxy-3-chloropropane (rac-2f).* [*Under formula of diol enantiomers* **1f** *and ent-***1f** *an illustrative part of 400 MHz PMR spectra in the presence of Eu(hfc)$_3$ as chiral shift reagent*[13] *are shown*]

Reagents: *i.)* PPL, H_2O, pH 7, r.t. (degree of conversion is given in parentheses); *ii.)* Ac_2O, cat. H_2SO_4, reflux, 15 min.; *iii.)* cat. NaOMe, MeOH, r.t.

Comparing the 90% enantiomeric purity of diol *ent*-1f prepared from *rac*-2f by the sequence of PPL hydrolysis (to 50% conversion) - reacetylation of the monoacetate fraction 3f+4f - PPL hydrolysis (to 60% conversion) to which obtained by the one-step hydrolysis (55%e.e. and 68%e.e. at 50% and 30% conversion, respectively) shows that significant improvement of enantiomeric purity can be achieved using consecutive hydrolyses, naturally, in charge of chemical yield.

From the viewpoint of practical applicability it is worth to mention that in case of *rac*-2a,b,c,f,g the diacetate (2) and monoacetate (3+4) fractions obtained after PPL hydrolysis are conveniently separable by using only extractive methods.

Conclusions

Analysis of data on lipase catalyzed hydrolysis of 1,2-diol diacetates compared to the lipase catalyzed acylation of 1,2-diols shows that contrarily to the acylation - hydrolysis of simple racemic alcohols and their esters where a common or very similar transition state for the hydrolysis or acylation is assumable[3] the hydrolytic process is mechanistically quite different from the acylation of the parent diol. The consequences of this difference are the very high regioselectivity parallel with moderate enantiomer selectivity and the poorer acceptance of the 1,2-diols as substrates in case of acylations and moderate and variable regioselectivity parallel with a higher enantiomer selectivity and a higher rate of transformation in case of hydrolyses. It means, that in synthetic procedures requiring high regioselectivity in transformation of 1,2-diols the acylation, while in syntheses needing higher enantiomer selectivity the hydrolysis of the diacetates are the method of choice.

EXPERIMENTAL

The ^{1}H-NMR spectra were measured on JEOL FX-100 (100 MHz) or Brucker AW-80 (80 MHz) spectrometers in $CDCl_3$ solutions containing TMS as internal standard. Enantiomer purity determinations[13] using Eu(hfc)$_3$ as chiral shift reagent were made in dry d_3-acetonitrile on a Varian VXR-400 (400 MHz) spectrometer. Optical rotations were determined on a Perkin Elmer 241 polarimeter. Thin-layer chromatography (TLC) was made using Merck Kieselgel 60 F_{254} aluminum sheets. TLC plates were developed using the following solvent systems: hexane-acetone = 5:2, A; diisopropyl ether-acetone = 2:1, B. Spots were visualized by treatment with 3% ethanolic phosphomolybdic acid solution and heating of the dried plates. Preparative vacuum-chromatography[24] was performed using Merck Kieselgel 60 F_{254}. Acetic anhydride and racemic diols (*rac*-1a,b,c,f) were purchased from Merck. The other diols (*rac*-1d,e,g,h) were synthesized by known procedures. Porcine pancreatic lipase (PPL, Type II) was obtained from Sigma. All solvents used were freshly distilled.

Acetylation of racemic diols (rac-1a-h): general procedure

Acetic anhydride (12.4 g, 0.12 mol) was added dropwise to the stirred diol (*rac*-1a-h, 0.10 mol) containing one drop of conc. H_2SO_4 at a rate providing gentle reflux. After introducing acetic anhydride the mixture was stirred for 15 min and then neutralized by adding sodium acetate. Product was isolated by vacuum distillation in 70-88% yield showing the appropriate IR and ^{1}H-NMR spectra.

rac-2a: yield: 70%, b.p.: 81-82°C (22 mbar/17 torr), *TLC*: Rf(A)= 0.59; *rac*-2b: yield: 73%, b.p.: 85°C (15 mbar/11 torr), *TLC*: Rf(A)= 0.58; *rac*-2c: yield: 78%, b.p.: 92-94°C (11 mbar/8 torr), *TLC*: Rf(A)= 0.59; *rac*-2d: yield: 81%, b.p.: 128-132°C (20 mbar/15 torr), *TLC*: Rf(A)= 0.60; *rac*-2e: yield: 81%, b.p.: 132-139°C (4 mbar/3 torr), *TLC*: Rf(A)= 0.62; *rac*-2f: yield: 77%, b.p.: 118-122°C (21 mbar/16 torr), *TLC*: Rf(A)= 0.48; *rac*-2g: yield: 88%, b.p.: 114-116°C (21 mbar/16 torr), *TLC*: Rf(A)= 0.45; *rac*-2h: yield: 72%, b.p.: 138-139°C (4 mbar/3 torr), *TLC*: Rf(A)= 0.59.

Hydrolysis of racemic diol diacetates (rac-2a-h): general procedure (on 50 mmol scale)

To a stirred emulsion of 1,2-diol diacetate (*rac*-2a-h, 50 mmol) and 80 ml of water PPL enzyme (1 g) was added and the pH value of the mixture was kept constant 7.4 by dropping 1M NaOH solution from an autoburette. After consumpting the desired amount of base (0.4 - 4 h) the mixture was extracted with ethyl acetate (4 x 60 ml). The combined ethyl acetate layers were washed with brine (40 ml) and dried ($MgSO_4$). After evaporating the solvent *in vacuo* the remaining oil was separated either by vacuum-chromatography[23] (*a*) or extraction (*b*) yielding diacetate (2a-h) and monoacetate (3+4a-h) fractions in 48-85% and 55-85% yield (based on conversion), respectively.

a) The remaining oil was applied onto a column filled with silica gel (100 g) and eluted first with hexane-acetone = 10:1 (approximately 1000 ml) then with hexane-acetone = 5:1 eluant mixtures. After analyzing the collected fractions the appropriate parts were combined and evaporated yielding diacetate (2a-h) and monoacetates (3+4a-h).

b) The remaining oil was dissolved in hexane (150 ml) and then extracted with water (3-4 x 150 ml). After reextracting the combined aqueous layers with hexane (100 ml) the unified hexane layers were dried ($MgSO_4$) and evaporated *in vacuo* giving diacetate (2a,b,c,f,g). The aqueous layer was then extracted with ethyl acetate (3-4 x 80 ml). Evaporation of the solvent from the combined and dried ($MgSO_4$) ethyl acetate layers *in vacuo* gave monoacetates (3+4a,b,c,f,g).

For calculated yields of fractions 2a-h and 3+4a-h and isomeric ratio of monoacetates (3 to 4) see Table. Physical properties (IR, ^{1}H-NMR spectra, TLC) of optically active diacetates (2a-h) were similar to the racemic compounds (*rac*-2a-h).

Hydrolysis of 1,2-diacetoxypropane (rac-2a)

a) Hydrolysis of *rac*-2a: (10 g) at 50% conversion yielded after extractive separation 2a (3.75 g) and 3+4a (2.36 g). 3+4a: *TLC*: Rf (A) = 0.39, *^{1}H-NMR*, δ 1.19 (d, J= 6Hz, 1.3H, 4a -CH_3), 1.22 (d, J= 6Hz, 1.7H, 3a -CH_3), 2.07 (s, 1.3H, CH_3), 2.09 (s, 1.7H, CH_3), 3.61 (d, J= 5Hz, 1.15H, 3a -OCH_2-), 3.8-4.3 (m, 1.3H, 4a -OCH_2- and OCH), 4.7-5.2 (m, 0.31H, 3a OCH).

b) Hydrolysis of *rac*-2a: (25 g) at 30% conversion yielded diacetate (11.16 g) and 3+4a (3.37 g).

c) Hydrolysis of diacetate fraction from *b*) at 57% conversion gave 2a (3.68 g) and monoacetates (2.41 g).

Hydrolysis of 1,2-diacetoxybutane (rac-2b)
a) Hydrolysis of *rac*-2b: (10 g) at 50% conversion gave after extractive separation 2b (2.90 g) and 3+4b (2.54 g). 3+4b: *TLC*: Rf (A) = 0.40, ^{1}*H-NMR*, δ 0.96 (m, 3H, CH_3), 1.25-2.0 (m, 2H, CH_2), 2.08 (br s, 3H, CO-CH_3), 3.55-3.77 (m, 1.05H, 3b OCH_2), 3.78-4.35 (m, 1.4H, 4b OCH_2 and OCH), 4.6-5.05 (m, 0.55H, 3a OCH).
b) Hydrolysis of *rac*-2b: (15 g) at 30% conversion yielded diacetate (6.82 g) and 3+4b (2.93 g).
c) Hydrolysis of diacetate fraction from *b*) at 57% conversion gave 2b (2.14 g) and monoacetates (2.35 g).

Hydrolysis of 1,2-diacetoxypentane (rac-2c)
a) Hydrolysis of *rac*-2c: (10 g) at 50% conversion gave after extractive separation 2c (3.85 g) and 3+4c (3.1 g).
b) Hydrolysis of *rac*-2c: (15 g) at 30% conversion yielded diacetate (6.82 g), 3c and 4c (total monoacetates: 3.02 g). Analytical data for the regioisomers separated by vacuum-chromatography on silica gel: 3c: *TLC*: Rf (A) = 0.39, ^{1}*H-NMR*, δ 0.93 (m, 3H, CH_3), 1.48 (mc, 4H, 2 CH_2), 2.09 (s, 3H, CO-CH_3), 3.67 (mc, 2H, OCH_2), 4.7-5.2 (m, 1H, OCH); 4c: *TLC*: Rf (A) = 0.41, ^{1}*H-NMR*, δ 0.93 (m, 3H, CH_3), 1.45 (mc, 4H, 2 CH_2), 2.06 (s, 3H, CO-CH_3), 3.7-4.3 (m, 3H, OCH_2 and OCH).
c) Hydrolysis of diacetate fraction from *b*) at 57% conversion gave 2c (2.14 g) and monoacetates (2.35 g).

Hydrolysis of 1,2-diacetoxyheptane (rac-2d)
a) Hydrolysis of *rac*-2d: (10 g) at 50% conversion gave after separation by vacuum-chromatography 2d (3.9 g) and 3+4d (2.9 g). Analytical data for the regioisomers: 3d: *TLC*: Rf (A) = 0.39, ^{1}*H-NMR*, δ 0.89 (m, 3H, CH_3), 1.38 (mc, 8H, 4 CH_2), 2.08 (s, 3 H, CO-CH_3), 3.67 (mc, 2H, OCH_2), 4.7-5.2 (m, 1H, OCH); 4d: *TLC*: Rf (A) = 0.42, ^{1}*H-NMR*, δ 0.89 (m, 3H, CH_3), 1.41 (mc, 8H, 4 CH_2), 2.06 (s, 3H, CO-CH_3), 3.7-4.3 (m, 3H, OCH_2 and OCH).
b) Hydrolysis of *rac*-2d: (20 g) at 30% conversion yielded diacetate (11.3 g) and 3+4d (3.87 g).
c) Hydrolysis of diacetate fraction from *b*) at 57% conversion gave 2d (4.05 g) and monoacetates (2.94 g).

Hydrolysis of 1,2-diacetoxydecane (rac-2e)
a) Hydrolysis of *rac*-2e: (10 g) at 50% conversion yielded after separation by vacuum-chromatography 2e (3.85 g) and 3+4e (2.87 g). 3e: *TLC*: Rf (A) = 0.41, 4e: *TLC*: Rf (A) = 0.43, 3+4e: ^{1}*H-NMR*, δ 0.89 (m, 3H, CH_3), 1.35 (mc, 14H, 7 CH_2), 2.06 (s, ca. 1.3H, CO-CH_3), 2.08 (s, ca. 1.7H, CO-CH_3), 3.64 (mc, 1.2H, 3e OCH_2), 3.75-4.3 (m, 1.45H, 4e OCH_2 and OCH), 4.7-5.2 (m, 0.6H, 3e OCH).
b) Hydrolysis of *rac*-2e: (10 g) at 30% conversion gave diacetate (5.2 g) and 3+4e (1.94 g).
c) Hydrolysis of diacetate fraction from *b*) at 57% conversion gave 2e (2.10 g) and monoacetates (1.87 g).

Hydrolysis of 3-chloro-1,2-diacetoxypropane (rac-2f)
a) Hydrolysis of *rac*-2f: (10 g) at 50% conversion yielded after extractive separation 2f (4.05 g) and 3+4f (2.94 g). 3+4f: *TLC*: Rf (A) = 0.32, ^{1}*H-NMR*, δ 2.10 (br s, 3H, CO-CH_3), 3.4-3.95 (m, 2.35H, Cl-CH_2 and 3f OCH_2), 3.95-4.5 (m, 2.45H, 4f OCH_2 and OCH), 4.8-5.3 (m, 0.2H, 3f OCH).
b) Hydrolysis of *rac*-2f: (20 g) at 30% conversion yielded diacetate (10.9 g) and 3+4f (3.20 g).
c) Hydrolysis of diacetate fraction from *b*) at 57% conversion gave 2f (3.43 g) and monoacetates (3.71 g).

Hydrolysis of 1,2-diacetoxy-3-methoxypropane (rac-2g)
a) Hydrolysis of *rac*-2g: (10 g) at 50% conversion gave after extractive separation 2g (3.76 g) and 3+4g (2.10 g). 3+4g: *TLC*: Rf (A) = 0.30, ^{1}*H-NMR*, δ 2.08 (s, 2.45H, 4g CO-CH_3), 2.10 (s, 0.55H, 3g CO-CH_3), 3.37(s, 3H, OCH_3), 3.42 (d, J= 5Hz, 1.65H, 4g CH_2-OMe), 3.56 (d, J= 5Hz, 0.35H, 3g CH_2-OMe), 3. 65-4.25 (m, 2.45H, 4g OCH_2 and OCH), 4.8-5.2 (m, 0.2H, 3g OCH).
b) Hydrolysis of *rac*-2g: (30 g) at 30% conversion yielded diacetate (14.7 g) and 3+4g (3.51 g).
c) Hydrolysis of diacetate fraction from *b*) at 57% conversion gave 2g (4.83 g) and monoacetates (4.82 g).

Hydrolysis of 3-benzyloxy-1,2-diacetoxypropane (rac-2h)
a) Hydrolysis of *rac*-2h: (3 g) at 50% conversion yielded after separation by vacuum-chromatography 2h (1.22 g) and 3+4h (0.92 g). 3h: *TLC*: Rf (A) = 0.37, 4h: *TLC*: Rf (A) = 0.41, 3+4h: ^{1}*H-NMR*, δ 2.04 (s, ca. 1.9H, 4h CO-CH_3), 2.07 (s, ca. 1.1H, 3h CO-CH_3), 3.4-4.3 (m, ca. 4.6H, BnO-CH_2, OCH_2, and 4h OCH), 4.51 (s, 2H, OCH_2Ph), 4.8-5.3 (m, ca. 0.4H, 3h OCH), 7.30 (m, 5H, ArH).
b) Hydrolysis of *rac*-2h: (3.1 g) at 30% conversion gave diacetate (1.87 g) and 3+4h (0.57 g).
c) Hydrolysis of diacetate fraction from *b*) at 57% conversion gave 2h (0.59 g) and monoacetates (0.62 g).

Deacetylation of diacetates (2a-h) or monoacetates (3,4a-h) to optically active diols (1a-h) or (ent-1a-h): general procedure

Acetylated 1,2-diol (2a-h or 3,4a-h; 20 mmol) was dissolved in 0.2% methanolic NaOMe solution (15 ml) and stirred at r.t. for 4 h. After neutralizing the mixture by 1*M* HCl methanol was evaporated off and the rest was purified by vacuum-chromatography using hexane-acetone= 2:1 as eluant to give diol (1a-h or *ent*-1a-h) in 70-85% yield.
1a or *ent*-1a: *TLC*: Rf(A)= 0.15; 1b or *ent*-1b: *TLC*: Rf(A)= 0.20; 1c or *ent*-1c: *TLC*: Rf(A)= 0.22; 1d or *ent*-1d: *TLC*: Rf(A)= 0.27; 1e or *ent*-1e: *TLC*: Rf(A)= 0.29; 1f or *ent*-1f: *TLC*: Rf(A)= 0.20, Rf(B)= 0.68; 1g or *ent*-1g: *TLC*: Rf(A)= 0.11, Rf(B)= 0.37, 1h or *ent*-1h: *TLC*: Rf(A)= 0.29. For optical rotation value, enantiomeric purity and configuration data of the diols (1a-h or *ent*-1a-h) prepared from the corresponding diacetates (2a-h) or monoacetates (3+4a-h) obtained by PPL hydrolyses of racemic diacetates (*rac*-2a-h) see Table.

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