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Review

Highly enantioselective deracemization of 1-phenyl-1,2-ethanediol and its derivatives by stereoinversion using *Candida albicans* in a one-pot process

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ABSTRACT

A very simple methodology was developed to transform racemic 1-(4-substitutedphenyl)-1,2-ethanediols using resting cells of *Candida albicans* CCT 0776 through a one-pot two-step process in which the (*R*)-stereoisomer was completely oxidized to the corresponding substituted-α-hydroxyacetophenones, which were completely reduced to produce (*S*)-1-(4-substitutedphenyl)-1,2-ethanediols in good isolated yield (60–85%) and with high enantiomeric excess (99% ee). The overall process corresponded to an enantioselective deracemization by stereoinversion of the (*R*)-enantiomer. The process was not achieved for other similar 1,2-diols using the same reaction conditions, which indicates a structural restriction of substrates by the active pocket of the enzymes of *C. albicans* involved in the stereoinversion process.

Contents

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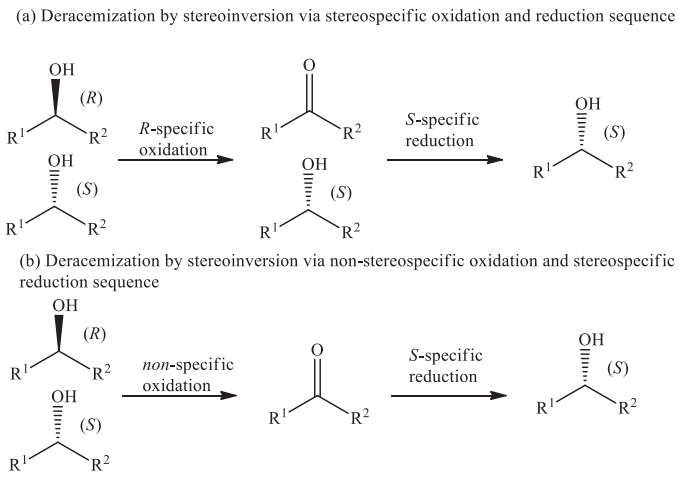


Fig. 1. Stereoinversion/deracemization technologies using alcohol dehydrogenases to transform one enantiomer into the opposite optical form.

1. Introduction

The exquisite chemo-, regio- and stereoselectivity displayed by enzymes has led to their widespread application as catalysts for stereocontrolled organic synthesis [1]. The industrial strategy most commonly used in the preparation of chiral compounds is the settlement of racemates. The separation of a racemate into its two enantiomers, commonly known as resolution, has been the most prominent way to separate two enantiomers in numerous applications. The kinetic resolution is a process in which the two enantiomers of a racemate are converted into products at different rates in an efficient process, such that only one of the enantiomers remains as the product. The limitation of this process is to obtain a maximum return of 50% of product, because only one of the enantiomers undergoes a reaction. Kinetic resolution of enantiomers occurs when $k_R \neq k_S$. To ensure high selectivity, the difference in the reactions rates in the individual enantiomers should be as large as possible (in ideal cases, $k_R/k_S = \infty$). Several strategies have been developed to overcome this limitation and allow the transformation of a racemic mixture into one of the corresponding enantiomers in theoretically 100% chemical yield and 100% optical purity, designated deracemization [2] processes. The cells of microorganisms possess several different enzymes necessary to realize their metabolism including alcohol dehydrogenases (ADHs), which lead to high oxidation, reduction and deracemization activities even toward unnatural substrates [2].

Deracemization by stereoinversion is described as a two-step interconversion reaction between the two enantiomers of the racemate in which the first step includes a stereospecific oxidation (Fig. 1a), or a non-stereospecific oxidation (Fig. 1b) of one alcohol enantiomer into the corresponding ketone and its simultaneous reduction to the mirror-image alcohol. This stereoinversions methodology, is usually achieved by employing one [3,4] or two catalysts [5]. In contrast to the chemical process, oxidation and reduction process can occur simultaneously in living cells. Several authors have reported deracemization through the stereoinversion of one alcohol enantiomer in the presence of fermenting or resting cells of microorganisms [6–10]. Different microorganisms have been tested for the deracemization of alcohols: *Geotrichum candidum* [11,12], *Candida parapsilosis* [13–15], *Alcaligenes faecallis* [16], *Serratia marcescens* [14], *Sphimgomonas* sp. [17], and *Sphingomonas paucimobilis* [18]. These reports present high substrate specificity, the requirement for low substrate concentrations to achieve high ee, high oxidation activity and long reaction times. A tandem biocatalysts system was developed for the deracemization of 1-phenylethanol using resting cells of *Microbacterium oxydans* for the oxidation step and *Rhodotorula* sp. to reduce the ketone [19]. A number of reports described only stereoselective oxidation of secondary alcohols achieving kinetic resolution [20,21].

Chiral 1,2-diols are a versatile group used in the synthesis of pharmaceuticals, agrochemicals, pheromones and other valuable molecules. In particular, (*S*)-1-phenyl-1,2-ethanediol (PED) is a precursor for the production of chiral biphosphines and an initiator for stereoselective polymerization [22]. Several methods for the preparation of chiral PED and other 1,2-diols have been developed by biocatalysis, including stereospecific dihydroxylation of styrene by naphthalene dioxygenase [23], resolution of PED by lipase-catalyzed transesterification [24], enantioselective oxidation by glycerol dehydrogenase [25], and microbial stereoinversion with a whole cell system [13,14]. This last procedure has been employed to avoid coenzyme addition or regeneration systems to obtain alcohols with high yield and ee from racemates [26–28]. For the preparation of optically active 1,2-diols from the corresponding racemates there are reports employing *C. parapsilosis* IFO0708 [14] and *C. parapsilosis* M203011 [13]. Recently, we used *Trichosporon cutaneum* to promote the deracemization of (±)-2-hydroxyindan-1-one to give (1*S*,2*R*)-1,2-indandiol in 90% yield and >99% ee by a dynamic kinetic resolution process [29]. Using the same fungus *T. cutaneum*, we achieved the diastereo- and enantioselective bioreduction of (±)-2-hydroxy-1-tetralone to the corresponding enantiopure (1*S*,2*R*)-*cis*-1,2-dihydroxy-1,2,3,4-tetrahydronaphtalene in 83% yield and >99% ee through dynamic kinetic resolution [30]. We also reported the enantioselective oxidation of (1*R*,2*S*)-1-phenyl-1,2-propanediol mediated by *Saccharomyces cerevisiae* to give (*S*)-1-phenyl-2-hydroxy-1-propanone in 64% yield and 93% ee [31].

In the present report, we investigate the deracemization of 1-phenyl-1,2-ethanediol (PED) and its derivatives with substituents at the phenyl moiety to obtain (*S*)-1-phenyl-1,2-ethanediol in high yield (80–90%) and high ee (99%), employing *Candida albicans* CCT 0776. Similar result was achieved using *C. parapsilosis* M203011 but the authors have not mentioned the reaction time, the mechanism was not studied with details and there is a misconception about the stereochemistry of the product since the structure in the scheme does not fit with assigned configuration [13]. Hasegawa et al. [14] obtained a slight better process using *C. parapsilosis* IFO0708, but they have not studied the mechanism and they have not scaled up the reaction for PED.

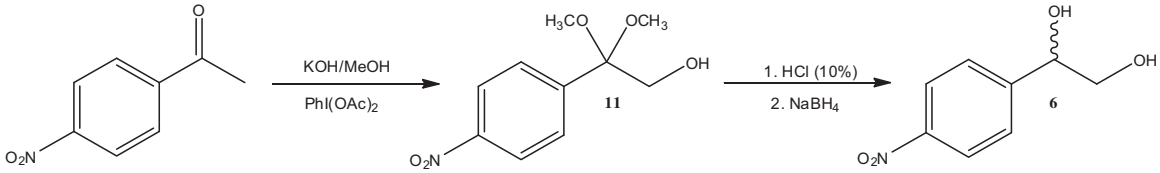
2. Experimental

2.1. General

The alcohols 1-phenyl-1,2-ethanediol (**1**) and 1-(2-nitrophenyl)-1,2-ethanediol (**7**) were purchased from Sigma–Aldrich. 1-(4-Methylphenyl)-1,2-ethanediol (**5**) and 1-(4-chlorophenyl)-1,2-ethanediol (**3**) were purchased from Spectra Group Limited Inc. All other commercial reagents and solvents were purchased with the highest purity available and were used as received. The NMR spectra were recorded in a Varian Gemini at 250 (^{1}H NMR) and 62.5 (^{13}C NMR) MHz, or an Avance at 500 and 600 (^{1}H NMR) and 125–150 (^{13}C NMR) MHz. The chemical shifts (δ') were reported in parts per million (ppm) and the coupling constants (*J*) were reported in Hertz (Hz). A BOMEM MB-100 FT-IR was used for the IR spectra. Optical rotations were measured using a Carl Weiss POLAMAT A polarimeter. The GC analysis was performed with an Agilent 6890 Series GC equipped with a DB1 silica capillary column from J&W Scientific (30 m × 0.25 mm ID × 0.25 μm film thickness) and helium as the carrier gas (0.9 mL/min) with a split ratio of 1:50. The temperature of the injector and the detector were maintained at 230 °C and 280 °C, respectively. The column temperature

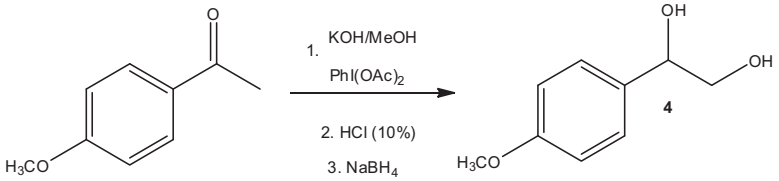
was held at 80 °C for 3 min, increased to 290 °C at a rate of 30 °C min^{-1} and then held constant for 3 min. One microliter of a 0.3 mg mL^{-1} solution of the compound or the extracted reaction aliquots in ethyl acetate was injected. The chiral GC/FID analyses were obtained on an Agilent 6850 Series GC system using a Hydrodex-β chiral capillary column (30 m × 0.25 mm × 0.25 μm). The temperature was sustained at 80 °C, increased to 180 °C at a rate of 5 °C min^{-1}, and then held constant for 10 min. The carrier gas was hydrogen (1 mL/min), the injector temperature was 200 °C and the detector temperature was 220 °C. The chiral HPLC analyses were performed on an Agilent Technologies 1200 series, using a Chiracel OB-H 250 mm × 4.6 mm × 5 μm column from Sigma–Aldrich. Thin layer chromatography (TLC) analyses were performed with precoated aluminum sheets of silica gel F254 nm. The *C. albicans* CCT 0776 yeast strains were stored at André Tosello Research Foundation (Campinas, SP, Brazil; http://www.fat.org.br). The type II lyophilized *S. cerevisiae* was purchased from Sigma–Aldrich and stored in a refrigerator.

2.2. Procedure for the synthesis of 1-(4-nitrophenyl)-1, 2-ethanediol **6** [32]



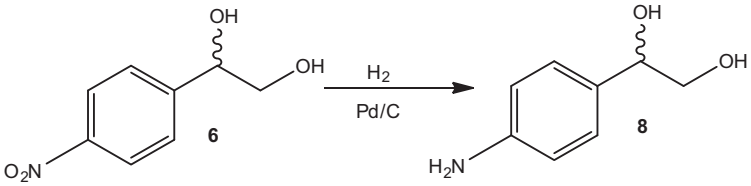
Potassium hydroxide (5.6 g; 0.1 mol) was dissolved in 50 mL of methanol and 4′-nitroacetophenone (1.65 g; 0.01 mol) was added over 10 min. $C_6H_5I(OAc)_2$ (6.44 g; 0.01 mol) was added over a 10 min period. The reaction mixture was stirred at room temperature overnight. Work-up followed by crystallization yielded **11** (1.25 g; 55%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.29 (s, 6H), 3.74 (s, 2H), 7.73 (d, 2H, *J* = 9.0 Hz), 8.26 (d, 2H, *J* = 9.0 Hz). Hydrolysis was conducted in HCl (10%) for 30 min. The crude product was dissolved in ethanol (5 mL) and $NaBH_4$ (0.378 g; 0.01 mol) was added. The reaction mixture was stirred at room temperature for 30 min. Work-up followed by crystallization yielded **6** (0.91 g, 90%) as yellow crystals. IR (KBr, cm^{-1}): 3445, 3112, 3077, 2946, 2836, 1607, 1523, 1491. MS *m*/*z* (rel. intensity %): 183 [M$^+$], (0.8), 152 (100), 136 (16), 122 (8), 106 (32), 94 (18), 77 (31). ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.66 (dd, *J* = 7.8, 11.4 Hz, 1H), 3.86 (dd, *J* = 3.6, 11.4 Hz, 1H), 4.97 (dd, *J* = 3.6, 7.8 Hz, 1H), 7.58 (d, *J* = 9.0 Hz, 2H), 8.23 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 49.37, 65.09, 101.76, 123.36, 128.46, 146.54, 147.93.

2.3. Procedure for the synthesis of 1-(4-methoxyphenyl)-1, 2-ethanediol **4** [32]



Compound **4** was obtained from 4′-methoxyacetophenone (1.5 g; 0.01 mmol) as a colorless solid (0.86 g; 50%). IR (KBr, cm^{-1}): ν_{max} 3279, 2958, 1611, 1513, 1246. MS *m*/*z* (rel. intensity %): 168 [M$^+$] (7), 150 (6), 137 (100), 109 (20), 94 (21), 77 (25), 65 (5). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.68 (dd, *J* = 8.0, 11.5 Hz, 1H), 3.75 (dd, *J* = 3.5, 11.5 Hz, 1H), 3.83 (s, 3H), 4.79 (dd, *J* = 3.5, 8.0 Hz, 1H), 6.92 (d, *J* = 9.0 Hz, 2H), 7.31 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 55.33, 68.09, 74.31, 113.99, 127.38, 132.65, 159.44.

2.4. Procedure for the synthesis of 1-(4-aminophenyl)-1, 2-ethanediol **7** [33]



To a solution of **6** (275 mg, 1.50 mmol) in ethyl acetate (10 mL) was added Pd/C (10%, w/w, 27 mg), and the mixture was stirred under a hydrogen atmosphere (balloon) at room temperature for 4 h. The catalyst was filtered on Celite and the filtrate was concentrated in vacuum to give **8** (215 mg, 95% yield) as a red solid mp 88–89 °C. MS *m*/*z* (rel. intensity %): 153 [M+] (13.3), 135 (15.0), 122 (100), 106 (84.9), 94 (36.3), 77(38.9), 65 (7.9). ^{1}H NMR (500 MHz, DMSO-*d*6): δ 4.36 (m, 1H), 4.55 (m, 1H), 4.86 (m, 1H), 6.50 (d, *J* = 8.5 Hz, 2H), 6.97 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR (150 MHz, DMSO-*d*6): δ 68.11, 74.26, 113.87, 127.31, 130.94, 147.96. HRMS calcd. for $C_8H_{11}NO_2$: [M+] = 153.0790, found [M+] 153.0785.

2.5. Procedure for the synthesis of 1-(2-aminophenyl)-1, 2-ethanediol **9**

The 1-(2-aminophenyl)-1,2-ethanediol **9** was obtained by the same methodology used for **8**, yielding **9** (210 mg, 93%) as a brown solid 89–90 °C. MS *m*/*z* (rel. intensity %): 153 [M+], (27), 122 (100), 117 (87), 106 (1), 94 (3.5), 77 (3), 65 (0.9). ^{1}H NMR (250 MHz, DMSO-*d*6): δ 3.45 (s, 2H), 4.58 (s, 2H), 5.16 (s, 1H), 6.48–6.59 (m, 2H), 6.87–6.93 (m, 1H), 7.04–7.07 (m, 1H). ^{13}C NMR (100 MHz, DMSO-*d*6): δ 65.64, 72.06, 115.80, 116.69, 126.54, 127.53, 127.85, 146.22. HRMS calcd. for $C_8H_{11}NO_2$: [M+] = 153.0790, found [M+] 153.0771.

2.6. Growth conditions of C. albicans CCT 0776

C. albicans CCT 0776 was grown in a yeast malt broth medium (1 L) in a 2 L Erlenmeyer flask incubated at 30 °C, and 180 rpm for 24 h. The cells were harvested by centrifuging the culture broth at 1844 × *g* for 30 min and were subsequently washed with distilled water. The wet cells were used for biotransformation. In total, 20 g of wet cells was obtained per 1 L medium.

2.7. General procedure for deracemization of 1,2-diols

To a 25 mL Erlenmeyer flask containing 3 g of wet cells of *C. albicans* CCT 0776 suspended in 10 mL of distilled water, 50 mg of 1,2-diols dissolved in 0.5 mL of ethanol as co-solvent was added and incubated at 30 °C, and 180 rpm in an orbital shaker, until complete deracemization was achieved.

In a preparative scale, 200 mg substrate (**3**, **4** and **5**) was added to a 150 mL Erlenmeyer flask containing a slurry of 12 g of yeast (wet weight) in 40 mL of water. The crude reaction was extracted with ethyl acetate (three times), and the organic layer was dried over anhydrous sodium sulfate. The solvent was removed by rotary evaporator, and enantiomerically pure (*S*)-diols were obtained after purification with silica gel chromatography using hexane/ethyl acetate as the mobile phase. For (±)-1-phenyl-1,2-ethanediol **1**, was used 500 mg of substrate in 500 mL flask containing 30 g of yeast in 100 mL of water.

2.7.1. (S)-1-Phenyl-1,2-ethanediol (S)-*1*

Colorless solid, mp 63–65 °C; $[\alpha]_D^{20}$ +66.0 (c 1.0 $CHCl_3$) 99% ee {lit. [34] $[\alpha]_D^{20}$ = +66.9 (c 1.0, $CHCl_3$)} 99% ee. ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.76 (dd, *J* = 3.5, 11.25, 1H), 3.66 (dd, *J* = 8.0, 11.25, 1H), 4.81 (dd, *J* = 3.5, 8.0 Hz, 1H), 7.26–7.37 (m, 5H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 68.0, 74.6, 126.0, 128.0, 128.5, 140.4.

2.7.2. (S)-1-(4-methylphenyl)-1,2-ethanediol (S)-*5*

Colorless solid, mp 65–67 °C; $[\alpha]_D^{20}$ +64.0 (c 1.8, $CHCl_3$) 99% ee {lit. [34] $[\alpha]_D^{20}$ = +68.5 (c 1.12, $CHCl_3$), 99% ee}. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.34 (s, 3H), 3.65 (dd, *J* = 8.0, 11.25, 1H) 3.74 (dd, *J* = 3.75, 11.25, 1H), 4.78 (dd, *J* = 3.75, 8.0 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 21.1, 68.0, 74.5, 125.9, 129.2, 137.4, 137.7. The enantiomeric excess was determined by HPLC analysis using a Chiracel OB-H column (eluent hexane/2-propanol 90:10, flow rate 0.5 mL/min) t_R = 97.636. min [(*R*)-isomer]; t_R = 102.534 min [(*S*)-isomer].

2.7.3. (S)-1-(4-chlorophenyl)-1,2-ethanediol (S)-*3*

Colorless solid, mp 79–80 °C; $[\alpha]_D^{20}$ +55.0 (c 1.6 $CHCl_3$) 99% ee {lit. [34] $[\alpha]_D^{20}$ = +52.0 (c 1.6, $CHCl_3$), 99% ee}. ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.61–3.72 (m, 2H), 4.78 (m, 1H), 7.26–7.36 (m, 4H). The enantiomeric excess was determined by HPLC analysis using a Chiracel OB-H column (eluent hexane/2-propanol 90:10, flow rate 0.5 mL/min) t_R = 76.024 min [(*R*)-isomer]; t_R = 78.761 min [(*S*)-isomer].

2.7.4. (S)-1-(4-methoxyphenyl)-1,2-ethanediol (S)-*4*

Colorless solid, mp 76–77 °C; $[\alpha]_D^{20}$ +61.0 (c 0.5 $CHCl_3$) 99% ee {lit. [34] $[\alpha]_D^{20}$ = +60.3 (c 0.5, $CHCl_3$), 99% ee}. The enantiomeric excess was determined by HPLC analysis using a Chiracel OB-H column (eluent hexane/2-propanol 90:10, flow rate 0.5 mL/min) t_R = 145.086 min [(*S*)-isomer]; t_R = 149.029 min [(*R*)-isomer].

2.7.5. 1-(4-aminophenyl)-2-hydroxyethanone *10*

Brown solid, mp 113–115 °C (decomposition). ^{1}H NMR (400 MHz, DMSO-*d*6): δ 4.62 (s, 2H), 6.58 (d, *J* = 8.8 Hz, 2H), 7.66 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-*d*6): δ 64.7, 113.1, 122.4, 130.4, 154.4, 196.3. MS *m*/*z* (rel. intensity %): 151 [M+] (11.5), 135 (0.9), 120 (100), 106 (0.9), 92 (30.1), 77 (1.8), 65 (22.1). HRMS calcd. for $C_8H_9NO_2$: [M^+] = 151.0633, found [M^+] 151.0626.

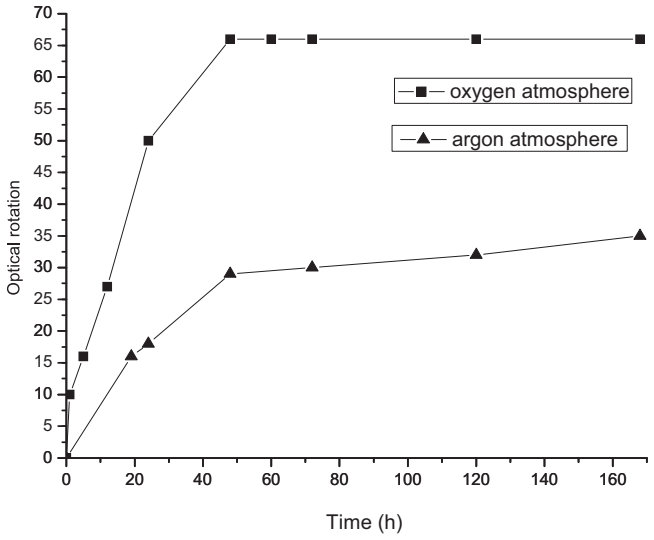
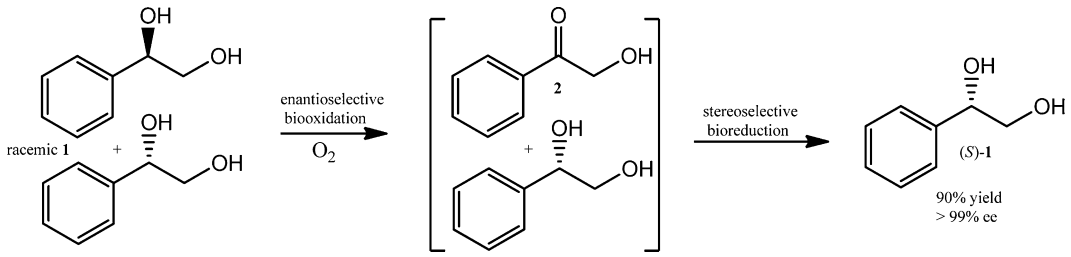


Fig. 2. Monitoring the deracemization of 1-phenyl-1,2-ethanediol **1** in oxygen and argon atmosphere.

3. Results and discussion

The deracemization of racemic (±)-1-phenyl-1,2-ethanediol **1** in an aqueous cells suspension of *C. albicans* in an orbital shaker at 30 °C, was monitored by measuring the optical rotation as shown in Fig. 1. After 48 h, the specific rotation $[\alpha]_D^{20}$ stabilized at +66 indicating a quantitative conversion to (*S*)-1-phenyl-1.2-ethanediol (*S*)-**1**, which was confirmed by chiral GC. Through a preparative scale reaction, 500 mg of (±)-**1** was incubated with *C. albicans* for 48 h to produce (*S*)-**1** in 80% yield and 99% ee. In an argon atmosphere, the reaction was slow, and only a partial deracemization occurred, because after 48 h, the $[\alpha]_D^{20}$ was only +30 and after 7 days it reached not more than +35 (see Fig. 2). Monitoring the reaction under saturated oxygen atmosphere by chiral GC, we observed after 1 h the presence of α-hydroxyacetophenone **2** in 3%, reached 10% after 7 h and then decreased to 3% after 48 h. The ketone **2** was isolated in 3–5% when the reaction was performed on a preparative scale, suggesting a deracemization process through a stereoinversion. It is known that the oxidation of the alcohol by some fungus strain occurs because of the presence of NADH-dependent stereoselective ADH(s) and NADH oxidase(s), which regenerated NAD^+ at the expense of molecular oxygen [16]. To obtain more mechanistic information, we studied the behavior of the enantiomer (*R*)-**1** in the presence of *C. albicans*, which was incubated with the same conditions used before for the deracemization of racemic **1**. When monitoring the reaction by GC, an immediate formation of α-hydroxyacetophenone **2** was observed, which was then promptly reduced to (*S*)-**1** after 2 days giving 99% ee. The cited stereoisomer (*R*)-**1** was prepared by performing the reduction of α-hydroxyacetophenone **2** with *S. cerevisae* to produce (*R*)-**1** in 90% yield and 92% ee after 20 h. In a separate reaction, we incubated ketone **2** with *C. albicans* and produced, after 22 h, (*S*)-**1** in 86% yield and 99% ee. Leaving that reaction for a long period, we observed that (*S*)-**1** was completely stable, indicating no further oxidation and conversion to its antipode. Considering all of the above facts, we propose a two-step one-pot deracemization of (±)-1-phenyl-1,2-ethanediol **1** by resting cells of *C. albicans*, in which an enantioselective oxidation of the transient enantiomer (*R*)-**1** to α-hydroxyacetophenone **2** initially occurred by an alcohol (*R*)-specific oxidase, and **2** was then enantioselectively reduced to



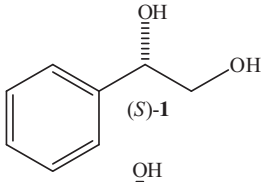
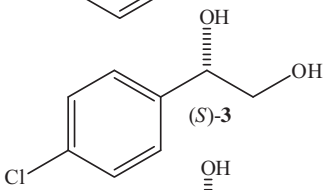
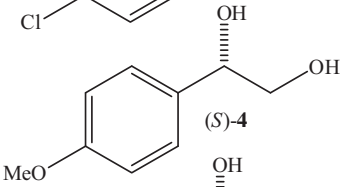
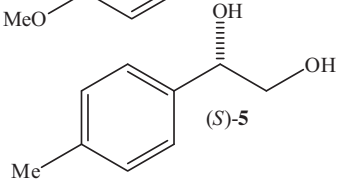
Scheme 1. Proposed mechanism for the deracemization of 1-phenyl-1,2-ethanediol **1** by stereoinversion using resting cells of *C. albicans*.

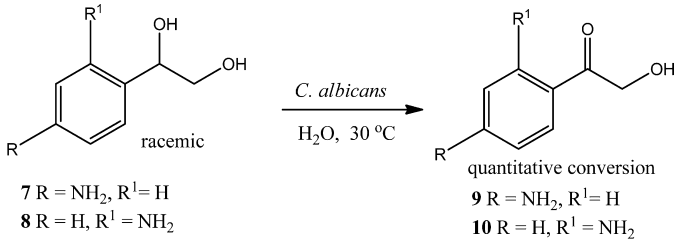
(*S*)-**1** by an alcohol (*S*)-specific dehydrogenase (Scheme 1). The cells of *C. albicans* possessed all of the enzymatic machinery required to perform the two steps of this highly stereoselective process of stereoinversion, including the recycling of all cofactors linked to each step. The overall process is the stereoinversion of (*R*)-**1** to its antipode (*S*)-**1**, which provided a green and efficient biocatalytic alternative to the chemical versatile Mitsunobu inversion reaction employing only one microorganism.

Because the deracemization of 1-phenyl-1,2-ethanediol **1** was so efficient, we extended our method to evaluate the generality and specificity of the stereoinversion of other similar secondary alcohols. Initially, we focused on similar structures of racemic alcohol **1** with different electron demand substituents at the para position of the aromatic ring. In Table 1, we summarize our results for four 1,2-diols that gave quantitative conversion of racemic 1,2-diols, with good isolated yield (60–85%) and excellent ee (>99%) of (*S*)-1-phenyl-1.2-ethanediols **1**–**5**. The deracemization process with *C. albicans* exhibited the same enantioselectivity [(*S*)-1,2-ethanediol] for all compounds with any differences independent of the electron demand of the substituents. With 1-(4-chlorophenyl)-1,2-ethanediol **3** and 1-(4-methoxyphenyl)-1,2-ethanediol **4**, the reaction was completed within 3 days, whereas with 1-(4-methylphenyl)-1,2-ethanediol **5**, it required 1 day. One possible explanation for the observed difference in the reaction time for deracemization of compounds **1**, **3**, **4** and **5** with different substituents in the aromatic ring, are their interactions in the active pocket of the enzyme to form the enzyme complex. The evaluation is difficult because we have a two-step process, where the substituent that facilitates the oxidation step hinders the reduction. For all four racemic compounds investigated, the deracemization was achieved by an efficient process of stereoinversion giving the enantiomers (*S*)-1,2-diol.

Other 1,2-diols were evaluated to determine the size of the molecule that can be recognized by the active pocket of the enzymes of *C. albicans* involved in the stereoinversion process. With 1-(4-nitrophenyl)-1,2-ethanediol **6** and 1-(2-nitrophenyl)-1,2-ethanediol **7**, no reaction was observed. Initially, we supposed that the nitro group was too strongly electron withdrawing to allow a reaction during the oxidation step of the stereoinversion process. With this in mind, the nitro group was chemically reduced to an amino group yielding the 1-(4-aminophenyl)-1,2-ethanediol **8** and 1-(2-aminophenyl)-1,2-ethanediol **9**. Both compounds were promptly oxidized by *C. albicans* to the respective ketones without stereoselectivity, giving 1-(4-aminophenyl)-2-hydroxyethanone **10** (after 2 h) and 1-(2-aminophenyl)-2-hydroxy-ethanone **11**, which was not stable enough during the reaction work-up to allow its full characterization. The α-hydroxyketones **10** and **11** were not reduced by *C. albicans* (Scheme 2). With this result, which showed high reactivity for the oxidation of amino-alcohol derivatives and a total inactivity for the oxidation of the nitro-derivatives, we

Table 1
Deracemization of 1-aryl-1,2-ethanediols in resting cells of *C. albicans*.

	Time (h)	ee (%)	Conversion (%) [yield (%)]
 (*S*)-**1**	48	>99	100 [85]
 (*S*)-**3**	72	>99	100 [71]
 (*S*)-**4**	72	>99	90 [60]
 (*S*)-**5**	24	>99	100 [69]



Scheme 2. Oxidation of 1-(4-aminophenyl)-1,2-ethanediol **8** and 1-(2-aminophenyl)-1,2-ethanediol **9** mediated by *C. albicans*.

conclude that the electron withdrawing nitro group is too strong of a deactivator for the oxidation of 1-(4-nitrophenyl)-1,2-ethanediol **6** and 1-(2-nitrophenyl)-1,2-ethanediol **7** by *C. albicans*.

To complement the evaluation, of different substrates, we focused on the deracemization of 1-(2-naphtyl)-1,2-ethanediol and 3-benzyloxy-1,2-propanodiol, which were both completely inactive when incubated with *C. albicans*.

In conclusion, a very simple one-pot green methodology was developed to transform racemic 1-(4-substitutedphenyl)-1,2-ethanediols using resting cells of *C. albicans* CCT 0776 through a two-step process in which the (*R*)-stereoisomer was completely oxidized to the corresponding substituted-α-hydroxyacetophenones and then reduced to produce (*S*)-(4-substitutedphenyl)-1,2-ethanediols in good isolated yield and with high ee. The overall process corresponds to an enantioselective deracemization by stereoinversion of the (*R*)-enantiomer. The process was not achieved for other similar substrates using *C. albicans* under same reaction conditions.

Acknowledgments

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.molcatb.2014.08.018.

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