Pergamon

Tetrahedron: *Asymmetry* 9 (1998) 589–598

TETRAHEDRON: *ASYMMETRY*

Lipase-catalyzed kinetic resolution of *threo*-configured 1,2-diols: a comparative study of transesterification versus hydrolysis

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Received 17 November 1997; accepted 28 January 1998

Abstract

The kinetic resolution of the α,β-unsaturated vicinal diols **3** has been investigated by irreversible transesterification in organic media and by hydrolysis of the corresponding diacetates **6** (Scheme 1). The best results were obtained in the hydrolysis of the diacetates with the lipase CAL-B from *Candida antarctica* as a catalyst.

1. Introduction

Optically active vicinal diols are valuable intermediates in the synthesis of biologically active compounds and natural products.[1] They are readily transformed into epoxides,[2] aziridines and amino alcohols.[3] Enantiomerically pure diols are precursors for the preparation of chiral crown ethers[4] and they have been successfully used as C_2-symmetric ligands in metal-catalyzed enantioselective reactions.[5]

Among the various classical methods reported for the preparation of optically active vicinal diols, the metal-catalyzed asymmetric dihydroxylation of alkenes is to date the most effective one.[6] Also, biocatalytic processes constitute attractive environmentally acceptable alternatives to obtain optically active 1,2-diols. Recently we have reported that horseradish peroxidase catalyzes the enantioselective reduction of racemic hydroxy hydroperoxides to afford the corresponding 1,2-diols in high enantiomeric excess.[7]

Vicinal diols with one primary and one secondary hydroxyl group, as well as *meso* derivatives, have been resolved by lipase-catalyzed kinetic resolution,[8] however, the lipase-catalyzed kinetic resolution of vicinal diols with two secondary hydroxyl functionalities appears to be unknown. To fill this gap, we have now investigated in detail the transesterification of the racemic *threo*-1,2-diols **3a**–**e** and, for comparison, hydrolysis of the corresponding diacetates **6a**–**e** by lipases (Scheme 1).

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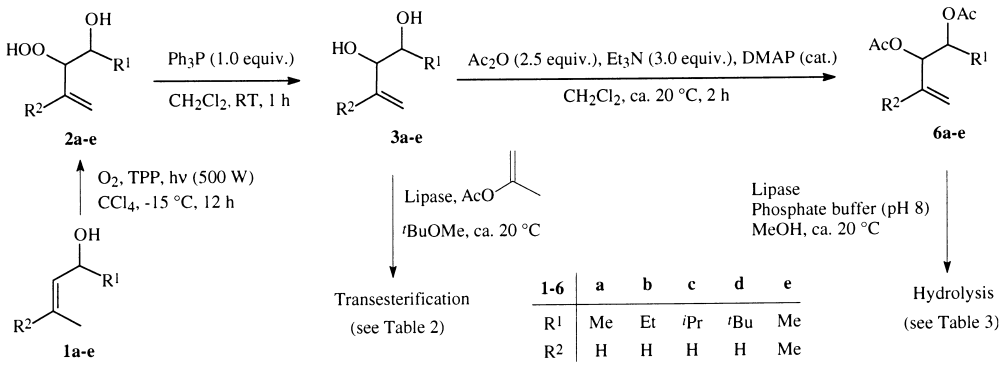
0957-4166/98/$19.00
PII: S0957-4166(98)00043-3



Scheme 1. Synthesis and kinetic resolution of the diols **3a–e** and their corresponding diacetates **6a–e**

2. Results and discussion

The photooxygenation of the allylic alcohols **1a–e**, according to the previously described procedure,[9] afforded the racemic hydroxy hydroperoxides **2a–e** as ca 90:10 *threo:erythro* diastereomeric mixtures.[9] Reduction of the diastereomeric mixtures of the hydroperoxides **2a–e** by triphenylphosphine gave the diols **3a–e**, which were subsequently acetylated to the corresponding diacetates **6a–e**. GC analysis of the racemic diol and diacetate has shown that the diastereomers of these substrates can be easily separated on a cyclodextrin column. Therefore, the rather cumbersome purification of the diastereomers has been avoided and the diols **3a–e** and diacetates **6a–e** were used as a *threo:erythro* mixture (ca 90:10) in the lipase-catalyzed transesterification and hydrolysis. Of the 16 lipases that were employed, those which required long reaction times (>10 days) for ca 50% conversion or gave very low enantiomeric excesses were not studied further, those that performed adequately are described in Table 1.

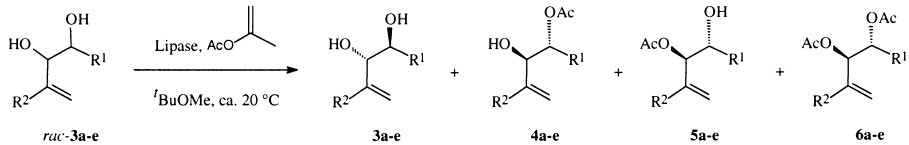
Table 1
Lipases used in Tables 2 and 3

Lipase[a]	Source	Activity (U/mg)[d]	Protein content[b] (mg)	Amount[c] (mg)
BSL (CHIRAZYME® L1)	*Burkholderia sp.*	225	0.10	50
CAL-B (CHIRAZYME® L2)	*Candida antarctica*, fraction B	130	0.30	10
PSL1 (CHIRAZYME® L4)	*Pseudomonas sp.*	8	0.60	50
PSL2 (CHIRAZYME® L6)	*Pseudomonas sp.*	400	0.20	50
MML (CHIRAZYME® L9)	*Mucor miehei*	>300	–	100
ChiroCLEC-PC	*Pseudomonas cepacia*	–	–	10

[a]As lyophilisate formulation, from Boehringer Mannheim except last entry from Altus. [b]Per mg lyophilisate according to Biuret. [c]Amount of lipase used per mmol of substrate. [d]Trybutyrin, pH 7.0, 25 °C.

The results of the transesterifications of the diols **3a–e** are summarized in Table 2. The diol **3a** reacted quite rapidly with the lipases BSL, CAL-B, PSL1 and PSL2 (entries 1–4). The less hindered hydroxyl group was preferentially acetylated to give the monoacetate **4a** as the major product, together with the regiomeric monoacetate **5a** and the remaining diol **3a**. Small amounts of diacetate **6a** were also observed. This regioselectivity is more pronounced for diol **3e** (entries 12–14), although considerably

Table 2
Lipase-catalyzed transesterification[a] of the racemic diols **3a–e**



rac-**3a-e** **3a-e** **4a-e** **5a-e** **6a-e**

Entry	Substrate	Lipase[b]	Time (h)	Conv.[c] (%)	Distribution (%)[d] 3	4	5	6	ee (%)[e] 3	4	5	E[f]
1	**3a**	BSL	0.5	69	31	47	18	4	45	56	22	2
2	**3a**	CAL-B	2	50	50	33	14	3	25	68	42	2
3	**3a**	PSL1	4	56	44	40	13	3	30	76	48	2
4	**3a**	PSL2	4	57	43	39	14	4	39	70	27	3
5	**3b**	CAL-B	7	52	48	25	19	8	42	63	63	3
6	**3b**	PSL1	21	49	51	19	24	6	38	62	63	3
7	**3b**	PSL2	21	38	62	12	22	4	31	76	75	4
8	**3c**	CAL-B	57	27	73	11	16	0	20	64	78	4
9	**3c**	PSL1	57	28	72	13	15	0	17	44	62	3
10	**3c**	PSL2	13	49	51	24	25	0	6	8	26	1
11	**3d**	PSL2	144	23	77	12	11	0	10	75	76	2
12	**3e**[g]	BSL	3	45	55	43	2	0	5	35	n.d.[h]	1
13	**3e**[g]	PSL1	17	41	59	31	10	0	36	73	n.d.	4
14	**3e**[g]	MML	62	39	61	33	6	0	57	96	n.d.	31

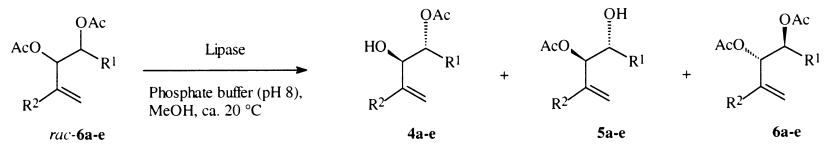
[a]Conducted in methyl *tert*-butyl ether with 10.0 equiv. of isopropenyl acetate as acyl donor; the diol was used as a *threo:erythro* mixture (>90:10). [b]Defined in Table 1. [c]Conversion of **3** determined by GC analysis on a Carlo Erba Strumentazione HRGC 5160 Mega Series (SE 54 column); conditions: started at 80 °C for 5 min, then heated at a rate of 2 °C/min to 100 °C; error ≤ 3%. [d]Normalized to 100%. [e]Determined by GC analysis on a Fisons-Instruments HRGC Mega Series 2 8560 on a permethylated β-cyclodextrin column packed with OV 1701 (25 m, 0.25-mm ID, 0.25-μm film); conditions: started at 80 °C, then heated at a rate of 1 °C/min to 100 °C for entries 1-7 and 11-14; started at 90 °C, then heated at a rate of 2 °C/min to 100 °C for entries 8-10; for the monoacetate **5e**, 80 °C isotherm; error ≤ 2%. [f]Enantioselectivity calculated from the expression E = ln [(1– conv.) (1– ee of substrate)] / ln [(1– conv.) (1+ ee of substrate)] (see Ref. 10). [g]Opposite configuration with respect to the other derivatives. [h]Not determined.

longer reaction times were needed for the same enzyme (compare entries 1 with 12 and 3 with 13). In fact, the transesterification was generally slower for bulkier R^1 groups and none of the lipases tested converted the sterically more demanding diol **3d** in acceptable reaction times. Also, the regioselectivity decreased for the diols **3b–d** (entries 5–11) and both monoacetates **4** and **5** were obtained in ca 1:1 ratio.

In these lipase-catalyzed asymmetric acetylations, the enantioselectivities (E values)[10] were low (Table 1, last column), except for the substrate **3e** with the lipase MML (entry 14). Even at high conversions, the ee values of the remaining diol **3** were only moderate (see entry 1). Similarly, for the monoacetates **4** and **5**, even at conversions under 30% (entries 8, 9 and 11), ee values up to ca 80% were obtained at best.

In view of these low E values in the lipase-catalyzed transesterification, the reverse process, namely the lipase-catalyzed hydrolysis of the corresponding diacetates **6a–e**, was investigated. The best results are listed in Table 3. Indeed, as has been previously described,[11] in our study the enantioselectivity for the enzymatic hydrolysis of the diacetate **6**, with CAL-B[12] as the catalyst, is superior compared to that observed for the acylation of the corresponding diol **3**.

Table 3
Lipase-catalyzed hydrolysis[a] of the racemic diacetates **6a–e**



rac-**6a-e** **4a-e** **5a-e** **6a-e**

Entry	Substrate	Lipase[b]	Time	Conv.[c]	Distribution (%)[d]			ee (%)[e]			E[f]
			(h)	(%)	**4**	**5**	**6**	**4**	**5**	**6**	
1	**6a**	BSL	99	47	24	23	53	65	35	41	4
2	**6a**	CAL-B	0.5	48	24	24	52	>98	>98	96	>500
3	**6a**	PSL1	28	42	23	19	5	56	60	54	12
4	**6a**	PSL2	3	49	25	24	51	>98	64	70	13
5	**6b**	BSL	26	37	19	18	63	72	72	43	10
6	**6b**	CAL-B	16	51	26	25	49	89	87	98	153
7	**6b**	PSL1	19	52	28	24	48	76	76	83	19
8	**6b**	PSL2	0.5	49	25	24	51	90	91	86	50
9	**6c**	BSL	96	10	5	5	90	5	7	1	1
10	**6c**	CAL-B[g]	116	45	21	23	56	>98	97	79	138
11	**6c**	PSL1	96	14	6	8	86	12	14	2	1
12	**6c**	PSL2	96	43	21	22	57	62	63	43	6
13	**6d**	CAL-B	144	3	not determined						
14	**6d**	PSL2	144	8	not determined						
15	**6d**	PLE2[h]	41	60	8	8	40[i]	n.d.[j]		79	2
16	**6e**[k]	CAL-B	25	54	29	25	46	98	95	>98	50
17	**6e**[k]	MML	72	60	32	28	40	19	47	48	1
18	**6e**[k]	ChiroCLEC-PC	72	39	21	18	61	50	30	32	4

[a]25% MeOH as cosolvent; the diacetate was used as a *threo:erythro* mixture (>90:10). [b]Lipases are defined in Table 1. [c]Conversion of **6**, *cf.* Footnote c in Table 2. [d]Normalized to 100%. [e]Determined by GC analysis on a Fisons-Instruments HRGC Mega Series 2 8560 on a permethylated β-cyclodextrin column (2,6-dimethyl-3-pentyl-β-cyclodextrin column for products **4e** and **6e**) packed with OV 1701 (25 m, 0.25-mm ID, 0.25-μm film); conditions: started at 80 °C and heated at a rate of 1 °C/min to 100 °C for entries 1-7 and 11-14; started at 90 °C, then heated at a rate of 2 °C/min to 100 °C for entries 8-10; for the monoacetate **5e**, 80 °C isotherm; error ≤ 2%. [f]*cf.* Footnote f in Table 2. [g]The reaction was carried out with dioxane as cosolvent. [h]Esterase from pig liver, fraction 2; no cosolvent was used. [i]The diol was formed as major product (44%). [j]Not determined. [k]Opposite configuration with respect to the other derivatives was obtained.

The enzyme screening revealed that the lipase CAL-B from *Candida antarctica* (fraction B) is the most efficient biocatalyst for the resolution of the diacetates **6a**–**e**. A ca 1:1 ratio of the regioisomeric monoacetates **4** and **5** was observed in the lipase-catalyzed hydrolysis of **6**, independent of the substituents and enzymes. These results may be rationalized in terms of intramolecular migration of the acyl group as reported in the literature.[13] Unfortunately, pure monoacetate **4** or **5** could not be prepared independently to assess the extent of acyl migration under hydrolysis conditions by control experiments. No significant amounts of diol **3** were observed in the lipase-catalyzed hydrolysis of diacetate **6**.

As to the enantioselectivity, the best ee values were uniformly found for the lipase CAL-B, which catalyzes the hydrolysis with a high degree of stereochemical control, to yield essentially enantiomerically pure monoacetates **4** and **5** and the remaining diacetate **6**. For the diacetate **6a**, nearly perfect kinetic resolution was achieved with CAL-B in a very short reaction time (entry 2). Excellent enantioselectivity was also observed for the diacetate **6e** (entry 16). The CAL-B lipase was sensitive to the steric hindrance of the substrate, since under the same reaction conditions, the hydrolysis of the more hindered diacetate **6c** (data not shown) was extremely slow and the enantiomeric excess was much lower than for diacetates **6a**,**b**. However dioxane, instead of methanol, as cosolvent gave the best results for this substrate (entry 10). The sterically most demanding diacetate **6d** was not resolved under any of the conditions examined for the lipases, the conversions were <10% even after 144 h reaction time (entries 13 and 14). However, the esterase from pig liver, fraction 2 (CHIRAZYME® E2 from Boehringer Mannheim) converted 60% of the substrate **6d** in 41 h (entry 15). In this case the diol **3d** was formed as a major product (44%) in 28% ee, while the remaining diacetate **6d** was obtained with better enantioselectivity (ee value 79%).

Lipase PSL2 yielded good enantioselectivities in the case of diacetate **6b** (entry 8). For the other substrates, PSL2 gave only moderate ee values (entries 4 and 12). Lipases BSL (entries 1, 5 and 9) and PSL1 (entries 3, 7 and 11) showed moderate enantioselectivities for substrates **6a**,**b** and the ee values decreased drastically for the bulkier diacetate **6c**. In the case of diacetate **6e**, better ee values were obtained for lipases MML and ChiroCLEC-PC (entries 17 and 18) in comparison with PSL1, PSL2 and BSL (data not shown), but much lower than those for CAL-B (entry 16).

The absolute configurations of all the diols **3a**–**e** are known, having been established by exciton coupled circular dichroism (ECCD) measurements on the corresponding chromophoric derivatives.[14] The absolute configurations of the optically active monoacetates **4** and **5** and diacetate **6** obtained after lipase-catalyzed kinetic resolution were determined by hydrolysis to the corresponding diols **3** with K_2CO_3 in methanol and comparison with authentic samples prepared by horseradish peroxidase-catalyzed reduction of the corresponding hydroxy hydroperoxides.[7]

The enzyme CAL-B, as well as the other lipases studied, recognize preferentially the (*R*,*R*) enantiomer in both the hydrolysis of the diacetates **6** and the transesterification of the diols **3**, except the derivatives **3e** and **6e** (R^2=Me), for which the (*S*,*S*) enantiomer is preferred. This may be rationalized in terms of the relative size of the substituents at the stereogenic sites by utilizing the empirical rules established for alcohols[15] to predict the sense of the enantioselectivity in lipase-catalyzed esterification, since not enough examples for diols are known in the literature. Figure 1 shows that the (*R*,*R*) enantiomers of the diols **3a**–**d** (structure **A**) agree well with the empirical model. In the case of diol **3e**, the 2-propenyl group is sterically larger than the 1-hydroxyethyl substituent and the preference is inverted (structure **B**).

In conclusion, for the substrates studied, the lipase-catalyzed hydrolysis of the diacetates **6a**–**e** is more efficient than the transesterification in organic solvent of the corresponding diols **3a**–**e** when lipase CAL-B from *Candida antarctica* (fraction B) is used. Except for the substrate **3d**, such enzymatic resolutions can be performed on the preparative scale to obtain these diols in enantiomerically pure form.

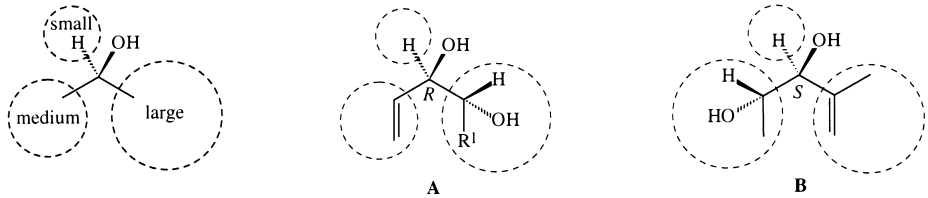


Fig. 1. Preferred enantiomer recognized by lipases in the transesterification of the diols **3a**–**e**

3. Experimental

3.1. Material and methods

All the solvents and isopropenyl acetate were distilled before use. The characteristics of the lipases are described in Table 1. ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker AC 250 (250 MHz) spectrometer. Melting points were determined on a Buchi B-545 apparatus and are uncorrected. IR spectra were recorded on an FT-IR Perkin–Elmer 1600 spectrophotometer. The optical rotations were measured on a Perkin–Elmer 241 polarimeter.

*3.2. Preparation of the hydroxy hydroperoxides **2***

Photooxygenation of 1.0 g (7.8–11.6 mmol) of the allylic alcohols **1a**–**e** in 70 mL dry CCl_4 in the presence of ca 50 mg tetraphenylporphine as a sensitizer according to the previously reported procedure,[9] afforded the corresponding hydroxy hydroperoxides **2a**–**e** as ca 90:10 *threo:erythro* diastereomeric mixtures in 80–93% yield.

*3.3. Reduction of the hydroxy hydroperoxides **2***

Triphenylphosphine (10.0 mmol, 2.62 g) was added at 0°C to the solution of 10.0 mmol (1.2–1.6 g) of the diastereomeric mixtures (d.r. ca 90:10) of the hydroxy hydroperoxides **2** in 50 mL dry dichloromethane. The solution was stirred for 30 min at 0°C, filtered and the solvent evaporated at reduced pressure (20°C/12 torr). Silica gel chromatography afforded the racemic diols **3a**–**e** in 82–92% yield (8.2–9.2 mmol).

*3.4. Diacetylation of the racemic diols **3***

To the solution of 5.0 mmol (0.5–0.7 g) of racemic diols **3** in 50 mL dry dichloromethane were added 2.4 equiv. (12.0 mmol, 1.1 mL) of acetic anhydride, 3.0 equiv. (15.0 mmol, 2.1 mL) of triethylamine and 1 mol% dimethylaminopyridine (DMAP) as catalyst. The reaction mixture was stirred at ca 20°C for 12 h, diluted with 50 mL of dichloromethane, quenched with 20 mL of saturated aqueous NH_4Cl solution, and extracted with dichloromethane (3×50 mL). The organic phase was washed subsequently with saturated aqueous $NaHCO_3$ solution (2×20 mL) and brine, and dried over $MgSO_4$. Silica gel chromatography afforded 4.2–4.7 mmol (84–95%) of diacetates **6a**–**e**.

3.5. General procedure for the lipase-catalyzed irreversible transesterification

Isopropenyl acetate (10.0 equiv.) and the lipase powder were added to the solution of the racemic diol (0.1 mmol) in *tert*-butylmethyl ether (1 mL). The mixture was vigorously stirred at ca 20°C for the time

indicated in Table 2, the enzyme was removed by filtration and the solvent evaporated at reduced pressure (20°C/12 torr). The crude samples were analyzed by gas chromatography.

3.6. General procedure for the lipase-catalyzed hydrolysis

The diacetates **6a**–**e** (0.1 mmol) were dissolved in 0.1 M phosphate buffer (1 mL, pH 8), which contained 25% methanol as a cosolvent. The lipase powder was added, the mixture was stirred at ca 20°C for the time indicated in Table 3, and extracted with Et_2O (4×3 mL). The crude samples were analyzed by gas chromatography.

For the preparative-scale experiments with CAL-B as the catalyst, the pH was kept constant by addition of 0.05 M NaOH solution. Silica gel chromatography afforded the enantiomerically pure diacetate **6** and a mixture of the regiosomeric acetates **4** and **5** in up to 98% ee. The latter were transformed into the corresponding diols or diacetates by standard procedures without loss of optical purity.

According to the general procedure, on the preparative scale the kinetic resolution of 130 mg (0.7 mmol) of **6a** gave 55.0 mg (42%) of (*S,S*)-**6a** (ee>98%) and a mixture of 39.0 mg (39%) of (*R,R*)-**4a** (ee 96%) and (*R,R*)-**5a** (ee 97%); 200 mg (1.0 mmol) of **6b** gave 75.0 mg (37%) of (*S,S*)-**6b** (ee>98%) and a mixture of 109.0 mg (45%) of (*R,R*)-**4b** (ee>98%) and (*R,R*)-**5b** (ee 93%); 129 mg of **6c** gave 50.0 mg (39%) of (*S,S*)-**6c** (ee 63%) and a mixture of 22 mg (21%) of (*R,R*)-**4c** (ee>98%) and (*R,R*)-**5c** (ee>98%); 140 mg of **6e** (0.7 mmol) gave 53.0 mg (38%) of (*R,R*)-**6e** (ee 96%) and a mixture of 46.0 mg (46%) of (*S,S*)-**4e** (ee>98%) and (*S,S*)-**5e** (ee>98%). The kinetic resolution of 200 mg of **6d** with the esterase PLE2 afforded 86.4 mg (43%) of (*S,S*)-**6d** (ee 59%).

3.7. Acetylation of the mixture of monoacetates *4* and *5*

For the acetylation of the optically active monoacetates **4** and **5**, the same procedure has been employed as for the diacetylation of the racemic diols **3**. According to this procedure, the acetylation of 32.0 mg (0.2 mmol) of the mixture of optically active **4e** and **5e** afforded 35.4 mg (90%) of the diacetate **6e** without any loss of optical purity (ee>98%).

3.8. Hydrolysis of the monoacetates *4a–c* and *5a–c*

The mixture of optically active monoacetates **4** and **5** (0.1 mmol, 14.4–17.2 mg) was dissolved in 2 mL of MeOH and 0.05 mmol of K_2CO_3 were added. The reaction was stirred at ca 20°C for 12 h, filtered, and the solvent was removed at 0°C under reduced pressure (1 torr). The residue was chromatographed on a silica gel column to afford 0.08–0.09 mmol (80–90%) of the optically active diols **3a**–**c** (ee 96% for **3a**, 95% for **3b** and 98% for **3c**).

By using the same procedure, the optically active diacetates **6a**–**e** were hydrolyzed to the corresponding diols **3a**–**e** in 81–93% yield without any loss of optical purity.

3.9. (2S,3S)-4-Penten-2,3-diol [(S,S)-*3a*]

Colorless oil; $[\alpha]_D^{20}=-30.7$ (c 0.4, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.15 (d, 3H, J=6.4 Hz), 3.13 (br s, 2H, OH), 3.61 (dq, 1H, J=7.0, 6.4 Hz), 3.82 (dd, 1H, J=7.0, 6.4 Hz), 5.20 (ddd, 1H, J=10.7, 1.5, 1.2 Hz), 5.32 (ddd, 1H, J=17.4, 1.5, 1.2 Hz), 5.81 (ddd, 1H, J=17.4, 10.7, 6.4 Hz); ^{13}C NMR (62.8 MHz, $CDCl_3$): δ 18.8 (q), 70.6 (d), 77.8 (d), 117.4 (t), 137.3 (d); IR ($CDCl_3$): ν 3616, 3579, 3441, 3085,

2981, 2933, 2890, 1644, 1602, 1450, 1426, 1396, 1379, 1263, 1117, 1045, 1020, 993 cm^{-1}. Anal. calcd for $C_5H_{10}O_2$ (102.1): C, 58.78; H, 9.87. Found: C, 58.50; H, 9.92.

*3.10. (3S,4S)-1-Hexen-3,4-diol [(S,S)-**3b**]*

Colorless oil; $[\alpha]_D^{20}=-23.9$ (c 1.1, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ 0.99 (dd, 3H, J=7.3, 7.3 Hz), 1.45 (ddq, 1H, J=14.0, 8.2, 7.3 Hz), 1.61 (ddq, 1H, J=14.0, 7.3, 4.3 Hz), 2.15 (br s, 2H, OH), 3.41 (ddd, 1H, J=8.2, 6.1, 4.3 Hz), 3.95 (dddd, 1H, J=6.1, 6.1, 1.2, 1.2 Hz), 5.24 (ddd, 1H, J=10.4, 1.5, 1.2 Hz), 5.35 (ddd, 1H, J=17.1, 1.5, 1.2 Hz), 5.87 (ddd, 1H, J=17.1, 10.4, 6.1 Hz); ^{13}C NMR (62.8 MHz, $CDCl_3$): δ 9.9 (q), 25.8 (t), 75.7 (d), 75.8 (d), 117.3 (t), 137.7 (d); IR ($CDCl_3$): ν 3685, 3614, 3575, 3456, 3084, 2968, 2937, 2879, 1602, 1463, 1396, 1383, 1261, 1241, 1118, 1056, 1032, 992, 971 cm^{-1}. Anal. calcd for $C_6H_{12}O_2$ (116.1): C, 62.02; H, 10.42. Found: C, 62.39; H, 10.48.

*3.11. (3S,4S)-5-Methyl-1-hexen-3,4-diol [(S,S)-**3c**]*

Colorless oil; $[\alpha]_D^{20}=-28.9$ (c 1.4, $CHCl_3$, for 100% ee). ^1H NMR (250 MHz, $CDCl_3$): δ 0.94 (d, 3H, J=6.7 Hz), 0.98 (d, 3H, J=6.7 Hz), 1.83 (m, 1H, J=6.7, 6.7, 5.2 Hz), 2.16 (br s, 2H, OH), 3.24 (dd, 1H, J=5.5, 5.2 Hz), 4.12 (dd, 1H, J=6.1, 5.5 Hz), 5.24 (ddd, 1H, J=10.4, 1.2, 1.2 Hz), 5.36 (ddd, 1H, J=17.1, 1.2, 1.2 Hz), 5.87 (ddd, 1H, J=17.1, 10.3, 6.1 Hz); ^{13}C NMR (62.8 MHz, $CDCl_3$): δ 16.5 (q), 19.8 (q), 29.5 (d), 73.7 (d), 78.8 (d), 116.8 (t), 137.9 (d); IR ($CDCl_3$): ν 3673, 3616, 3574, 3462, 3084, 2965, 2933, 2911, 2875, 1644, 1602, 1470, 1425, 1389, 1369, 1249, 994 cm^{-1}. Anal. calcd for $C_7H_{14}O_2$ (130.1): C, 64.57; H, 10.84. Found: C, 64.26; H, 10.61.

*3.12. (3S,4S)-5,5-Dimethyl-1-hexen-3,4-diol [(S,S)-**3d**]*

Colorless needles; mp 81–82°C (from hexane–CH_2Cl_2); $[\alpha]_D^{20}=-11.3$ (c 0.9, $CHCl_3$, for 100% ee). ^1H NMR (250 MHz, $CDCl_3$): δ 0.97 (s, 9H), 2.39 (br s, 2H, OH), 3.16 (d, 1H, J=2.4 Hz), 4.26 (dddd, 1H, J=5.8, 2.4, 1.2, 1.2 Hz), 5.18 (ddd, 1H, J=10.4, 1.2, 1.2 Hz), 5.30 (ddd, 1H, J=17.1, 1.2, 1.2 Hz), 5.93 (ddd, 1H, J=17.1, 10.4, 5.8 Hz); ^{13}C NMR (62.8 MHz, $CDCl_3$): δ 26.4 (3×q), 34.8 (s), 71.3 (d), 80.1 (d), 115.6 (t), 140.2 (d); IR ($CDCl_3$): ν 3617, 3563, 3084, 2961, 2908, 2871, 1479, 1396, 1366, 1177, 1120, 1071, 1012, 993 cm^{-1}. Anal. calcd for $C_8H_{16}O_2$ (144.1): C, 66.61; H, 11.19. Found: C, 66.18; H, 11.37.

*3.13. (2R,3R)-4-Methyl-4-penten-2,3-diol [(R,R)-**3e**]*

Colorless oil; $[\alpha]_D^{20}=+5.7$ (c 0.5, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ 1.16 (d, 3H, J=6.1 Hz), 1.74 (dd, 3H, J=1.5, 0.9 Hz), 2.33 (br s, 1H, OH), 2.39 (br s, 1H, OH), 3.74–3.85 (m, 2H), 4.96 (dq, 1H, J=1.5, 1.5 Hz), 5.02 (br dd, 1H, J=1.5, 0.9 Hz); ^{13}C NMR (62.8 MHz, $CDCl_3$): δ 17.8 (q), 18.9 (q), 68.7 (d), 80.6 (d), 113.8 (t), 144.6 (s); IR ($CDCl_3$): ν 3683, 3616, 3574, 3451, 3080, 2978, 2920, 1826, 1649, 1602, 1448, 1396, 1377, 1264, 1122, 1055, 1022 cm^{-1}.

*3.14. (2S,3S)-2,3-Diacetoxypent-4-ene [(S,S)-**6a**]*

Colorless oil; $[\alpha]_D^{20}=-36.6$ (c 0.4, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ 1.20 (d, 3H, J=6.7 Hz), 2.04 (s, 3H), 2.08 (s, 3H), 5.04 (dq, 1H, J=6.7, 6.4 Hz), 5.25–5.37 (m, 3H), 5.75 (dddd, 1H, J=17.1, 10.4, 1.5, 1.2 Hz); ^{13}C NMR (62.8 MHz, $CDCl_3$): δ 16.1 (q), 20.9 (q), 21.0 (q), 70.3 (d), 75.6 (d), 119.2 (t), 132.4 (d), 169.9 (s), 170.2 (s); IR ($CDCl_3$): ν 3090, 2990, 2939, 1736, 1651, 1602, 1449, 1427, 1347,

1255, 1235, 1140, 1061, 1025, 989 cm^{-1}. Anal. calcd for $C_9H_{14}O_4$ (186.1): C, 58.04; H, 7.58. Found: C, 57.79; H, 7.38.

*3.15. (3S,4S)-3,4-Diacetoxyhex-1-ene [(S,S)-**6b**]*

Colorless oil; $[\alpha]_D^{20}=-61.6$ (c 1.2, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ 0.89 (dd, 3H, J=7.6, 7.3 Hz), 1.56 (ddq, 2H, J=7.9, 7.6, 7.3 Hz), 2.05 (s, 3H), 2.07 (s, 3H), 4.97 (ddd, 1H, J=7.9, 5.2, 5.2 Hz), 5.24 (ddd, 1H, J=10.4, 1.2, 1.2 Hz), 5.30 (ddd, 1H, J=17.1, 1.2, 1.2 Hz), 5.34 (dddd, 1H, J=6.1, 5.2, 1.2, 1.2 Hz), 5.73 (ddd, 1H, J=17.1, 10.4, 6.1 Hz); ^{13}C NMR (62.8 MHz, $CDCl_3$): δ 9.4 (q), 20.8 (q), 20.9 (q), 23.4 (t), 74.5 (d), 74.7 (d), 118.8 (t), 132.6 (d), 169.9 (s), 170.5 (s); IR ($CDCl_3$): ν 3091, 2974, 2939, 2882, 1732, 1647, 1603, 1463, 1426, 1373, 1232, 1082, 1021 cm^{-1}. Anal. calcd for $C_{10}H_{16}O_4$ (200.1): C, 59.97; H, 8.06. Found: C, 59.74; H, 8.08.

*3.16. (3S,4S)-3,4-Diacetoxy-5-methylhex-1-ene [(S,S)-**6c**]*

Colorless oil; $[\alpha]_D^{20}=-68.8$ (c 0.9, $CHCl_3$, for 100% ee). ^1H NMR (250 MHz, $CDCl_3$): δ 0.90 (d, 3H, J=6.7 Hz), 0.91 (d, 3H, J=7.0 Hz), 1.89 (m, 1H, J=7.0, 6.7, 6.1 Hz), 2.06 (s, 3H), 2.08 (s, 3H), 4.89 (dd, 1H, J=6.1, 5.8 Hz), 5.24 (ddd, 1H, J=10.4, 1.2, 1.2 Hz), 5.31 (ddd, 1H, J=17.1, 1.2, 1.2 Hz), 5.44 (dddd, 1H, J=6.1, 6.1, 1.2, 1.2 Hz), 5.72 (ddd, 1H, J=17.1, 10.4, 6.1 Hz); ^{13}C NMR (62.8 MHz, $CDCl_3$): δ 17.2 (q), 19.2 (q), 20.8 (q), 20.9 (q), 28.5 (d), 73.7 (d), 77.6 (d), 118.6 (t), 132.8 (d), 169.9 (s), 170.6 (s); IR ($CDCl_3$): ν 2970, 2939, 2874, 1737, 1602, 1467, 1426, 1374, 1252, 1234, 1141, 1099, 1024 cm^{-1}. Anal. calcd for $C_{11}H_{18}O_4$ (214.1): C, 61.64; H, 8.47. Found: C, 61.28; H, 8.46.

*3.17. (3S,4S)-3,4-Diacetoxy-5,5-dimethyl-1-ene [(S,S)-**6d**]*

Colorless oil; $[\alpha]_D^{20}=-70.9$ (c 1.5, $CHCl_3$, for 100% ee). ^1H NMR (250 MHz, $CDCl_3$): δ 0.95 (s, 9H), 2.08 (s, 3H), 2.09 (s, 3H), 4.84 (d, 1H, J=3.0 Hz), 5.17 (ddd, 1H, J=10.4, 1.5, 1.2 Hz), 5.21 (ddd, 1H, J=17.1, 1.5, 1.2 Hz), 5.57 (dddd, 1H, J=5.5, 3.0, 1.2, 1.2 Hz), 5.72 (ddd, 1H, J=17.1, 10.4, 5.5 Hz); ^{13}C NMR (62.8 MHz, $CDCl_3$): δ 20.7 (q), 21.2 (q), 26.7 (3×q), 34.6 (s), 72.7 (d), 78.9 (d), 117.2 (t), 134.3 (d), 169.8 (s), 170.6 (s); IR ($CDCl_3$): ν 2968, 2931, 2874, 1736, 1646, 1602, 1479, 1425, 1374, 1235. Anal. calcd for $C_{12}H_{20}O_4$ (228.1): C, 63.12; H, 8.83. Found: C, 62.63; H, 8.79.

*3.18. (2R,3R)-2,3-Diacetoxy-4-methylpent-4-ene [(R,R)-**6e**]*

Colorless oil; $[\alpha]_D^{20}=-19.4$ (c 0.9, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ 1.13–1.19 (m 3H), 1.73 (br dd, 3H, J=1.5, 0.9 Hz), 2.01 (s, 3H), 2.06 (s, 3H), 4.96 (dq, 1H, J=1.5, 1.5 Hz), 5.02 (br s, 1H), 5.09–5.20 (m, 2H); ^{13}C NMR (62.8 MHz, $CDCl_3$): δ 16.4 (q), 18.7 (q), 20.9 (q), 21.0 (q), 69.3 (d), 78.4 (d), 115.2 (t), 140.2 (s), 169.9 (s), 170.3 (s); IR ($CDCl_3$): ν 3085, 2987, 2940, 1732, 1654, 1447, 1374, 1249, 1236, 1161, 1145, 1117, 1067, 1025, 978 cm^{-1}. Anal. calcd for $C_{10}H_{16}O_4$ (200.1): C, 59.97; H, 8.06. Found: C, 60.00; H, 8.01.

Acknowledgements

This work was supported by the Deutsche Forschungsgemeinschaft (SFB 347, Selektive Reaktionen Metall-aktivierter Moleküle), the Bayerische Forschungsstiftung (Bayerischer Forschungsver-

bund Katalyse-FORKAT) and the Fonds der Chemischen Industrie. M.T.D. thanks the Alexander-von-Humboldt Foundation for a postdoctoral fellowship (1997). We are grateful to Boehringer Mannheim GmbH for the generous gift of enzymes.

References

1. (a) Plattner, J. J.; Rapoport, H. *J. Am. Chem. Soc*. **1971**, *93*, 1758–1761. (b) Rao, A. V. R.; Bose, D. S.; Gurjar, M. K.; Ravindranathan, T. *Tetrahedron* **1989**, *45*, 7031–7040. (c) Wright, A. E.; Schäfer, M.; Midland, S.; Munnecke, D. E.; Sims, J. J. *Tetrahedron Lett*. **1989**, *30*, 5699–5702. (d) Fang, X.; Anderson, J. E.; Chang, C.; Mclaughlin, J. L. *Tetrahedron* **1991**, *47*, 9751–9758. (e) Niwa, H.; Ogawa, T.; Okamoto, O.; Yamada, K. *Tetrahedron* **1992**, *48*, 10531–10548.
2. Kolb, H. C.; Sharpless, K. B. *Tetrahedron* **1992**, *48*, 10515–10530.
3. (a) Lohray, B. B.; Gao, Y.; Sharpless, K. B. *Tetrahedron Lett*. **1989**, *30*, 2623–2626. (b) Lohray, B. B.; Ahuja, J. R. *J. Chem. Soc., Chem. Commun*. **1991**, 95–97.
4. Hayward, R. C.; Overton, C. H.; Whitham G. H. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2413–2415.
5. Orsini, F.; Pelizzoni, F. *Tetrahedron: Asymmetry* **1996**, *7*, 1033–1040.
6. Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev*. **1994**, *94*, 2483–2547.
7. Adam, W.; Hoch, U.; Humpf, H.-U.; Saha-Möller, C. R.; Schreier, P. *J. Chem. Soc., Chem. Commun*. **1996**, 2701–2702.
8. (a) Bosetti, A.; Bianchi, D.; Cesti, P.; Golini, P.; Spezia, S. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2395–2398. (b) Theil, F.; Weidner, J.; Ballschuh, S.; Kunath, A.; Schick, H. *J. Org. Chem*. **1994**, *59*, 388–393. (c) Theil, F.; Lemke, K.; Ballschuh, S.; Kunath, A.; Schick, H. *Tetrahedron: Asymmetry* **1995**, *6*, 1323–1344. (d) Egri, G.; Baitz-Gács, E.; Poppe, L. *Tetrahedron: Asymmetry* **1996**, *7*, 1437–1448. (e) Hof, R. P.; Kellogg, R. M. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2051–2060. (f) Nicolosi, G.; Patti, A.; Piattelli, M.; Sanfilipo, C. *Tetrahedron: Asymmetry* **1995**, *6*, 519–524.
9. Adam, W.; Nestler, B. *J. Am. Chem. Soc*. **1993**, *115*, 5041–5049.
10. Chen, C.-S.; Fujimoto, Y.; Girdaukas, G.; Sih, C. J. *J. Am. Chem. Soc*. **1982**, *104*, 7294–7299.
11. Poppe, L.; Novák, L.; Kajtár-Peredy, M.; Szántay, C. *Tetrahedron: Asymmetry* **1993**, *4*, 2211–2217.
12. (a) Gais, H.-J. Weiden, I. *Tetrahedron: Asymmetry* **1996**, *7*, 1523–1526. (b) Adam, W.; Groer, P.; Saha-Möller, C. R. *Tetrahedron: Asymmetry* **1997**, *8*, 833–836. (c) Rotticci, D.; Orrenius, C.; Hult, K.; Norin, T. *Tetrahedron: Asymmetry* **1997**, *8*, 359–362.
13. Mbappé, M.-A.; Sicsic, S. *Tetrahedron: Asymmetry* **1993**, *4*, 1035–1040.
14. Hoch, U.; Humpf, H.-U.; Schreier, P.; Saha-Möller, C. R.; Adam, W. *Chirality* **1997**, *9*, 69–74.
15. Kazlauskas, R. J.; Weissfloch, A. N. E.; Rappaport, A. T.; Cuccia, L. A. *J. Org. Chem*. **1991**, *56*, 2656–2665.