

Article

Enzymatic Kinetic Resolution of *tert*-Butyl 2-(1-Hydroxyethyl)phenylcarbamate, A Key Intermediate to Chiral Organoselenanes and Organotelluranes

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Abstract: The enzymatic kinetic resolution of *tert*-butyl 2-(1-hydroxyethyl) phenylcarbamate *via* lipase-catalyzed transesterification reaction was studied. We investigated several reaction conditions and the carbamate was resolved by *Candida antarctica* lipase B (CAL-B), leading to the optically pure (*R*)- and (*S*)-enantiomers. The enzymatic process showed excellent enantioselectivity ($E > 200$). (*R*)- and (*S*)-*tert*-butyl 2-(1-hydroxyethyl)phenylcarbamate were easily transformed into the corresponding (*R*)- and (*S*)-1-(2-aminophenyl)ethanols.

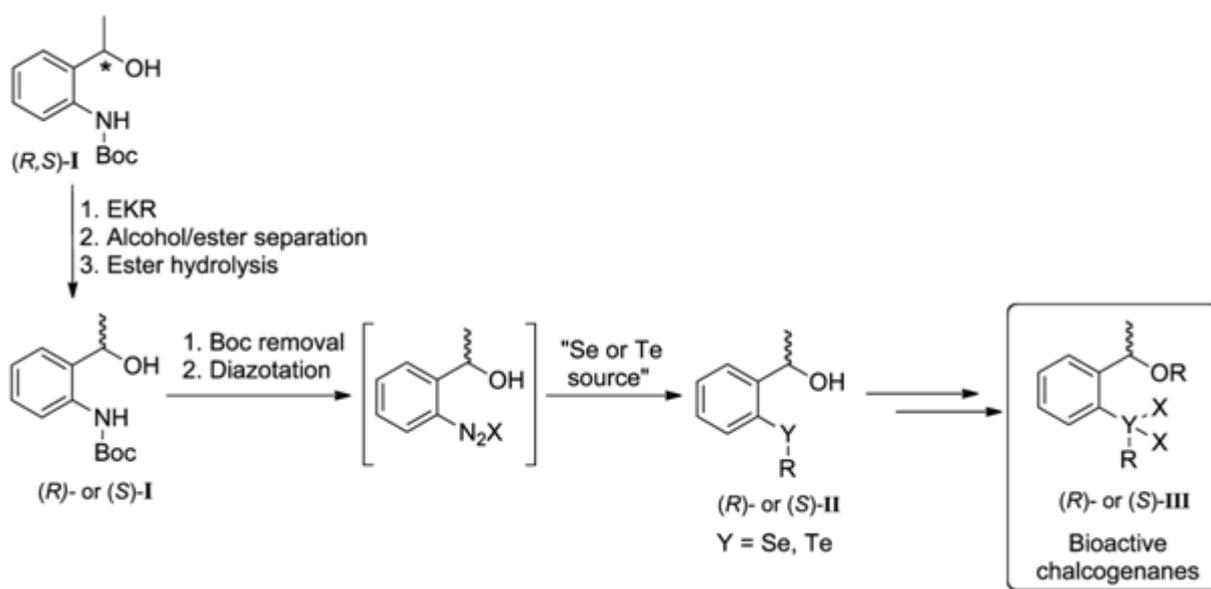
Keywords: alcohols; carbamates; lipases; kinetic resolution; enatiopure

1. Introduction

Selenium- and tellurium-containing compounds have drawn the attention of the scientific community due to their biological properties [1-4]. Notwithstanding the intense activity in the field of selenium and tellurium chemistry over the last three decades, organometallic reagents are commonly employed on the preparation of organo-selenium and -tellurium compounds. Moreover, hypervalent organoselenium(IV) compounds (organoselenanes) and organotellurium(IV) compounds (organotelluranes) have been investigated as cysteine protease [5-8], protein tyrosine phosphatase [9] and poliovirus 3C proteinase inhibitors [10]. Considering the biological activities of organoselenanes

and telluranes, we have described chemoenzymatic methodologies to synthesize selenium compounds without employing organolithium or organomagnesium reagents [11,12]. Herein, we report the preparation of enantiopure organochalcogenane precursors, (*R*)- and (*S*)-*tert*-butyl 2-(1-hydroxyethyl) phenylcarbamate, employing enzymatic kinetic resolution (EKR) catalyzed by lipases. The chiral building blocks [(*R*)-**I** and (*S*)-**I**] could be applied as advanced synthetic intermediates of organotelluranes and organoselenanes **III**, containing an asymmetric center (Scheme 1). It is possible to transform (*R*)-**I** and (*S*)-**I** into their respective arene diazonium salts, followed by a reaction with a nucleophilic selenium/tellurium specie to give selenides/tellurides **II**, direct precursors of selenanes and telluranes [12].

Scheme 1. Synthetic route to bioactive chalcogenanes [5-6,9,12].



2. Results and Discussion

As outlined in Scheme 2, chiral building blocks (*R*)-**3** and (*S*)-**3** could be synthesized from commercially available 1-(2-aminophenyl)ethanone (**1**). Initially, the amine protection leads to the *N*-Boc-protected arylketone **2**, which by reduction of the ketone group affords (*R,S*)-**3**. Then, the latter could be submitted to an enzymatic kinetic resolution (EKR) and, at the end of the process, both enantiomers could be easily separated.

2.1. Synthesis of the (*R,S*)-*tert*-butyl 2-(1-Hydroxyethyl)phenylcarbamate (**3**)

Several methods were evaluated to synthesize *tert*-butyl (2-acetylphenyl)carbamate (**2**) (Table 1). The protection of amine group was carried out by reacting 1-(2-aminophenyl)ethanone (**1**) with *tert*-butyl dicarbonate [(Boc)₂O]. For example, by using dichloromethane (CH₂Cl₂) as solvent and DMAP as additive, after 24 h at room temperature, compound **2** was obtained in 60% yield (Entry 1). It is worth mentioning that the intermediate **1a** was observed, then easily transformed to the compound **2** [13]. A second method, employing THF as solvent and under reflux was evaluated. However, a slight yield improvement (compound **2**, 67%) was observed with a shorter reaction time, 12 h (Entry 2). Other

reaction conditions were evaluated; however, the yields were lower than 40% (Entries 3–5). Next, we decided to apply the second method (Entry 2) to prepare the compound **2** in a preparative scale (5 mmol).

Scheme 2. Synthetic route to enantiopure *tert*-butyl 2-(1-hydroxyethyl)phenylcarbamates.

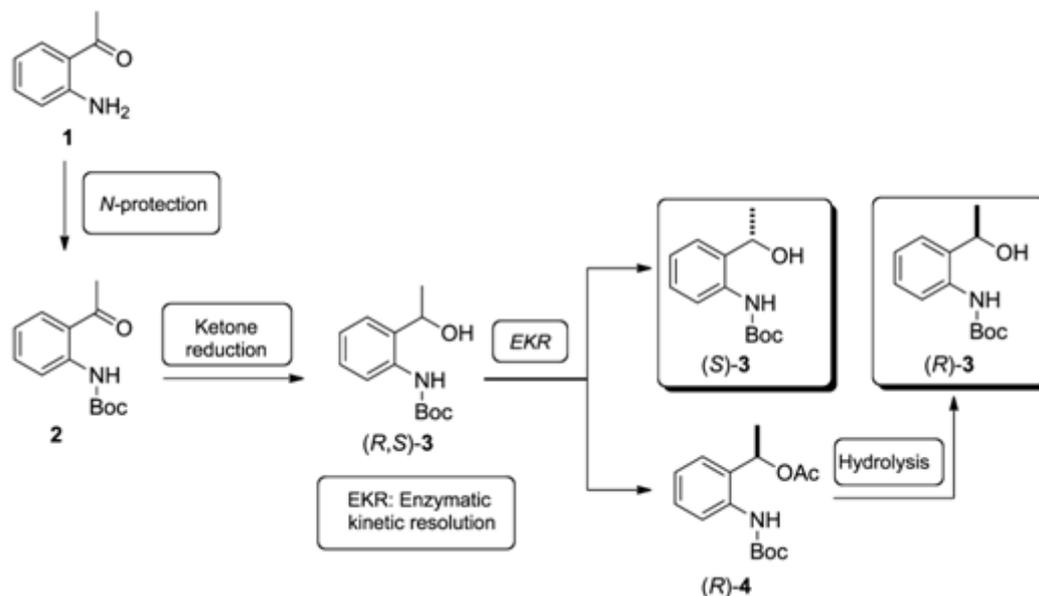
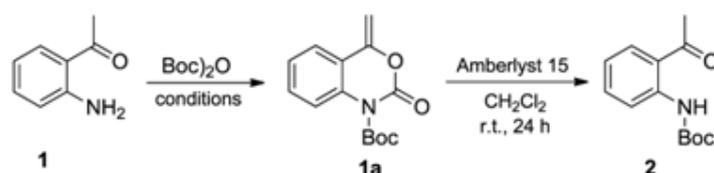


Table 1. Synthesis of *tert*-butyl (2-acetylphenyl)carbamate (**2**).



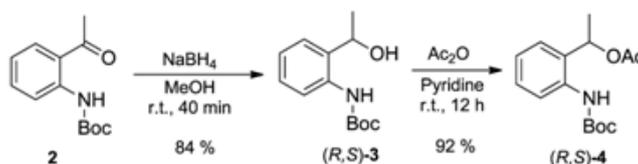
Entry	Additive (amount)	Solvent	t (°C)	Time (h)	Yield 2 (%)	Ref.
1	DMAP (1 equiv.)	CH ₂ Cl ₂	r.t.	24	60	[13]
2	DMAP (1 equiv.)	THF	reflux	12	67	[13,14]
3	I ₂ (2 equiv.)	--	r.t.	12	37 ^a	[15]
4	NaHCO ₃ (2 equiv.)	Dioxane	r.t.	12	traces ^a	[16]
5	NaOH (2 equiv.)	Dioxane	0–r.t.	12	traces ^a	[17]

Reaction conditions: Compound **1** (0.5 mmol), Boc₂O (1 mmol), solvent (5 mL), additive;

^a Determined by GC analysis; r.t. = room temperature.

The reduction of *tert*-butyl (2-acetylphenyl)carbamate (**2**) with NaBH₄ gave (*R,S*)-*tert*-butyl 2-(1-hydroxyethyl)phenylcarbamate (**3**) in 84% yield (Scheme 3). The acylated derivative (*R,S*)-**4** was efficiently synthesized from (*R,S*)-**3** and acetic anhydride (92% yield, Scheme 3).

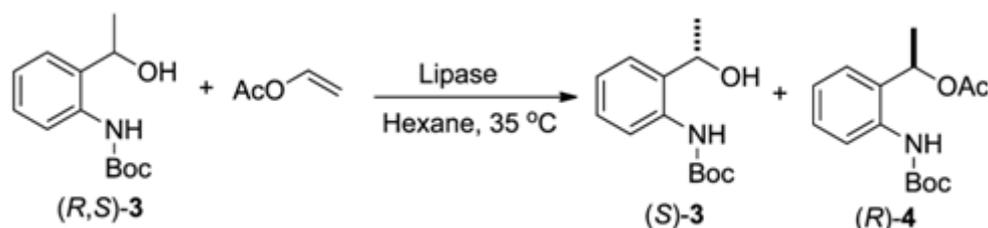
Scheme 3. Synthesis of racemic compounds **3** and **4**.



2.2. Enzymatic Kinetic Resolution of the (*R,S*)-*tert*-butyl 2-(1-Hydroxyethyl)phenylcarbamate (**3**)2.2.1. Screening of Lipases for Kinetic Resolution of (*R,S*)-**3**

A screening set with 12 different lipases was carried out, looking for an enzyme able to mediate the transesterification of (*R,S*)-**3** with high enantioselectivity and conversion in a short reaction time (Table 2).

Table 2. Screening of lipases for kinetic resolution of (*R,S*)-**3c**.



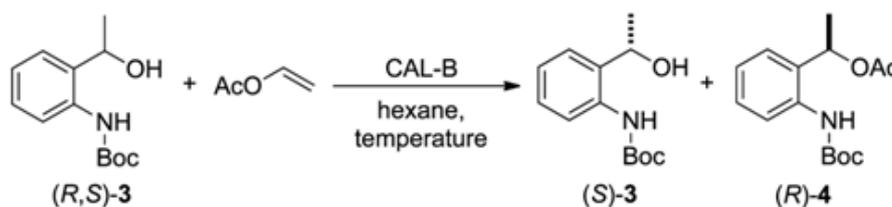
Entry	Lipase	Time (h)	c ^a (%)	ee ^b (%)		E ^c
				(<i>S</i>)- 3	(<i>R</i>)- 4	
1	<i>Candida antarctica</i>	12	47	88	>99	>200
2	(Novozym [®] 435; immobilized on	24	50	>99	>99	>200
3	acrylic resin)	48	51	>99	95	>200
4	<i>Pseudomonas cepacia</i> (immobilized on ceramics)	12	33	49	>99	>200
5		24	44	77	>99	>200
6		48	49	95	>99	>200
7	<i>Pseudomonas cepacia</i> (immobilized on diatomite)	12	16	19	>99	>200
8		24	26	34	>99	>200
9		48	36	56	>99	>200
10	<i>Candida rugosa</i>	12	14	13	81	10
11		24	17	17	81	11
12		48	21	21	80	11
13	<i>Candida cylindracea</i>	12	12	11	84	12
14		24	15	14	81	10
15		48	18	17	80	10
16	<i>Candida</i> sp. (Novozymes [®] CALB L)	24	<5 ^d	nd	nd	nd
17	<i>Thermomyces lanuginosus</i>	24	<5 ^d	nd	nd	nd
18	<i>Rhizomucor miehei</i>	24	<5 ^d	nd	nd	nd
19	Porcine pancreas lipase	24	<5 ^d	nd	nd	nd
20	<i>Aspergillus niger</i>	24	<5 ^d	nd	nd	nd
21	<i>Pseudomonas fluorescens</i>	24	<5 ^d	nd	nd	nd
22	<i>Penicillium camemberti</i>	24	<5 ^d	nd	nd	nd
23	<i>Mucor javanicus</i>	24	<5 ^d	nd	nd	nd
24	<i>Pseudomonas cepacia</i>	24	<5 ^d	nd	nd	nd

Reaction conditions: Compound (*R,S*)-**3** (0.25 mmol), lipase (20 mg), vinyl acetate (1 mmol), hexane (1 mL), 35 °C, 160 rpm; ^a conversion: $c = 100 \times (ee_s/ee_s + ee_p)$; ^b enantiomeric excess: determined by HPLC analysis; ^c Enantiomeric ratio: $E = \ln\{[ee_p(1 - ee_s)]/(ee_p + ee_s)\} / \ln\{[ee_p(1 + ee_s)]/(ee_p + ee_s)\}$; ^d determined by GC analysis; nd: not determined due to low conversion.

Table 3. Cont.

Entry	Solvent	Time (h)	c ^a (%)	ee ^b (%)		E ^c
				(S)-3	(R)-4	
1	Hexane	12	47	88	>99	>200
2		24	50	99	>99	>200
3	Toluene	12	38	61	>99	>200
4		24	47	87	>99	>200
5	Methyl <i>tert</i> -butyl ether (MTE)	12	42	73	>99	>200
6		24	49	94	>99	>200
7	Tetrahydrofuran (THF)	24	<30 ^d	nd	nd	nd
8	Chloroform (CHCl ₃)	24	<30 ^d	nd	nd	nd
9	Isobutylic alcohol (<i>i</i> -BuOH)	24	<30 ^d	nd	nd	nd
10	Diethyl ether (Et ₂ O)	24	<30 ^d	nd	nd	nd

Reaction conditions: Compound (*R,S*)-3 (0.25 mmol), CAL-B (20 mg), vinyl acetate (1 mmol), solvent (1 mL), 35 °C, 160 rpm; ^a conversion: $c = 100 \times (ee_s/ee_s + ee_p)$; ^b enantiomeric excess: determined by HPLC analysis; ^c Enantiomeric ratio: $E = \ln\{[ee_p(1 - ee_s)]/(ee_p + ee_s)\}/\ln\{[ee_p(1 + ee_s)]/(ee_p + ee_s)\}$; ^d determined by GC analysis; nd: not determined due to low conversion.

Table 4. Influence of temperature in the lipase-catalyzed transesterification of (*R,S*)-3.

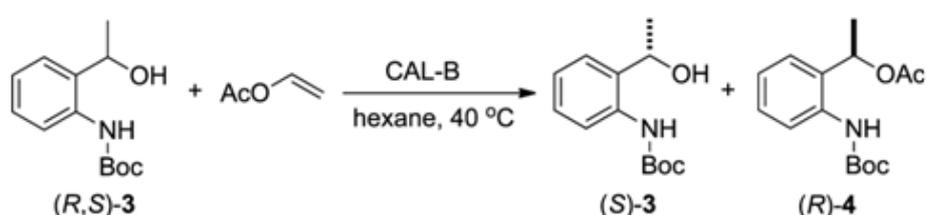
Entry	Temperature (°C)	Tempo (h)	c ^a (%)	ee ^b (%)		E ^c
				(S)-3	(R)-4	
1	25	12	45	80	>99	>200
2	25	16	46	86	>99	>200
3	25	20	49	95	>99	>200
4	25	24	50	>99	>99	>200
5	35	12	48	89	>99	>200
6	35	16	50	>99	>99	>200
7	35	20	50	>99	>99	>200
8	35	24	50	>99	>99	>200
9	40	12	50	>99	>99	>200
10	40	16	50	>99	>99	>200
11	40	20	51	>99	98	>200
12	40	24	52	>99	97	>200
13	50	12	50	>99	98	>200
14	50	16	50	>99	98	>200
15	50	20	52	>99	97	>200
16	50	24	53	>99	94	>200

Reaction conditions: Compound (*R,S*)-3 (0.25 mmol), CAL-B (20 mg), vinyl acetate (1 mmol), hexane (1 mL), 160 rpm; ^a conversion: $c = 100 \times (ee_s/ee_s + ee_p)$; ^b enantiomeric excess: determined by HPLC analysis; ^c Enantiomeric ratio: $E = \ln\{[ee_p(1 - ee_s)]/(ee_p + ee_s)\}/\ln\{[ee_p(1 + ee_s)]/(ee_p + ee_s)\}$.

2.2.4. Study of the Ratio of Enzyme to Substrate for Kinetic Resolution of (*R,S*)-**3**

The ratio enzyme/substrate was also investigated for EKR of (*R,S*)-**3** at 40 °C and 12 h (Table 5). It was observed that 10 mg of CAL-B was not enough to reach 50% of conversion (Entry 3). By using 20 and 40 mg the desired result was achieved just at the end of the experiments (Entries 6 and 9). However, the reaction with 80 mg of CAL-B showed 50% of conversion after 8 h (Entry 11) and for the reaction with 100 mg only 6 h were needed to obtain the desired results (Entry 13), but we considered the ratio of 100 mg CAL-B to 0.25 mmol substrate impracticable, so 20 mg was chosen as the optimal amount to achieve excellent values of conversion and enantiomeric excess.

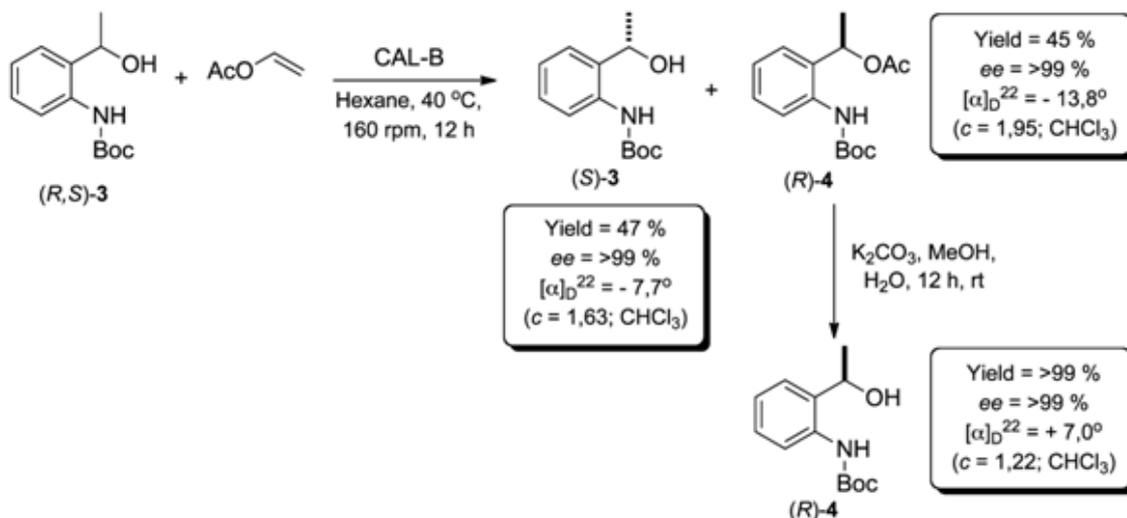
Table 5. Study of ratio CAL-B/substrate for kinetic resolution of (*R,S*)-**3**.



Entrada	Massa (mg)	Tempo (h)	c (%) ^a	<i>ee</i> (%) ^b		<i>E</i> ^c
				3	4	
1	10	6	30	63	>99	>200
2	10	8	39	75	>99	>200
3	10	12	45	90	>99	>200
4	20	6	40	84	>99	>200
5	20	8	45	93	>99	>200
6	20	12	50	>99	>99	>200
7	40	6	43	86	>99	>200
8	40	8	48	97	>99	>200
9	40	12	50	>99	>99	>200
10	80	6	48	97	>99	>200
11	80	8	50	>99	>99	>200
12	80	12	51	>99	97	>200
13	100	6	50	>99	>99	>200
14	100	8	50	>99	>99	>200
15	100	12	52	>99	95	>200

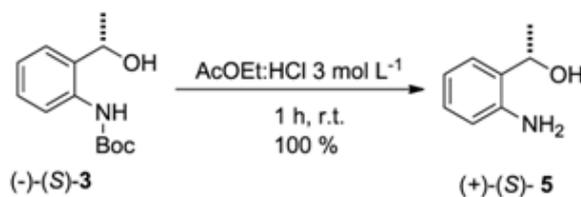
Reaction conditions: Compound (*R,S*)-**3** (0.25 mmol), CAL-B, vinyl acetate (1 mmol), hexane (1 mL), 40 °C, 160 rpm; ^a conversion: $c = 100 \times (ee_s/ee_s + ee_p)$; ^b enantiomeric excess: determined by HPLC analysis; ^c Enantiomeric ratio: $E = \ln\{[ee_p(1 - ee_s)]/(ee_p + ee_s)\} / \ln\{[ee_p(1 + ee_s)]/(ee_p + ee_s)\}$.

In order to obtain the compounds (*S*)-**3** and (*R*)-**3** and to assign the absolute configuration, a reaction on a preparative scale (5 mmol) was carried out. After quenching the reaction, the compounds (*S*)-**3** and (*R*)-**4** were separated by flash gel column chromatography. Then, the ester (*R*)-**4** was submitted to a hydrolysis reaction to give the alcohol (*R*)-**3** (Scheme 4). In this way, both enantiomers of **3** were obtained in high enantiomeric purity (*ee* > 99%) and yields (>45%).

Scheme 4. Synthesis of (*R*)- and (*S*)-3.

The absolute configuration of the compound **3** was indirectly attributed after deprotection of the amino group of (–)-(*S*)-**3** [18]. Then, the optical rotation of the resulting amino-alcohol **5** was measured, and by comparison with literature data [18] its absolute configuration was attributed to (*S*)-**5** (Table 6). Consequently, the configuration of the *NH*-Boc protected precursor was also attributed to (*S*)-**3**.

Table 6. Assignment of the absolute configuration of *tert*-butyl 2-(1-hydroxyethyl)phenylcarbamate (**3**).



#	<i>ee</i> (%)	$[\alpha]_D$
Literature [18]	93	+52, 5 (<i>c</i> = 1,0; CHCl ₃)
This work	>99	+63,1 (<i>c</i> = 1,1; CHCl ₃)

3. Experimental Section

Commercially available materials were used without further purification. Lipase from *Candida antarctica* (fraction B, CAL-B) immobilized, and commercially available as Novozym® 435 was kindly donated by Novozymes Latin America Ltda. All solvents were HPLC or ACS grade. Solvents used for moisture sensitive operations were distilled from drying reagents under a nitrogen atmosphere: THF was distilled from Na/benzophenone.

Analytical thin-layer chromatography (TLC) was performed using aluminum-backed silica plates coated with a 0.25 mm thickness of silica gel 60 F₂₅₄ (Merck), visualized with an ultraviolet light ($\lambda = 254$ nm), followed by exposure to *p*-anisaldehyde solution or vanillin solution and heating. Standard chromatographic purification methods were followed using 35–70 mm (240–400 mesh) silica gel purchased from Acros Organics®.

Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AC 200 spectrometer at operating frequencies of 200 (^1H -NMR) and 50 MHz (^{13}C -NMR). The ^1H -NMR chemical shifts are reported in ppm relative to TMS peak. The data are reported as follows: chemical shift (δ), multiplicity (s = singlet, d = doublet, t = triplet, qd = quadruplet, dd = double doublet, td = triple doublet, m = multiplet), and coupling constant (J) in Hertz and integrated intensity. The ^{13}C -NMR chemical shifts are reported in ppm relative to CDCl_3 signal.

Reaction products were analyzed by a Shimadzu model GC-17A (FID) gas chromatograph equipped with a J&W Scientific HP5 column (30 m \times 0.25 mm I.D.; 0.25 μm). The chromatographic conditions were as follows: Oven temperature initiated at 50 $^\circ\text{C}$ and increased at 10 $^\circ\text{C}/\text{min}$; run time 20 min; injector temperature 230 $^\circ\text{C}$; detector temperature 250 $^\circ\text{C}$; injector split ratio 1:20; hydrogen carrier gas at a pressure of 100 kPa. The enantiomeric excesses of the products were determined by HPLC analyses performed in a Shimadzu model SPD-10Av instrument with UV-Vis detector (deuterium lamp 190–600 nm) and equipped with a Chiralcel[®] OD-H column (25 cm \times 0.46 cm I.D.; Daicel Chemical Ind.) eluted with *n*-hexane (60%) and 2-propanol (99:1).

High-resolution mass spectra (HRMS) were acquired using a Bruker Daltonics MicroTOF instrument, operating in the electrospray ionization (ESI) mode.

Infrared spectra were recorded from KBr discs or from a thin film between NaCl plates on FTIR spectrometer (Bomem Michelson model 101). Absorption maxima (ν_{max}) are reported in wavenumbers (cm^{-1}).

Optical rotations were measured on a Perkin Elmer-343 digital polarimeter in a 1 mL cuvette with a 1 dm pathlength. All values are reported in the following format: $[\alpha]_{\text{D}}(\text{temperature of measurement}) = \text{specific rotation (concentration of the solution reported in units of 10 mg sample per 1 mL solvent used)}$.

3.1. Synthesis of *tert*-butyl (2-Acetylphenyl)carbamate (**2**) (Adapted from References [13,14])

To a solution of the 1-(2-aminophenyl)ethanone (**1**, 1.35 g, 10 mmol) in anhydrous THF (100 mL) Boc_2O (6.48 g, 30 mmol) was added, followed by DMAP (122 mg, 1 mmol). The solution was stirred under reflux for 12 h then concentrated to dryness and partitioned between 0.5 mol L^{-1} HCl (100 mL) and EtOAc (100 mL). The aqueous layer was extracted with EtOAc (2 \times 100 mL) and the combined organic phases were washed with brine (50 mL), dried over MgSO_4 , filtered and concentrated to afford the crude *tert*-butyl (2-acetylphenyl)carbamate (**2**) and the di-Boc derivative products. These compounds were separated by flash silica gel column chromatography eluted with hexane/EtOAc 9:1. (2-Acetylphenyl)carbamate (**2**) and the di-Boc derivative were isolated in 45% and 31% yields, respectively. The di-Boc compound (1.00 g) was dissolved in CH_2Cl_2 (100 mL) and Amberlyst 15 resin (1.00 g) was added. The mixture was stirred for 24 h in an orbital shaker. Then, the solvent was removed and the residue filtered through a silica gel column with hexane/EtOAc 9:1. The compound **2** was obtained in 67% yield. ^1H -NMR (200 MHz, CDCl_3); δ (ppm): 10.95 (s, 1H); 8.46 (d, 1H, $J = 8.3$ Hz); 7.84 (dd, 1H, $J_{\text{A}} = 7.9$ Hz; $J_{\text{B}} = 1.32$ Hz); 7.50 (td, 1H, $J_{\text{A}} = 8.3$ Hz; $J_{\text{B}} = 1.3$ Hz); 7.01 (t, 1H, $J = 7.9$ Hz); 2.64 (s, 3H); 1.53 (s, 9H). ^{13}C -NMR (50 MHz, CDCl_3); δ (ppm): 202.5; 153.4; 142.0; 135.2; 131.9; 121.6; 121.2; 119.4; 80.7; 28.8. IR (KBr), cm^{-1} : 3432; 2947; 1713; 1656; 1562; 1239; 1108; 739. HRMS (ESI), $[\text{M}+\text{Na}]^+$: Calculated for $\text{C}_{13}\text{H}_{17}\text{NO}_3\text{Na}$: 258.1106. Found: 258, 1104.

3.2. Synthesis of Racemic *tert*-butyl (2-(1-Hydroxyethyl)phenyl)carbamate [(*R,S*)-**3**]

To a solution of *tert*-butyl (2-acetylphenyl)carbamate (**2**, 1.175 g, 5 mmol) in methanol (50 mL) NaBH₄ (0.21 g, 5.5 mmol) at 0 °C was added. After adding NaBH₄, the ice bath was removed and the solution was stirred at room temperature for 2 h then concentrated to dryness. To residue water (30 mL) was added and the pH adjusted to 6.0. In the sequence the mixture was extracted with CH₂Cl₂ (3 × 15 mL), dried over MgSO₄, filtered and concentrated to afford the crude *tert*-butyl (2-(1-hydroxyethyl)phenyl)carbamate (**3**). This was purified by flash silica gel column chromatography eluted with hexane/EtOAc 9:1 to afford **3** in 84% yield. ¹H-NMR (200 MHz, CDCl₃); δ (ppm): 8.01 (s, 1H); 7.90 (d, 1H, *J* = 8.3 Hz); 7.26 (t, 1H, *J* = 7.5 Hz); 7.14 (d, 1H, *J* = 7.5 Hz); 7.00 (t, 1H, *J* = 7.5 Hz); 4.95 (qd, 1H, *J* = 6.6 Hz); 1.54 (m, 12H). ¹³C-NMR (50 MHz, CDCl₃); δ (ppm): 153.5; 136.7; 132.7; 127.9; 126.4; 122.9; 121.4; 80.0; 69.5; 28.2; 22.1. IR (film), cm⁻¹: 3457; 3343; 2979; 1761; 1727; 1524; 1449; 1254. HRMS (ESI), [M+Na]⁺: Calculated for C₁₃H₁₉NO₃Na: 260.1263. Found: 260.1262.

3.3. Synthesis of Racemic 1-(2-((*tert*-Butoxycarbonyl)amino)phenyl)ethyl acetate [(*R,S*)-**4**]

To a solution of the (2-(1-hydroxyethyl)phenyl)carbamate (**3**, 237 g, 1 mmol) in pyridine (2 mL) was added Ac₂O (0.10 g, 1 mmol). The solution was stirred at room temperature overnight then diluted in EtOAc (20 mL) and washed with CuSO₄ (5 mL portions) to the complete removal of the pyridine. The organic phase was dried over MgSO₄, filtered and concentrated to afford the crude 1-(2-((*tert*-butoxycarbonyl)amino)phenyl)ethyl acetate (**4**). The crude material was purified by flash silica gel column chromatography eluted with hexane/EtOAc 9:1 to afford **4** in 92% yield. ¹H-NMR (200 MHz, CDCl₃); δ (ppm): 7.78 (d, 2H, *J* = 8.1 Hz); 7.66 (s, 1H); 7.32 (m, 2H); 7.12 (td, 1H, *J*_A = 7.5 Hz; *J*_B = 0.8 Hz); 5.98 (qd, 1H, *J* = 6.4 Hz); 2.0 (s, 3H); 1.61 (d, 3H, *J* = 6.4 Hz); 1.5 (s, 9H). ¹³C-NMR (50 MHz, CDCl₃); δ (ppm): 170.2; 152.8; 135.1; 130.7; 128.1; 126.3; 123.6; 122.9; 79.3; 68.1; 27.6; 20.3; 20.0. IR (film), cm⁻¹: 3432; 3338; 2980; 1731; 1591; 1519; 1453; 1241; 1160. HRMS (ESI), [M+Na]⁺: Calculated for C₁₅H₂₁NO₄Na: 302.1368. Found 302.1364.

3.4. Enzymatic Kinetic Resolution of the (*R,S*)-*tert*-butyl 2-(1-Hydroxyethyl)phenylcarbamate [(*R,S*)-**3**]

To solution of racemic *tert*-butyl (2-(1-hydroxyethyl)phenyl)carbamate (**3**, 1.185 g; 5 mmol) in hexane (20 mL), CAL-B (Novozym[®] 435; 400 mg) and vinyl acetate (1.72 g; 20 mmol) were added. The mixture was stirred in an orbital shaker at 40 °C for 12 h (160 rpm). Following that, the enzyme was filtered off and washed with dichloromethane (3 × 20 mL). The solvent was removed under reduced pressure and the residue was purified by flash silica gel column chromatography eluted with hexane/EtOAc 9:1 to afford (*S*)-**3** (*ee* > 99%) in 47% yield and (*R*)-**4** (*ee* > 99%) in 45% yield.

3.5. HPLC Analysis of (*S*)- and (*R*)-*tert*-butyl 2-(1-Hydroxyethyl)phenylcarbamate (**3**)

HPLC conditions: Chiralcel[®] OD-H column, *n*-hexane/*i*-PrOH (99:1), 1.0 mL min⁻¹, 254 nm UV detector. (*S*)-**3**: isolated yield = 45%; retention time: 23.7 min; *ee* > 99%; [α]_D²² = -7.7 (*c* = 1.63; CHCl₃). (*R*)-**3**: Isolated yield = 45%; retention time: 29.2 min; *ee* > 99%; [α]_D²² = 7.0 (*c* = 1.22; CHCl₃).

3.6. General Procedure to Remove Boc-Protecting Group (Adapted from Reference [19])

To a mixture of AcOEt:HCl 3 mol L⁻¹ 1:1 (5 mL), *N*-Boc protected compound (1 mmol) was added. The mixture was stirred at room temperature for 1 h. After that, the solvent was removed under vacuum. The residue was dissolved in CH₂Cl₂ (10 mL) and washed with saturated NaHCO₃ solution (3 × 3 mL). Then, the organic layer was dried over MgSO₄, filtered and concentrated to dryness under vacuum. The product was obtained in quantitative yield without further purification.

4. Conclusions

In summary, we have described an efficient methodology to obtain (*R*)- and (*S*)-*tert*-butyl 2-(1-hydroxyethyl)phenylcarbamates in enantiopure form (*ee* > 99%), using a kinetic resolution process mediated by lipase as a biocatalyst. Both enantiomers can be employed in the preparation of organochalcogenanes for further application in biological studies.

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