

Article

Lipase-Catalyzed Kinetic Resolution of Aryltrimethylsilyl Chiral Alcohols

Dayvson J. Palmeira, Juliana C. Abreu and Leandro H. Andrade *

Institute of Chemistry, University of São Paulo, Av. Prof. Lineu Prestes, n°. 748, SP 05508-900, São Paulo, Brazil; E-Mails: dayvson.palmeira@gmail.com (D.J.P.); jukinhabreu@hotmail.com (J.C.A.)

* Author to whom correspondence should be addressed; E-Mail: leandroh@iq.usp.br;
Tel.: +55-11-3091-2287.

Received: 27 September 2011; in revised form: 28 October 2011 / Accepted: 17 November 2011 /

Published: 23 November 2011

Abstract: Lipase-catalyzed kinetic resolution of aryltrimethylsilyl chiral alcohols through a transesterification reaction was studied. The optimal conditions found for the kinetic resolution of *m*- and *p*-aryltrimethylsilyl chiral alcohols, led to excellent results, high conversions ($c = 50\%$), high enantiomeric ratios ($E > 200$) and enantiomeric excesses for the remaining (*S*)-alcohol and (*R*)-acetylated product ($>99\%$). However, kinetic resolution of *o*-aryltrimethylsilyl chiral alcohols did not occur under the same conditions applied to the other isomers.

Keywords: lipase; aryltrimethylsilyl chiral alcohols; kinetic resolution; transesterification

1. Introduction

The chemistry of organosilicon compounds is well-established nowadays due to its importance in organic synthesis, in which these compounds can be used for carbon-carbon bond formation as well as protecting-group reagents [1,2]. In addition, most of the organosilicon compounds are generally easy to handle and store. They are thermal stable and present low toxicity [3,4]. These characteristics make the organosilicon compounds a good choice for diverse organic synthesis methodologies. Aryltrimethylsilyl compounds have attracted special attention because they are involved in some interesting desilylative functionalizations, such as aryne formation [5–10], oxyarylation of alkenes [11,12], phosphazene base-promoted functionalization [13], metal-catalyzed cross-coupling reactions [14–18] and palladium-catalyzed oxidative coupling reaction [19].

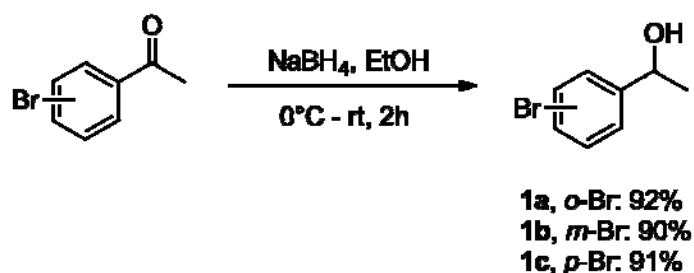
Although silicon-containing organic compounds find a remarkable application in organic synthesis, there is a general lack of biocatalyzed studies using these compounds as substrates, and only a few such biocatalyzed transformations of organosilanes have been reported, such as the stereoselective microbial reduction of racemic acetyl(*t*-butyl)methylphenyl silane [20], preparation of *p*-(trimethylsilyl)phenylalanine through an amidohydrolase produced by a bacterium [21], enantioselective microbial reduction of acyl silanes [22], the synthesis of (*R*)-2-trimethylsilyl-2-hydroxyethylcyanide by a (*R*)-oxynitrilase-catalyzed hydrogen cyanide addition [23], biocatalytic cleavage of silicon-oxygen bonds [24,25] and enzyme-catalyzed siloxane bond formation [26–28]. Reports on lipase-catalyzed kinetic resolution of organosilanes are even scarcer. To our knowledge, just a few publications have focused on this type of biocatalytic reaction, such as the synthesis of optically active 2-sila-1,3-propanediols through a regioselective transesterification reaction catalyzed by a series of lipases [29], the preparation of optically active silylmethanol derivatives through lipase-catalyzed enantioselective esterification and transesterification [30], enantioselective transesterification of 1-trimethylsilyl-1-alkyn-3-ols catalyzed by immobilized *Pseudomonas cepacia* lipase PS and *Pseudomonas fluorescens* [31–33], and the kinetic resolution of 4-(phenyldimethylsilyl)-3-butyne-2-ol for the preparation of enantioenriched allenylsilanes [34]. However, there are no reports in the literature, in which aryltrimethylsilyl compounds have been used in lipase-catalyzed kinetic resolution. The aim of this work was therefore to carry out an extensive study on the lipase-catalyzed kinetic resolution of aryltrimethylsilyl chiral alcohols *via* transesterification reaction.

2. Results and Discussion

2.1. Synthesis of Aryltrimethylsilyl Chiral Alcohols 2a–f

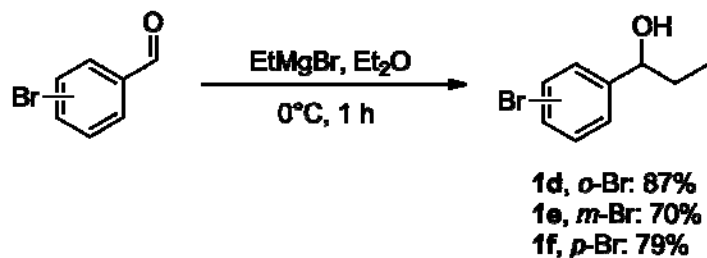
1-(Bromo-phenyl)ethanols **1a–f** were synthesized in excellent yields (90–92%) by reacting *o*-, *m*-, and *p*-bromo-substituted acetophenones with NaBH₄ (Scheme 1) [35].

Scheme 1. Reduction of bromo-substituted acetophenones to afford chiral alcohols **1a–c**.



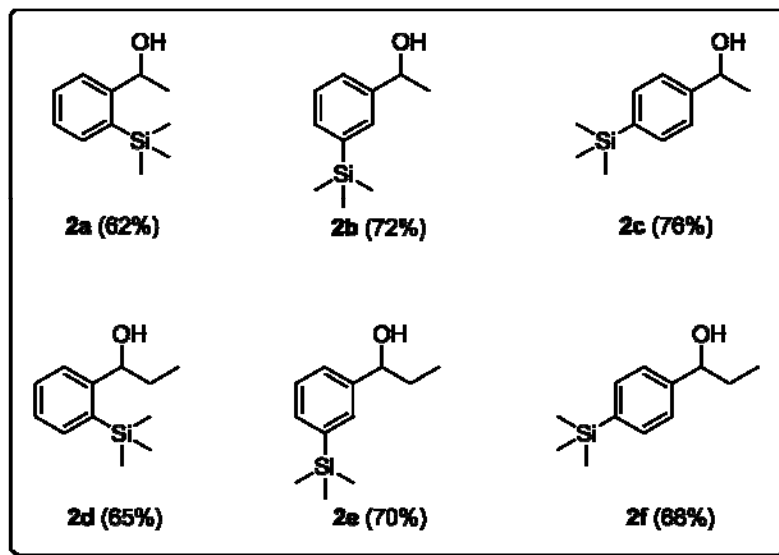
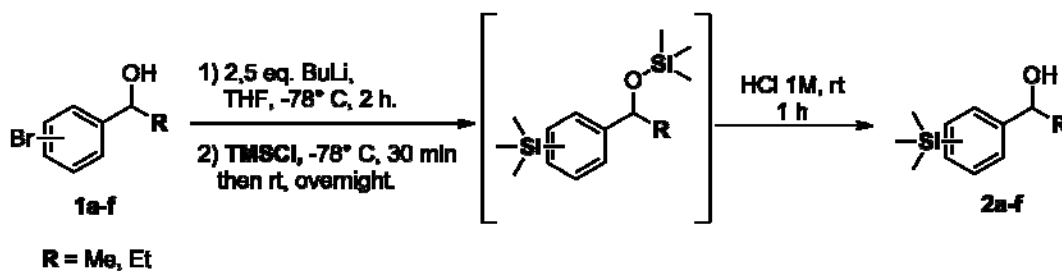
The addition of a Grignard reagent to the *o*-, *m*-, and *p*-bromo-substituted benzaldehydes gave the chiral alcohols **1d–f** bearing an ethyl group attached at the benzylic carbon, in good yields (70%–87%, Scheme 2).

Scheme 2. Carbonyl addition of a Grignard reagent to bromo-substituted benzaldehydes to give chiral alcohols **1d–f**.



With the aryl bromides precursors **1a–f** in hand, we next synthesized aryltrimethylsilyl chiral alcohols. The compounds **1a–f** were submitted to the bromo-lithium exchange reaction with *n*-butyllithium, THF at -70°C , followed by addition of trimethylsilyl chloride. The disilylated intermediates were generated *in situ*, and after acid hydrolysis reaction, aryltrimethylsilyl chiral alcohols **2a–f** were obtained in moderate to good yields (62%–76%, Scheme 3).

Scheme 3. Synthesis of the aryltrimethylsilyl chiral alcohols **2a–f**.

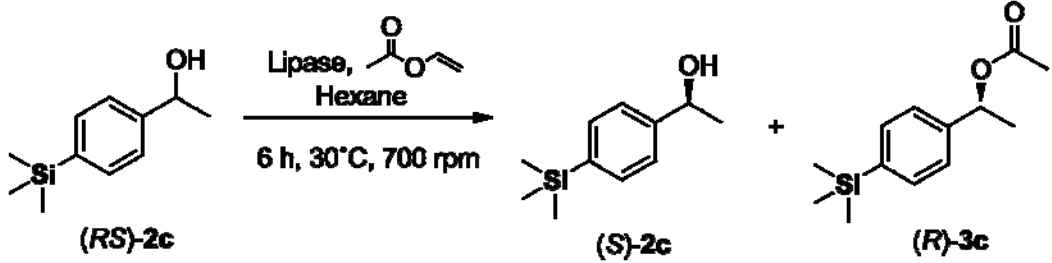


2.2. Enzymatic Kinetic Resolution of the Aryltrimethylsilyl Chiral Alcohols **2a–f**

Initially, we focused our study on choosing the best lipase source for the enzymatic kinetic resolution (EKR) of aryltrimethylsilyl chiral alcohols through transesterification reaction. For the lipase screening, vinyl acetate was chosen as the acyl donor, hexane as the solvent, and the compound

(*RS*)-2c as the model substrate. Eleven types of lipase sources were used in the kinetic resolution of compound (*RS*)-2c. The results are summarized in Table 1.

Table 1. Screening of lipases for the kinetic resolution of (*RS*)-2c ^a.

					
Entry	Lipase (source)	<i>ee</i> (%) ^b		<i>c</i> (%) ^c	<i>E</i> ^d
		(<i>S</i>)-2c	(<i>R</i>)-3c		
1	<i>Mucor javanicus</i> (Amano M)	—	—	—	—
2	<i>Candida cylindracea</i> (Fluka)	—	—	—	—
3	<i>Candida antarctica</i> (CAL-B, Novozym 435)	74	>99	43	>200
4	<i>Pseudomonas cepacia</i> (Amano PS)	48	>99	33	>200
5	<i>Aspergillus niger</i> (Amano A)	—	—	—	—
6	<i>Pseudomonas cepacia</i> (Amano PS-D I)	98	>99	49	>200
7	<i>Candida rugosa</i> (Amano, type VII)	—	—	—	—
8	<i>Pseudomonas cepacia</i> (Amano PS-C II)	>99	>99	50	>200
9	<i>Mucor meihei</i> (Sigma)	—	—	—	—
10	<i>Pseudomonas fluorescens</i> (Amano AK)	58	>99	37	>200
11	Porcine pancreas (Sigma, type II)	—	—	—	—

^a General conditions: Substrate (0.05 mmol), lipase (2 mg), vinyl acetate (0.11 mmol), hexane (200 μ L);

^b Determined by chiral GC analysis; ^c Conversion: $c = ee_S/(ee_S + ee_P)$; ^d $E = \ln\{[ee_P(1 - ee_S)/(ee_P + ee_S)]\}/\ln\{[ee_P(1 + ee_S)/(ee_P + ee_S)]\}$; (—) = No reaction.

Lipases from *Mucor javanicus*, *Candida cylindracea*, *Aspergillus niger*, *Candida rugosa*, *Mucor meihei* and porcine pancreas (Table 1, entries 1, 2, 5, 7, 9 and 11) showed no activity for the transesterification reaction of (*RS*)-2c, and only unreacted racemic alcohol was recovered at the end of the process. On the other hand, high enantiomeric ratios ($E > 200$) and excellent enantiomeric excess for (*R*)-3c ($ee > 99\%$) were achieved when lipases from *Candida antarctica* (CAL-B), *Pseudomonas cepacia* [free form (Amano PS), immobilized on diatomite (Amano PS-DI) or immobilized on ceramic (Amano PS-CII)] and *Pseudomonas fluorescens* (entries 3, 4, 6, 8 and 10) were used as biocatalysts.

When *Pseudomonas cepacia* immobilized on diatomite (Amano PS-DI) or ceramic (Amano PS-CII) (entries 6 and 8) were used, high conversions were obtained (49% and 50%, respectively). Based on these results and aiming future application in the chemoenzymatic dynamic resolution of aryltrimethylsilyl chiral alcohols, the lipase from *Pseudomonas cepacia* Amano PS-C II (Table 1, entry 8) was chosen for the subsequent studies. The amount of enzyme and reaction time were also evaluated in order to achieve the perfect kinetic resolution process (Table 2).

Table 2. Evaluation of reaction time and enzyme/substrate ratio for kinetic resolution of (*RS*)-**2c** ^a.

Entry	Substrate (mmol)	Amano PS-C II (mg)	Time (h)	<i>ee</i> (%) ^b		<i>c</i> (%) ^c	<i>E</i> ^d
				(<i>S</i>)- 2c	(<i>R</i>)- 3c		
1	0.05	2	6	>99	>99	50	>200
2	0.05	2	3	>99	>99	50	>200
3	0.05	1	6	>99	>99	50	>200
4	0.05	1	3	>99	>99	50	>200
5	0.05	1	1.5	86	>99	46	>200
6	0.1	1	6	>99	>99	50	>200
7	0.1	1	3	83	>99	45	>200
8	0.1	1	1.5	48	>99	33	>200

^a General conditions: vinyl acetate (2.2 equiv.), hexane (200 μ L); ^b Determined by chiral GC analysis; ^c Conversion: $c = ee_S/(ee_S + ee_P)$; ^d $E = \ln\{[ee_P(1 - ee_S)/(ee_P + ee_S)]\}/\ln\{[ee_P(1 + ee_S)/(ee_P + ee_S)]\}$.

After 6 hours reaction, a decrease in the enzyme amount and an increase in substrate quantities (entries 1, 3 and 6) led to perfect kinetic resolution of (*RS*)-**2c**. However, excellent results were also achieved after 3 hours (entries 2 and 4), even with a decrease in enzyme concentration (entry 4). Maintaining the reaction time (3 h), 1 mg of enzyme, but increasing the amount of substrate (entry 7), a small decrease in conversion was observed. Reactions performed in 1.5 h (entries 5 and 8) presented the lowest conversions, indicating that the kinetic resolution of (*RS*)-**2c** did not occur completely.

Thus, the optimized conditions, considering reaction time and amount of substrate and enzyme (entry 4), was then applied to enzymatic kinetic resolution of several aryltrimethylsilyl chiral alcohols **2a,b,d,e,f** (Table 3).

The EKR of compounds (*R,S*)-**2b,f** (Table 3, entries 3 and 9, respectively) performed in 3 h led to very good results with high conversions (47% and 49%, respectively) and excellent enantioselectivity ($E > 200$ in both cases). We extended the reaction time to 16 h (Table 3, entries 4 and 10), and a perfect kinetic resolution of (*R,S*)-**2b,f** was achieved (conversion of 50% and enantiomeric excesses for (*S*)-**2** and (*R*)-**3** >99%, in both cases). In regards to compound (*R,S*)-**2e**, a three-hour reaction (Table 3, entry 7) led to low conversion ($c = 35\%$). Only when the reaction time and enzyme amount were increased to 24 h and 2 mg, respectively (Table 3, entry 8), excellent conversion ($c = 50\%$), enantioselectivity ($E > 200$) and enantiomeric excesses ($ee > 99\%$ for both (*S*)-**2e** and (*R*)-**3e**) were found.

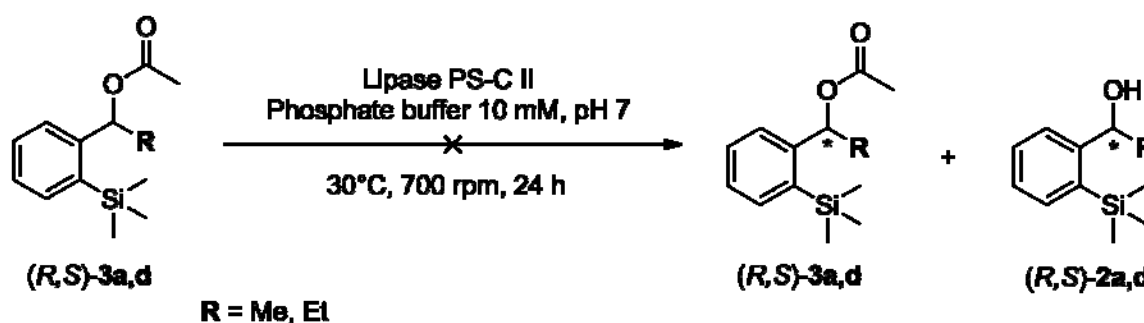
Table 3. Enzymatic kinetic resolution of aryltrimethylsilyl chiral alcohols **2a,b,d,e,f**^a.

Entry	Substrate	Time (h)	<i>ee</i> (%) ^b		<i>c</i> (%) ^c	<i>E</i> ^d
			(<i>S</i>)- 2	(<i>R</i>)- 3		
1	(<i>RS</i>)- 2a	3	—	—	—	—
2	(<i>RS</i>)- 2a	16	—	—	—	—
3	(<i>RS</i>)- 2b	3	87	>99	47	>200
4	(<i>RS</i>)- 2b	16	>99	>99	50	>200
5	(<i>RS</i>)- 2d	3	—	—	—	—
6	(<i>RS</i>)- 2d	16	—	—	—	—
7	(<i>RS</i>)- 2e	3	54	>99	35	>200
8	(<i>RS</i>)- 2e ^e	24	>99	>99	50	>200
9	(<i>RS</i>)- 2f	3	96	>99	49	>200
10	(<i>RS</i>)- 2f	16	>99	>99	50	>200

^a General conditions: substrate (0.05 mmol), enzyme (1 mg), vinyl acetate (0.11 mmol), hexane (200 μ L); ^b Determined by chiral GC analysis; ^c Conversion: $c = ee_S/(ee_S + ee_P)$; ^d $E = \ln\{[ee_P(1 - ee_S)/(ee_P + ee_S)]\}/\ln\{[ee_P(1 + ee_S)/(ee_P + ee_S)]\}$; ^e Amount of enzyme: 2 mg; (—) = No reaction.

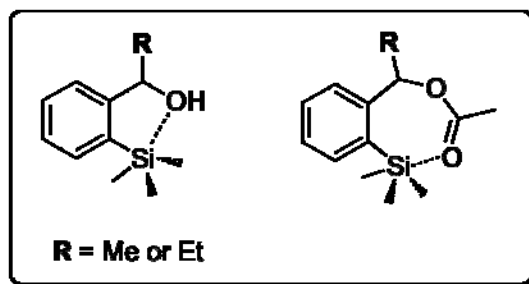
As it can be seen, after three-hour reaction, *p*-trimethylsilyl-substituted phenyl chiral alcohols **2c,f** (Table 2, entry 4 and table 3, entry 9) showed better conversion than *m*-trimethylsilyl substituted analogues **2b,e** (Table 3, entries 3 and 7). The size of the alkyl chain (methyl: **2b**, ethyl: **2e**) attached to the chiral carbon has a small influence in the conversion of alcohols **2b,e** into esters **3b,e**. For example, the enzymatic kinetic resolution of alcohol **2b** presented 47% conversion whereas for the alcohol **2e** presented 35% (Table 3, entries 3 and 7). Nevertheless, in all cases excellent enantioselectivities were achieved.

Lipase-catalyzed transesterification of *o*-trimethylsilyl substituted phenyl chiral alcohols (*RS*)-**2a,d** did not occur neither after 3 h (entries 1 and 5) nor 16 h (entries 2 and 6). To overcome this obstacle, attempts towards the enantioselective hydrolysis of (*RS*)-**3a,d** were made (Scheme 4) [36].

Scheme 4. Attempts towards the enantioselective hydrolysis of (*RS*)-**3a,d**.

However, by using PS-C II lipase, phosphate buffer solution (10 mM, pH 7) and ester (*RS*)-**3a,d** as substrate, no hydrolysis products (**2a,d**) were obtained. A possible explanation for these results may involve a non-bonded Si $\cdots$ O attraction by pseudo-pentacoordinated species (Figure 1).

Figure 1. Possible pseudo-pentacoordinated species that can be present on the active site of the enzyme.



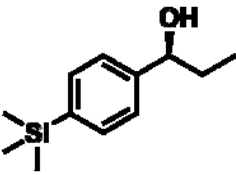
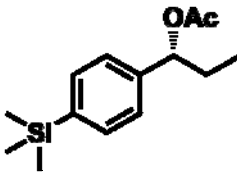
Pseudo-pentacoordinated species have been evidenced in studies involving silyl formates [37], di- and trisilanes bearing the (dimethylamino)-1-naphthyl group [38,39], *N*-substituted trimethylsilyl carbamates [40] and *N*-trimethylsilylated cyclic ureas [41]. Assuming the five- and seven-membered pseudo-rings formed from this intramolecular interaction, a steric hindrance, due to a rigid array of these structures, could be unfavorable for the formation of enzyme-substrate complexes.

This proposal is endorsed by the results obtained for the *m*- and *p*-trimethylsilyl substituted phenyl chiral alcohols, in which the non-bonded Si...O attraction should be less intense and pseudo-pentacoordinated species can hardly be formed. In these cases the kinetic resolution proceed as expected. Motivated by the excellent results, we decided to carry out the enzymatic kinetic resolution of (*R,S*)-**2b,c** and (*R,S*)-**2e,f** on a higher scale (Table 4).

Table 4. Lipase-catalyzed kinetic resolution of compounds (*R,S*)-**2b,c** and (*R,S*)-**2e,f**^a.

Entry	Substrate	Isolated yield % (ee %) ^b	
1	<i>(RS)</i> - 2b		
		(<i>S</i>)- 2b , 44 (>99)	(<i>R</i>)- 3b , 49 (>99)
2	<i>(RS)</i> - 2c ^c		
		(<i>S</i>)- 2c , 31 (>99)	(<i>R</i>)- 3c , 46 (>99)
3	<i>(RS)</i> - 2e ^d		
		(<i>S</i>)- 2e , 38 (>99)	(<i>R</i>)- 3e , 49 (>99)

Table 4. Cont.

Entry	Substrate	Isolated yield % (ee %) ^b	
4	(R,S)-2f		
		(S)-2f, 39 (>99)	(R)-3f, 34 (>99)

^a General conditions: substrate (1 mmol), enzyme (20 mg), vinyl acetate (2.2 mmol, 203 μ L), hexane (4 mL), reaction time of 16 h; ^b Determined by chiral GC analysis; ^c Reaction time of 3 h;

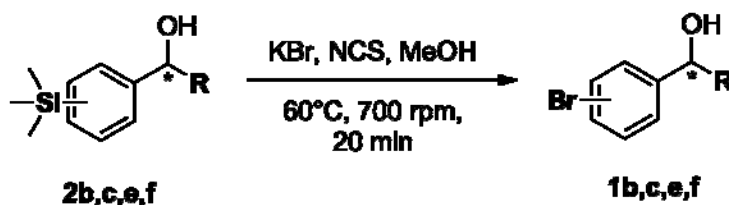
^d Reaction time of 24 h and amount of enzyme = 40 mg.

According to the results on Table 4, the lipase-catalyzed kinetic resolution of (R,S)-2b,c and (R,S)-2e,f led to excellent results with enantiomeric excesses >99% in all cases and isolated yields of up to 49%.

2.3. Determination of Absolute Configuration of Enantioenriched Aryltrimethylsilyl Chiral Alcohols (2b, 2c, 2e and 2f)

The enantioenriched compounds 2b, 2c, 2e and 2f were submitted to a bromodesilylation reaction in order to obtain the corresponding bromides (Scheme 5).

Figure 5. Bromodesilylation of enantioenriched compounds 2b, 2c, 2e and 2f.



The enantioenriched bromides 1b, 1c, 1e and 1f were submitted to chiral GC and HPLC analysis, and the retention times were compared with those described in the literature [42–45]. Thus, absolute configuration of enantioenriched aryltrimethylsilyl (S)-alcohols and (R)-acetates were determined by analogy to the results found for the bromophenyl (S)-alcohols. The stereochemistry found for the resolved aryltrimethylsilyl chiral alcohols and acetates is in accordance with the Kaslauskas' rule prediction [46].

3. Experimental

3.1. General Methods

All the enzymes were purchased from the Sigma-Aldrich Chemical Company and stored at 4 °C. All solvents used were HPLC or ACS grade. THF and Et₂O were distilled from Na/benzophenone. CH₂Cl₂ was distilled from CaH₂. Nuclear magnetic resonance (NMR) spectra were recorded on a Varian Gemini 200 or Bruker DPX 300 spectrometer at operating frequencies of 200 and 300 MHz (¹H-NMR) or 50 and 75 MHz (¹³C-NMR). The ¹H-NMR chemical shifts are reported in ppm relative

to TMS peak. Data are reported as follows: chemical shift (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (J) in Hertz and integrated intensity. The ^{13}C -NMR chemical shifts are reported in ppm relative to CDCl_3 signal. Infrared spectra were recorded from KBr discs on a Bomem Michelson model 101 FTIR spectrometer. Absorption maxima (ν_{max}) are reported in wavenumbers (cm^{-1}). Low-resolution mass spectra were obtained on a GC/MS Shimadzu spectrometer, operating at 70 eV. High-resolution mass spectra (HRMS) were acquired using a Bruker Daltonics MicroTOF instrument, operating electrospray ionization (ESI) mode. Gas chromatography (GC) analysis for measurement of enantiomeric excess was obtained using a Shimadzu 17-A Gas Chromatograph, Flame Ionization Detector (FID), and a chiral column Varian CP-Chirasil-DEX CB β -cyclodextrin ($25\text{ m} \times 0.32\text{ mm} \times 0.25\text{ }\mu\text{m}$). Temperature of the detector and injector was $250\text{ }^\circ\text{C}$; oven temperature: from $100\text{ }^\circ\text{C}$ to $150\text{ }^\circ\text{C}$, $1\text{ }^\circ\text{C}/\text{min}$; flow = 80 kPa , H_2 as gas carrier.

3.2. Synthetic Procedures

3.2.1. General Procedure for the Preparation of 1-(Bromophenyl)ethanols **1a–c** [35,47]

Ketone (10 mmol, 1.99 g) was added to a 250 mL round-bottomed flask containing ethanol (20 mL) cooled at $0\text{ }^\circ\text{C}$, followed by the addition of NaBH_4 (11 mmol, 0.42 mg) in small portions. The mixture was stirred for 30 min at $0\text{ }^\circ\text{C}$ and for 2.5 h at room temperature. The ethanol was evaporated under reduced pressure and H_2O (20 mL) was added to the organic residue. The mixture was treated with aqueous acid solution (1 M HCl) until pH 6, and extracted with CH_2Cl_2 ($3 \times 20\text{ mL}$). Organic phase was dried over anhydrous MgSO_4 , and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography using *n*-hexane/ethyl acetate (8:2) as eluent. All spectral data of compounds **1a–c** were in agreement with those described in the literature [48].

3.2.2. General Procedure for the Preparation of 1-(Bromophenyl)propanols **1d–f** [49]

To a 100 mL, two-necked, round-bottom flask fitted with a reflux condenser and containing a suspension of magnesium (15 mmol, 0.36 g) in Et_2O (4 mL), a solution of bromoethane (15 mmol, 1.63 g, 1.12 mL) in Et_2O (12 mL) was added dropwise under N_2 atmosphere. The mixture was refluxed for 30 min. Then the solution of ethylmagnesium bromide was cooled to $-5\text{ }^\circ\text{C}$ and a solution of the appropriate brom-benzaldehyde (10 mmol, 1.85 g) in Et_2O (8 mL) was added dropwise. The mixture was stirred for 1 h at r.t., poured on ice, and acidified with 6 M HCl . The organic layer was separated, and the aqueous layer was extracted with Et_2O ($3 \times 5\text{ mL}$). The organic solutions were combined, washed with 10% NaHCO_3 solution ($2 \times 5\text{ mL}$), H_2O ($2 \times 5\text{ mL}$), brine ($2 \times 5\text{ mL}$), and dried over anhydrous MgSO_4 . The crude product was purified by column chromatography using *n*-hexane/ethyl acetate (9:1) as eluent. All spectral data of the compounds **1d–f** were in agreement with those described in the literature [42].

3.2.3. General Procedure for the Preparation of Aryltrimethylsilyl Chiral Alcohols **2a–f** [11,50]

A 50 mL, two-necked, round-bottom flask under N_2 atmosphere was charged with a solution of the appropriate alcohol **1a–f** (5 mmol) in THF (15 mL). The mixture was cooled to $-70\text{ }^\circ\text{C}$ and, a solution of *n*-butyllithium (12.5 mmol, 1.6 M in hexanes, 7.80 mL) was added dropwise. The mixture was

stirred at $-70\text{ }^{\circ}\text{C}$ for 2 h. Trimethylsilyl chloride (14 mmol, 1.52 g, 1.78 mL) was added, and after 30 min at $-70\text{ }^{\circ}\text{C}$, the solution was allowed to warm to room temperature and stirred overnight. The reaction was quenched by the addition of aqueous acid solution (1 M HCl, 15 mL) and stirred for 1 hour. The organic layer was separated and the aqueous layer extracted with ethyl acetate ($3 \times 10\text{ mL}$). The combined organic layers were washed with saturated solution of NaHCO_3 ($2 \times 25\text{ mL}$) and brine ($2 \times 25\text{ mL}$), dried over anhydrous MgSO_4 and concentrated *in vacuo*. The residue was purified by column chromatography using *n*-hexane/ethyl acetate (9:1) as eluent.

1-(2-(Trimethylsilyl)phenyl)ethanol (2a). Yield: 606 mg (62%). White solid. $^1\text{H-NMR}$ (200 MHz, CDCl_3) δ = 0.35 (s, 9H), 1.49 (d, J = 6.0 Hz, 3H), 5.11 (q, J = 6.0 Hz, 1H), 7.23–7.64 (m, 4H). $^{13}\text{C-NMR}$ (50 MHz, CDCl_3): δ = 0.85, 25.38, 69.84, 125.32, 127.21, 130.07, 134.42, 137.06, 151.65. FT-IR (KBr) ν_{max} = 3284, 3058, 2956, 1930, 1630, 1432, 1247, 1099, 1072, 1000, 848, 731 cm^{-1} . LRMS (EI) m/z (%) = 179(15), 161(100), 145(62), 133(21), 119(8), 104(12), 91(10), 75(33), 59(9), 43(49). HRMS (ESI): Calculated for $\text{C}_{11}\text{H}_{18}\text{OSiNa}$ $[\text{M} + \text{Na}]^+ = 217.1025$; found: 217.1018.

1-(3-(Trimethylsilyl)phenyl)ethanol (2b). Yield: 702 mg (72%). Colourless oil. $^1\text{H-NMR}$ (200 MHz, CDCl_3) δ = 0.27 (s, 9H), 1.50 (d, J = 6.0 Hz, 3H), 4.86 (q, J = 6.0 Hz, 1H), 7.30–7.52 (m, 4H). $^{13}\text{C-NMR}$ (50 MHz, CDCl_3): δ = -0.93 , 25.32, 70.84, 126.08, 128.09, 130.46, 132.75, 141.02, 145.05. FT-IR (KBr) ν_{max} = 3343, 3048, 2956, 1594, 1450, 1248, 1098, 858, 837, 753 cm^{-1} . LRMS (EI) m/z (%) = 194(7) $[\text{M}]^+$, 179(100), 161(33), 145(8), 135(15), 119(10), 104(11), 91(8), 75(54), 59(9), 43(60). HRMS (ESI): Calculated for $\text{C}_{11}\text{H}_{18}\text{OSiNa}$ $[\text{M} + \text{Na}]^+ = 217.1025$; found: 217.1015.

1-(4-(Trimethylsilyl)phenyl)ethanol (2c). Yield: 743 mg (76%). White waxy solid. $^1\text{H-NMR}$ (200 MHz, CDCl_3) δ = 0.30 (s, 9H), 1.51 (d, J = 6.0 Hz, 3H), 4.86 (q, J = 6.0 Hz, 1H), 7.37 (d, J = 8.0 Hz, 2H), 7.53 (d, J = 8.0 Hz, 2H). $^{13}\text{C-NMR}$ (50 MHz, CDCl_3): δ = -0.94 , 25.20, 70.57, 124.96, 133.75, 139.83, 146.53. FT-IR (KBr) ν_{max} = 3323, 3068, 2955, 1918, 1601, 1410, 1247, 1082, 1071, 1003, 857, 822 cm^{-1} . LRMS (EI) m/z (%) = 194(8) $[\text{M}]^+$, 179(100), 163(6), 151(4), 135(8), 119(7), 105(12), 91(7), 73(23), 59(3), 43(38). HRMS (ESI): Calculated for $\text{C}_{11}\text{H}_{18}\text{OSiNa}$ $[\text{M} + \text{Na}]^+ = 217.1025$; found: 217.1019.

1-(2-(Trimethylsilyl)phenyl)propanol (2d). Yield: 673 mg (65%). Colourless oil. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ = 0.34 (s, 9H), 1.01 (t, J = 6.0 Hz, 3H), 1.69–1.88 (m, 2H), 4.83 (m, 1H), 7.23–7.55 (m, 4H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ = 0.96, 11.01, 32.11, 75.22, 125.57, 127.17, 129.94, 134.53, 137.63, 150.67. FT-IR (KBr) ν_{max} = 3387, 3056, 2959, 1590, 1459, 1250, 1105, 968, 838, 730 cm^{-1} . LRMS (EI) m/z (%) = 193(16), 175(87), 163(100), 145(18), 135(12), 117(15), 105(14), 91(12), 75(53), 59(94), 45(39). HRMS (ESI): Calculated for $\text{C}_{12}\text{H}_{20}\text{OSiNa}$ $[\text{M} + \text{Na}]^+ = 231.1181$; found: 231.1175.

1-(3-(Trimethylsilyl)phenyl)propanol (2e). Yield: 725 mg (70%). Colourless oil. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ = 0.27 (s, 9H), 0.92 (t, J = 6.0 Hz, 3H), 1.68–1.86 (m, 2H), 4.55 (t, J = 6.0 Hz, 1H), 7.30–7.47 (m, 4H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ = -0.94 , 10.40, 32.06, 76.38, 126.60, 127.94, 131.03, 132.67, 140.75, 143.92. FT-IR (KBr) ν_{max} = 3351, 3052, 2958, 1586, 1441, 1248, 1121, 860, 837, 753 cm^{-1} . LRMS (EI) m/z (%) = 208(4) $[\text{M}]^+$, 193(32), 179(100), 163(10), 145(4), 135(10), 119(7), 105(10), 91(9), 73(94), 59(26), 43(31). HRMS (ESI): Calculated for $\text{C}_{12}\text{H}_{20}\text{OSiNa}$ $[\text{M} + \text{Na}]^+ = 231.1181$; found: 231.1171.

1-(4-(Trimethylsilyl)phenyl)propanol (2f). Yield: 706 mg (68%). White solid. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ = 0.26 (s, 9H), 0.30 (t, J = 6.0 Hz, 3H), 1.70–1.85 (m, 2H), 4.57 (t, J = 6.0 Hz, 1H), 7.31 (d, J = 9.0 Hz, 2H), 7.49 (d, J = 9.0 Hz, 2H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ = −0.92, 10.38, 31.97, 76.19, 125.53, 133.64, 139.81, 145.36. FT-IR (KBr) ν_{max} = 3323, 3068, 2957, 1598, 1453, 1401, 1248, 1111, 1094, 853, 837 cm^{-1} . LRMS (EI) m/z (%) = 208(3) $[\text{M}]^+$, 193(51), 179(100), 163(14), 151(7), 135(14), 119(8), 105(11), 91(13), 73(76), 59(8), 43(28). HRMS (ESI): Calculated for $\text{C}_{12}\text{H}_{20}\text{OSiNa}$ $[\text{M} + \text{Na}]^+ = 231.1181$; found: 231.1176.

3.2.4. General Procedure for the Preparation of Aryltrimethylsilyl Chiral Acetates **3a–f** [51]

To a 25 mL round-bottom flask containing a solution of the appropriate aryltrimethylsilyl chiral alcohol (0.5 mmol) in CH_2Cl_2 (5 mL), was added acetic anhydride (0.6 mmol, 0.06 g, 56.3 μL), pyridine (2 mmol, 0.16 g, 161.5 μL) and DMAP (0.1 mmol, 12.2 mg), sequentially. The mixture was stirred overnight at r.t. Then the solvent was evaporated under reduced pressure and ethyl acetate (15 mL) was added to the organic residue. The organic layer was washed with aq. 1 M CuSO_4 (2×10 mL), brine (2×10 mL), dried over anhydrous MgSO_4 and concentrated *in vacuo*. The residue was purified by column chromatography using *n*-hexane/ethyl acetate (9:1) as eluent.

1-(2-(Trimethylsilyl)phenyl)ethyl acetate (3a). Yield: 112 mg (95%). Colourless oil. $^1\text{H-NMR}$ (200 MHz, CDCl_3) δ = 0.36 (s, 9H), 1.50 (d, J = 6.0 Hz, 3H), 2.06 (s, 3H), 6.06 (q, J = 6.0 Hz, 1H), 7.24–7.55 (m, 4H). $^{13}\text{C-NMR}$ (50 MHz, CDCl_3): δ = 0.63, 21.61, 23.62, 72.43, 125.97, 127.38, 129.77, 134.48, 137.29, 147.73, 170.37. FT-IR (KBr) ν_{max} = 3024, 2960, 1740, 1599, 1436, 1237, 1019, 1037, 838 cm^{-1} . LRMS (EI) m/z (%) = 221(5), 193(3), 177(3), 161(30), 145(25), 133(8), 117(67), 103(6), 91(3), 75(19), 59(7), 43(100). HRMS (ESI): Calculated for $\text{C}_{13}\text{H}_{20}\text{O}_2\text{SiNa}$ $[\text{M} + \text{Na}]^+ = 259.1130$; found: 259.1128.

1-(3-(Trimethylsilyl)phenyl)ethyl acetate (3b). Yield: 115 mg (98%). Colourless oil. $^1\text{H-NMR}$ (200 MHz, CDCl_3) δ = 0.27 (s, 9H), 1.53 (d, J = 6.0 Hz, 3H), 2.07 (s, 3H), 5.85 (q, J = 6.0 Hz, 1H), 7.33–7.48 (m, 4H). $^{13}\text{C-NMR}$ (50 MHz, CDCl_3): δ = −0.95, 21.56, 22.44, 72.70, 126.72, 128.04, 131.15, 133.11, 140.90, 140.99, 170.50. FT-IR (KBr) ν_{max} = 3050, 2956, 1739, 1587, 1448, 1247, 1065, 1024, 839 cm^{-1} . LRMS (EI) m/z (%) = 236(4) $[\text{M}]^+$, 221(1), 193(11), 177(4), 161(28), 135(4), 117(30), 103(5), 91(2), 75(33), 59(4), 43(100). HRMS (ESI): Calculated for $\text{C}_{13}\text{H}_{20}\text{O}_2\text{SiNa}$ $[\text{M} + \text{Na}]^+ = 259.1130$; found: 259.1125.

1-(4-(Trimethylsilyl)phenyl)ethyl acetate (3c). Yield: 114 mg (97%). Colourless oil. $^1\text{H-NMR}$ (200 MHz, CDCl_3) δ = 0.30 (s, 9H), 1.52 (d, J = 6.0 Hz, 3H), 2.07 (s, 3H), 5.86 (q, J = 6.0 Hz, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.49 (d, J = 8.0 Hz, 2H). $^{13}\text{C-NMR}$ (50 MHz, CDCl_3): δ = −0.98, 21.51, 22.29, 72.48, 125.60, 133.71, 140.31, 142.30, 170.50. FT-IR (KBr) ν_{max} = 3020, 2955, 1738, 1602, 1447, 1241, 1063, 1022, 850 cm^{-1} . LRMS (EI) m/z (%) = 236(2) $[\text{M}]^+$, 221(7), 194(8), 177(4), 161(14), 151(14), 133(4), 119(11), 103(7), 91(4), 75(19), 59(5), 43(100). HRMS (ESI): Calculated for $\text{C}_{13}\text{H}_{20}\text{O}_2\text{SiNa}$ $[\text{M} + \text{Na}]^+ = 259.1130$; found: 259.1131.

1-(2-(Trimethylsilyl)phenyl)propyl acetate (3d). Yield: 121 mg (97%). Colourless oil. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ = 0.38 (s, 9H), 0.96 (t, J = 6.0 Hz, 3H), 1.71–1.91 (m, 2H), 2.07 (s, 3H), 5.93 (t, J = 6 Hz, 1H), 7.23–7.51 (m, 4H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ = 0.78, 10.59, 21.44, 31.16, 77.09, 125.88,

127.23, 129.53, 134.63, 137.61, 147.11, 170.54. FT-IR (KBr) $\nu_{\max}$ = 3058, 2967, 1738, 1591, 1434, 1372, 1235, 1085, 1046, 840 cm^{-1} . LRMS (EI) m/z (%) = 235(1), 207(1), 175(4), 163(11), 145(6), 135(4), 117(55), 105(4), 91(3), 75(15), 59(25), 43(100). HRMS (ESI): Calculated for $\text{C}_{14}\text{H}_{22}\text{O}_2\text{SiNa}$ $[\text{M} + \text{Na}]^+ = 273.1287$; found: 273.1283.

1-(3-(Trimethylsilyl)phenyl)propyl acetate (3e). Yield: 118 mg (95%). Colourless oil. ^1H -NMR (300 MHz, CDCl_3) δ = 0.27 (s, 9H), 0.89 (t, J = 6.0 Hz, 3H), 1.76–1.97 (m, 2H), 2.08 (s, 3H), 5.68 (t, J = 6 Hz, 1H), 7.31–7.46 (m, 4H). ^{13}C -NMR (75 MHz, CDCl_3): δ = −0.94, 10.19, 21.46, 29.62, 77.72, 127.13, 127.93, 131.64, 133.04, 139.88, 140.83, 170.61. FT-IR (KBr) $\nu_{\max}$ = 3050, 2957, 1740, 1459, 1372, 1237, 1085, 1020, 839 cm^{-1} . LRMS (EI) m/z (%) = 250(4) $[\text{M}]^+$, 235(1), 221(3), 207(9), 175(20), 163(8), 135(4), 117(34), 105(4), 91(4), 75(32), 59(8), 43(100). HRMS (ESI): Calculated for $\text{C}_{14}\text{H}_{22}\text{O}_2\text{SiNa}$ $[\text{M} + \text{Na}]^+ = 273.1287$; found: 273.1288.

1-(4-(Trimethylsilyl)phenyl)propyl acetate (3f). Yield: 119 mg (96%). Colourless oil. ^1H -NMR (200 MHz, CDCl_3) δ = 0.25 (s, 9H), 0.89 (t, J = 6.0 Hz, 3H), 1.73–2.00 (m, 2H), 2.07 (s, 3H), 5.65 (t, J = 6 Hz, 1H), 7.28 (d, J = 8.0 Hz, 2H), 7.47 (d, J = 8.0 Hz, 2H). ^{13}C -NMR (50 MHz, CDCl_3): δ = −0.97, 10.14, 21.42, 29.43, 77.54, 126.05, 133.58, 140.17, 141.20, 170.61. FT-IR (KBr) $\nu_{\max}$ = 3024, 2960, 1740, 1599, 1436, 1237, 1085, 1019, 838 cm^{-1} . LRMS (EI) m/z (%) = 250(5) $[\text{M}]^+$, 235(4), 221(8), 208(15), 179(23), 165(9), 135(4), 117(33), 105(6), 91(4), 75(27), 59(7), 43(100). HRMS (ESI): Calculated for $\text{C}_{14}\text{H}_{22}\text{O}_2\text{SiNa}$ $[\text{M} + \text{Na}]^+ = 273.1287$; found: 273.1282.

3.3. Determination of the Enantiomeric Excess (ee)

The enantiomeric excesses of the aryltrimethylsilyl chiral alcohols **2a–f** and esters **3a–f** were measured by chiral GC analysis. The analysis was carried out on Varian CP-Chirasil-DEX CB β -cyclodextrin (25 m $\times$ 0.32 mm $\times$ 0.25 μm). Temperature of the detector and injector was 250 $^\circ\text{C}$; oven temperature: from 100 $^\circ\text{C}$ to 150 $^\circ\text{C}$, 1 $^\circ\text{C}/\text{min}$; flow = 80 kPa, H_2 as gas carrier.

Retention times (t_R):

- (**2a**): t_R = 19.8 min for (*S*) and t_R = 20.9 min for (*R*);
- (**2b**): t_R = 19.6 min for (*S*) and t_R = 20.1 min for (*R*);
- (**2c**): t_R = 26.5 min for (*S*) and t_R = 25.6 min for (*R*);
- (**2d**): t_R = 21.6 min for (*S*) and t_R = 22.6 min for (*R*);
- (**2e**): t_R = 25.0 min for (*S*) and t_R = 24.4 min for (*R*);
- (**2f**): t_R = 31.2 min for (*S*) and t_R = 30.3 min for (*R*);
- (**3a**): t_R = 16.0 min for (*S*) and t_R = 16.2 min for (*R*);
- (**3b**): t_R = 16.2 min for (*S*) and t_R = 16.8 min for (*R*);
- (**3c**): t_R = 23.7 min for (*S*) and t_R = 25.9 min for (*R*);
- (**3d**): t_R = 63.4 min for (*S*) and t_R = 63.6 min for (*R*) (oven: 50 $^\circ\text{C}$ to 150 $^\circ\text{C}$, 1 $^\circ\text{C}/\text{min}$);
- (**3e**): t_R = 22.0 min for (*S*) and t_R = 20.4 min for (*R*);
- (**3f**): t_R = 26.3 min for (*S*) and t_R = 27.1 min for (*R*);

3.4. Enzymatic Procedures

3.4.1. General Procedure for Small Scale Enzymatic Reactions

A 1.5 mL Eppendorf tube (2 mL) was charged with the appropriate aryltrimethylsilyl chiral alcohol **2a–f** (0.05 mmol), hexanes (HPLC grade, 200 μ L), CAL-B (enzyme amount as indicated in Tables 1–3) and vinyl acetate (2.2 equiv., 0.11 mmol, 10 μ L). The reaction mixture was sealed and stirred on a thermomixer (30 °C, 700 rpm) until the appropriate time. After that, the mixture was filtered and the solvent evaporated under reduced pressure.

3.4.2. General Procedure for Preparative-Scale Enzymatic Reactions

A 10 mL glass tube was charged with the appropriate aryltrimethylsilyl chiral alcohol **2a–f** (1 mmol), hexanes (HPLC grade, 4 mL), CAL-B (enzyme amount as indicated on Table 4) and vinyl acetate (2.2 mmol, 203 μ L). The reaction mixture was sealed and stirred on a thermomixer (30 °C, 700 rpm) until the appropriate time. After that, the mixture was filtered and the solvent evaporated under reduced pressure. The purification of alcohol **2** and acetate **3** was performed by column chromatography using *n*-hexane/ethyl acetate (9:1) as eluent.

(*S*)-**2b**: isolated yield = 44%; enantiomeric excess > 99%; $[\alpha]_D^{20} = -37.0$ ($c = 1.0$; CHCl₃).

(*R*)-**3b**: isolated yield = 49%; enantiomeric excess > 99%; $[\alpha]_D^{20} = +70.8$ ($c = 1.0$; CHCl₃).

(*S*)-**2c**: isolated yield = 31%; enantiomeric excess > 99%; $[\alpha]_D^{20} = -31.2$ ($c = 1.0$; CHCl₃).

(*R*)-**3c**: isolated yield = 46%; enantiomeric excess > 99%; $[\alpha]_D^{20} = +93.9$ ($c = 1.0$; CHCl₃).

(*S*)-**2e**: isolated yield = 38%; enantiomeric excess > 99%; $[\alpha]_D^{20} = -32.9$ ($c = 1.0$; CHCl₃).

(*R*)-**3e**: isolated yield = 49%; enantiomeric excess > 99%; $[\alpha]_D^{20} = +76.8$ ($c = 1.0$; CHCl₃).

(*S*)-**2f**: isolated yield = 39%; enantiomeric excess > 99%; $[\alpha]_D^{20} = -34.1$ ($c = 1.0$; CHCl₃).

(*R*)-**3f**: isolated yield = 34%; enantiomeric excess > 99%; $[\alpha]_D^{20} = +91.3$ ($c = 1.0$; CHCl₃).

3.5. Determination of the Absolute Configuration

3.5.1. General Procedure for Transformation of Enantioenriched Aryltrimethylsilyl Chiral Alcohols **2b**, **2c**, **2e** and **2f** to Their Bromide Derivatives [52]

To a solution of the appropriate enantioenriched aryltrimethylsilyl chiral alcohol (0.05 mmol) dissolved in MeOH (1.0 mL) was added KBr (0.05 mmol, 6 mg) and NCS (0.05 mmol, 7 mg). The mixture was stirred for 20 min at 60 °C. The reaction was quenched with H₂O (2 mL) and extracted with CH₂Cl₂ (2 $\times$ 5 mL). The organic layer was washed with brine (2 $\times$ 2 mL), dried over anhydrous MgSO₄ and concentrated *in vacuo*. The residue was purified by column chromatography using *n*-hexane/ethyl acetate (9:1) as eluent.

3.5.2. Determination of Absolute Configuration of Enantioenriched Aryltrimethylsilyl Chiral Alcohols **2b**, **2c**, **2e** and **2f**

The enantioenriched alcohols **1b**, **1c**, **1e** and **1f** obtained from the bromodesilylation reactions (section 3.4.1) were submitted to chiral GC and HPLC analysis, and the values found for retention

times were in agreement with enantiopure samples and those described in the literature for enantioenriched compounds [42–45]. The absolute configuration of compounds **2b**, **2c**, **2e** and **2f** were attributed by analogy of those found to its bromide derivatives.

4. Conclusions

An extensive study of lipase-catalyzed kinetic resolution of aryltrimethylsilyl chiral alcohols through an enantioselective transesterification was described. The best lipase source found for kinetic resolution of these silicon-containing compounds was *Pseudomonas cepacia* (Amano PS-C II). Different enzyme/substrate ratios were evaluated and a very small amount of lipase proved to be satisfactory for the kinetic resolution in most cases. The kinetic resolution of *o*-substituted phenyl chiral alcohols did not occur under the conditions evaluated. The reason for this surprisingly results is still opened for further studies, but a possible explanation is that a pseudo-pentacoordinated species generated by a non-bonded Si $\cdots$ O attraction, should create a steric hindrance that made the kinetic resolution more difficult to occur. On the other hand, perfect kinetic resolutions were achieved for the *m*- and *p*-substituted phenyl chiral alcohols, in which (*S*)-alcohols and (*R*)-acetates were obtained in high yields (up to 49%) and excellent enantiomeric excesses (>99%).

Acknowledgments

The authors want to thank FAPESP (State of São Paulo Research Foundation), CNPq (National Counsel of Technological and Scientific Development) and CAPES (Coordination for the Improvement of Higher Level -or Education-Personnel) for their fellowship and financial support.

References and Notes

1. Colvin, E.W. *Silicon Reagents in Organic Synthesis*, 1st ed.; Academic Press: San Diego, CA, USA, 1988; pp. 7–137.
2. Patai, S.; Rappoport, Z. *The Chemistry of Organic Silicon Compounds*, 1st ed.; Wiley: New York, NY, USA, 1998; Volume 2, pp. 1667–1793.
3. Gilman, H.; Dunn, G.E. Relationships between analogous organic compounds of silicon and carbon. *Chem. Rev.* **1953**, *52*, 77–115.
4. Burkhard, C.A.; Rochow, E.G.; Booth, H.S.; Hartt, J. The present state of organosilicon chemistry. *Chem. Rev.* **1947**, *41*, 97–149.
5. Yoshida, H.; Sugiura, S.; Kunai, A. Facile synthesis of *N*-alkyl-*N'*-arylimidazolium salts via addition of imidazoles to arynes. *Org. Lett.* **2002**, *4*, 2767–2769.
6. Dockendorff, C.; Sahli, S.; Olsen, M.; Milhau, L.; Lautens, M. Synthesis of dihydronaphthalenes via aryne Diels-Alder reactions: Scope and diastereoselectivity. *J. Am. Chem. Soc.* **2005**, *127*, 15028–15029.
7. Liu, Z.; Larock, R.C. Highly efficient route to fused polycyclic aromatics via palladium-catalyzed aryne annulation by aryl halides. *J. Org. Chem.* **2007**, *72*, 223–232.
8. Xie, C.; Liu, L.; Zhang, Y.; Xu, P. Copper-catalyzed Alkyne-aryne and alkyne-alkene-aryne coupling reactions. *Org. Lett.* **2008**, *10*, 2393–2396.

9. Gebara, K.S.; Casagrande, G.A.; Raminelli, C. An efficient fluoride-mediated *O*-arylation of sterically hindered halophenols with silylaryl triflates under mild reaction conditions. *Tetrahedron Lett.* **2011**, *52*, 2849-2852.
10. McAusland, D.; Seo, S.; Pintori, D.G.; Finlayson, J.; Greaney, M.F. The benzyne Fischer-indole reaction. *Org. Lett.* **2011**, *13*, 3667-3669.
11. Brenzovich, W.E.; Brazeau, J.-F.; Toste, F.D. Gold-catalyzed oxidative coupling reactions with aryltrimethylsilanes. *Org. Lett.* **2010**, *12*, 4728-4731.
12. Ball, L.T.; Green, M.; Lloyd-Jones, G.C.; Russell, C.A. Arylsilanes: Application to gold-catalyzed oxyarylation of alkenes. *Org. Lett.* **2010**, *12*, 4724-4727.
13. Suzawa, K.; Ueno, M.; Wheatley, A.E.H.; Kondo, Y. Phosphazene base-promoted functionalization of aryltrimethylsilanes. *Chem. Commun.* **2006**, 4850-4852.
14. Nakao, Y.; Imanaka, H.; Sahoo, A.K.; Yada, A.; Hiyama, T. Alkenyl- and aryl[2-(hydroxymethyl)phenyl]dimethylsilanes: An entry to tetraorganosilicon reagents for the silicon-based cross-coupling reaction. *J. Am. Chem. Soc.* **2005**, *127*, 6952-6953.
15. Nakao, Y.; Imanaka, H.; Chen, J.; Yada, A.; Hiyama, T. Synthesis and cross-coupling reaction of alkenyl[(2-hydroxymethyl)phenyl]dimethylsilanes. *J. Organomet. Chem.* **2007**, *692*, 585-603.
16. Chen, J.; Tanaka, M.; Sahoo, A.K.; Takeda, M.; Yada, A.; Nakao, Y.; Hiyama, T. Synthesis of biaryls and oligoarenes using aryl[2-(hydroxymethyl)phenyl]dimethylsilanes. *Bull. Chem. Soc. Jpn.* **2010**, *83*, 554-569.
17. Nakao, Y.; Takeda, M.; Matsumoto, T.; Hiyama, T. Cross-coupling reactions through the intramolecular activation of alkyl(triorgano)silanes. *Angew. Chem. Int. Ed.* **2010**, *49*, 4447-4450.
18. Denmark, S.E. The interplay of invention, discovery, development, and application in organic synthetic methodology: A case study. *J. Org. Chem.* **2009**, *74*, 2915-2927.
19. Rauf, W.; Brown, J.M. Catalytic amide-mediated methyl transfer from silanes to alkenes in fujiwara-moritani oxidative coupling. *Angew. Chem. Int. Ed.* **2008**, *47*, 4228-4230.
20. Tacke, R.; Brakmann, S.; Wuttke, F. Stereoselective microbial reduction of racemic acetyl(*t*-butyl)methylphenylsilane by *Trigonopsis variabilis* (DSM 70714) and *Corynebacterium dioxydans* (ATCC 21766). *J. Organomet. Chem.* **1991**, *403*, 29-41.
21. Yamanaka, H.; Kawamoto, T.; Tanaka, A. Efficient preparation of optically active *p*-trimethylsilylphenylalanine by using cell-free extract of *Blastobacter* sp. A17p-4. *J. Ferment. Bioeng.* **1997**, *84*, 181-184.
22. Zani, P. Biotransformations of organosilicon compounds: enantioselective reduction of acyl silanes by means of baker's yeast. *J. Mol. Catal. B: Enzym.* **2001**, *11*, 279-285.
23. Li, N.; Zong, M.-H.; Peng, H.-S.; Wu, H.-C.; Liu, C. (*R*)-Oxynitrilase-catalyzed synthesis of (*R*)-2-trimethylsilyl-2-hydroxyl-ethylcyanide. *J. Mol. Catal. B: Enzym.* **2003**, *22*, 7-12.
24. Maraite, A.; Ansorge-Schumacher, M. B.; Ganchegui, B.; Leitner, W.; Grogan, G. On the biocatalytic cleavage of silicon-oxygen bonds: A substrate structural approach to investigating the cleavage of protecting group silyl ethers by serine-triad hydrolases. *J. Mol. Catal. B: Enzym.* **2009**, *56*, 24-28.
25. Frampton, M.B.; Simionescu, R.; Dudding, T.; Zelisko, P.M. The enzymatic cleavage of Si-O bonds: A kinetic analysis of the biocatalyzed hydrolysis of phenyltrimethoxysilane. *J. Mol. Catal. B: Enzym.* **2010**, *66*, 105-112.

26. Bassindale, A.R.; Brandstadt, K.F.; Lane, T.H.; Taylor, P.G. Enzyme-catalysed siloxane bond formation. *J. Inorg. Biochem.* **2003**, *96*, 401–406.
27. Abbate, V.; Bassindale, A.R.; Brandstadt, K.F.; Lawson, R.; Taylor, P.G. Enzyme mediated silicon–oxygen bond formation; the use of *Rhizopus oryzae* lipase, lysozyme and phytase under mild conditions. *Dalton Trans.* **2010**, *39*, 9361–9368.
28. Abbate, V.; Bassindale, A.R.; Brandstadt, K.F.; Taylor, P.G. A large scale enzyme screen in the search for new methods of silicon-oxygen bond formation. *J. Inorg. Biochem.* **2011**, *105*, 268–275.
29. Djerourou, A.-H.; Blanco, L. Synthesis of optically active 2-sila-1,3-propanediols derivatives by enzymatic transesterification. *Tetrahedron Lett.* **1991**, *32*, 6325–6326.
30. Fukui, T.; Kawamoto, T.; Tanaka, A. Enzymatic preparation of optically active silylmethanol derivatives having a stereogenic silicon atom by hydrolase-catalyzed enantioselective esterification. *Tetrahedron: Asymmetry* **1994**, *5*, 73–82.
31. Burgess, K.; Jennings, L.D. Enantioselective esterifications of unsaturated alcohols mediated by a lipase prepared from *Pseudomonas* sp. *J. Am. Chem. Soc.* **1991**, *113*, 6129–6139.
32. Allevi, P.; Ciuffreda, P.; Anastasia, M. Lipase catalysed resolution of (*R*)- and (*S*)-1-trimethylsilyl-1-alkyn-3-ols—Useful intermediates for the synthesis of optically active γ -lactones. *Tetrahedron: Asymmetry* **1997**, *8*, 93–99.
33. Ratnayake, A.S.; Hemscheidt, T. Olefin cross-metathesis as a tool in natural product degradation. The stereochemistry of (+)-Falcarindiol. *Org. Lett.* **2002**, *4*, 4667–4669.
34. Brawn, R.A.; Panek, J.S. Preparation and use of enantioenriched allenylsilanes for the stereoselective synthesis of homopropargylic ethers. *Org. Lett.* **2007**, *9*, 2689–2692.
35. Andrade, L.H.; Omori, A.T.; Porto, A.L.M.; Comasseto, J.V. Asymmetric synthesis of arylselenoalcohols by means of the reduction of organoseleno acetophenones by whole fungal cells. *J. Mol. Catal. B: Enzym.* **2004**, *29*, 47–54.
36. Bianchi, D.; Battistel, E.; Bosetti, A.; Cesti, P.; Fekete, Z. Effects of chemical modification on stereoselectivity of *Pseudomonas cepacia* lipase. *Tetrahedron: Asymmetry* **1993**, *4*, 777–782.
37. Ignatyev, I.S. Intramolecular coordination of silicon in silyl formates: Spectroscopic evidence confirmed by ab initio calculations. *J. Mol. Struct.* **1991**, *245*, 139–145.
38. Tamao, K.; Asahara, M.; Sun, G.-R.; Kawachi, A. Synthesis, structure, and reactivity of 1, ω -bis(pseudo-pentacoordinated) 1, ω -difluoro-oligosilanes bearing 8-(dimethylamino)-1-naphthyl groups. *J. Organomet. Chem.* **1999**, *574*, 193–205.
39. Tamao, K.; Asahara, M.; Saeki, T.; Toshimitsu, A. Enhanced nucleophilicity of ambiphilic silylene and silylenoid bearing 8-(dimethylamino)-1-naphthyl group. *J. Organomet. Chem.* **2000**, *600*, 118–123.
40. Pongor, G.; Kolos, Z.; Szalay, R.; Knausz, D. Pseudo-pentacoordination in silylcarbamates: structure-based prediction of silylating power. *J. Mol. Struct. (THEOCHEM)* **2005**, *714*, 87–97.
41. Szalay, R.; Pongor, G.; Harmat, V.; Böcskei, Z.; Knausz, D. Surprisingly great difference in reactivity depending upon the ring size: Solvolysis and molecular structure study of some *N*-trimethylsilylated cyclic ureas. *J. Organomet. Chem.* **2005**, *690*, 1498–1506.
42. Solís, A.; García, S.; Pérez, H.I.; Manjarrez, N.; Luna, H. Screening of liver acetone powders in the resolution of 1-phenylethanols and 1-phenylpropanols derivatives. *Tetrahedron: Asymmetry* **2008**, *19*, 549–553.

43. Salvia, N.A.; Chattopadhyay, S. Asymmetric reduction of halo-substituted arylalkanones with *Rhizopus arrhizus*. *Tetrahedron: Asymmetry* **2008**, *19*, 1992-1997.
44. Machado, L.L.; Lemos, T.L.G.; de Mattos, M.C.; de Oliveira, M.C.F.; de Gonzalo, G.; Gotor-Fernández, V.; Gotor, V. Immobilized *Manihot esculenta* preparation as a novel biocatalyst in the enantioselective acetylation of racemic alcohols. *Tetrahedron: Asymmetry* **2008**, *19*, 1419-1424.
45. Araújo, L.S.; Kagohara, E.; Garcia, T.P.; Pellizari, V.H.; Leandro, H.; Andrade, L.H. Screening of microorganisms producing cold-active oxidoreductases to be applied in enantioselective alcohol oxidation. An antarctic survey. *Mar. Drugs* **2011**, *9*, 889-905.
46. Kazlauskas, R.J.; Weissfloch, A.N.E.; Rappaport, A.T.; Cuccia, L.A. A rule to predict which enantiomer of a secondary alcohol reacts faster in reactions catalyzed by cholesterol esterase, lipase from *Pseudomonas cepacia*, and lipase from *Candida rugosa*. *J. Org. Chem.* **1991**, *56*, 2656-2665.
47. Andrade, L.H.; Polak, R.; Porto, A.L.M.; Schoenlein-Crusius, I.H.; Comasseto, J.V. Application of bioreduction by microorganisms in the enantioselective synthesis of alpha-substituted-1-phenylethanols. *Lett. Org. Chem.* **2006**, *3*, 613-618.
48. Nakamura, K.; Matsuda, T. Asymmetric reduction of ketones by the acetone powder of *Geotrichum candidum*. *J. Org. Chem.* **1998**, *63*, 8957-8964.
49. Zaidlewicz, M.; Wolan, A. Syntheses with organoboranes. XIII. Synthesis of ω -(4-bromophenyl)alkanoic acids and their borylation. *J. Organomet. Chem.* **2002**, *657*, 129-135.
50. Achmatowicz, B.; Raubo, P.; Wicha, J. Synthesis of four stereoisomeric tetrose derivatives from propargyl alcohol. One-carbon homologation of vinylsilanes via alpha, beta-epoxy silanes. *J. Org. Chem.* **1992**, *57*, 6593-6598.
51. Demasi, M.; Felicio, A.L.; Pacheco, A.O.; Leite, H.G.; Lima, C.; Andrade, L.H. Studies on terrein as a new class of proteasome inhibitors. *J. Braz. Chem. Soc.* **2010**, *21*, 299-305.
52. Wilbur, D.S.; Stone, W.E.; Anderson, K.W. Regiospecific incorporation of bromine and iodine into phenols using (trimethylsilyl)phenol derivatives. *J. Org. Chem.* **1983**, *48*, 1542-1544.

Sample Availability: Not available.

© 2011 by the authors; licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution license (<http://creativecommons.org/licenses/by/3.0/>).