Enantioselective Synthesis of Both Enantiomers of Cathinone *via* the Microbiological Reduction of 2-Azido-1-phenyl-1-propanone

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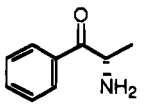
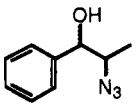
Cathinone, **1a**, or (−)-(2*S*)-2-amino-1-phenyl-1-propanone is the main active constituent of the products extracted from the fresh leaves of *Catha edulis* (Khat)[1] which is found in several countries of East Africa and the Arabian peninsula. The biological activity of cathinone is analogous to that of amphetamines, especially on the cardiovascular system[2] and the metabolism of dopamine.[3] Berrang *et al.*[1] have reviewed all the previous studies and racemic syntheses of cathinone. They have also discussed the puzzling results obtained for the physical constants of the natural **1a** and presented a synthesis of both enantiomers of cathinone.[4]



1a



2

We have shown, in previous work on the microbiological reduction of α-azido ketones,[5,6] that by the appropriate choice of the microorganism, all the chiral isomers of the corresponding β-azido alcohols can be obtained with excellent enantiomeric excesses. A fast and effective synthesis of both enantiomers of **1** was envisaged using the β-azido alcohol **2** from the microbiological reduction of the corresponding azido ketone, thus avoiding the problem of the resolution of a racemic mixture. In this paper, we describe the preparation of the optically pure synthon **2** by microbiological reduction as well as its conversion into both enantiomers of 2-amino-1-phenyl-1-propanone (**1**).

Results and Discussion

Microbiological Reduction of 2-Azido-1-phenyl-1-propanone (4). The microbiological reduction of 2-azido-1-phenyl-1-propanone, **4**, was studied in order to prepare the corresponding azido alcohols, **2**. Ketone **4** was obtained by treatment of the corresponding bromo ketone **3** with sodium azide following a method described previously[7] (Scheme 1).

The study of the microbiological reduction of **4** was realized with the same microorganisms as those previously used for the reduction of α-azido ketones:[6] the yeasts (*Saccharomyces cerevisiae* and *Rhodotorula glutinis*), the fungi (*Beauveria sulfurescens, Cunninghamella elegans*, *Geotrichum candidum*, *Mortierella isabellina* and *Sporotrichum exile*) and the bacterium *Lactobacillus kefir*. The bakers' yeast (*S. cerevisiae*) was used freeze-dried under nonfermenting conditions, *i.e.* suspended in water without added sugar. The bioconversions with the other microorganisms were done with washed resting cells, except *R. glutinis*. Growing cells were used for this microorganism.

First, a rate study was conducted with each microorganism. The results showed that all the microorganisms reduced **4** after an incubation time of 24 h, except *C. elegans* and *S. exile*, which subsequently were not used for quantitative assays. The percent conversion of α-azido ketone was determined by studying the residue from the bioconversion by GC, but the diastereomeric azido alcohols gave a single peak regardless of the GC conditions. The proportions of each isomer were determined, in consequence, by the use of ^{1}H NMR spectroscopy, which distinguished clearly between the *syn* and *anti* diastereomers of **2**.

Quantitative assays were carried out for an incubation time of 24 h with all the microorganisms which reduced **4**. However, separation of the two diastereoisomers required their derivatization with TBDMS-triflate.[8] Silyl ether formation was quantitative, and the *syn* **5a** and *anti* **5b** diastereoisomers could be separated by semi-preparative HPLC (Table 1).

Only *L. kefir* and *M. isabellina* yielded an alcohol with the (*S*) absolute configuration. But both diastereoisomers exhibited medium enantiomeric excesses of 44% for the *syn* and 61% for the *anti* isomer with *L. kefir*, and very low with *M. isabellina*. All the other microorganisms gave the (*R*) alcohol and in all cases, the *anti* diastereoisomers were optically pure. Bakers' yeast and *R. glutinis* were the only microorganisms yielding the *syn* diastereoisomer with an excellent enantiomeric excess. The indicated chemical yields are those of the TBDMS-protected azido alcohols after purification. The low yields obtained with bakers' yeast and *L. kefir* were due to the recovered quantity of α-azido ketone which did not react (60 and 30%, respectively). In all other cases, the reduction was complete and the yields were good or even excellent as with *R. glutinis* (92%).

Determination of the enantiomeric excess of each diastereoisomer required the initial hydrolysis of the silyl group and the use of ^{1}H NMR on the azido alcohol in the presence of the chiral europium derivative: Eu(tfc)$_3$. Under these conditions, preferential shielding of the methyl group located at 1.15 ppm was observed, and the proportion of each enantiomer could be determined from their integration. The only disadvantage of this method is its precision (5%), and so an optically pure compound is noted as ee ≥95%.

Absolute configurations were determined by comparing the azido alcohols coming from the microbiological reduc-

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(2) Kohli, J. D.; Goldberg, L. I. *J. Pharm. Pharmacol.* **1982**, *34*, 338.
(3) Kalix, P. *Life Sci.* **1983**, *32*, 801.
(4) The synthesis of both enantiomers of **1**, as their hydrochlorides, was based on the resolution of (±)-norephedrine, with *O,O*-dibenzoyl-*d*-tartaric acid. A three-step sequence of N-protection, oxidation to the ketone, and N-deprotection yielded the natural cathinone and its enantiomer.
(5) Besse, P.; Veschambre, H. *Tetrahedron: Asymmetry* **1993**, *4*, 1271.
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(8) Gassman, P. G.; Haberman, L. M. *J. Org. Chem.* **1986**, *51*, 5010.

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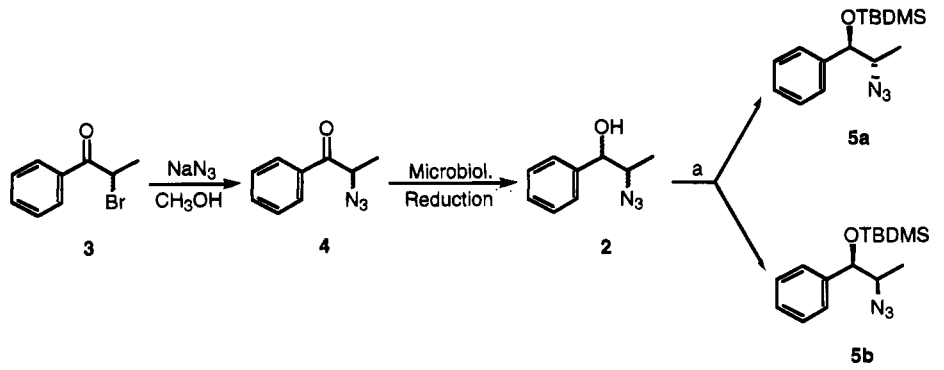
Scheme 1[a]



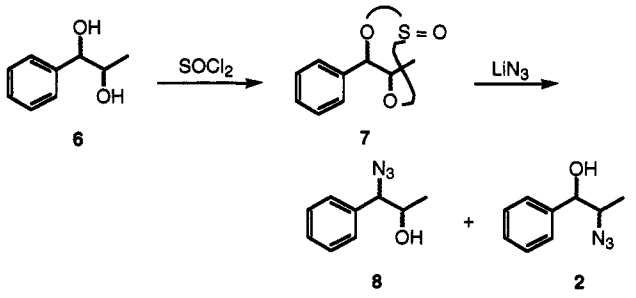
3 4 2 5a 5b

[a] Reaction conditions: (a) (i) TBDMS-triflate, (ii) HPLC.

Table 1. Microbiological Reduction of 2-Azido-1-phenyl-1-propanone (4)

	syn TBDMS derivatives			*anti* TBDMS derivatives			
	$[\alpha]^{25}_J$	ee, %	config	$[\alpha]^{25}_J$	ee, %	config	yield, %
Rhodotorula glutinis	−139	≥95	(1*R*,2*R*)	−60	≥95	(1*R*,2*S*)	92 (55/45)
bakers' yeast	−139	≥95	(1*R*,2*R*)	−60	≥95	(1*R*,2*S*)	35 (50/50)
Geotrichum candidum	−28	20	(1*R*,2*R*)	−60	≥95	(1*R*,2*S*)	72 (35/65)
Beauveria sulfurescens	+14	10	(1*S*,2*S*)	−60	≥95	(1*R*,2*S*)	85 (70/30)
Mortierella isabellina	+9	6	(1*S*,2*S*)	+12	23	(1*S*,2*R*)	75 (55/45)
Lactobacillus kefir	+61	44	(1*S*,2*S*)	+32	61	(1*S*,2*R*)	45 (70/30)

Scheme 2



6 7 8 2

tion with their counterparts obtained by a stereospecific synthesis from the β-diol **6** *via* the formation of cyclic sulfite **7** by the method of Lohray[9] (Scheme 2). The opening of the sulfite is not regioselective and a mixture of two isomeric azido alcohols (**8** and **2**) is obtained.

The stereochemistry of the reaction being known, the absolute configuration of the azido alcohol is deduced directly from that of the starting diol. From the (1*R*,2*S*) and (1*S*,2*S*)-1-phenyl-1,2-propanediols **6**, the (1*R*,2*R*) and (1*S*,2*R*)-2-azido-1-phenyl-1-propanols were prepared (for complete experimental data see ref 6) and converted into the corresponding TBDMS derivatives. Comparison of their physical constants (optical rotation, ^1H and ^{13}C NMR) with those of the TBDMS-protected azido alcohols from the microbiological reduction allowed the assignment of all absolute configurations.

Although all possible diastereoisomers were not obtained optically pure, the screening was not extended. Indeed, during the conversion of these synthons into the enantiomers of cathinone, the alcohol function becomes a ketone, and only the presence of a (2*S*) or (2*R*) optically pure asymmetric carbon is necessary. The microbiological reduction with *R. glutinis* gave two diastereoisomeric azido alcohols in near equal proportion with excellent chemical (92%) and optical yields (≥95% ee for each diastereoisomer). For shorter incubation times, the ratio of the azido alcohols *syn/anti* (55/45) did not change.

Synthesis of the Enantiomers of 2-Amino-1-phenyl-1-propanone (1). Initially, a synthesis of both enantiomers of cathinone was made from each of the TBDMS-derivatives **5a** and **5b**.[10] During this synthesis, it was observed that the diastereoisomers of a racemic mixture of N-Boc and O-TBDMS protected amino alcohols, one of the intermediates, could be separated easily by column chromatography on silica gel. Thus a new synthetic pathway was envisaged, starting directly from the diastereomeric mixture of **2a** and **2b** coming from the microbiological reduction of **4** (Scheme 3).

We considered it prudent to convert the azide group into a protected amine, before oxidizing the alcohol to the ketone, as it has been shown that cathinone, **1**, is prone to racemization if the amine is free.[1] The method of Saito *et al.*[11] constituted a very convenient one-pot protocol for the direct conversion of the azido group to the N-Boc amino group. Treatment of the diastereomeric mixture (**2a** and **2b**) with di-*tert*-butyl dicarbonate (Boc_2O) in a suspension of 10% Pd/C in ethyl acetate under a hydrogen atmosphere gave the compounds **9a** and **9b** in a 92% yield. They were separated by column chromatography on silica gel. Oxidation of each isomer, **9a** and **9b**, was done following the method of Cossio *et al.*,[12] who used pyridinium chlorochromate (PCC). Compounds **10a** and **10b** were obtained in a 86% yield and were characterized by their NMR spectra, specific rotations, and their elemental analyses. Hydrolysis with 3 N hydrochloric acid of **10a** or **10b** gave, in the last step, the two optically

(9) Lohray, B. B.; Ahuja, J. R. *J. Chem. Soc., Chem. Commun.* **1991**, 95.

(10) **5a** or **5b** was treated with $(Boc)_2O$ under a hydrogen atmosphere according to Saito *et al.*,[11] and the compounds obtained were oxidized with PDC in the presence of $SiMe_3Cl$ according to Cossio *et al.*[12] Hydrolysis in acidic medium (3 N HCl) led to **1a** and **1b** with a 24 and 30% yield, respectively.

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(12) Cossio, F. P.; Aizpurua, J. M.; Palomo, C. *Can. J. Chem.* **1986**, *64*, 225.

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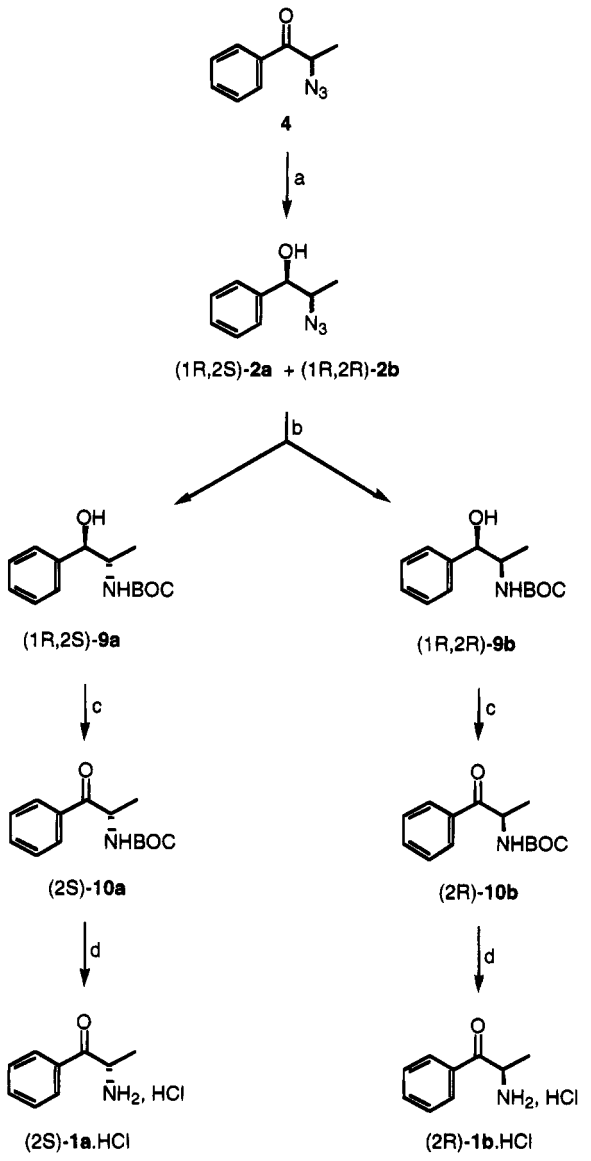
Scheme 3[a]



[a] Reaction conditions: (a) Microbiological reduction with *R. glutinis*; (b) (i) 10% Pd/C, H_2, $(Boc)_2O$, EtOAc, (ii) column chromatography; (c) PCC; (d) 3 N HCl–EtOAc.

pure enantiomers of 2-amino-1-phenyl-1-propanone hydrochloride, **1**·HCl. They were found to have, after recrystallization, the same physical constants (melting points and specific rotations) as those described by Berrang *et al.*[1]

The enantiomeric excesses of the isomers of **9** and **10** were identical to those of the starting compound, **2**, because the chemical reactions take place without affecting the asymmetric carbon atoms.

This new synthesis of cathinone avoids the resolution of norephedrine used by Berrang *et al.*[1] Both enantiomers **1a** and **1b** were obtained in four steps from **4** with an overall yield of 33 and 40%, respectively.

Experimental Section

Melting points are uncorrected. Optical rotations were recorded at the mercury J line (λ = 578 nm) in $CHCl_3$ solution. NMR spectra were recorded in $CDCl_3$ or CD_3OD at 400 MHz (^1H) and 100.61 MHz (^{13}C). Chemical shifts are relative to $CDCl_3$ or CD_3OD. All reaction solvents were distilled before use.

Gas phase chromatography (GC) analyses were performed by using a 25m × 0.32 mm capillary column coated with Carbowax 20 M. Reactions were monitored by TLC using silica gel Kieselgel 60 PF plates and the purification of products was performed on silica gel Merck 60 (70–230 μm) with mixtures of pentane and Et_2O as the mobile phase.

The microorganisms were all laboratory-grown except freeze-dried bakers' yeast, which was a commercial product (ANCEL S. A. Strasbourg). Preculture and culture conditions as well as bioconversion conditions have been described elsewhere.[5]

2-Azido-1-phenyl-1-propanone (4). To a solution of 2.1 g (10 mmol) of 2-bromo-1-phenyl-1-propanone[5] in 3 mL of CH_3OH, with stirring and cooling at 0 °C, was added 0.650 g (10 mmol) of NaN_3. After stirring overnight at room temperature, the methanol was evaporated under vacuum. The residue was diluted with H_2O and extracted three times with Et_2O. The organic phase was dried over anhydrous $MgSO_4$. After evaporation of Et_2O, the pure azido ketone **4** (1.6 g) was obtained in a 95% yield. ^1H NMR ($CDCl_3$) δ: 1.59 (d, 3H, J = 7 Hz); 4.73 (q, 1H, J = 7 Hz); 7.40–7.58 (m, 2H); 7.59–7.72 (m, 1H); 7.88–8.05 (m, 2H). ^{13}C NMR δ: 16.5; 58.5; 128.7; 129.0; 134.0; 134.4; 196.8. Anal. Calcd for $C_9H_9ON_3$: C: 61.70; H: 5.18; N: 23.98. Found: C: 61.70; H: 5.20; N: 23.90.

Microbiological Reduction of 2-Azido-1-phenyl-1-propanone (4). Incubation time was 24 h. GC oven temperature was 170 °C. After isolation of the diastereomeric azido alcohols **2**, the alcohol functionality was protected by TBDMS, according to the described method,[8] in order to separate the two diastereoisomers by HPLC.

2-Azido-1-(*tert*-butyldimethylsilyloxy)-1-phenylpropane (5). To an ice-cold solution of 715 mg of dry and freshly distilled pyridine (2.0 equiv) and 800 mg (1 equiv, 4.5 mmol) of **2** in 4.5 mL of dry CH_2Cl_2 was added slowly 1.56 mL (1.5 equiv, 6.8 mmol, 1.80 g) of TBDMS-triflate. After 30 min, the reaction mixture was diluted with Et_2O and poured into a saturated solution of $NaHCO_3$ (10 mL). After several extractions with Et_2O, the organic extracts were dried over anhydrous $MgSO_4$ and evaporated under vacuum. The residue was purified by column chromatography (eluent: pentane) and gave 1.25 g (95% yield) of **5**. Then, the two diastereoisomers **5a** and **5b** were separated by semipreparative HPLC by using a Nucleosil 5 μm column. The eluent was isooctane, 2 mL/min.

Results obtained with *Rhodotorula glutinis*. From ten flasks, 45% (−)-(1*R*,2*S*)-**5a** and 55% (−)-(1*R*,2*R*)-**5b** were obtained. Yield: 92%.

(−)-(1*R*,2*S*)-2-Azido-1-(*tert*-butyldimethylsilyloxy)-1-phenylpropane (5a): 0.345 g; R_f (eluent: pentane): 0.02. GC t_R = 280 s. ^1H NMR ($CDCl_3$) δ: −0.12 (s, 3H); 0.11 (s, 3H); 0.91 (s, 9H); 1.18 (d, 3H, J = 8 Hz); 3.51 (td, 1H, J_{2-1} = 5 Hz; J_{2-3} = 8 Hz); 4.68 (d, 1H, J_{1-2} = 5 Hz); 7.25–7.35 (m, 5H). ^{13}C NMR δ: −3.8; −3.3; 13.6; 18.2; 25.9; 63.2; 77.9; 126.8, 128.2; 127.8; 141.4. Anal. Calcd for $C_{15}H_{25}N_3OSi$: C: 61.81; H: 8.64; N: 14.42; Si: 9.64. Found: C: 61.93; H: 8.64; N: 14.39; Si: 9.61. $[\alpha]^{25}_J$ = −60 (*c* 0.01, $CHCl_3$); ee ≥95%.

(−)-(1*R*,2*R*)-2-Azido-1-(*tert*-butyldimethylsilyloxy)-1-phenylpropane (5b): 0.420 g; R_f (eluent: pentane): 0.02. GC t_R = 280 s. ^1H NMR ($CDCl_3$) δ: −0.12 (s, 3H); 0.10 (s, 3H); 0.91 (s, 9H); 1.10 (d, 3H, J = 7 Hz); 3.47 (qu, 1H, J = 7 Hz); 4.52 (d, 1H, J = 7 Hz); 7.20–7.35 (m, 5H). ^{13}C NMR δ: −3.8; −3.4; 16.2; 18.1; 25.8; 63.8; 79.5; 127.0, 128.2; 127.9; 141.7. Anal. Calcd for $C_{15}H_{25}N_3OSi$: C: 61.81; H: 8.64; N: 14.42; Si: 9.64. Found: C: 61.88; H: 8.65; N: 14.46; Si: 9.61. $[\alpha]^{25}_J$ = −139 (*c* 0.04, $CHCl_3$); ee ≥95%.

Results obtained with Bakers' yeast (*S. cerevisiae*). From seven flasks, 60% 2-azido-1-phenyl-1-propanone (**4**), 20% (−)-(1*R*,2*S*)-**5a**, and 20% (−)-(1*R*,2*R*)-**5b** were obtained. Yield: 35%.

(−)-(1*R*,2*S*)-2-Azido-1-(*tert*-butyldimethylsilyloxy)-1-phenylpropane (5a): 0.100 g; $[\alpha]^{25}_J$ = −60 (*c* 0.02, $CHCl_3$); ee ≥95%.

(−)-(1*R*,2*R*)-2-Azido-1-(*tert*-butyldimethylsilyloxy)-1-phenylpropane (5b): 0.100 g; $[\alpha]^{25}_J$ = −139 (*c* 0.02, $CHCl_3$); ee ≥95%.

Results obtained with *Geotrichum candidum*. From five flasks, 65% (−)-(1*R*,2*S*)-**5a** and 35% (−)-(1*R*,2*R*)-**5b** were obtained. Yield: 72%.

(−)-(1*R*,2*S*)-2-Azido-1-(*tert*-butyldimethylsilyloxy)-1-phenylpropane (5a): 0.195 g; $[\alpha]^{25}_J$ = −60 (*c* 0.03, $CHCl_3$); ee ≥95%.

(−)-(1*R*,2*R*)-2-azido-1-(*tert*-butyldimethylsilyloxy)-1-phenylpropane (5b): 0.105 g; $[\alpha]^{25}_J = -28$ (*c* 0.02, $CHCl_3$); ee = 20%.

Results obtained with *Beauveria sulfurescens*. From seven flasks, 30% (−)-(1*R*,2*S*)-**5a** and 70% (+)-(1*S*,2*S*)-**5** were obtained. Yield: 85%.

(−)-(1*R*,2*S*)-2-Azido-1-(*tert*-butyldimethylsilyloxy)-1-phenylpropane (5a): 0.150 g; $[\alpha]^{25}_J = -60$ (*c* 0.03, $CHCl_3$); ee ≥95%.

(+)-(1*S*,2*S*)-2-Azido-1-(*tert*-butyldimethylsilyloxy)-1-phenylpropane: 0.345 g; $[\alpha]^{25}_J = +14$ (*c* 0.05, $CHCl_3$); ee = 10%.

Results obtained with *Mortierella isabellina*. From six flasks, 45% (+)-(1*S*,2*R*)-**5** and 55% (+)-(1*S*,2*S*)-**5** were obtained. Yield: 75%.

(+)-(1*S*,2*R*)-2-Azido-1-(*tert*-butyldimethylsilyloxy)-1-phenylpropane: 0.170 g; $[\alpha]^{25}_J = +12$ (*c* 0.02, $CHCl_3$); ee = 23%.

(+)-(1*S*,2*S*)-2-Azido-1-(*tert*-butyldimethylsilyloxy)-1-phenylpropane: 0.205 g; $[\alpha]^{25}_J = +9$ (*c* 0.03, $CHCl_3$); ee = 6%.

Results obtained with *Lactobacillus kefir*. From six flasks, 30% 2-azido-1-phenyl-1-propanone (**4**), 20% (+)-(1*S*,2*R*)-**5**, and 50% (+)-(1*S*,2*S*)-**5** were obtained. Yield: 45%.

(+)-(1*S*,2*R*)-2-Azido-1-(*tert*-butyldimethylsilyloxy)-1-phenylpropane: 0.070 g; $[\alpha]^{25}_J = +32$ (*c* 0.01, $CHCl_3$); ee = 61%.

(+)-(1*S*,2*S*)-2-Azido-1-(*tert*-butyldimethylsilyloxy)-1-phenylpropane: 0.165 g; $[\alpha]^{25}_J = +61$ (*c* 0.04, $CHCl_3$); ee = 44%.

Synthesis of Enantiomers of 2-Amino-1-phenyl-1-propanone Hydrochloride from 2-Azido-1-phenyl-1-propanol (2). After the preparation and growth of the *Rhodotorula glutinis* for 60 h at 27 °C as previously described,[13] the substrate, ketone **4**, was added to the culture (50 μL/100 mL of culture) under sterile conditions. After a 24 h incubation at 27 °C on a rotary shaker set at 200 rpm, the mixture was centrifugated at 8000 rpm. The liquor was extracted continuously with Et_2O for 24 h, and the ethereal solution was dried over anhydrous $MgSO_4$. The residue was filtered rapidly on a short column of silica gel (eluent: pentane/ether 90/10). A mixture of pure diastereoisomers (1*R*,2*S*) and (1*R*,2*R*) of **2** was obtained with 97% yield. **2a** and **2b** described below were obtained after the hydrolysis of **5a** and **5b**.

(+)-(1*R*,2*S*)-2-Azido-1-phenyl-1-propanol (2a). R_f (eluent: pentane/ether 90/10): 0.20. GC t_R = 910 s. ^1H NMR ($CDCl_3$) δ SPCLN 1.21 (d, 3H, J_{3-2} = 6 Hz); 1.60 (s, 1H, exchangeable with D_2O); 3.75 (qd, 1H, J_{2-3} = 6 Hz, J_{2-1} = 4.5 Hz); 4.76 (dd, 1H, J_{1-2} = 4.5 Hz, $J_{1\text{-}OH}$ = 2 Hz); 7.30−7.45 (m, 5H). ^{13}C NMR δ: 13.6; 62.5; 76.5; 126.5; 128.2; 128.6; 140.2. Anal. Calcd for $C_9H_{11}ON_3$: C: 61.35; H: 5.72; N: 23.85. Found: C: 61.40; H: 5.75; N: 23.78. $[\alpha]^{25}_J = +50$ (*c* 0.01, $CHCl_3$); ee ≥98%.

(−)-(1*R*,2*R*)-2-Azido-1-phenyl-1-propanol (2b). R_f (eluent: pentane/ether 90/10): 0.19. GC t_R = 910 s. ^1H NMR ($CDCl_3$) δ SPCLN 1.12 (d, 3H, J_{3-2} = 7 Hz); 2.50 (s, 1H, exchangeable with D_2O); 3.68 (q, 1H, J = 7 Hz); 4.48 (d, 1H, J_{1-2} = 7.5 Hz); 7.30−7.40 (m, 5H). ^{13}C NMR δ: 15.9; 63.5; 78.1; 126.8; 128.4; 128.6; 140.4. Anal. Calcd for $C_9H_{11}ON_3$: C: 61.35; H: 5.72; N: 23.85. Found: C: 61.29; H: 5.80; N: 23.92. $[\alpha]^{25}_J = -140$ (*c* 0.03, $CHCl_3$); ee ≥98%.

2-*N*-Boc-Amino-1-phenyl-1-propanol (9). A suspension of 40 mg of Pd/C (10%) in 4 mL of EtOAc was stirred vigorously under a hydrogen atmosphere for 2 h. To this was added a mixture of 370 mg (1 equiv, 2.1 mmol) of **2a** and **2b** and 592 mg (1.2 equiv, 2.71 mmol) of $(Boc)_2O$ in 2 mL of EtOAc, and the resulting mixture was stirred under hydrogen at room temperature for 24 h. The mixture was then filtered through a celite pad to eliminate the catalyst. The filtrate was concentrated *in vacuo* and the residue (700 mg) was purified on a silica gel column (120 g), eluent pentane/ether 70/30, to give 215 mg of **9a** and 262 mg of **9b** (92% total yield).

(−)-(1*R*,2*S*)-2-*N*-Boc-Amino-1-phenyl-1-propanol (9a): mp 91−93 °C. ^1H NMR ($CDCl_3$) δ: 0.97 (d, 3H, J = 6.9 Hz); 1.47 (s, 9H); 3.77 (s, 1H, exchangeable with D_2O); 3.97 (s, 1H); 4.77−4.95 (m, 1H); 4.85 (d, 1H, J = 8.5 Hz); 7.20−7.40 (m, 5H). ^{13}C NMR δ: 14.2; 28.3; 51.9; 76.2; 79.5; 126.2, 127.2; 128.0; 141.1; 159.1. Anal. Calcd for $C_{14}H_{21}NO_3$: C: 66.91; H: 8.42; N: 5.57. Found: C: 66.87; H: 8.44; N: 5.56. $[\alpha]^{25}_J = -63$ (*c* 0.06, $CHCl_3$); ee ≥95%.

(−)-(1*R*,2*R*)-2-*N*-Boc-Amino-1-phenyl-1-propanol (9b): mp 85−87 °C. ^1H NMR ($CDCl_3$) δ: 1.06 (d, 3H, J = 6.7 Hz); 1.50 (s, 9H); 3.50 (s,1H, exchangeable with D_2O); 3.86 (m, 1H); 4.50−4.58 (m, 1H); 4.75 (s, 1H); 7.15−7.45 (m, 5H). ^{13}C NMR δ: 17.6; 28.3; 52.3; 77.6; 79.6; 126.6, 127.6; 128.2; 141.7; 156.4. Anal. Calcd for $C_{14}H_{21}NO_3$: C: 66.91; H: 8.42; N: 5.57. Found: C: 66.87; H: 8.46; N: 5.54. $[\alpha]^{25}_J = -32$ (*c* 0.05, $CHCl_3$); ee ≥95%.

2-*N*-Boc-Amino-1-phenyl-1-propanone (10). To a suspension of PCC (1.19 mmol, 255 mg) in 10 mL of CH_2Cl_2 (freshly distilled from P_2O_5) was added a solution of 200 mg (0.8 mmol) of **9a** or **9b** in 2 mL of CH_2Cl_2 and the dark-brown reaction mixture was stirred at room temperature for 1.5 h. A volume of 10 mL of dry ether was added and the mixture was filtered through a Florisil column. The black deposit was washed with dry Et_2O and filtered as well. The filtrate was concentrated under vacuum to give 170 mg (86% yield) of **10**.

(−)-(2S)-2-*N*-Boc-Amino-1-phenyl-1-propanone (10a): mp 70−72 °C. ^1H NMR ($CDCl_3$) δ: 1.40 (d, 3H, J = 7 Hz); 1.50 (s, 9H); 5.30 (qu, 1H, J = 7 Hz); 5.61 (d, 1H, J = 7 Hz); 7.45−7.55 (m, 2H); 7.55−7.65 (m, 1H); 7.98 (d, 2H, J = 9.5 Hz). ^{13}C NMR δ: 19.9; 28.4; 51.1; 79.7; 128.7, 128.8; 133.7; 134.3; 155.2; 199.5. Anal. Calcd for $C_{14}H_{19}NO_3$: C: 67.45; H: 7.68; N: 5.62. Found: C: 67.32; H: 7.70; N: 5.64. $[\alpha]^{25}_J = -2$ (*c* 0.03, $CHCl_3$); ee ≥95%.

(+)-(2*R*)-2-*N*-Boc-Amino-1-phenyl-1-propanone (10b). Same melting point and NMR spectra as its (2*S*) enantiomer. $[\alpha]^{25}_J = +2$ (*c* 0.02, $CHCl_3$); ee ≥95%.

2-Amino-1-phenyl-1-propanone Hydrochloride (1). A suspension of 100 mg (0.40 mmol) of **10a** or **10b** in 3 mL of a mixture of 3 N HCl in EtOAc (3 N HCl:EtOAc 1:2) was stirred vigorously at room temperature for 30 min. The mixture was evaporated to dryness, and the residue was recrystallized from *i*-PrOH−Et_2O. After the sample was dried overnight, 75 mg of **1**·HCl was obtained (95% yield).

(−)-(2S)-2-Amino-1-phenyl-1-propanone Hydrochloride (1a.HCl). Overall yield = 33%. mp 180−182 °C. ^1H NMR (CD_3OD) δ: 1.80 (d, 3H, J = 7.5 Hz); 5.35 (q, 1H, J = 7.5 Hz); 7.70−7.85 (m, 2H); 7.85−7.95 (m, 1H); 8.27 (d, 2H, J = 8.1 Hz). ^{13}C NMR δ: 18.0; 53.1; 130.2; 130.6; 134.5; 136.1; 197.6. $[\alpha]^{25}_J = -48$ (*c* 0.02, H_2O); Lit.[1] $[\alpha]^{21}_D = -46.9$ (*c* 1, H_2O).

(+)-(2*R*)-2-Amino-1-phenyl-1-propanone Hydrochloride (1b·HCl). Overall yield = 40%. mp 181−182 °C. Same NMR spectra as its (2*S*) enantiomer. $[\alpha]^{25}_J = +48$ (*c* 0.07, H_2O); lit.[1] $[\alpha]^{23}_D = +47.3$ (*c* 1, H_2O).