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Tetrahedron: *Asymmetry* 15 (2004) 2615–2620

Chemoenzymatic syntheses of (*R*)-2-bromo-, (*R*)-2-chloro- and (*R*)-2-azido-1-(1,3-benzodioxol-5-yl)-1-ethanol

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Received 6 May 2004; revised 15 July 2004; accepted 27 July 2004
Available online 21 August 2004

Abstract—Enantioselective reductions of 2-X-1-(1,3-benzodioxol-5-yl)-1-ethanones, (X = Cl, Br, N_3) by *Rhodothorula glutinis* CCT 2182 afforded the corresponding (*R*)-ethanols in good to excellent yields (57–99%) and excellent enantiomeric excesses (>99%). These alcohols may be used as raw materials for the preparation of the pharmaceuticals (*R*)-(−)-epinephrine, (*R*)-(−)-norepinephrine and (*R*)-(−)-isoproterenol.

1. Introduction

The synthesis of enantiomerically pure 1,2-aminoalcohols attracted many research groups due to the importance of the use of these compounds as therapeutic drugs, chiral auxiliaries and synthetic intermediates in organic synthesis.[1] The actual needs require enantiomers with high purity and ee value that should generally be >98%. For this purpose, simple, more efficient and more practical methods for the preparation of chiral C2 building units are desired. Bioreductions of 2-halo-1-phenyl-1-ethanones[2] and 2-halo- and 2-azido-1-phenyl-1-propanones[3] have been used to obtain chiral halohydrins that are employed for the synthesis of 1,2-aminoalcohols in high enantiomeric excess.[4] There are few examples in the literature reporting the bioreduction of 2-halo-1-aryl-1-ethanones in spite of the useful functional group in the products.[5]

Rhodothorula glutinis is a soil yeast for which various authors have explored the enzymatic machinery, such as mono-oxygenases,[6] epoxy-hydrolases,[7] invertase[8] and used it in resolutions of relevant compounds. However, only a small number of papers have used this yeast for the reduction of ketones. Larchevêque et al. have reduced 3-aryl-3-oxopropionic esters to obtain 3-hydroxy-propionates in high yields and good ee.[9] Zymanczyk-Duda et al. have employed five different species of microorganisms for enantioselective reductions of a variety of 1-oxoalkylphosphonates and found *R. glutinis* as the best biocatalyst.[10] Patel et al. have reduced α-chloroketone to α-chlorohydrin[11] and 2′-bromo-4′-fluorophenyl-2-ethanona to the corresponding (*S*)-alcohol[12] in good yields and high ee. Homann et al. using a screening methodology, found *R. glutinis* as an active microorganism among 60 cultures that were shown to selectively reduce various ketones providing *R* and *S* enantiomers of the corresponding alcohols.[13] Very recently, we reported the synthesis of (*S*)-2-ethyl-1-phenylpropan-1-one by the bioreduction of 2-ethyl-2-phenylprop-2-en-1-one in high yield and high ee using resting cells of *R. glutinis*.[14]

Herein, we report the enantioselective preparation of synthetically useful compounds through the bioreduction of 2-substituted-1-(1,3-benzodioxol-5-yl)-1-ethanones mediated by the yeast *R. glutinis*, as a microbiological alternative route[15] for the preparation of catecholamines such as (*R*)-(−)-epinephrine **1**, (*R*)-(−)-norepinephrine **2** and (*R*)-(−)-isoproterenol **3**, that are part of a class of compounds that exhibit pharmacological activities such as bronchodilator, vasoconstrictor and neurotransmitter of the sympathetic nervous system.[16]

2. Results and discussion

The ketones **4b** and **4e** were prepared applying the Kaufman and Wyman methodology[17] by chlorination of **4a** with sulfuryl chloride in CH_2Cl_2. Ketone **4b** was obtained by running the experiment at 0 °C, while **4e** was obtained when the chlorination temperature was 20 °C.

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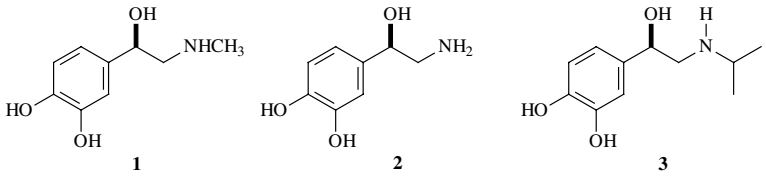
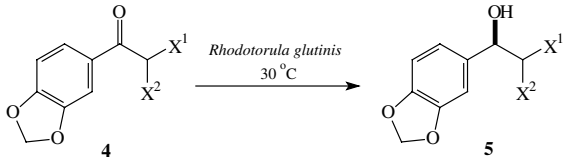
doi:10.1016/j.tetasy.2004.07.029



The bromination of **4a** in CH_2Cl_2 afforded a separable mixture of **4c** and **4f** and the ketone **4d** was obtained by the reaction of **4c** with NaN_3 in DMF at rt. The bioreduction of ketones **4a–f** was mediated by *R. glutinis* in nutrient broth (YM) at temperature of 30 °C (Scheme 1). Inoculation of substrates **4b**, **4c** and **4d** afforded (−)-**5b**, (−)-**5c** and (−)-**5d** in 98%, 57% and 99% yield, respectively, in excellent ee >99% (Table 1).



a $X^1 = H$, $X^1 = H$
b $X^1 = Cl$, $X^2 = H$
c $X^1 = Br$, $X^2 = H$
d $X^1 = N_3$, $X^2 = H$
e $X^1 = Cl$, $X^2 = Cl$
f $X^1 = Br$, $X^2 = Br$

Scheme 1.

For the determination of the absolute configuration of the obtained azidoalcohol (−)-**5d**, the azido group was reduced by H_2/Pd–C furnishing (−)-2-amino-1-(1,3-benzodioxol-5-yl)-1-ethanol (−)-**6**. The obtained aminoalcohol **6** shows specific rotation of −38.7 (*c* 2, $CHCl_3$). The attribution of the absolute configuration to (−)-**6** as being *R* was done by comparison with the literature value ($[\alpha]_D^{25} = -38.7$ (*c* 2, $CHCl_3$), configuration *R*).[18] Therefore the absolute configuration of the obtained azidoalcohol (−)-**5d** is *R*.

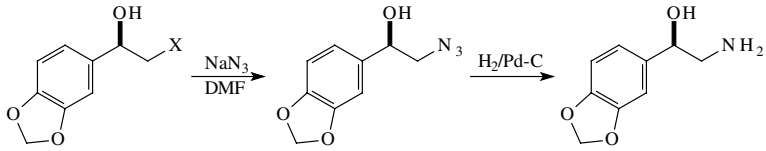
Nucleophilic substitution reactions of (−)-**5b** and (−)-**5c** with sodium azide were carried out for elucidation of the absolute configurations of these halohydrins. The attribution of the absolute configurations of the obtained azidoalcohol products as being *R* was achieved by coinjection on GC using a chiral stationary phase and a genuine sample of (*R*)-(−)-**5d**. Therefore the absolute configuration of the obtained halohydrins (−)-**5b** and (−)-**5c** is *R* (Scheme 2).

These results suggest that the reductions of **4b–c** are by hydride transfer from NADH or NADPH, mediated by a dehydrogenase present in the cells, to the carbonyl carbon of **4** rather than by electron transfer[19] or glutathione-dependent[20] mechanisms where dehalogenated products are obtained. It is known that the reduction rate of 1-(4-substituted-phenyl)-1-etanone mediated by *Saccharomyces cerevisiae* is decreased by electron-donating groups and therefore 1-(4-methoxyphenyl)-1-ethanone is not reduced by this microorganism.[21] In the same way, it was observed that the 3,4-methylenedioxyphenyl group deactivates the carbonyl carbon to undergo a nucleophilic attack by the hydride in the reduction of 1-(1,3-benzodioxol-5-yl)-1-ethanone **4a** mediated by *S. cerevisiae*[22] and in this work, by

Table 1. Bioreduction of ketones **4a–f** by *R. glutinis* CCT 2182[a]

Ketone	Alcohol	Yield (%)	$[\alpha]_D^{25}$[b]	$[\theta]$ (λ, nm) in MeOH	Ee[c] (%)
4a	—	—	—	—	—
4b	**5b**	98	−36.0	−7202 (197)	>99 (*R*)
4c	**5c**	57	−33.2	−523 (216)	>99 (*R*)
4d	**5d**	99	−70.0	−14,234 (200)	>99 (*R*)
4e	**5e**	88	−19.0	−330 (217)	76 (*R*)[d]
4f	**5f**	92	−11.7	−4638 (200)	72 (*R*)[d]

[a] *T* = 30 °C, 24 h, 2 mmol of ketone/1.5 mL of EtOH was added to 10 g of yeast (wet weight)/400 mL of YM (yeast–malt extract) nutrient broth.
[b] *c* 1, $CHCl_3$.
[c] Determined by GC–MS analysis (chiral capillary column CHIRASIL-DEX).
[d] The configuration attribution was tentatively made through the comparison of it circular dichroism spectrum and the spectra of alcohols **5b** and **5c**.



(-)-**5b**, **X = Cl**
(-)-**5c**, **X =Br**

(-)-**5d**

(-)-**6**

Scheme 2.

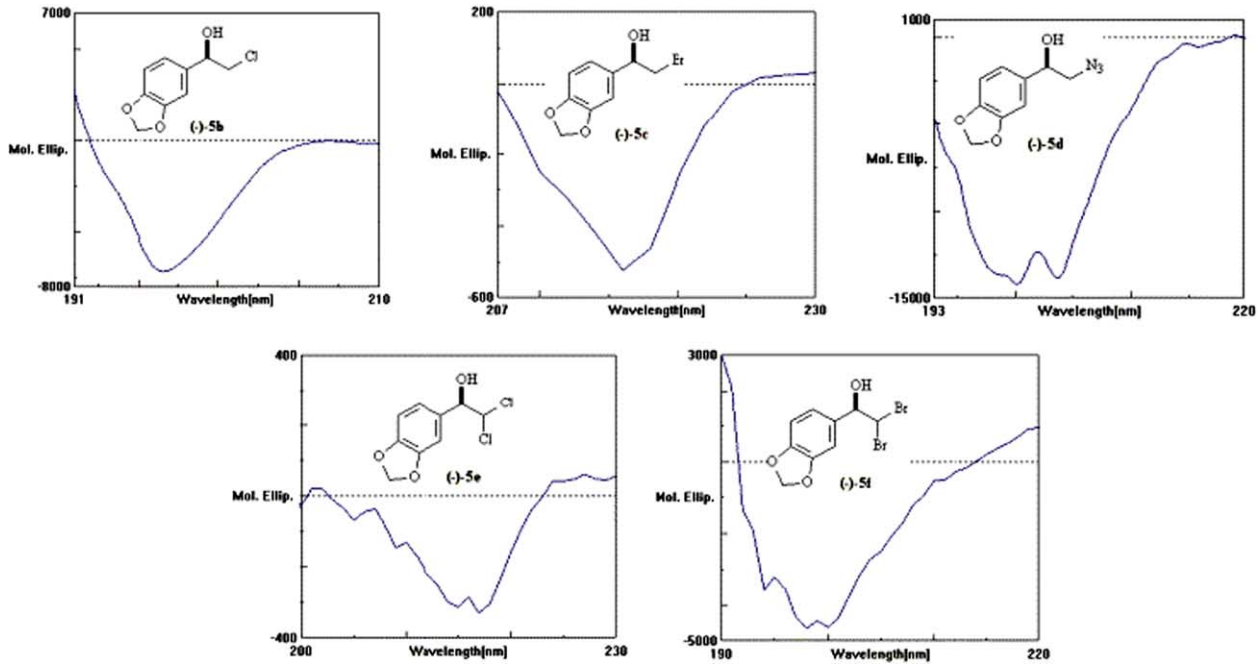


Figure 1. CD spectra of halohydrins **5b–c**, azidoalcohol **5c** and dihaloalcohols **5e–f** in methanol at 25 °C.

R. glutinis (see Table 1). On the other hand, electronegative groups as Cl, Br and N_3, on the α carbon, seems to be responsible for the activation of the carbonyl carbon to undergo reduction mediated by *R. glutinis* in spite of the above mentioned effect of the 3,4-methylenedioxyphenyl group.

It is interesting to observe that **4e** and **4f**, having two electronegative groups bound to the α-carbon, were reduced by *R. glutinis* but the enantiomeric excesses of the obtained products (−)-**5e** and (−)-**5f** were low, 76% and 72% ee, respectively.

The configuration attributions to (−)-**5e** and (−)-**5f** were tentatively made through the comparison of the circular dichroism spectra with the spectra of (−)-(*R*)-**5b–d**. As shown in Figure 1, the Cotton effect for these halohydrins is negative due to a strong absorption of the aromatic ring around 203–217 nm. Due to the similarity of CE spectra we can assume that the compounds **5b–f** have the same configuration.

The hydride transfers from NADH or NADPH to the carbonyl carbon, mediated by the enzyme for reduction of **5b–f** are to the *si* face of those ketones. The Prelog rule[23] has been followed in these reductions taking into account that the bulk of 3,4-methylenedioxybenzene group is bigger than the $–CH_2Cl$, $–CH_2Br$, $–CHCl_2$, $–CHBr_2$ and $–CH_2N_3$ groups.[24]

The great importance of obtaining halohydrins (*R*)-(−)-**5b–c** in excellent yield and ee is that it may be used as raw materials for the preparation of (*R*)-aminoalcohols such as (*R*)-(−)-epinephrine **1**, (*R*)-(−)-norepinephrine **2** and (*R*)-(−)-isoproterenol **3** through its epoxidation followed by epoxide ring opening reaction with amines[1d] and the deprotection of the phenolic groups.[15d]

3. Conclusions

The excellent enantioselectivity and good to excellent yields of the bioreduction of the ketones **4b–d**, presented in this work, provide alcohols (*R*)-(−)-**5b–d** that could be used as intermediates for the enantioselective synthesis of the chiral aminoalcohols. Electronegative groups as Cl, Br and N_3, on the α carbon, seem to be responsible for the activation of the carbonyl carbon to undergo bioreduction in spite of the presence of the 3,4-methylenedioxybenzene group in ethanones **4b–f**.

4. Experimental

IR spectra were recorded on a Bomem MB Series spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini 300 spectrometer in $CDCl_3$. The melting points were obtained in MQAPF-301-MicroQuímica equipment. The gas chromatographic analysis was performed using a Shimadzu GC/MS Class 5000, with helium as a carrier gas, with fused silica capillary columns of SUPELCO SIMPLICITY 1™ (30 m × 0.25 mm × 0.25 μm) and CHIRASIL-DEX (25 m × 0.25 mm × 0.25 μm). Optical rotations and CD spectra were measured with a J-720 VRDM306 JASCO, spectropolarimeter (589.3 nm, 25 °C).

Compound **4a** was acquired from the Aldrich Co. Racemic **5b–f** were prepared by reduction of corresponding **4b–f** with $NaBH_4$ in MeOH. All other solvents and reagents were reagent grade.

4.1. Growth conditions for yeast culture

The yeast *R. glutinis* CCT 2182 is stored at 'André Tosello' Research Foundation[25] and it was cultivated in

YM (yeast–malt extract) nutrient broth (400 mL), for two days incubation at 30 °C on an orbital shaker (200 rpm) before use. Sterile material was used to perform the experiments and the yeast was manipulated in a laminar flow cabinet.

4.2. Synthesis of substrates

4.2.1. 1-(1,3-Benzodioxol-5-yl)-2-chloro-1-ethanone 4b. Sulfuryl chloride (2.0 mL, 28.2 mmol) was added dropwise over a period of 30 min to a solution of 3.0 g (18.3 mmol) of **4a** dissolved in 20 mL of CH_2Cl_2 at 0 °C in a flask equipped with a condenser, dropping funnel, magnetic stirrer and protected from the atmosphere with an anhydrous calcium chloride drying tube. The reaction was maintained at 0 °C under stirring for 1 h. After that, 100 mL of cold water were added to the reaction mixture and the crude product was extracted with ethyl acetate. The organic solution was dried with $MgSO_4$ and the solvent was evaporated to give 2.0 g (55% yield) of yellow crystals, mp 88 °C. IR (KBr) 3111, 3089, 3054, 2955, 2906, 1674, 1601, 1503, 1448, 1256, 1107, 1045, 931, 810, 785, 755, 718 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.63 (s, 2H), 6.07 (s, 2H), 6.87 (d, 1H, $J = 8.0$ Hz), 7.52 (d, 1H, $J = 1.8$ Hz), 7.55 (dd, 1H, $J = 8.0$ Hz, $J = 1.8$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 45.6, 102.0, 108.1, 108.2, 126.0, 128.8, 148.3, 152.4, 189.1; MS *m/z* (rel int. %): 200–198 (M^+, 8–26), 185 (25), 183 (76), 157 (8), 155 (26), 125 (11), 99 (21), 62 (44), 43 (100).

4.2.2. 1-(1,3-Benzodioxol-5-yl)-2-bromo-1-ethanone 4c and 1-(1,3-benzodioxol-5-yl)-2,2-dibromo-1-ethanone 4f. A solution of 3.0 g (18.3 mmol) of **4a** and crystals of *p*-toluene sulfonic acid dissolved in 50 mL of CH_2Cl_2 was cooled to 0 °C and treated dropwise with 1.0 mL (19.4 mmol) of bromine in 15 mL of CH_2Cl_2. The mixture was stirred vigorously for 48 h. The product was diluted with a solution of sodium bisulfite and extracted with ether. The organic phase was dried on $MgSO_4$. Evaporation of the solvent furnished crude mixture of ketones **4c** and **4f**. Purification was achieved by flash column chromatography using hexane/ethyl acetate (7:3), affording pure **4c**, a white crystalline solid recrystallized from ethyl ether–hexane (1:1), mp 89 °C, 68% yield, and **4f** a crystalline solid, recrystallized from ethyl ether–hexane (2:1), mp 101 °C, 32% yield. Compound **4c**: IR (KBr): 3082, 2999, 2951, 2914, 1682, 1603, 1506, 1445, 1246, 1109, 1040, 932, 804 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.37 (s, 2H), 6.07 (s, 2H), 6.87 (d, 1H, $J = 8.1$ Hz), 7.44 (d, 1H, $J = 1.8$ Hz), 7.56 (dd, 1H, $J = 8.1$ Hz, $J = 1.8$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 30.51, 101.91, 107.9, 108.4, 125.4, 128.4, 148.2, 152.2, 189.2; MS *m/z* (rel int. %): 244–242 (M^+, 7–7), 149 (100), 135 (11), 121 (19), 105 (3), 91 (6), 77 (13). Compound **4f**: IR (KBr): 3107, 3082, 3059, 2913, 1673, 1599, 1499, 1442, 1279, 1241, 1139, 1032, 925, 886, 821, 758, 727, 707 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 6.09 (s, 2H), 6.63 (s, 1H), 6.88 (dd, 1H, $J = 8.1$ Hz, $J = 1.8$ Hz), 7.57 (d, 1H, $J = 1.8$ Hz), 7.70 (dd, 1H, $J = 8.1$ Hz, $J = 1.8$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$): 39.5, 102.1, 108.0, 109.2, 124.8, 126.2, 148.2, 149.5, 184.0; MS *m/z* (rel int. %): 324–322–320 (M^+, 1–2–1), 149 (100), 121 (12), 107 (3), 91 (3).

4.2.3. 2-Azido-1-(1,3-benzodioxol-5-yl)-1-ethanone 4d. To a solution of 1.0 g (4.1 mmol) of **4c** in 30 mL of DMF, 1.1 g (16.9 mmol) of sodium azide were added under stirring. The mixture was stirred for 30 min at room temperature. The product was diluted with water and extracted with ether. The organic phase was dried on $MgSO_4$. The solvent was evaporated affording crude ketone **4d**. Purification was achieved by flash column chromatography using hexane/ethyl acetate (7:3), affording pure **4d** a yellow crystalline solid, mp 76 °C, 98% yield. IR (KBr) 3111, 3062, 2922, 2145, 1685, 1617, 1603, 1506, 1281, 1098, 1038, 931, 739, 712 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.47 (s, 2H), 6.07 (s, 2H), 6.86 (d, 1H, $J = 8.1$ Hz), 7.40 (d, 1H, $J = 1.8$ Hz), 7.47 (dd, 1H, $J = 8.1$ Hz, $J = 1.8$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 54.6, 101.9, 107.5, 108.0, 124.1, 128.9, 148.3, 152.5, 190.9; MS *m/z* (rel int. %): 205 (M^+, 1), 177 (11), 149 (100), 121 (35), 91 (11), 74 (6), 65 (43), 63 (42).

4.2.4. 1-(1,3-Benzodioxol-5-yl)-2,2-dichloro-1-ethanone 4e. Sulfuryl chloride (2.0 mL, 28.2 mmol) was added dropwise over a period of 30 min to a solution of 3.0 g (18.3 mmol) of **4a** dissolved in CH_2Cl_2 in a flask equipped with a condenser, dropping funnel, magnetic stirrer and protected from the atmosphere by an anhydrous calcium chloride drying tube. The reaction was very exothermic and the temperature was maintained between 20 °C by a cold-water bath. Both sulfur dioxide and hydrogen chloride were rapidly evolved during the reaction. After the addition was completed, the dark brown solution was diluted with 100 mL of cold water and extracted with ethyl acetate. The crude **4e** was recrystallized from hexane/ethyl acetate 9:1 as white crystalline solid, mp 98 °C, 47% yield. IR (KBr) 3111, 3063, 3022, 2919, 1680, 1600, 1444, 1249, 1113, 1033, 927, 888, 777, 762 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 6.08 (s, 2H), 6.62 (s, 1H), 6.89 (dd, 1H, $J = 8.4$ Hz, $J = 1.8$ Hz), 7.52 (d, 1H, $J = 1.8$ Hz), 7.70 (dd, 1H, $J = 8.4$ Hz, $J = 1.8$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 67.6, 102.1, 108.0, 109.1, 125.4, 126.3, 148.2, 152.8, 183.9; MS *m/z* (rel int. %): 234–232 (M^+, 4–3), 169 (4), 149 (100), 121 (21), 91 (6), 75 (8), 65 (24), 63 (25).

4.3. General procedure for bioreduction of ketones

The ketone **4** (2 mmol), dissolved in 1.5 mL of ethanol, was added to a slurry of growing yeast (400 mL). The resulting suspension was stirred in an orbital shaker (200 rpm) at 30 °C until full conversion of **4** (24 h). The product was extracted with CH_2Cl_2 and was purified in column chromatography using hexane/ethyl acetate (7:3).

4.4. (*R*)-1-(1,3-Benzodioxol-5-yl)-2-chloro-1-ethanol 5b

When **4b** (0.40 g, 2 mmol) was subjected to the general procedure for bioreduction, the isolated product was **5b** (0.39 g, 98%) as oil; $[\alpha]_D^{25} = -36.0$ (*c* 1, $CHCl_3$); ee >99% determined by GC using a chiral column; IR

(film) 3407, 3075, 3010, 2899, 1610, 1504, 1443, 1245, 1037, 981, 863, 816, 739 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.66 (br s, 1H), 3.58–3.70 (m, 2H), 4.81 (d, 1H, $J = 5.5$ Hz), 5.96 (s, 2H), 6.77–6.89 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 76.3, 78.5, 101.1, 107.2, 108.0, 120.8, 130.9, 147.8, 147.9; MS *m/z* (rel int. %): 202–200 (M^+, 3–10), 182 (2), 151 (76), 135 (7), 123 (17), 93 (100), 77 (17), 65 (93).

4.4.1. (*R*)-1-(1,3-Benzodioxol-5-yl)-2-bromo-1-ethanol 5c. When **4c** (0.485 g, 2 mmol) was subjected to the general procedure for bioreduction, the isolated product was **5c** (0.280 g, 57%) as oil; $[\alpha]_D^{25} = -33.2$ (*c* 1, $CHCl_3$), ee >99% determined by GC using a chiral column; IR (film) 3421, 3074, 2961, 2896, 1503, 1487, 1247, 1055, 929, 814 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.78 (br s, 1H), 3.44–3.58 (m, 2H), 4.80 (dd, 1H, $J = 8.8$ Hz, $J = 3.0$ Hz), 5.95 (s, 2H), 6.76–6.86 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 40.0, 73.5, 101.0, 106.2, 108.1, 119.4, 134.1, 147.3, 147.6; MS *m/z* (rel int. %): 246–244 (M^+, 7–7), 151 (100), 135 (8), 123 (13), 93 (82), 77 (14), 65 (51).

4.4.2. (*R*)-2-Azido-1-(1,3-benzodioxol-5-yl)-1-ethanol 5d. When **4d** (0.410 g, 2 mmol) was subjected to the general procedure for bioreduction, the product isolated was **5d** (0.410 g, 99%) as oil; $[\alpha]_D^{25} = -70.0$ (*c* 1, $CHCl_3$); ee >99% determined by GC using a chiral column; IR (film) 3406, 2973, 2905, 2102, 1503, 1488, 1443, 1248, 1036, 930, 812 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.40 (br s, 1H), 3.41 (dd, 2H, $J = 4.2$ Hz, $J = 12.4$ Hz), 3.45 (dd, 2H, $J = 8.0$ Hz, $J = 12.4$ Hz), 4.77 (q, 1H, $J = 4.2$ Hz, $J = 8.0$ Hz), 5.95 (s, 2H), 6,77 (m, 2H), 6.86 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 57.9, 73.1, 100.9, 106.1, 108.1, 119.2, 134.2, 147.2, 147.6; MS *m/z* (rel int. %): 207 (M^+, 3), 179 (6), 151 (51), 150 (43), 149 (100), 135 (2), 121 (33), 93 (45), 65 (41), 63 (27).

4.4.3. (*R*)-1-(1,3-Benzodioxol-5-yl)-2,2-dichloro-1-ethanol 5e. When **4e** (0.465 g, 2 mmol) was subjected to the general procedure for bioreduction, the isolated product was **5e** (0.415 g, 88%) as oil; $[\alpha]_D^{25} = -19.0$ (*c* 1, $CHCl_3$); ee = 76% determined by GC using a chiral column; IR (film) 3470, 2994, 2899, 1610, 1504, 1490, 1446, 1250, 1039, 927, 864, 782, 746, 716 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.17 (br s, 1H), 4.84 (d, 1H, $J = 5.5$ Hz), 5.72 (d, 1H, $J = 5.5$ Hz), 5.95 (s, 2H), 6.77–6.90 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 76.2, 78.4, 101.1, 107.2, 107.9, 120.8, 131.0, 147.5, 147.7; MS *m/z* (rel int. %): 236–234 (M^+, 4–6), 151 (100), 135 (5), 123 (19), 93 (91), 77 (14), 65 (70), 63 (23).

4.4.4. (*R*)-1-(1,3-Benzodioxol-5-yl)-2,2-dibromo-1-ethanol 5f. When **4f** (0.64 g, 2 mmol) was subjected to the general procedure for bioreduction, the isolated product was **5f** (0.60 g, 92%) as oil; $[\alpha]_D^{25} = -11.7$ (*c* 1, $CHCl_3$); ee = 72% determined by GC using a chiral column; IR (film) 3421, 3074, 2961, 2896, 1607, 1503, 1487, 1444, 1247, 1010, 929, 814, 796, 762, 719 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.94 (br s, 1H), 4.94 (d, 1H, $J = 5.5$ Hz), 5.80 (d, 1H, $J = 5.5$ Hz), 5.98 (s, 2H), 6.78–6.93 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 52.1, 78.6, 101.1, 107.3, 108.0, 120.6, 131.5, 147.5, 147.8; MS *m/z* (rel int. %): 324 (M^+, 3), 151 (100), 135 (8), 123 (9), 93 (50), 77 (8), 65 (25), 63 (13).

Acknowledgements

We thank FAPESP and CNPq for financial support.

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