Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron: *Asymmetry* 15 (2004) 3945–3954
Tetrahedron: Asymmetry

Enzymatic resolution of (*RS*)-β-hydroxy selenides in organic media

Carlos E. Costa,[a,*] Giuliano C. Clososki,[a] Henrique B. Barchesi,[a] Sandra P. Zanotto,[b] M. Graça Nascimento[b] and João V. Comasseto[a,*]

[a]*Instituto de Química, Universidade de São Paulo, C.P. 26077, 05599-070, São Paulo SP, Brazil*
[b]*Departamento de Química, Universidade Federal de Santa Catarina, C.P. 26077, 88040-900, Florianópolis SC, Brazil*

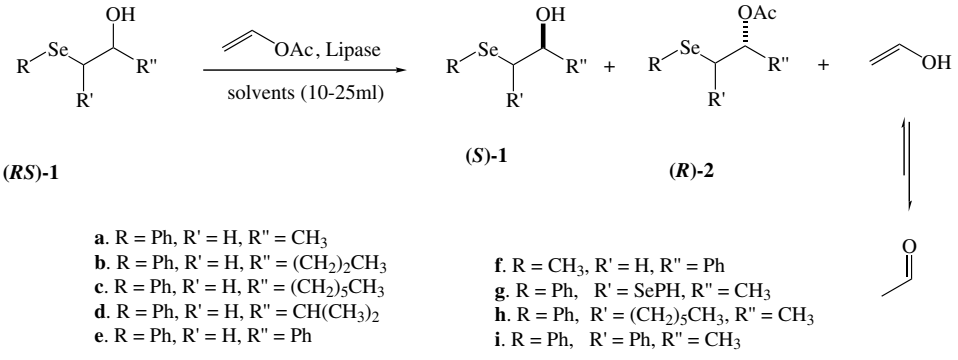
Received 1 October 2004; accepted 1 November 2004

Abstract—Kinetic resolutions of a number of β-hydroxy selenides promoted by enzymes were performed using PPL (free *Porcine pancreatic* lipase), PSL (Amano PS—free *Pseudomonas* sp. lipase) and CALB (NOVOZYM 435®—immobilized *Candida Antarctica* lipase type B) with (*RS*)-1-phenylselanyl-propan-2-ol. CALB gave the best results and provided both (*R*)- and (*S*)-enantiomers in high enantiomeric purity. A comparative study of the effect of temperature, solvent, enzyme immobilization and the structure of the substrates on the resolution is presented.

1. Introduction

Biocatalysis is a powerful synthetic tool to obtain enantiopure building blocks for organic synthesis.[1] Selenium organic compounds have been widely used in useful synthetic transformations[2] and enantioselective methodologies involving this element have been developed.[3] However, to our knowledge only one application of biocatalysis to prepare enantiopure selenium compounds has been published to date.[4] With the aim of combining the synthetic potential of the biocatalysis with the organoselenium chemistry, we initiated a program to apply biocatalysis in the preparation of enantiopure chiral selenium organic compounds.[5] The selanyl group of β-hydroxy selenides can be used in radical carbon–carbon bond formation, especially the intramolecular type (radical cyclizations),[6] which is useful for synthesis of organic molecules.[7]

Lipases tolerate unnatural substrates and reaction conditions very well and are ideal candidates to explore possibilities to prepare enantiopure selenium compounds in transesterification reactions in organic media. Herein, we report the enzymatic resolution of a number of β-hydroxy selenides in organic media (Scheme 1) using free and immobilized lipases in the presence of vinyl acetate under different experimental conditions.



Scheme 1. Lipase-catalyzed transesterification of (*RS*)-β-hydroxy selenides in organic media.

* Corresponding authors. Tel.: +55 11 3091 2176; fax: +55 11 3815 5579; e-mail: jvcomass@iq.usp.br

0957-4166/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2004.11.007

2. Results and discussion

2.1. Enzymatic resolution

The evaluation of the enzyme enantioselectivity in the transesterification of β-hydroxy selenides was carried out with (***RS***)-**1a** as the substrate and vinyl acetate as the acetate donor in organic media. Three lipases, PPL (free *Porcine pancreatic* lipase—42 units/mg prot), PSL (Amano PS—free *Pseudomonas* sp. Lipase—30,000 u/g) and CALB (NOVOZYM 435®—immobilized *Candida antarctica* lipase type B—10,000 PLU/g), were chosen as the enzymes.

Initially, the influence of the temperature was studied using PPL, PSL and CALB in typical experiments at 5, 10, 20, 32 and 40 °C. The conversions were determined by analyzing the formed products by chiral-GC. Table 1 shows the effects of the temperature on the enzymes in the resolution of (***RS***)-**1a**. The results demonstrated that the enzymatic activity depends on the temperature employed. The temperature also had considerable effect on the enantioselectivity, but no influence in the stereochemical preference for the (***R***)-1-phenylselanyl-propan-2-ol enantiomer. It was observed that this enantiopreference agrees with the Kazlauskas' rule, an extension of Prelog's rule for hydrolases.[8]

The highest stereoselectivities were obtained using PSL and CALB at 20–40 °C, and the best relation between enantiomeric excess and conversion was observed at 32 °C. In the reaction with PSL both the (***S***)-**1a** and (***R***)-**2a** were obtained in more than 92% ee at 32 °C (Table 1, entries 11 and 12), while the best enantioselectivity was achieved for the reaction with CALB, when both the (***S***)-**1a** and (***R***)-**2a** were obtained in more than 98% ee at 32 °C (Table 1, entries 18 and 19). Control of the reaction time and temperature, when PSL or CALB were used as biocatalysts, allowed the isolation of both (***S***)-**1a** and (***R***)-**2a** with >99% ee (Table 1, entries 9, 12, 17 and 19).

The influence of the solvent was also evaluated in the acylation of (***RS***)-**1a** using PSL and CALB in typical experiments at 32 °C in some dry solvents. The conversions were determined measuring the yield of the products at 24 h for PSL and 6 h for CALB (Fig. 1). It was observed that the solvent influenced conversion of the substrate (enzymatic activity), but no effect in the enzyme enantioselectivity and enantiopreference, showing the same preference for the (*R*)-1-phenylselanyl-

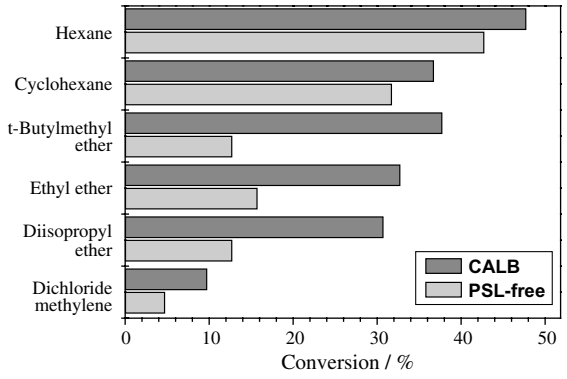


Figure 1. Effect of the solvent in the lipase-catalyzed kinetic resolution of (*RS*)-1-phenylselanyl-propan-2-ol (**1a**) at 32 °C.

Table 1. Enzymatic resolution[a] of (***RS***)-1-phenylselanyl-propan-2-ol (**1a**) using different lipases at different temperatures

Entry	Lipase	Temperature (°C)	Time (h)	Conversion (%)	Ee (***S***)-**1a**[b] (%)	Ee (***R***)-**2a**[c] (%)	*E*[d]
1	PPL	5	24	30	40	94	47
2		10	24	39	57	90	33
3		20	24	41	63	89	32
4		32	24	40	59	88	28
5		32	98	49	81	84	28
6		40	24	34	46	88	24
7	PSL	5	24	27	37	99	>200
8		10	24	28	39	99	>200
9		20	24	31	45	**>99**	>200
10		32	24	45	80	97	161
11		32	49	51	98	95	179
12		32	72	52	**>99**	92	>125
13		40	24	47	85	95	106
14	CALB	5	6	43	76	**>99**	>200
15		10	6	47	88	**>99**	>200
16		20	6	48	90	**>99**	>200
17		32	2	45	80	**>99**	>200
18		32	4	49	98	99	>200
19		32	6	50	**>99**	99	>200
20		40	5	51	**>99**	98	>200

[a] The reactions were performed with 0.5 mmol of (***RS***)-**1a** and **1g** of PPL, 100 mg of PSL or 15 mg of CALB in hexane (25 mL for PPL and PSL or 10 mL for CALB).
[b] Enantiomeric excess of the recovered alcohol (***S***)-**1a**.
[c] Enantiomeric excess of the acetate (***R***)-**2a**.
[d] Enantiomeric ratio: this parameter describes the enantioselectivity of the enzyme.

propan-2-ol **1a** enantiomer. In all solvents (***R***)-**2a** was obtained in more than 97% ee using PSL and in more than 99% ee using CALB. The highest enzymatic activities were observed in nonpolar solvents as hexane and cyclohexane, while in polar solvents the enzymatic activity decreased.

Enzyme immobilization is a valuable tool for modifying the kinetic resolution parameters. For instance, PSL immobilized in agar gel, silica, sodium caseinate film, poly(ethylene oxide) (PEO) film and montmorillonite K10. The influence of the support was evaluated by reacting compound (***RS***)-**1a** with the supported enzymes, under the same experimental conditions used for the free enzyme reaction. The results showed the dependence of the enzymatic activity on the kind of support employed (Fig. 2). No product was detected using

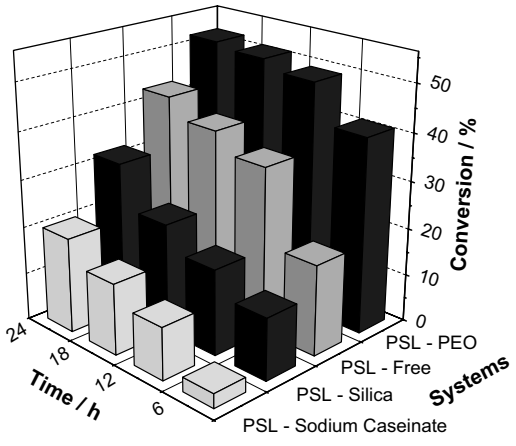


Figure 2. Immobilized *Pseudomonas* sp. lipase (PSL) versus time in the resolution of (*RS*)-1-phenylselanyl-propan-2-ol **1a** in hexane at 35 °C.

PSL immobilized in agar gel and montmorillonite K10, while using silica or sodium caseinate film as the support the enzymatic activity decreased. However, the immobilization of PSL in PEO increased its activity. A rationalization for this result could be based on the diffusion processes of the reagents and products from the support to the reaction medium and also due to the maintenance of the enzyme original structure. Using PEO, the diffusion was faster than when agar gel was used.[9] In all employed systems (***R***)-**2a** was obtained in more than 92% ee at 35 °C. The product (***R***)-**2a** was obtained with 92% ee and the unreacted substrate (***S***)-**1a** with >99% ee with 52% of conversion within 24 h reaction time, while 45% of conversion and 80% ee for (***S***)-**1a** and 97% ee for (***R***)-**2a** were obtained using the free lipase. The stereochemical preference for the (***R***)-1-phenylselanyl-propan-2-ol **1a** enantiomer leading to the acetate (***R***)-**2a** is the same with PSL-free or immobilized, regardless of the support used.

As discussed above, CALB in hexane at 32 °C was found to be the system of choice to perform the kinetic resolution of (***R***,***S***)-**1a**. These experiments aimed to investigate the influence of the R″ substituent in the resolution parameters. In this way, the kinetic resolutions of selenides (***R***,***S***)-**1b**–**e** (Scheme 1) were performed by mixing of the substrate (0.5 mmol), CALB (300 mg) and vinyl acetate in hexane. Initially, the reaction with (***R***,***S***)-**1b** was performed at 32 °C. However at this temperature the reaction presented low enzymatic activity (Table 2, entries 1–3). In view of this fact all reactions were then performed at 40 °C, since at this temperature the enzymatic activity of CALB is higher (Table 1, entry 20). In all cases, the stereochemical preference for the *R*-enantiomer was evidenced. The results in Table 2 show that the reaction time and the enantioselectivity are affected by the size of the *R*″ group. The presence of a

Table 2. Enzymatic resolution[a] of β-hydroxy selenides with CALB at different temperatures

Entry	Substrate	Temperatures (°C)	Time (days)	Conversion (%)	Ee 1 (%)[b]	Ee 2 (%)[c]	Absolut. config.[d]	*E*[e]
1	(***RS***)-**1b**	32	4	46	66	91	(***S***)	42
2			12	56	99	78	(***S***)	41
3			16	58	**>99**	71	(***S***)	41
4		40	2	41	62	88	(***S***)	29
5			7	58	98	72	(***S***)	27
6			9	59	**>99**	70	(***S***)	28
7	(***RS***)-**1c**	40	5	35	22	41	(***S***)	3
8			7	46	32	37	(***S***)	3
9			9	59	42	33	(***S***)	3
10	(***RS***)-**1d**	40	12	29	36	90	(***S***)	27
11			15	35	47	89	(***S***)	27
12			20	45	69	86	(***S***)	29
13	(***RS***)-**1e**	40	20	<1	—	—	—	—
14	(***RS***)-**1f**	40	10	23	24	79	(***R***)	10
15			15	32	32	76	(***R***)	10
16			20	36	41	74	(***R***)	10

[a] The reactions were performed with CALB (300 mg) in hexane (10 mL).
[b] Enantiomeric excess of the recovered alcohol **1**.
[c] Enantiomeric excess of the acetate **2**.
[d] Absolute configuration of the recovered alcohol **1**.
[e] Enantiomeric ratio: this parameter describes the enantioselectivity of the enzyme.

large-sized substitute [compounds (***RS***)-**1b** and **c**] or a ramification [compound (***RS***)-**1d**] had a negative influence on the kinetic resolution and, in the case of compound (***RS***)-**1e**, no acetylated product was detected (Table 2, entry 13).

These results are in agreement with the literature on the structural requirements that a secondary alcohol needs to be successfully resolved with lipases.[10] A recent study using CALB, showed that alcohols bearing a medium-sized substituent larger than an ethyl group or a large-sized substituent smaller than a *n*-propyl group led to poor enantiomeric ratio (*E*) values.[11] According to Kazlauskas's rule,[8] our results showed that, for the β-hydroxy selenides (***RS***)-**1a–e**, the phenyl seleno group behaved as a large substituent. To evaluate the effect of the size of the seleno group in the resolution of the β-hydroxy selenides, (***RS***)-**1f** was synthesized. This compound has a phenyl group as the *R′* group (large-sized) and a methyl seleno group instead of the phenyl seleno group (R = Me). The enzymatic resolution of (***RS***)-**1f** presented the stereochemical preference for the *S*-enantiomer, differently of the others compounds (Table 2, entries 14–16). According to Kazlauskas's rule,[8] the methyl seleno group behaved as a medium-sized group, larger than the ethyl group in the enzymatic resolution using CALB, leading to poor enantiomeric ratio (*E*) values (Table 2, entries 14–16).

Considering these results, we realized that β-hydroxy selenides need a medium-sized substituent smaller than the ethyl group in order to be successfully resolved by CALB, like the methyl group in (***RS***)-**1a**. In this way, the enzymatic resolution of the β-hydroxy selenides (±)-**1g–i** (which have a methyl group as the R″ group) was performed by mixing the substrate (0.5 mmol), CALB (15 mg) and vinyl acetate in hexane at 32 °C.

Under these conditions, compounds **1g–i** were successfully resolved. The stereochemical preference for the *R*-configuration in the stereogenic carbinyl center was observed, in accordance with our previous results. The (*S*)-enantiomer (unreacted substrate) was obtained with >92% ee and the product [(*R*)-enantiomer] with >99% ee (Table 3). These results demonstrated that (***RS***)-β-hydroxy selenides bearing a medium-sized substituent smaller than the ethyl group as the *R″* group, and an alkyl or aryl group as *R′* group (Scheme 1) can be successfully resolved by CALB.

2.2. Determination of the enantiomeric excesses

The enantiomeric excesses (ee) of the alcohols **1a–i** and esters **2a–i** were calculated from the chiral-GC chromatograms comparing with the racemic samples. For compounds **1g–i** and **2c–i**, direct analyses were not possible in view of the poorly resolved chiral chromatograms. In this way, alcohol **1g** was transformed into the β-hydroxy selenide **1a** by reductive deselenenylation, alcohol **1h** was transformed into its corresponding allyl alcohol **3**, alcohol **1i** was transformed into its corresponding selenium free alcohol **4** and esters **2c–i** were transformed into their corresponding alcohols prior to the chiral GC analysis (Scheme 2).

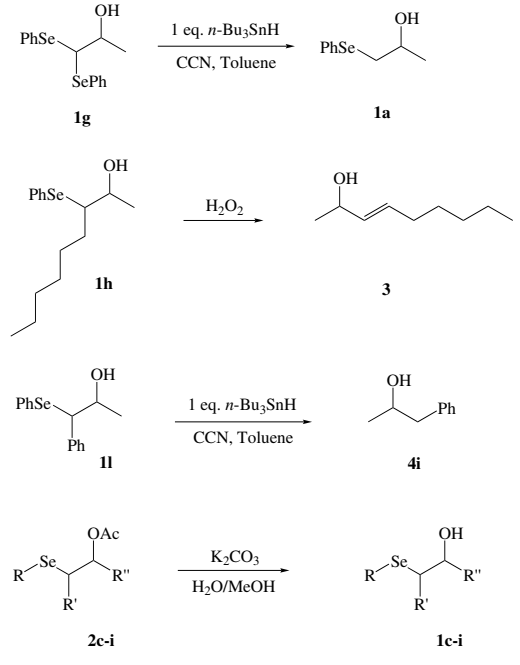
Table 3. Enzymatic resolution[a] of **1g–i** with CALB at 32 °C

Entry	Substrate	Time (h)	Conv. (%)	Ee (%)	Ee (%)	E[b]
1	(***RS***)-**1g**	25	50	99[c]	>99[d]	>200
2	(***RS***)-**1h**	50	48	93[e]	>99[f]	>200
3	(***RS***)-**1i**	72	48	92[g]	>99[h]	>200

[a] Reactions were performed with 0.5 mmol of (***RS***)-**1** and CALB (15 mg) in hexane (10 mL).
[b] Enantiomeric ratio.
[c] Enantiomeric excess of the recovered alcohol **1g**.
[d] Enantiomeric excess of the acetate **2g**.
[e] Enantiomeric excess of the recovered alcohol after selenoxide elimination.
[f] Enantiomeric excess of the acetate after selenoxide elimination.
[g] Enantiomeric excess of the recovered alcohol after the phenyl seleno group removal.
[h] Enantiomeric excess of the acetate after the phenyl seleno group removal.

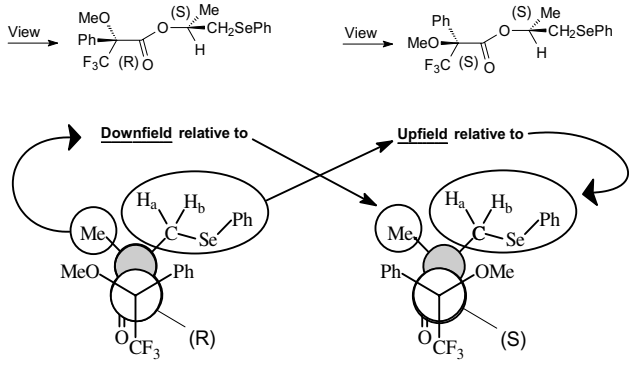
2.3. Determination of the absolute configuration

The absolute stereochemistry of alcohol **1a** was determined by NMR. The unreacted substrate (**1a** >99% ee) of the kinetic resolution was derivatized with the two stereoisomers of α-methoxy-α-trifluoromethylphenylacetyl chloride (MTPA-Cl). The proton NMR spectra of the resulting diastereoisomeric derivatives presented different chemical shifts. According to Mosher's model,[12] the differences were originated by the anisotropic effect of the aromatic ring in a preferred



c. R = Ph, R' = H, R'' = $(CH_2)_5CH_3$
d. R = Ph, R' = H, R'' = $CH(CH_3)_2$
e. R = Ph, R' = H, R'' = Ph
f. R = CH_3, R' = H, R'' = Ph
g. R = Ph, R' = SePh, R'' = CH_3
h. R = Ph, R' = $(CH_2)_5CH_3$, R'' = CH_3

Scheme 2. Transformations to determine the ee.

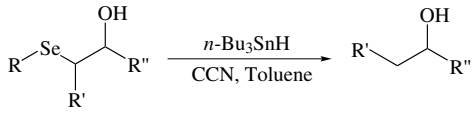


	(*RS*)	(*SS*)
δ_{Ha}(ppm) =	3.14	3.17
δ_{Hb}(ppm) =	2.93	3.02
$\delta_{H\text{-}Me}$(ppm) =	1.44	1.35
δ_{Se}(ppm) =	269.99	271.12
$\delta_{C\text{-}Se}$(ppm) =	32.20	32.40
$\delta_{C\text{-}Me}$(ppm) =	19.70	19.60

Figure 3. Mosher's model for compound **1a**.

conformation. This effect allowed the assignment of the position of the groups on the carbonyl carbon. In addition, the ^{13}C NMR and ^{77}Se NMR spectra presented the same effect in their chemical shifts (Fig. 3). Thus the absolute stereochemistry of alcohol **1a** was determined as being (***S***).

The β-hydroxy selenides **1b**, **1d**, **1f**, **1h** and **1i** were transformed into their corresponding selenium free alcohols by reductive deselenenylation using *n*-BuSnH (Scheme 3) or by selenoxide elimination (**1h**—Scheme 2). The absolute stereochemistry of these alcohols was determined by comparison of their optical rotations with the data published in the literature.[13–15] The absolute stereochemistry of β-hydroxy selenide **1c** was determined by comparison of its optical rotation with the data published in the literature for the (*R*)-enantiomer.[16] Compound **1g** was transformed into β-hydroxy selenide **1a** by reductive deselenenylation using *n*-BuSnH (Scheme 2) and the absolute stereochemistry was determined by comparison of its optical rotation with our data for (***S***)-**1a**.



1

b. R = Ph, R' = H, R'' = $(CH_2)_2CH_3$
d. R = Ph, R' = H, R'' = $CH(CH_3)_2$
f. R = CH_3, R' = H, R'' = Ph
i. R = Ph, R' = Ph, R'' = CH_3

4

b. R = H, R' = $(CH_2)_2CH_3$
d. R = H, R' = $CH(CH_3)_2$
f. R = H, R' = Ph
i. R = Ph, R' = CH_3

Scheme 3. Transformations for determination of the absolute configuration.

3. Conclusions

This work demonstrated that the presence of a selenium group in the structure of a secondary alcohol did not inhibit the lipase activity and that enantiopure β-hydroxy selenide **1a** can be obtained by enzymatic resolution using PSL or CALB in organic medium, providing both (*R*)- and (*S*)-enantiomers in high enantiomeric purity. It should be also mentioned that the immobilization of PSL in PEO increased its activity, and decreased the time of the kinetic resolution. This method represents a simple enantioselective alternative to afford enantiomericaly enriched β-hydroxy selenides, which are important building blocks in organic synthesis.

4. Experimental

4.1. General

The NMR spectra were recorded on Bruker AC-200, Varian FT-300 or Bruker DRX-500 spectrometers using as solvent $CDCl_3$ and as internal reference TMS (^1H NMR), the central peak of the $CDCl_3$ signal (^{13}C NMR) and a capillary of diphenyl diselenide 1 M (^{77}Se NMR). Infrared spectra (IR) were recorded on a Perkin–Elmer 1600 spectrophotometer. The mass spectra were performed on GC–MS Shimadzu GC-17A/QP5050A. Optical rotations were measured on a Jasco, DIP 370 Digital polarimeter. The chiral GC analyses were performed on a Shimadzu GC-17A instrument equipped with flame ionization detector (FID) and ALFA DEX™ 120 chiral capillary column (packed α-cyclodextrin, 30 m × 0.25 mm × 0.25 μm, SUPELCO®), BETA DEX™ 120 chiral capillary column (packed β-cyclodextrin, 30 m × 0.25 mm × 0.25 μm, SUPELCO), GAMA DEX™ 120 chiral capillary column (packed γ-cyclodextrin, 30 m × 0.25 mm × 0.25 μm, SUPELCO®) or CHIRASIL-DEX CB (packed β-cyclodextrin, 25 m × 0.25 mm × 0.25 μm, CRHOMOPACK-Varian®). H_2 was used as a carrier gas in the analyses. CAL-B (NOVOZYM 435® immobilized lipase-B from *C. antarctica*) was kindly provided by Novozymes Inc., PSL (*Pseudomonas* sp. lipase free) was kindly provided by Amano Pharmaceutical Co., PPL (*Porcine pancreatic* lipase) was purchased from Sigma–Aldrich Chemical Co.

4.2. Synthesis

4.2.1. General procedure for the preparation of the racemic substrates (*RS*)-1a and (*RS*)-1e. In a two necked flask, under nitrogen, diphenyl diselenide (5 mmol) was dissolved in dry ethanol (30 mL) and then sodium borohydride was added slowly at room temperature until the solution became colourless. To the solution was added the corresponding epoxide (propylene oxide or styrene oxide—11 mmol) and the mixture was stirred for 2 h. A 10% aqueous solution of Na_2CO_3 (20 mL) was added and the reaction mixture was extracted with ethyl acetate (3 × 20 mL). The organic phase was washed with brine, dried with $MgSO_4$ and evaporated. The residue was purified by silica gel column

chromatography eluting with hexane–ethyl acetate (85:15).

4.2.1.1. (*RS*)-1-(Phenylseleno)-2-propanol, (*RS*)-1a. Oil; yield: 1.913 g (89%); CAS NR: 25570-56-3; ^{1}H NMR (300 MHz): δ 1.27 (d, 3H, J = 6.2 Hz), 2.46 (br s, 1H), 2.88 (dd, 1H, J = 8.3, 12.7 Hz), 3.10 (dd, 1H, J = 3.9, 12.7 Hz), 3.84–3.88 (m, 1H), 7.23–7.28 (m, 3H), 7.50–7.56 (m, 2H); ^{13}C NMR (75 MHz): δ 22.4, 38.5 ($J^1_{^{13}C-^{77}Se}$ = 64 Hz), 66.1, 127.3, 129.3, 129.2, 133.1; NMR ^{77}Se (95 MHz): δ 240.8; IR 3390, 3070, 3056, 3016, 2971, 2927, 1578, 1478, 1371, 736, 691 cm^{-1}; MS *m*/*z* (rel int): 216 (60), 215 (4), 172 (47), 158 (57), 157 (50), 91 (100), 77 (72), 78 (89), 59 (68), 51 (63), 45 (53); Anal. Calcd for $C_9H_{12}OSe$: C, 50.24; H, 5.62. Found: C, 49.86; H, 5.63.

4.2.1.2. (*RS*)-1-Phenyl-2-(phenylseleno)-ethanol, (*RS*)-1e. Oil; yield: 1.800 g (65%); CAS NR: 51558-95-3; NMR ^{1}H (300 MHz): δ 2.83 (d, 1H, J = 2.8 Hz), 3.13 (dd, 1H, J = 9.3, 12.8 Hz), 3.29 (dd, 1H J = 3.8, 12.8 Hz), 4.73 (dd, 1H, J = 3.8, 9.3 Hz), 7.24–7.33 (m, 8H), 7.52–7.55 (m, 2H); NMR ^{13}C (75 MHz): δ 38.5, 72.3, 125.8, 127.4, 127.9, 128.5, 129.3, 133.1, 133.2, 142.5; NMR ^{77}Se (95 MHz): δ 251.9; IR 693, 736, 1085, 1437, 1453, 1477, 1578, 2880, 2932, 2983, 3000, 3029, 3058, 3907 cm^{-1}; MS *m*/*z* (rel int): 278 (25), 277 (3), 172 (100), 157 (18), 121 (4), 107 (60), 91 (54), 79 (83), 77 (83); 51 (43), 43 (29); Anal. Calcd for $C_{14}H_{14}OSe$: C, 60.66; H, 5.09. Found: C, 60.51; H, 5.34.

4.2.2. General procedure for the preparation of the racemic substrates (*RS*)-1b–d, (*RS*)-1h and i. In a two necked flask, under nitrogen, the appropriate seleno-acetal (2 mmol)[2,17] was dissolved in dry THF (8 mL). *n*-Butyl lithium (2 mmol in hexane) was added slowly at −78 °C and the reaction mixture was stirred for 30 min. To the solution was added the corresponding aldehyde (propynaldehyde, isobutyraldehyde, heptaldehyde, acetaldehyde—2 mmol) and the mixture was stirred for 20 min at −78 °C and then for 1 h at room temperature. After this period, NH_4Cl solution was added and the reaction mixture was extracted with ethyl acetate. The organic phase was washed with brine, dried with $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography eluting with hexane–ethyl acetate (85:15).

4.2.2.1. (*RS*)-1-(Phenyseleno)-2-pentanol, (*RS*)-1b. Oil; yield: 0.350 g (72%); NMR ^{1}H (300 MHz): δ 0.89 (t, 3H, J = 7.20 Hz), 1.33–1.37 (m, 1H), 1.44–1.54 (m, 3H), 2.18 (br s, 1H), 2.88 (dd, 1H, J = 8.61, 12.73 Hz), 3.14 (dd, 1H, J = 3.51, 12.73 Hz), 3.66–3.71 (m, 1H), 7.24–7.27 (m, 3H), 7.52–7.53 (m, 2H); NMR ^{13}C (75 MHz): δ 14.2, 19.2, 37.5 ($J^1_{^{13}C-^{77}Se}$ = 64 Hz), 39.0, 69.91, 127.5, 129.4, 129.7, 133.3; NMR ^{77}Se (95 MHz): δ 234.2; IR 691, 737, 1436, 1459, 1474, 1578, 2870, 2928, 2958, 3063, 3401 cm^{-1}; MS *m*/*z* (rel int): 244 (60), 243 (4), 172 (100), 158 (63), 157 (61), 91 (86), 78 (81), 77 (74), 69 (44), 55 (85), 51 (51), 45 (90), 41 (89); Anal. Calcd for $C_{11}H_{16}OSe$: C, 54.32; H, 6.63. Found: C, 54.08; H, 6.85.

4.2.2.2. (*RS*)-1-(Phenylseleno)-2-octanol, (*RS*)-1c. Oil; yield: 0.473 g (83%); CAS NR: 52954-45-7; NMR ^{1}H (500 MHz): 0.87 (t, 3H, J = 7.1 Hz), 1.25–1.31 (m, 8H), 1.51–1.54 (m, 2H), 2.14 (br s, 1 H), 2.87 (dd, 1H, J = 8.6, 12.7 Hz), 3.14 (dd, 1H, J = 3.5, 12.7 Hz), 3.63–3.68 (m, 1H), 7.24–7.27 (m, 3H), 7.51–7.54 (m, 2H); NMR ^{13}C (125 MHz): δ 14.0, 22.5, 29.23, 31.7, 36.6, 37.2, 69.8, 127.2, 129.2, 133.0; NMR ^{77}Se (95 MHz): δ 237.0; IR 691, 736, 1024, 1070, 1478, 1578, 1712, 1799, 1873, 1946, 2855, 2928, 3056, 3070, 3399 cm^{-1}; MS *m*/*z* (rel int): 286 (68), 172 (96), 158 (71), 129 (23), 91 (78), 77 (70), 69 (96), 55 (100), 51 (48), 45 (42); Anal. Calcd for $C_{14}H_{22}OSe$: C, 58.94; H, 7.77. Found: C, 59.31; H, 7.97.

4.2.2.3. (*RS*)-1-(Phenylseleno)-3-methyl-2-butanol, (*RS*)-1d. Oil; yield: 0.379 g (78%); CAS NR: 68395-98-2; NMR ^{1}H (500 MHz): δ 0.89–0.93 (m, 6H), 1.74–1.80 (m, 1H), 2.89 (dd, 1H, J = 9.5, 12.7 Hz), 3.17 (dd, 1H, J = 3.0, 12.7 Hz), 3.40–3.44 (m, 1H), 7.23–7.28 (m, 3H), 7.50–7.54 (m, 2H); NMR ^{13}C (125 MHz): δ 17.7, 18.7, 33.3, 34.9, 74.5, 127.2, 129.2, 129.3, 133.0; NMR ^{77}Se (95 MHz): δ 240.8; IR 691, 737, 1472, 1578, 1801, 1874, 2874, 2960, 3429; MS *m*/*z* (rel int): 244 (57), 183 (4), 172 (71), 157 (72), 91 (74), 77 (76), 69 (100), 51 (60), 45 (44); Anal. Calcd for $C_{11}H_{16}OSe$: C, 54.32; H, 6.63. Found: C, 54.75; H, 7.05.

4.2.2.4. (*RS*)-1-Hexyl-1-(phenylseleno)-2-propanol, (*RS*)-1h. Diastereoisomeric mixture; oil; yield: 0514 g (86%); NMR ^{1}H (300 MHz): δ 0.85–0.93 (m, 6H), 1.18–1.76 (m, 26H), 2.08 (br s, 1H), 2.12 (br s, 1H), 2.97–3.03 (m, 1H), 3.25–3.76 (m, 1H), 3.65–3.76 (m, 1H), 3.80–3.88 (m, 1H), 7.20–7.30 (m, 6H), 7.56–7.60 (m, 4H); NMR ^{13}C (75 MHz): δ 14.0, 19.8, 20.5, 22.6, 28.1, 28.4, 29.0, 29.1, 31.1, 31.6, 31.7, 31.9, 57.8, 58.0, 68.9, 69.3, 127.5, 127.6, 129.0, 129.1, 129.6, 134.4, 134.9; MS *m*/*z* (rel int): 300 (30), 255 (6), 172 (5), 158 (59), 157 (24), 91 (16), 78 (49), 77 (40), 69 (100), 55 (96), 51 (20), 45 (63); Anal. Calcd for $C_{15}H_{24}OSe$: C, 60.19; H, 8.08. Found: C, 60.34; H, 8.37.

4.2.2.5. (*RS*)-1-Phenyl-1-(phenylseleno)-2-propanol, (*RS*)-1i. Diastereoisomeric mixture; oil; yield: 0.512 g (88%); CAS NR: 623575-61-1; NMR ^{1}H (200 MHz): δ 1.15 (d, 3H, J = 5.7 Hz), δ 1.24 (d, 3H, J = 5.7 Hz), 1.95 (br s, 2H), 4.07–4.26 (m, 4H), 7.02–7.37 (m, 20H); NMR ^{13}C (75 MHz): δ 20.5, 20.6, 57.3, 60.1, 69.2, 69.6, 127.1, 127.4, 128.3, 128.4, 128.9, 129.0, 135.1, 135.5; MS *m*/*z* (rel int): 292 (11), 247 (4), 158 (30), 157 (15), 135 (86), 117 (51), 91 (62), 78 (32), 77 (39), 57 (73), 51 (25), 43 (100).

4.2.3. General procedure for the preparation of the racemic substrate (*RS*)-1f. To a suspension of elemental selenium (5 mmol) in dry THF (25 mL) under nitrogen and with magnetic stirring was added *n*-butyllithium (in hexane—5 mmol). A yellow solution was formed. To this solution was added styrene oxide (5 mmol). The mixture was then heated at reflux for 24 h. After this period, the mixture was cooled to room temperature, treated with NH_4Cl solution and extracted with ethyl acetate. The organic phase was washed with

brine, dried with $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography eluting with hexane–ethyl acetate (85:15).

4.2.3.1. (*RS*)-1-Phenyl-2-(metheylseleno)-ethanol, (*RS*)-1f. Oil; yield: 0.828 g (77%); CAS NR: 56051-09-3; NMR ^{1}H (200 MHz): δ 1.95 (s, 3H), 2.79 (dd, 1H, J = 8.8, 12.7 Hz), 2.92 (dd, 1H, J = 3.9 12.7 Hz), 4.77 (dd, 1H, J = 3.9, 8.8 Hz), 7.24–7.39 (m, 5H); NMR ^{13}C (50 MHz): δ 4.7, 35.8, 72.1, 125.7, 127.7, 128.4; NMR ^{77}Se (95 MHz): δ 30.6; MS *m*/*z* (rel int): 216 (53), 121(65), 107(94), 91(80), 77(100), 51(66).

4.2.4. General procedure for the preparation of the racemic substrate, (*RS*)-1g. In a two necked flask, under nitrogen, bis(phenylseleno)methane[2] (2 mmol) was dissolved in dry THF (8 mL), LDA (2 mmol) was slowly added at −78 °C and the reaction mixture was stirred for 30 min. To the resulting solution was added acetaldehyde (2 mmol) and the mixture was stirred for 20 min at −78 °C and 1 h at room temperature. After this period, NH_4Cl solution was added and the reaction mixture was extracted with ethyl acetate. The organic phase was washed with brine, dried with $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography eluting with hexane–ethyl acetate (9:1).

4.2.4.1. (*RS*)-1,1-Bis(phenylseleno)propan-2-ol, (*RS*)-1g. Oil; yield: 0.540 g (73%); CAS NR: 77461-31-5; NMR ^{1}H (200 MHz): δ 1.38 (d, 3H, J = 6.1 Hz), 2.46 (br s, 1H), 3.89–3.99 (m, 1H), 4.49 (d, 1H, J = 3.1 Hz), 7.24–7.30 (m, 6H), 7.53–7.62 (m, 4H); NMR ^{13}C (50 MHz): 20.8, 55.3 ($J^1_{^{13}C-^{77}Se}$ = 86.8 Hz), 69.2, 128.1, 128.2, 129.2, 129.3, 129.9, 130.3, 134.3, 135.5; NMR ^{77}Se (95 MHz): δ 355.0, 357.9; MS *m*/*z* (rel int): 372 (6), 314 (13), 215 (31), 157 (62), 117 (22), 91 (77), 77 (93), 51 (72), 43 (100).

4.2.5. General procedure for the preparation of the racemic esters. In a two necked flask, under nitrogen, the β-hydroxy selenide (3.6 mmol) was dissolved in dry pyridine (5 mL) and then acetic anhydride (2 mL, 21 mmol) was slowly added at 0 °C. The reaction mixture was stirred at room temperature and monitored by TLC. After 4 h, 10% aqueous HCl (5 mL) was added and the reaction mixture was extracted with ethyl acetate (10 mL). The organic phase was washed with $CuSO_4$ solution (3 × 15 mL) and brine, dried with $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography eluting with hexane–ethyl acetate (9:1).

4.2.5.1. (*RS*)-*O*-Acetyl-1-(phenylseleno)-2-propanol, (*RS*)-2a. Oil; yield: 0.842 g (91%); NMR ^{1}H (300 MHz): δ 1.33 (d, 3H, J = 6.30 Hz), 1.94 (s, 3H), 2.99 (dd, 1H, J = 6.2, 12.8 Hz), 3.10 (dd, 1H J = 6.1, 12.8 Hz), 5.04–5.10 (m, 1H), 7.21–7.30 (m, 3H), 7.50–7.54 (m, 2H); NMR ^{13}C (75 MHz): δ 19.8, 21.1, 33.0, 70.3, 127.1, 129.1, 129.9, 132.8, 170.4; NMR ^{77}Se (95 MHz): δ 264,3; IR 691, 738, 1242, 1371, 1438, 1453, 1478, 1578, 1737, 2932, 2980, 3057, 3071 cm^{-1}; MS *m*/*z* (rel int): 257 (1), 215 (1), 198 (12), 181 (4), 157(5), 101 (13), 78 (7), 77 (11), 43 (100); Anal. Calcd for $C_{11}H_{14}O_2Se$: C, 51.37; H, 5.49. Found: C, 51.50; H, 5.54.

4.2.5.2. (*RS*)-*O*-Acetyl-1-(phenylseleno)-2-pentanol, (*RS*)-2b. Oil; yield: 0.944 g (92%); NMR ^{1}H (500 MHz): δ 0.89 (t, 3H, J = 7.4 Hz), 1.24–1.36 (m, 2H), 1.94 (s, 3H), 3.07 (d, 2H, J = 6.0 Hz), 5.01–5.06 (m, 1H), 7.21–7.33 (m, 3H), 7.51–7.54 (m, 2H); NMR ^{13}C (125 MHz): 13.8, 18.5, 21.0, 31.6, 35.9, 73.2, 127.1, 129.1, 130.1, 132.8, 170.6; NMR ^{77}Se (95 MHz): δ 260.3; IR 692, 738, 1237, 1372, 1435, 1459, 1474, 1578, 1739, 2872, 2960, 3057 cm^{-1}; MS *m*/*z* (rel int): 286 (27), 285 (3), 226 (51), 157 (35), 129 (41), 116 (49), 91 (52), 78 (45), 77(51), 69 (80), 51 (44), 43 (100); Anal. Calcd for $C_{13}H_{18}O_2Se$: C, 54.74; H, 6.36. Found: C, 54.60; H, 6.36.

4.2.5.3. (*RS*)-*O*-Acetyl-1-(phenylseleno)-2-octanol, (*RS*)-2c. Oil; yield: 0.965 g (82%); CAS NR: 67007-28-7; NMR ^{1}H (500 MHz): δ 0.86 (t, 3H, J = 7.2 Hz), 1.23–1.29 (m, 8H), 1.62–1.70 (m, 2H), 1.93 (s, 3H), 3.06 (d, 2H, J = 6.0 Hz), 4.99–5.04 (m, 1H), 7.21–7.28 (m, 3H), 7.51–7.54 (m, 2H); NMR ^{13}C (125 MHz): δ 14.0, 21.0, 22.5, 25.2, 29.1, 31.6, 33.8, 73.4, 127.6, 129.9, 132.8, 140.9, 170.6; NMR ^{77}Se (95 MHz): δ 264,0; IR 691, 736, 1022, 1239, 1579, 1738, 2858, 2959, 2955, 3016, 3058 cm^{-1}; MS *m*/*z* (rel int): 328 (15), 268 (44), 171 (25), 158 (6), 91 (46), 77 (38), 69 (89), 43 (100); Anal. Calcd for $C_{16}H_{24}O_2Se$: C, 58.71; H, 5.39. Found: C, 59.12; H, 7.67.

4.2.5.4. (*RS*)-*O*-Acetyl-1-(phenylseleno)-3-methyl-2-butanol, (*RS*)-2d. Oil; yield: 0.985 g (96%); NMR ^{1}H (200 MHz): δ 0.77–0.98 (m, 7H), 1.95 (s, 3H), 3.05–3.09 (m, 2H), 4.85–4.97 (m, 1H), 7,23–7.32 (m, 3H), 7.50–7.55 (m, 2H); NMR ^{13}C (125 MHz): δ 17.3, 18.4, 18.7, 20.8, 47.9, 77.4, 127.0, 129.0, 129.1, 132.9, 170.7; NMR ^{77}Se (95 MHz): δ 265.4; IR 694, 739, 1021, 1301, 1474, 1578, 1744, 2874, 2934, 2965, 3032, 3058 cm^{-1}; MS *m*/*z* (rel int): 286 (20), 226 (44), 171 (10), 157 (24), 91 (45), 77 (42), 69 (96), 43 (100); Anal. Calcd for $C_{13}H_{18}O_2Se$: C, 54.74; H, 6.36. Found: C, 54.91; H, 6.31.

4.2.5.5. (*RS*)-*O*-Acetyl-1-phenyl-2-(methylseleno) ethanol, (*RS*)-2f. Oil; yield: 0.851 g (92%); CAS NR: 56268-17-8; NMR ^{1}H (200 MHz): δ 1.91 (s, 3H), 2.09 (s, 3H), 2.87 (dd, 1H, J = 6.6, 12.9 Hz), 3.00 (dd, 1H, J = 7.46, 12.9 Hz), 5.86–5.93 (m, 1H), 7.26–7.38 (m, 5H); NMR ^{13}C (50 MHz): 5.0, 21.1, 30.7, 75.4, 126.7, 128.3, 128.5, 139.6, 170.0; NMR ^{77}Se (95 MHz): δ 64.3; MS *m*/*z* (rel int): 258 (14), 198 (48), 181 (10), 163 (42), 149 (6), 104 (50), 91 (37), 77 (48), 43 (100).

4.2.5.6. (*RS*)-*O*-Acetyl-1,1-bis(phenylseleno)propan-2-ol, (*RS*)-2g. Oil; yield: 1.424 g (96%); NMR ^{1}H (200 MHz): δ 1.45 (d, 3H, J = 6.6 Hz), 1.88 (s, 3H), 4.52 (d, 1H, J = 3.5 Hz), 5.14–5.25 (m, 1H), 7.22–7.33 (m, 6H), 7.52–7.55 (m, 4H); NMR ^{13}C (50 MHz): δ 18.2, 20.8, 48.8, 72.7, 128.1, 128.2, 129.1, 129.2, 130.2, 130.5, 134.2, 134.9, 170.22; NMR ^{77}Se (95 MHz): δ 374.7, 382.4; MS *m*/*z* (rel int): 414 (7), 257 (46), 215 (58), 197 (52), 157 (46), 116 (34), 91 (31), 77 (64), 51

(52), 43 (100); Anal. Calcd for $C_{17}H_{18}O_2Se_2$: C, 49.53; H, 4.40. Found: C, 49.41; H, 4.68.

4.2.5.7. (*RS*)-*O*-Acetyl-1-hexyl-1-(phenylseleno)propan-2-ol, (*RS*)-2h. Diastereoisomeric mixture; oil; yield: 1.154 g (94%); NMR ^{1}H (300 MHz): δ 0.84–0.90 (m, 6H), 1.24–1.29 (m, 16H), 1.31 (d, 3H, J = 6.3 Hz), 1.36 (d, 3H, J = 6.3 Hz), 1.50–1.80 (m, 4H), 1.81 (s, 3H), 1.99 (s, 3H), 3.17–3.23 (m, 1H), 3.27–3.34 (m, 1H), 5.01-5-16 (m, 2H), 7.24–7.27 (m, 6H), 7.55–7.59 (m, 4H); NMR ^{13}C (75 MHz): δ 14.0, 17.2, 17.2, 20.9, 21.1, 22.5, 28.0, 29.0, 31.4, 31.6, 31.7, 50.5, 51.7, 72.6, 73.0, 127.2, 127.4, 128.9, 129.9, 130.0, 134.0, 134.7, 170.4; MS *m*/*z* (rel int): 342 (2), 282 (4), 157 (20), 91 (4), 77 (30), 69 (100), 55 (94), 51 (18); Anal. Calcd for $C_{17}H_{26}O_2Se$: C, 59.82; H, 7.68. Found: C, 60.4; H, 7.82.

4.2.5.8. (*RS*)-*O*-Acetyl-1-phenyl-1-(phenylseleno)propan-2-ol, (*RS*)-2i. Diastereoisomeric mixture; oil; yield: 1.103 g (92%); NMR ^{1}H (200 MHz): δ 1.20 (d, 3H, J = 6.1 Hz), 1.30 (d, 3H, J = 6.1 Hz), 1.90 (s, 3H), 1.98 (s, 3H), 4.27–4.37 (m, 2H), 5.33–5.49 (m, 2H), 7.11–7.28 (m, 16H), 7.35–7.43 (m, 4H); NMR ^{13}C (125 MHz): 18.9, 20.9, 21.1, 53.4, 53.7, 72.4, 73.4, 127.3, 127.7, 127.9, 128.2, 128.4, 128.7, 128.9, 129.1, 129.5, 135.0, 135.4, 170.2, 170.4; MS *m*/*z* (rel int): 334 (11), 274 (8), 177 (52), 158 (11), 157 (19), 135 (73), 117 (61), 91 (41), 78 (39), 77 (44), 57 (38), 51 (35), 43 (100); Anal. Calcd for $C_{17}H_{18}O_2Se$: C, 61.26; H, 5.44. Found: C, 61.42; H, 5.56.

4.3. General procedure for the enzymatic resolution

To a solution of the substrate (0.5 mmol) in the appropriate solvent (10–25 mL) was added the lipase (15 mg–1 g—Tables 1–3) and vinyl acetate (5 equiv). The reaction mixture was monitored by chiral GC and stirred until the conversion reached ca. 50%. The enzymes, free or immobilized, were removed by filtration and the resulting solution was concentrated. The organic residues were subjected to silica gel chromatography to obtain the acetylated product and the unreacted enantiomer.

4.3.1. (*S*)-1-(Phenylseleno)-2-propanol, (*S*)-1a. Oil; >99% ee; yield: 0.049 g (46%); $[\alpha]_D^{22}$ = +56 (*c* 2.0, CH_2Cl_2).

4.3.2. (*R*)-*O*-Acetyl-1-(phenylseleno)-2-propanol, (*R*)-2a. Oil; >99% ee; yield: 0.054 g (42%); $[\alpha]_D^{22}$ = −7 (*c* 2.0, CH_2Cl_2).

4.3.3. (*S*)-1-(Phenyseleno)-2-pentanol, (*S*)-1b. Oil; >99% ee; yield: 0.036 g (30%); $[\alpha]_D^{23}$ = +41 (*c* 2.0, CH_2Cl_2).

4.3.4. (*R*)-*O*-Acetyl-1-(phenylseleno)-2-pentanol, (*R*)-2b. Oil; 94% ee; yield: 0.050 g (35%); $[\alpha]_D^{28}$ = +1 (*c* 2.0, CH_2Cl_2).

4.3.4.1. (*S*)-1-(Phenylseleno)-2-octanol, (*S*)-1c. Oil 70% ee; $[\alpha]_D^{22}$ = +12 (*c* 2.0, $CHCl_3$); lit.[16] for the (*R*)-enantiomer: $[\alpha]_D^{19}$ = −35.5 (*c* 0.986, $CHCl_3$) 93% ee.

4.3.5. (*R*)-*O*-Acetyl-1-(phenylseleno)-2-octanol, (*R*)-2c. Oil; 33% ee; $[\alpha]_D^{22}$ = +2 (*c* 2.0, CH_2Cl_2).

4.3.6. (*S*)-1-(Phenylseleno)-3-methyl-2-butanol, (*S*)-1d. Oil; 69% ee; $[\alpha]_D^{20}$ = +47 (*c* 2.0, CH_2Cl_2).

4.3.7. (*R*)-*O*-Acetyl-1-(phenylseleno)-3-methyl-2-butanol, (*R*)-2d. Oil; 86% ee; $[\alpha]_D^{20}$ = −12 (*c* 2.0, CH_2Cl_2).

4.3.8. (*R*)-1-Phenyl-2-(methylseleno)-ethanol, (*R*)-1f. Oil; ee = 41%; $[\alpha]_D^{22}$ = −55 (*c* 2.0, CH_2Cl_2).

4.3.9. (*S*)-*O*-Acetyl-1-phenyl-2-(methylseleno) ethanol, (*S*)-2f. Oil; 74% ee; $[\alpha]_D^{22}$ = +12 (*c* 2.0, CH_2Cl_2).

4.3.10. (*S*)-1,1-Bis(phenylseleno)propan-2-ol, (*S*)-1g. Oil; >99% ee; $[\alpha]_D^{21}$ = −43 (*c* 2.0, CH_2Cl_2).

4.3.11. (*R*)-*O*-Acetyl-1,1-bis(phenylseleno)propan-2-ol, (*R*)-2g. Oil; 99% ee; $[\alpha]_D^{21}$ = +1 (*c* 2.0, CH_2Cl_2).

4.4. Determination of the enantiomeric excesses

Conditions for GC analysis are as follows. (***RS*)-1a**: GAMA DEX^{TM}, 135 °C, 40 min hold, t_R1 = 24.7 min, t_R2 = 25.2 min; (***RS*)-1b**: GAMA DEX^{TM}, 140 °C, 70 min hold, t_R1 = 59.5 min, t_R2 = 61.2 min; (***RS*)-1c**: GAMA DEX^{TM}, 150 °C, 120 min hold, t_R1 = 106.2 min, t_R2 = 107.9 min; (***RS*)-1d**: GAMA DEX^{TM}, 135 °C, 70 min hold, t_R1 = 47.1 min, t_R2 = 48.3 min; (***RS*)-1f**: GAMA DEX^{TM}, 125 °C, 85 min hold, t_R1 = 75.6 min, t_R2 = 77.6 min; (***RS*)-2a**: BETA DEX^{TM}, 125 °C, 40 min hold, t_R1 = 38.0 min, t_R2 = 38.8 min; (***RS*)-2b**: BETA DEX^{TM}, 120 °C, 60 min hold, t_R1 = 54.6 min, t_R2 = 55.1 min; (***RS*)-3**: CHIRASIL-DEX CB, 60 °C, 40 min hold, 60–120 °C, 0.5 °C/min, 15 min hold, t_R1 = 92.0 min, t_R2 = 95.2 min; (***RS*)-4**: ALFA DEX^{TM}, 50 °C, 60 min hold, 50–190 °C, 1 °C/min, t_R1 = 171.8 min, t_R2 = 173.7 min. The E values were calculated from the enantiomeric excesses (ee) of products and substrates, according to Sih, Sharpless and Fajans's equation $\{E = \ln[1 - c(1 + ee_p)]/\ln[1 - c(1 - ee_p)]$, where $c = ee_s/(ee_s + ee_p)\}$.[18]

4.4.1. General procedure for the hydrolysis of the acetates 2c–i. In a flask the acetate of the appropriate β-hydroxy selenide (1 mmol) was dissolved in methanol (5 mL) and then H_2O (2 mL) was added. To the solution was added K_2CO_3 (0.2 mmol) and the mixture was stirred overnight. After this period, the mixture was extracted with ethyl acetate and the organic phase was washed with brine, dried and concentrated to give a residue which was purified by flash chromatography on silica gel.

4.5. Determination of the absolute configuration

4.5.1. Esterification of (*S*)-1-(phenylseleno)-2-propanol (*S*)-1a with Mosher's acid cloride. In a two necked flask, under nitrogen, the alcohol (***S*)-1a** (0.1 mmol), Et_3N (1.2 mmol) and DMAP (0.1 mmol) were dissolved in dry CH_2Cl_2 (10 mL). The α-methoxy-α-trifluoromethyl-phenylacetyl chloride (0.5 mmol) was dissolved

in dry CH_2Cl_2 (5 mL) and added to the solution of the alcohol (*S*)-**1a**. After 15 min the solution was washed with H_2O, dried and concentrated to give a residue which was purified by flash chromatography on silica gel.

4.5.1.1. (1*S*,2*R*)-1-Methyl-2-(phenylseleno)ethyl 3,3,3-trifluoro-2-methoxy-2-phenylpropionate. Oil; yield: 0.029 g (67%); NMR ^{1}H (500 MHz): δ 1.44 (d, 3H, J = 6.29 Hz), 2.93 (dd, 1H, J = 6.76, 12.82 Hz), 3.14 (dd, 1H, J = 6.30, 12.82 Hz), 3.55 (s, 3H), 5.25–5.31 (m, 1H), 7.23–7.55 (m, 10H); NMR ^{13}C (125 MHz, $CDCl_3$), δ (ppm): 19.7, 32.2, 55.5, 73.1, 165.9; RMN ^{77}Se (95 MHz, $CDCl_3$), δ (ppm): 269.8; E.M., *m*/*z* (% rel.): 431 (19), 275 (43), 217 (11), 198 (68), 189 (100), 157 (64), 105(49), 91 (37), 77 (78), 69 (17), 51 (32).

4.5.1.2. (1*S*,2*S*)-1-Methyl-2-(phenylseleno)ethyl 3,3,3-trifluoro-2-methoxy-2-phenylpropionate. Oil; yield: 0.030 g (69%); NMR ^{1}H (500 MHz): δ 1.35 (d, 3H, J = 6.26 Hz), 3.02 (dd, 1H, J = 6.07, 12.88 Hz), 3.17 (dd, 1H, J = 6.99, 12.88 Hz), 3.58 (s, 3H), 5.24–5.30 (m, 1H), 7.25–7.57 (m, 10H); NMR ^{13}C (125 MHz): δ 20.0, 32.8, 56.1, 73.5, 166.4; NMR ^{77}Se (95 MHz): δ 271.0; E.M., *m*/*z* (% rel.): 431 (13), 275 (36), 217 (11), 198 (65), 189 (100), 157 (68), 105 (54), 91 (42), 77 (88), 69 (20), 51 (39).

4.5.2. General procedure for the reductive deselenenylation. In a two necked flask, under nitrogen, a catalytic amount of CCN [1,1′-azobis(cyclohexanecarbonitrile)] and the β-hydroxy selenide (0.2 mmol) were dissolved in dry toluene (3 mL). To the solution was added triphenyltin hydride (0.2 mmol) and the mixture was stirred under reflux for 4 h. After this period, the system was cooled to room temperature, hexane was added and the mixture was extracted with acetonitrile. The acetonitrile phase was evaporated and the residue was purified by silica gel column chromatography eluting with hexane–ethyl acetate (9:1).

4.5.2.1. (*R*)-Pentan-2-ol (4b) from (*S*)-1b. Ee >99%; $[\alpha]_D^{19} = -12$ (*c* 1.0, $CHCl_3$); lit.[13] for the (*S*)-enantiomer: $[\alpha]_D = +10.25$ ($CHCl_3$) 79% ee.

4.5.2.2. (*R*)-3-Methyl-2-butanol (4d) from (*S*)-1d. Ee = 69%; $[\alpha]_D^{20} = -2$ (*c* 2.0, $CHCl_3$); lit.[13] for the (*R*)-enantiomer: $[\alpha]_D = -2.74$ ($CHCl_3$) 86% ee.

4.5.2.3. (*S*)-1-Phenylethanol 4f from (*R*)-1f. Ee = 41%; $[\alpha]_D^{20} = -24$ (*c* 2.0, $CHCl_3$); lit.[14] for the (*S*)-enantiomer: $[\alpha]_D^{25} = -55.1$ (*c* 1.63, $CHCl_3$) >99% ee.

4.5.2.4. (*S*)-1-Phenyl-2-propanol (4i) from [(1*R*,2*S*)-1-phenyl-1-(phenylseleno)-2-propanol and (1*S*,2*S*)-1-phenyl-1-(phenylseleno)-2-propanol]. Oil; 92% ee; $[\alpha]_D^{21} = +37$ (*c* 2.0, $CHCl_3$); lit.[14] for the (*S*)-enantiomer: $[\alpha]_D^{25} = +41.7$ (*c* 1.19, $CHCl_3$) >99% ee.

4.5.3. Selenoxide elimination. In a flask, the β-hydroxy selenide (*RS*)-**1h** (0.2 mmol) was dissolved in THF (5 mL) and hydrogen peroxide (30% sol.—0.6 mmol) was slowly added at room temperature. The mixture was stirred for 4 h, diluted with water and extract with several portions of ether. The organic phase was washed with concentrated aqueous Na_2CO_3 solution and brine, dried with $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography eluting with hexane–ethyl acetate (9:1).

4.5.3.1. (*S*)-3-Nonen-2-ol 3 from (1*R*,2*S*)-1-hexyl-1-(phenylseleno)-2-propanol and (1*S*,2*S*)-1-hexyl-1-(phenylseleno)-2-propanol. Oil; yield: 0.027 g (95%); CAS NR: 173144-01-9; NMR ^{1}H (200 MHz): δ 0.89 (t, 3H, J = 4.50 Hz), 1.25–1.39 (m, 8H), 1.97–2.04 (m, 3H), 4.22–4.31 (m, 1H), 5.50 (dd, 1H, J = 4.35, 10.45 Hz), 5.67 (dt, 1H, J = 4.40, 10.45 Hz); E.M., *m*/*z* (% rel.): 142 (1), 124 (25), 84 (23), 71 (100), 68 (72), 58 (30), 54 (55), 43 (12); 92% ee; $[\alpha]_D^{21} = -8$ (*c* 1.5, $CHCl_3$); lit.[15] for the (*R*)-enantiomer: $[\alpha]_D^{19} = +10.68$ (*c* 1.03, $CHCl_3$) 97% ee.

Acknowledgements

We thank FAPESP and CNPq for support. Amano Pharmaceutical Co. and Novozymes Inc. are acknowledged for their generous gifts of lipases.

References

1. (a) Davis, B. G.; Boyer, V. *Nat. Prod. Rep.* **2001**, *18*, 618–640; (b) Roberts, S. M. *Biocatalysis for fine chemical synthesis*; Oxford University Press: Oxford, 1999.
2. *Organoselenium Chemistry*; Back, T., Ed.; Oxford University Press: Oxford, 1999.
3. Tiecco, M. Topics in Current Chemistry: Organoselenium Chemistry: Modern Developments in Organic Synthesis. In *Electrophilic Selenium, Selenocyclizations*; Wirth, T., Ed.; Springer-Verlag: Heidelberg, 2000.
4. Ferraboschi, P.; Grisenti, P.; Santaniello, E. *Synlett* **1990**, 545.
5. (a) Comasseto, J. V.; Omori, A. T.; Porto, A. L. M.; Andrade, L. H. *Tetrahedron Lett.* **2004**, *45*, 473–476; (b) Andrade, L. H.; Omori, A. T.; Porto, A. L. M.; Comasseto, J. V. *J. Mol. Catal. B: Enzym.* **2004**, *29*, 47–54; (c) Comasseto, J. V.; Andrade, L. H.; Omori, A. T.; Assis, L. F.; Porto, A. L. M. *J. Mol. Catal. B: Enzym.* **2004**, *29*, 55–61.
6. Tiecco, M.; Testaferri, L.; Bagnoli, L.; Purgatorio, V.; Temperini, A.; Marini, F.; Santi, C. *Tetrahedron: Asymmetry* **2004**, *15*, 405–412.
7. Besev, M.; Engman, L. *Org. Lett.* **2002**, *4*, 3023–3025.
8. Kazlauskas, R. J.; Weissfloch, A. N. E.; Rappaport, A. T.; Cuccia, A. *J. Org. Chem.* **1991**, *56*, 2656–2665.
9. Queiroz, N.; Nascimento, M. G. *Tetrahedron Lett.* **2002**, *43*, 5225–5227.
10. Faber, K. *Biotransformation in Organic Chemistry*, 4th ed.; Springer-Verlag: Berlin, 2000.
11. Rotticci, D.; Hæffner, F.; Orrenius, C.; Norin, T.; Hult, K. *J. Mol. Catal. B: Enzym.* **1998**, *5*, 267–272.
12. Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*(2), 512.
13. Keinan, E.; Hafeli, E. K.; Seth, K. K.; Lamed, R. *J. Am. Chem. Soc.* **1986**, *108*, 162–169.
14. Nakamura, K.; Matsuda, T. *J. Org. Chem.* **1998**, *63*, 8957–8964.
15. Ohkuma, T.; Koizumi, M.; Doucet, H.; Pham, T.; Kozawa, M.; Murata, K.; Katayama, E.; Yokozawa, T.;

Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1998**, *120*, 13529–13530.
16. Toshimitso, A.; Nakano, K.; Mukai, T.; Tamao, K. *J. Am. Chem. Soc.* **1996**, *118*, 2756–2757.
17. Clarembeau, M.; Cravador, A.; Dumont, W.; Hevesi, L.; Krief, L.; Lucchetti, J.; Ende, D. V. *Tetrahedron* **1985**, *41*, 4793–4812.
18. Sir, C. J.; Wu, S. H. *Topics Stereochem.* **1989**, *19*, 63.