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A green route to enantioenriched (*S*)-arylalkyl carbinols by deracemization via combined lipase alkaline-hydrolysis/Mitsunobu esterification

Zahia Houiene [a], Mounia Merabet-Khelassi [a], Nassima Bouzemi [a], Olivier Riant [b,*], Louisa Aribi-Zouioueche [a,*]

[a] *Ecocompatible Asymmetric Catalysis Laboratory (LCAE), Badji Mokhtar Annaba-University, B.P. 12, 23000 Annaba, Algeria*
[b] *Institute of Condensed Matter and Nanosciences Molecules, Solids and Reactivity (IMCN/MOST), Université Catholique de Louvain, Bâtiment Lavoisier, Place Louis Pasteur, 1, bte 3, 1348 Louvain La Neuve, Belgium*

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ABSTRACT

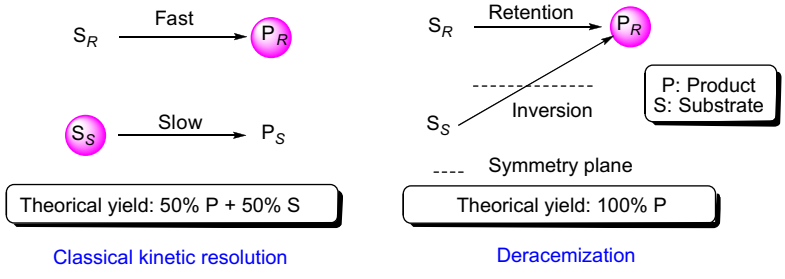
Herein we report results of the chemoenzymatic deracemization of a range of secondary benzylic acetates **1a–9a** via a sequence of hydrolysis with CAL-B lipase in non-conventional media, combined with esterification of the recovered alcohol according to the Mitsunobu protocol following an enzymatic kinetic resolution (KR). The KR of racemic acetates **1a–9a** via an enzymatic hydrolysis, with CAL-B lipase and Na_2CO_3, in non-aqueous media was optimized and gave high selectivities ($E \gg 200$) at good conversions (C >49%) for all of the substrates studied. This method competes well with the traditional one performed in a phosphate buffer solution. The deracemization using Mitsunobu inversion gave the (*S*)-acetates in moderate to excellent enantiomeric excess 75% < ee < 99%, in acceptable isolated yields 70% < yield < 89%, and with some variations according to the acetate structure.

1. Introduction

Biocatalysts, such as lipases are powerful catalytic tools for modern synthetic chemistry and are recognized as important tools for the enantioselective synthesis of functionalized substrates via an enzymatic kinetic resolution[1] under mild and eco-friendly conditions.[2] Kinetic resolution is one of the most useful methodologies and can be carried out by transesterification in organic solvents[3] or hydrolysis in water,[4] albeit with the main inconvenience of a limitation in the theoretical yield of 50%.

Over the last decade, efficient methods for deracemization[5] have been developed and have led to access to single enantiomers with high enantiomeric purity and good chemical yields. The unwanted enantiomer recovered after the classical enzymatic kinetic resolution can be recycled, via spontaneous racemization,[6] direct stereoinversion[7] or by an oxido-reduction driven racemization of the substrates.[8]

Among the deracemization methods, stereoinversion combined with enzymatic kinetic resolution (Scheme 1) is one of the most



Scheme 1. Principle of deracemization via stereoinversion.

* Corresponding authors. Fax: +32 (0)10474168 (O.R.); fax: +213 (0)38871712 (L.A.-Z.).
E-mail addresses: olivier.riant@uclouvain.be (O. Riant), louisa.zouioueche@univ-annaba.org (L. Aribi-Zouioueche).

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important methods for the production of enantioenriched alcohols.[7]

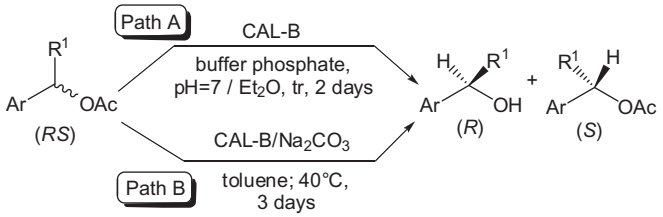
This method uses an in situ transformation of the remaining alcohol to the corresponding carboxylic ester with inversion of configuration at the stereogenic centre. One of the most powerful methods used so far is the Mitsunobu protocol[9] since it uses an activation of the alcohol and S_N2 mechanism with a carboxylate to yield the desired ester with clean stereoinversion.

Hydrolysis via an enzymatic kinetic resolution is modestly employed[10] due to the difficulty of solubility of organic substrates in aqueous media, which results in moderate yields and selectivities.[11] Recently we have reported a novel approach for the enzymatic hydrolysis[12] of various ester derivatives triggered by simple carbonate salts that allowed the use of non-aqueous media under mild conditions. This methodology of alkali-mediated enzymatic hydrolysis can be easily incorporated into a deracemization process via stereoinversion with the Mitsunobu esterification. In a previous investigation,[7e] deracemization through sequential enzymatic acylation/Mitsunobu inversion gave access to the (*R*)-acetates of arylalkylcarbinols in good yields and with high enantiomeric excesses.

In continuation of our investigations, we herein report an enantiocomplementary pathway by integrating the alkali-mediated enzymatic hydrolysis in non-aqueous media coupled to the Mitsunobu esterification, to give access to the corresponding (*S*)-acetates of arylalkylcarbinols in a straightforward and practical manner.

2. Results and discussion

The enzymatic hydrolysis of the secondary aromatic acetates **1a–9a** (Scheme 2) was carried out with the *Candida antarctica* lipase fraction B immobilized on acrylic resin (CAL-B), following two methods for comparison (Scheme 3).



Scheme 3. Enzymatic hydrolysis.

The first method uses the conventional hydrolysis in a biphasic medium and the second uses our protocol involving sodium carbonate in organic solvent. We have examined the selectivity and the reactivity obtained by each hydrolysis method.

2.1. Enzymatic hydrolysis in biphasic media

The enzymatic hydrolysis of racemic acetates **1a–9a** was performed in a biphasic system: phosphate buffer solution/Et_2O (v/v) (6/1) pH 7, according to the classical protocols.[13]

One equivalent of the racemic acetate, diluted in 1 mL of ether, was hydrolysed in the presence of 150 mg of CAL-B (specific activity UA = 4500 U/g), in 6 mL of phosphate solution pH 7, at room temperature for two days (Scheme 3, path A).

Both enantiomers of the residual acetates and alcohols formed were recovered after filtration of the lipase and liquid–liquid extraction. The course and selectivity of the enzymatic hydrolysis were quantified by chiral chromatography, and the results are summarized in Table 1.

The results from Table 1, demonstrate the important influence of CAL-B on both selectivity and reactivity depending directly on the structure of the acetates studied during the course of the enzymatic hydrolysis. The CAL-B displays (*R*)-enantiopreference since the (*R*)-acetate was selectively hydrolysed in all cases.

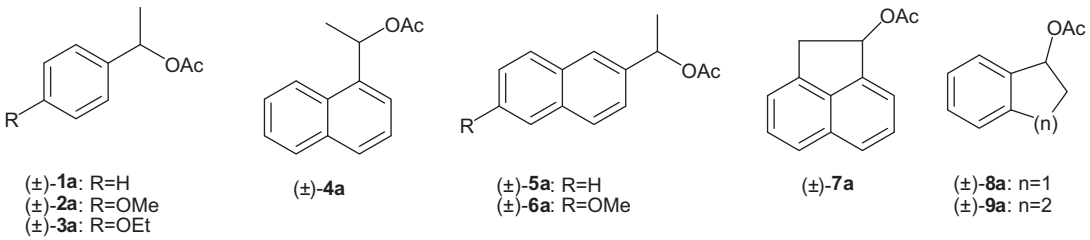
Table 1
Enzymatic hydrolysis of acetates **1a–9a**

Entry	Substrate[a]	ee_P (%)[b] (*R*)[d]	ee_S (%)[b] (*S*)[d]	*C*[c] (%)	*E*[c]
1	**1a**	>99	>99	50	≫200
2	**2a**	89	>99	53	91
3	**3a**	94	>99	51	>150
4	**4a**	87	75	46	37
5	**5a**	>99	89	49	≫200
6	**6a**	>99	98	49	≫200
7	**7a**	>99	6	6	200
8	**8a**	96	44	32	68
9	**9a**	98	83	46	≫200

[a] Reaction conditions: 1 mmol of racemic acetate, 12 mL of buffer phosphate pH 7, 2 mL Et_2O, 150 mg of CAL-B, at room temperature for 2 days.
[b] Measured by chiral chromatography, GC or HPLC (see Section 5).
[c] Conversion and selectivity:[14] $C = ee_S/(ee_P + ee_S)$; $E = \mathrm{Ln}[(1 - C)(1 - ee_{(S)})]/\mathrm{Ln}[(1 - C)(1 + ee_{(S)})]$.
[d] Absolute configuration was determined by the sign of the specific rotation of the isolated product with the literature (see Section 5).

The enzymatic hydrolysis was performed according to the conventional protocol (phosphate buffer pH 7) and showed a great diversity of results, with reactivities in the range of $6\% < C < 53\%$ and selectivities ranging $37 < E \ll 200$, for various acetate structures. The best results were obtained with the acetates **1a**, **2a, 3a**, **5a**, **6a** and **9a** (entries 1, 2, 3, 5, 6 and 9), with high selectivities $91 < E \ll 200$ and conversions $46\% < C < 52\%$. The comparison between the results obtained with **2a** and **3a** and **1a**, shows that the substitution of the *para*-position on the aromatic ring with methoxy- and ethoxy-groups, respectively, led to a decrease in the selectivity factor $E \gg 200$ to $E = 91$ (entry 1 vs 2) with a slight improvement of the conversion. However, the presence of a polar moiety on the naphthyl ring of structure **6a** compared to **5a**, did not have any influence on the reactivity or on the selectivity (entry 5 vs 6).

When a monocyclic aryl ring was replaced with an α-naphthyl **4a**, the reactivity of the lipase was preserved, albeit with a strong decrease in the selectivity ($C = 46\%$; $E = 37$; entry 4). However, in the case of isomer **5a**, the lipase gave excellent selectivity while



(±)-**1a**: R=H
(±)-**2a**: R=OMe
(±)-**3a**: R=OEt

(±)-**4a**

(±)-**5a**: R=H
(±)-**6a**: R=OMe

(±)-**7a**

(±)-**8a**: n=1
(±)-**9a**: n=2

Scheme 2. Substrate models.

keeping excellent conversion $C = 49\%$ and $E \gg 200$ (entry 5). Low to moderate reactivity was observed with cyclic substrates **7a** and **8a**, albeit with a high selectivity for **7a** (entries 7 and 8). Finally, an excellent selectivity was observed for the flat cyclic substrate **9a**, with only a slight decrease in the overall reactivity (entry 8).

This large diversity of results and the lack of obvious structure–activity relationship could be attributed to the structure of the substrates, and also to their moderate solubility in the aqueous media.

2.2. Enzymatic-alkaline hydrolysis in non-aqueous media

We carried out the enzymatic-alkaline hydrolysis of acetates **1a–9a** in toluene, according to the literature.[12] The hydrolysis reaction was carried out in 1 mmol of substrate (Scheme 3, path B), 3 mL of toluene, in the presence of 50 mg of CAL-B, for three days at 40 °C. We checked the influence of the amount of sodium carbonate (0.5 and 1 equiv) in order to assess the generality, flexibility and reproducibility of our method on various substrates (Table 2).

The carbonate promoted hydrolysis presented in Table 2 showed good to high reactivities and selectivities ($42.5\% < C < 50\%$, $E > 150$) within the range of the acetates studied.

We also saw that a stoichiometric equivalent of sodium carbonate gave the best conversions, while keeping the best selectivities $E > 200$ at optimal conversions in all cases.

Recapitulative histograms of the two sets of experiments (Fig. 1) allow a comparative illustration (conversion C and selectivity E) between both methods of enzymatic acetate hydrolysis. It is obvious from both figures that our new method performs better than the conventional hydrolytic method in aqueous media, within the range of substrates studied.

The alkaline-enzymatic hydrolysis using Na_2CO_3 is thus a very attractive method due to the high reactivities and selectivities recorded. It also facilitates the work-up procedure and avoids the use of liquid–liquid extraction, thus providing an economy of solvent and optimization of the isolated chemical yields. These advantages of our non-conventional methodology make it an ideal candidate to be combined with the Mitsunobu esterification protocol (Fig. 2), in order to establish deracemization via stereoinversion. The two steps can be combined through a simple filtration of the enzyme, and addition of the Mitsunobu reagents immediately to the reaction mixture without any prior work-up.

3. Deracemization through a selective alkaline-enzymatic hydrolysis/Mitsunobu esterification sequence

The reaction mixture containing the (*S*)-remaining acetate and the (*R*)-recovered alcohol from hydrolysis reaction underwent the Mitsunobu reaction to yield the (*S*)-acetate (Scheme 4).

Acetates **1a–9a** were hydrolysed according to the conditions established below. After three days at 40 °C, the enzyme was filtered. The enantiomeric excesses of the remaining acetate and the recovered alcohol were evaluated by chiral chromatography (GC or HPLC). Next, 1.2 equiv of triphenyl phosphine, and 1.2 equiv of acetic acid were added directly to the filtrate. The diisopropylazodicarboxylate (DIAD) (1.2 equiv) was added slowly at 0 °C, to convert the (*R*)-alcohol into the (*S*)-acetate. The desired acetate was then isolated after standard work-up and purification by silica-gel column chromatography. The enantiomeric purity was determined by chiral chromatography (GC or HPLC), and the absolute configuration was determined by the sign of the specific rotation compared to the literature data. The results are shown in Table 3.

The results detailed in Table 3 show that the (*S*)-acetates **1a–9a** were obtained quantitatively in moderate to high enantiomeric excesses $57\% < ee < 99\%$. We have noted in some cases some notable loss in the enantiomeric purity of the acetates, whereas the starting materials present excellent enantiomeric excesses $96\% < ee_P < 99\%$. This decrease was recorded after the Mitsunobu esterification. The (*S*)-acetates **1a**, **4a** and **7a** were recovered with clean stereoinversion of the (*R*)-alcohol obtained after hydrolysis with ee >99% (entries 1, 4 and 7); in these cases the enantiomeric purities of the initial alcohols were conserved through the (*S*)-acetates, which were recovered in excellent enantiomeric purity ee >99% and good isolated chemical yields (70–89%). However, for alcohols **5**, **8** and **9** ($98\% < ee < 99\%$ after hydrolysis), partial racemization occurred during the Mitsunobu reaction to yield the corresponding (*S*)-acetates with an overall decrease of the enantiomeric excesses of approximately 10% (entries 5, 8 and 9). This effect was even more important with substrates **2a**, **3a** and **6a** since the enantiomeric excesses of the remaining acetates after Mitsunobu esterification decreased to $57\% < ee < 65\%$ (entries 2, 3 and 6). This shows that these alcohols underwent the Mitsunobu reaction with almost full racemization.

Table 2
Optimization of the enzymatic alkaline-hydrolysis in non aqueous media

Entry	Substrate[a]	Amount of Na_2CO_3 (mmol)	ee_s (%)[b] (*S*)[e]	ee_p (%)[b] (*R*)[e]	*C*[c] (%)	*E*[c]
1	**1a**	0.5	>99	>99	50	≫200
2		1	83	99.5	45.5	≫200
3	**2a**	0.5	>99	93	52	144
4		1	95	98	49	≫200
5	**3a**	0.5	>99	>99	50	≫200
6		1	96	97	50	≫200
7	**4a**	0.5	73	>99	42.5	≫200
8		1	>99	>99	50	≫200
9	**5a**	0.5	84	>99	46	≫200
10		1	98	98	50	≫200
11	**6a**	0.5	ND[d]	ND[d]	ND[d]	ND[d]
12		1	93	96	49	>150
13	**7a**	0.5	ND[d]	ND[d]	ND[d]	ND[d]
14		1	>99	>99	50	≫200
15	**8a**	0.5	ND[d]	ND[d]	ND[d]	ND[d]
16		1	98	>99	50	≫200
17	**9a**	0.5	89	>99	47.5	≫200
18		1	>99	>99	50	≫200

[a] Reaction conditions: 2 mmol of racemic acetate, appropriate amount of Na_2CO_3, 6 mL of toluene, 50 mg of CAL-B, 40 °C for 3 days.
[b] Measured by chiral chromatography, GC or HPLC (see Section 5).
[c] Conversion and selectivity:[14] $C = ee_S/ee_P + ee_s$; $E = \mathrm{Ln}[(1 - C)(1 - ee_{(S)})]/\mathrm{Ln}[(1 - C)(1 + ee_{(S)})]$.
[d] Not determined.
[e] Absolute configuration was determined by the comparison of sign of the specific rotation of the isolated product with the literature (see Section 5).

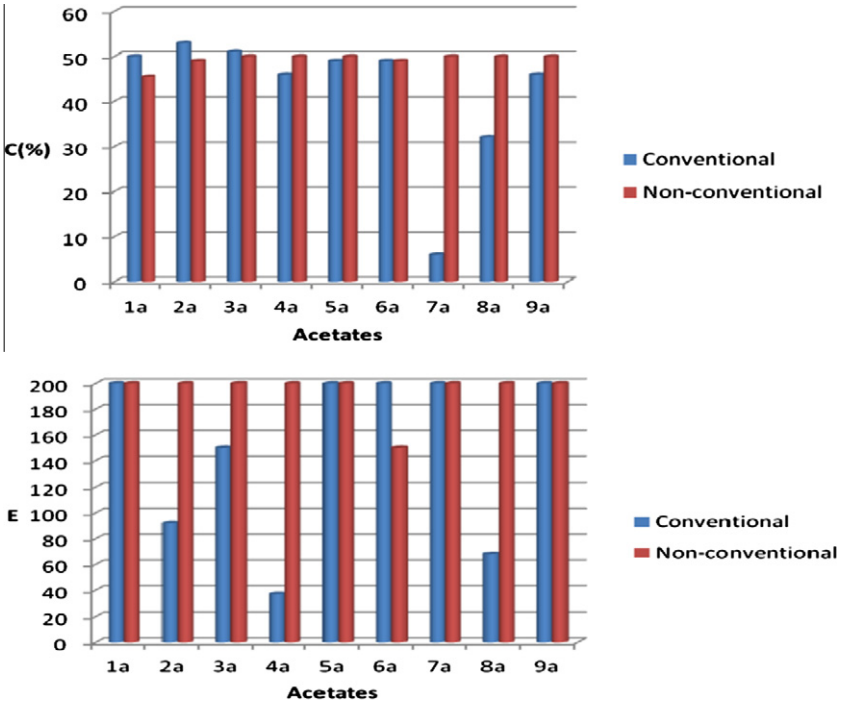


Figure 1. Comparison between the efficiency of the alkaline hydrolysis and the conventional one.

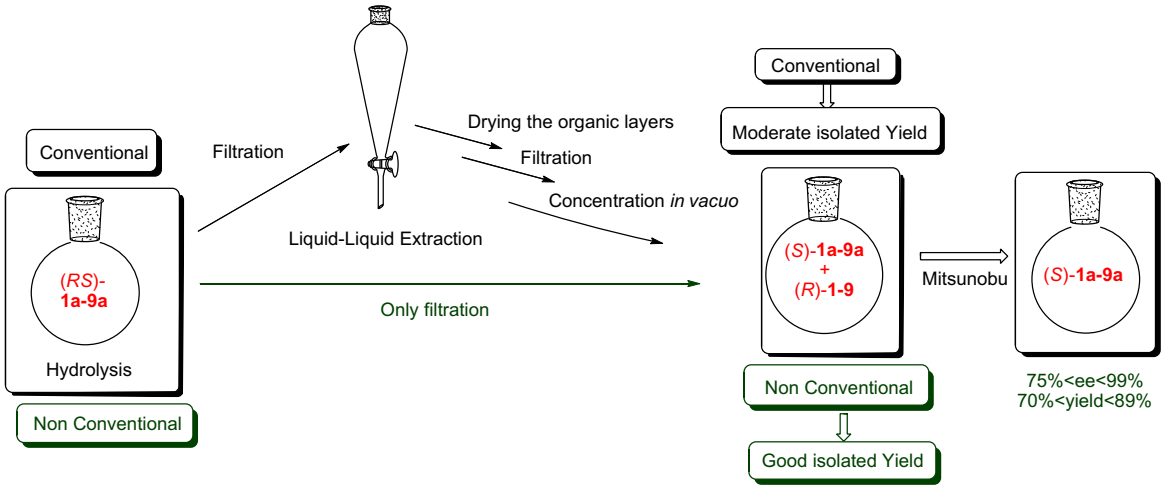
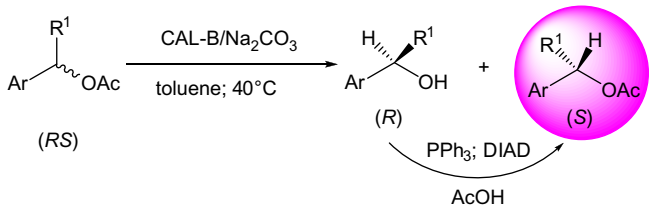


Figure 2. Comparison between the two processes.



Scheme 4. Deracemization via a combined enzymatic-alkaline hydrolysis/Mitsunobu inversion.

Similar observations were also noted in our previous investigations regarding deracemization through enzymatic acetylation/Misunobu esterification, under the same conditions, where a racemization phenomenon occurred during the enantioselective synthesis of (*R*)-acetates.[7e]

In our case, we observed a strong decrease in the enantioselectivity for the substrates bearing a strong electrodonating group on the aryl ring. Recently, a similar observation was reported regarding a racemization occurring over the course of an enantioselective synthesis via Mitsunobu substitution.[15] This loss of enantiomeric purity may arise from a competitive substitution process that proceeds via an attack of the carbocation intermediate, via a non-stereoselective (S_N1) process to generate the racemic product,[16] which in our case will give rise to an overall decrease in the enantiomeric excess of recovered (*S*)-acetates.

Table 3
Deracemization via a combination of the alkaline enzymatic hydrolysis with Mitsunobu inversion

Entry	Substrate[a]	Enzymatic alkaline hydrolysis[c]			Mitsunobu inversion	
		ee_s (%)[b] (*S*)-remaining acetate	ee_p (%)[b] (*R*)-recovered alcohol	*E*[c]	ee (%)[b] (*S*)-acetate	Yield[d] (%)
1	**1a**	>99	>99	>500	>99	70
2	**2a**	95	98	>300	57	72
3	**3a**	96	97	>200	60	89
4	**4a**	>99	>99	>500	>99	82
5	**5a**	98	98	>500	92	87
6	**6a**	93	96	>150	65	77
7	**7a**	>99	>99	>500	>99	89
8	**8a**	98	>99	>500	90	81
9	**9a**	>99	>99	>500	90	74

[a] Reaction conditions: 2 mmol of racemic acetate.
[b] Measured by chiral chromatography, GC or HPLC (see Section 5).
[c] Conversion and selectivity:[14] $C = ee_S/ee_P + ee_s$; $E = \mathrm{Ln}[(1 - C)(1 - ee_{(S)})]/\mathrm{Ln}[(1 - C)(1 + ee_{(S)})]$.
[d] Isolated yield.

4. Conclusion

We have prepared (*S*)-arylalkylcarbinol acetates **1a**–**9a** through deracemization via alkaline-hydrolysis catalysed by CAL-B lipase combined with Mitsunobu esterification. The hydrolysis using CAL-B in the presence of Na_2CO_3 gave high selectivities and reactivities *C* >49% for all of the studied substrates, and we have shown that this method is more advantageous than the traditional one in an aqueous media buffer. This process reduces the number of steps and gives a more practical experimental protocol. After optimization of the amount of the sodium carbonate used, this hydrolysis pathway was combined with Mitsunobu esterification after simple filtration. The recovered *(S)*-acetates after the stereoinversion protocol were isolated in excellent enantiomeric purity ee >99% for **1a**, **4a** and **7a**, to good ee >99% for **5a**, **8a** and **9a** and moderate ee >57% for **2a**, **3a** and **6a**. For these three cases, we observed almost full racemization during the nucleophilic substitution reaction due to the presence of an electron donating substituent on the aromatic ring.

5. Experimental

5.1. General

NMR spectra were performed with Bruker spectrometers (300 MHz for ^{1}H, 75 MHz for ^{13}C). Chemical shifts were reported in δ ppm from tetramethylsilane with the solvent resonance as internal standard for ^{1}H NMR and chloroform-*d* (δ 77.0 ppm) for ^{13}C NMR. The enantiomeric excesses were measured by gas chromatography (ThermoFinnigan Trace GC) equipped with an automatic autosampler and using a CHIRALSIL-DEX CB column (25 m; 0.25 mm; 0.25 μm), or by a chiral stationary phase HPLC on Chiralcel-ODH column. Retention times are reported in minutes. Optical rotations were determined using a Perkin–Elmer 241 Polarimeter at room temperature using a cell of 1 dm length at 589 nm.

5.2. General procedure for the synthesis of racemic acetates 1a–9a

The acetates were synthesized by chemical acetylation from the corresponding racemic alcohol (1 equiv), using 1.5 equiv of acetic anhydride, 1.2 equiv of Et_3N and a catalytic amount of 4-dimithylaminopyridine (0.1 equiv) diluted in ether. The acetates were obtained with enough purity after standard work up. The ^{1}H NMR spectra of these products were in good agreement with the literature.

5.3. General procedure for the conventional hydrolysis of racemic acetates 1a–9a with *Candida antarctica*-B lipase

At first, 2 mmol of racemic acetates **1a**–**9a** was dissolved in 2–3 mL of ether and added to 12 mL of phosphate buffer pH 7. Next, 300 mg of CAL-B (UA = 4500 U) was added. The suspension was stirred at room temperature for two days. The reaction mixture was filtered on Celite and concentrated in vacuo. The acetate formed and the remaining alcohol were separated by flash chromatography on silica gel (petroleum ether/ethyl acetate: 80/20) and analysed by chiral HPLC or GC.

5.4. General procedure for the alkaline-hydrolysis of racemic acetates 1a–9a with *Candida antarctica*-B lipase

A dry Schlenk tube was charged with 1 mmol of racemic acetates **1a–9a**, which was dissolved in 3 mL of solvent before the addition of 1 mmol of sodium carbonate and 50 mg of CAL-B. The suspension was stirred at 40 °C for the indicated time. The reaction mixture was filtered on Celite and concentrated in vacuo. The acetate formed and the remaining alcohol were separated by flash chromatography on silica gel (petroleum ether/ethyl acetate: 80/20) and analysed by chiral HPLC or GC.

5.5. General procedure for the esterification under Mitsunobu conditions

To the filtrate recovered after the enzymatic-alkaline hydrolysis, 1.2 equiv of AcOH and 1.2 equiv of PPh_3 were added; followed by the slow addition of 1.2 equiv of DIAD, at 0 °C. The reaction mixture was stirred vigorously at room temperature for 24 h. The solvent was removed under reduced pressure and the crude product was purified by silica-gel column chromatography using petroleum ether/ethyl acetate (80/20).

5.6. Chiral GC analysis and/or chiral HPLC analysis

The absolute configurations of all chiral compounds (isolated after chromatography) were determined by polarimetry by comparison with the literature. The conditions for the analysis of alcohols (*R*)-**1–9** and acetates (*S*)-**1a–9a** are reported below.

5.6.1. (*R*)-(+)-1-Phenylethanol 1

GC (Chiralsil-Dex CB,): t_R = 3.9 min, t_S = 4.1 min (T_{column} = 140 °C, flow 1.2 mL/min).

5.6.2. (*R*)-(+)-1-(4-Methoxyphenyl) ethanol 2

GC (Chiralsil-Dex CB): t_R = 12.7 min, t_S = 13.5 min (T_{column} = 135 °C, flow 1.2 mL/min).

5.6.3. (*R*)-(+)-1-(4-Ethoxyphenyl) ethanol 3

GC (Chiralsil-Dex CB): t_R = 13.1 min, t_S = 13.9 min (T_{column} = 155 °C, flow 1.2 mL/min).

5.6.4. (*R*)-(+)-1-(Naphthalene-1-yl) ethanol 4

Chiral HPLC: *Chiracel* OD-H column, t_R = 20.05 min, t_S = 28.90 min. Eluant (v,v): hexane/*i*-PrOH: 90/10; flow 0.5 mL/min.

5.6.5. (*R*)-(+)-1-(2-Naphthyl) ethanol 5

GC (Chiralsil-Dex CB): t_R = 10.2 min, t_S = 10.5 min (T_{column} = 170 °C, flow 1.2 mL/min).

5.6.6. (*R*)-(+)-1-(6-Methoxynaphthalen-2-yl) ethanol 6

GC (Chiralsil-Dex CB): t_R = 17.2 min, t_S = 17.7 min (T_{column} = 180 °C, flow 1.2 mL/min).

5.6.7. (*R*)-(−)-Acenaphthenol 7

Chiral HPLC: Chiracel OD-H column, t_R = 28.80 min, t_S = 34.67 min. Eluant (v,v): hexane/*i*-PrOH: 95/5; flow 0.5 mL/min.

5.6.8. (*R*)-(−)-1-Indanol 8

GC (Chiralsil-Dex CB), t_R = 51.2 min, t_S = 51.9 min (T_{column} = 80 °C for 7 min, after 135 °C for 5 min, flow 1.2 mL/min).

5.6.9. (*R*)-(−)-1,2,3,4-Tetrahydronaphthalen-1-ol 9

GC (Chiralsil-Dex CB), t_S = 63.7 min, t_R = 65.0 min (T_{column} = 80 °C for 7 min, then 135 °C for 5 min, flow 1.2 mL/min).

5.6.10. (*S*)-(−)-1-(Phenylethyl) acetate 1a

GC (Chiralsil-Dex CB), t_S = 2.9 min, t_R = 3.2 min (T_{column} = 140 °C, flow 1.2 mL/min). $[\alpha]_D^{20} = -136$ (*c* 0.1, $CHCl_3$) for 99% ee, {Lit. $[\alpha]_D$ = +135.9 (*c* 1, $CHCl_3$) for 99% ee (*R*)].[17]

5.6.11. (*S*)-(−)-1-(4-Methoxyphenyl)ethyl acetate 2a

GC (Chiralsil-Dex CB), t_S = 10.9 min, t_R = 12.1 min (T_{column} = 135 °C, flow 1.2 mL/min). $[\alpha]_D^{20} = -8$ (*c* 0.2, $CHCl_3$) for 57% ee, {Lit. $[\alpha]_D$ = +11.4 (*c* 1.2, $CHCl_3$) for 84% ee (*R*)].[17]

5.6.12. (*S*)-(−)-1-(4-Ethoxyphenyl)ethyl acetate 3a

GC (Chiralsil-Dex CB), t_S = 12.2 min, t_R = 13.4 min (T_{column} = 155 °C, flow 1.2 mL/min). $[\alpha]_D^{20} = -70.8$ (*c* 0.5, $CHCl_3$) for 60% ee, {Lit. $[\alpha]_D$ = −113.1 (*c* 0.9, $CHCl_3$) for >85% ee (*S*)}.[18]

5.6.13. (*S*)-(−)-1-(Naphthalen-1-yl) ethyl acetate 4a

Chiral HPLC: Chiracel OD-H column, t_R = 9.87 min, t_S = 13.50 min. Eluant (v,v): hexane/*i*-PrOH: 90/10; flow 0.5 mL/min. $[\alpha]_D^{20} = -46.5$ (*c* 0.2, $CHCl_3$) for 99% ee, {Lit. $[\alpha]_D$ = +49.5 (*c* 1, $CHCl_3$) for 99% ee (*R*)}.[17]

5.6.14. (*S*)-(−)-1-(Naphthalen-2-yl) ethyl acetate 5a

GC (Chiralsil-Dex CB), t_S = 8.6 min, t_R = 8.9 min (T_{column} = 170 °C, flow 1.2 mL/min). $[\alpha]_D^{20} = -104$ (*c* 0.2, $CHCl_3$) for 92% ee, {Lit. $[\alpha]_D$ = +110.2 (*c* 1, $CHCl_3$) for 99% ee (*R*)}.[17]

5.6.15. (*S*)-(−)-1-(6-Methoxynaphthalen-2-yl) ethyl acetate 6a

GC (Chiralsil-Dex CB), t_S = 16.2 min, t_R = 16.6 min (T_{column} = 180 °C, flow 1.2 mL/min). $[\alpha]_D^{20} = -64.5$ (*c* 0.3, $CHCl_3$) for 65% ee, {Lit. $[\alpha]_D$ = +110 (*c* 1, EtOH) for 99% ee (*R*)}.[17]

5.6.16. (*S*)-(−)-1-Acenaphthyl acetate 7a

Chiral HPLC: Chiracel OD-H column. t_S = 11.88 min, t_R = 12.52 min. Eluant (v,v): hexane/*i*-PrOH: 95/5; flow 0.5 mL/min; $[\alpha]_D^{20} = -79.4$ (*c* 0.2, $CHCl_3$) for 90% ee, {Lit. $[\alpha]_D$ = −85.2 (*c* 2.4, $CHCl_3$); 99% ee (*S*)}.[13a]

5.6.17. (*S*)-(−)-2,3-Dihydro-*1H*-inden-yl acetate 8a

GC (Chiralsil-Dex CB): t_S = 46.1 min, t_R = 46.9 min (T_{column} = 80 °C for 7 min, after 135 °C for 5 min, flow 1.2 mL/min). $[\alpha]_D^{20}$ −100 (*c* 0.5, $CHCl_3$) for 90% ee, {Lit. $[\alpha]_D$ = +85 (*c* 1, $CHCl_3$) for 80% ee (*R*)}.[17]

5.6.18. (*S*)-(−)-1,2,3,4-Tetrahydronaphthalen-1-yl acetate 9a

GC (Chiralsil-Dex CB): t_R = 57.4 min, t_S = 58.6 min (T_{column} = 80 °C for 7 min, after 135 °C for 5 min, flow 1.2 mL/min). $[\alpha]_D^{20} = -97.5$ (*c* 0.5, $CHCl_3$) for 90% ee, {Lit. $[\alpha]_D$ = +105 (*c* 1, $CHCl_3$) for 92% ee (*R*)}.[17]

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References

1. (a) Kirchner, G.; Scollar, M. P.; Klibanov, A. M. *J. Am. Chem. Soc.* **1985**, *107*, 7072–7076; (b) Klibanov, A. M. *CHEMTECH* **1986**, *16*, 354–359; (c) Klibanov, A. M. *J. Am. Chem. Soc.* **1986**, *108*, 2767–2768; (d) Faber, K.; Riva, S. *J. Synth. Org. Chem.* **1992**, 895–910; (e) Zhu, B.; Panek, J. S. *Org. Lett.* **2000**, *2*, 2575–2578; (f) Reetz, M. T. *Curr. Opin. Chem. Biol.* **2002**, *6*, 145–150; (g) Pavel, R. N. *Curr. Opin. Drug Disc. Dev.* **2003**, *6*, 902–920; (h) Faber, K. *Biotransformations in Organic Chemistry*, 6th ed.; Springer-Verlag: Berlin Heidelberg, 2011; (i) Ahmed, M.; Kelly, T.; Ghanem, A. *Tetrahedron* **2012**, *68*, 6781–6802.
2. (a) Trost, B. M. *Science* **1991**, 1471–1477. *Angew. Chem., Int. Ed.* **1995**, *107*, 285–307: Trost, B.M. *Angew. Chem., Int. Ed.* **1995**, *34*, 259–281; (b) Anastas, P. T.; Warner, J. C. *Green Chemistry: Theory and Practice*; Oxford University Press: New York, 1998; (c) Anastas, P. T.; Li, P. T. *Water as a Green Solvent*; John Wiley & Sons, 2010; (d) Anastas, P. T.; Eghbali, N. *Chem. Soc. Rev.* **2010**, *39*, 301–312.
3. (a) Carrera, G.; Riva, S. *Angew. Chem., Int. Ed.* **2000**, *39*, 2227–2254; (b) Ghanem, A. *Tetrahedron* **2007**, *63*, 1721–1754; (c) Merabet-Khellassi, M.; Aribi-Zouioueche, L.; Riant, O. *Tetrahedron: Asymmetry* **2009**, *20*, 1371–2377; (d) Chênevert, R.; Pelchet, N.; Morin, P. *Tetrahedron: Asymmetry* **2009**, *20*, 1191–1196; (e) Merabet-Khelassi, M.; Bouzemi, N.; Fiaud, J.-C.; Riant, O.; Aribi-Zouioueche, L. *C. R. Chim.* **2011**, *14*, 978–986.
4. (a) Boland, W.; Frossl, C.; Lorenz, M. *Synthesis* **1991**, 1049–1072; (b) Kawasaki, M.; Nakamura, K.; Kawabata, S. *J. Mol. Catal. B: Enzym.* **1999**, *6*, 447–451; (c) Kang, S.-K.; Jeon, J.-H.; Yamaguchi, T.; Kim, J.-S.; Ko, B.-S. *Tetrahedron: Asymmetry* **1995**, *6*, 2139–2142; (d) Aoyagi, N.; Ogawa, N.; Izumi, T. *Tetrahedron Lett.* **2006**, *47*, 4797–4801; (e) Reddipalli, G.; Venkataiah, M.; Fadnavis, N. W. *Tetrahedron: Asymmetry* **2010**, *21*, 320–324; (f) Bora, P. P.; Bez, G.; Anal, J. M. H. *J. Mol. Catal. B: Enzym.* **2011**, *72*, 270–275.
5. (a) Stercher, H.; Faber, K. *Synthesis* **1997**, 1–16; (b) Strauss, U. T.; Felfer, U. F.; Faber, K. *Tetrahedron: Asymmetry* **1999**, *10*, 107–117; (c) Faber, K. *Chem. Eur. J.* **2001**, *7*, 5005–5010; (d) Turner, N. J. *Curr. Opin. Biotechnol.* **2003**, *14*, 401–406; (e) Pàmies, O.; Bäckvall, J.-E. *Curr. Opin. Biotechnol* **2003**, *14*, 407–413; (f) Matute, B. M.; Bäckvall, J.-E. *Curr. Opin. Chem. Biol.* **2007**, *11*, 226–232; (g) Kamal, A.; Azhar, M. A.; Krishnaji, T.; Malik, M. H.; Azeeza, S. *Coord. Chem. Rev.* **2008**, 569–592; (h) Merabet-Khelassi, M.; Vriamont, N.; Riant, O.; Aribi-Zouioueche, L. *Tetrahedron: Asymmetry* **2011**, *22*, 1790–1796; (i) Pellissier, H. *Tetrahedron* **2011**, *67*, 3769–3802.
6. (a) van den Heuvel, M.; Cuiper, A. D.; van der Deen, H.; Kellogg, R. M.; Feringa, B. L. *Tetrahedron Lett.* **1997**, *38*, 1655–1658; (b) El Ghihani, M. T.; Williams, J. M. *J. Curr. Opin. Chem. Biol.* **1999**, *3*, 11–15.
7. (a) Takano, S.; Suzuki, M.; Ogasawara, K. *Tetrahedron: Asymmetry* **1993**, *4*, 1043–1046; (b) Vanttinen, E.; Kanerva, L. T. *Tetrahedron: Asymmetry* **1995**, *6*, 1779–1786; (c) Liu, H. L.; Anthonsen, T. *Chirality* **2002**, *14*, 25–27; (d) Wallner, A.; Mang, H.; Glieck, S. M.; Steinreiber, A.; Mayer, S. F.; Faber, K. *Tetrahedron: Asymmetry* **2003**, *14*, 2427–2432; (e) Bouzemi, N.; Aribi-Zouioueche, L.; Fiaud, J. C. *Tetrahedron: Asymmetry* **2006**, *17*, 797–800.
8. (a) Voss, C. V.; Gruber, C. C.; Faber, K.; Knaus, T.; Macheroux, P.; Kroutil, W. *J. Am. Chem. Soc.* **2008**, *130*, 13969–13972; (b) Mu, X. Q.; Xu, Y.; Yang, M.; Sun, Z. H. *Process Biochem.* **2011**, *46*, 233–239.
9. Mitsunobu, O.; Yamada, M. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2380.
10. (a) Danda, T.; Nagatomi, T.; Maehara, A.; Umemura, T. *Tetrahedron* **1991**, *47*, 8701–8716; (b) Steinreiber, A.; Stadler, A.; Mayer, S. F.; Faber, K.; Kappe, O. *Tetrahedron Lett.* **2001**, *42*, 6283–6286; (c) Shimada, Y.; Usuda, K.; Okabe, H.; Suzuki, T.; Matsumoto, K. *Tetrahedron: Asymmetry* **2009**, *20*, 2802–2808.
11. Rakels, J. L. L.; Straathof, A. J. J.; Heijneii, J. J. *Tetrahedron: Asymmetry* **1994**, *5*, 93–100.
12. Merabet-Khelassi, M.; Houiene, Z.; Aribi-Zouioueche, L.; Riant, O. *Tetrahedron: Asymmetry* **2012**, *23*, 823–833.

13. (a) Bidjou, C.; Aribi-Zouioueche, L.; Fiaud, J.-C. *J. Soc. Alg. Chim.* **1999**, *9*, 261–268; (b) Aribi-Zouioueche, L.; Fiaud, J.-C. *Tetrahedron Lett.* **2000**, *41*, 4085–4088; (c) Bidjou, C.; Aribi-Zouioueche, L.; Fiaud, J.-C. *Tetrahedron Lett.* **2002**, *43*, 3025–3027.
14. (a) Chen, C. S.; Fujimoto, Y.; Sih, C. J. *J. Am. Chem. Soc.* **1982**, *104*, 7294–7299; (b) Kagan, H. B.; Fiaud, J.-C. In *Kinetic Resolution Topics in Stereochemistry*; Eliel, E. L., Wilen, S. H., Eds.; J. Wiley & Sons, Inc.: New York, 1988; Vol. 18, pp 249–330.
15. Thvedt, T. H. K.; Fuglseth, E.; Sundby, E.; Hoff, B. H. *Tetrahedron* **2010**, *66*, 6733–6743.
16. (a) Warmerdam, E. G. J. C.; Brussee, J.; Kruse, C. G.; Van der Gen, A. *Phosphorus, Sulfur Silicon Relat. Elem.* **1993**, *75*, 3–6; (b) Hillier, M. C.; Desrosiers, J. N.; Marcoux, J. F.; Grabowski, E. J. J. *Org. Lett.* **2004**, *9*, 573–576.
17. Bouzemi, N.; Debbeche, H.; Aribi-Zouioueche, L.; Fiaud, J.-C. *Tetrahedron Lett.* **2004**, *45*, 627–630.
18. Naemura, K.; Murata, M.; Tanaka, R.; Yano, M.; Hirose, K.; Tobe, Y. *Tetrahedron: Asymmetry* **1996**, *7*, 1581–1584.