

Stereoselective Reduction of Prochiral Ketones by Plant and Microbial Biocatalysts

K. JAVIDNIA, E. FAGHIIH-MIRZAEI^{1*}, R. MIRI, M. ATTARROSHAN AND K. ZOMORODIAN²

Medicinal and Natural Products Chemistry Research Center, Shiraz University of Medical Sciences, ²Department of Mycology and Parasitology, Faculty of Medicine, Shiraz University of Medical Sciences, Shiraz, ¹Department of Medicinal Chemistry, School of Pharmacy, Kerman University of Medical Sciences, Kerman, Iran

Javidnia, *et al.*: Stereoselective Reduction of Prochiral Ketones

Chiral alcohols are the key chiral building blocks to many enantiomerically pure pharmaceuticals. The biocatalytic approach in asymmetric reduction of corresponding prochiral ketones to the preparation of these optically pure substances is one of the most promising routes. The stereoselective reduction of different kinds of prochiral ketones catalyzed by various plants and microorganisms was studied in this work. Benzyl acetoacetate, methyl 3-oxopentanoate, ethyl 3-oxopentanoate, and ethyl butyryl acetate were chosen as the model substrates for β -ketoesters. Benzoyl acetonitrile, 3-chloro propiophenone, and 1-acetyl naphthalene were chosen as aromatic aliphatic ketones. Finally, 2-methyl benzophenone and 4-chloro benzophenone were selected as diaryl ketones. Plant catalysis was conducted by *Daucus carota*, *Brassica rapa*, *Brassica oleracea*, *Pastinaca sativa*, and *Raphanus sativus*. For microbial catalysis, *Aspergillus foetidus*, *Penicillium citrinum*, *Saccharomyces carlbergensis*, *Pichia fermentans*, and *Rhodotrula glutinis* were chosen. Chiral alcohols were obtained in high yields and with optical purity. A superiority in the microorganisms' performance in the bioreduction of prochiral ketones was detected. Among microorganisms, *Rhodotrula glutinis* showed remarkable results with nearly all substrates and is proposed for future studies.

Key words: Stereoselective, reduction, biocatalysts, prochiral ketones

The importance of obtaining enantiopure substances in the chemical or pharmaceutical industry has inspired considerable efforts to search for methods of constructing chiral precursors, especially optically active alcohols^[1,2]. These alcohols are important intermediates and building blocks for the synthesis of pharmaceutically active compounds such as orphenadrine, fluoxetine, tomoxetine, cloperastine, neobenodine, and carbinoxamine^[3].

Chiral alcohols with high optical purity can be obtained from the stereoselective reduction of prochiral ketones either by chemical or biological methods. Despite the vast progress of organic chemistry in chiral synthesis, biocatalysis as an alternative has attracted much attention recently from the viewpoint of green chemistry^[4].

Biocatalysis performed by whole cell living organisms is regarded as one of the most effective and promising routes because of its regio- and

stereoselectivity, mild and environment-friendly condition. This method appears advantageous over enzymatic reduction of carbonyl compounds using an isolated enzyme, since the oxido-reductase, cofactor (NAD(P)H) and its regenerating system are all located within the cell^[5,6].

There are numerous works on the asymmetric reduction reaction catalyzed by whole cell biocatalysts with excellent enantioselectivity and yield. The previously reported works can be divided into two periods. Before the year 2000, the focus was on microorganisms as biocatalysts. Baker's yeast was then the microorganism most widely used for the reduction of prochiral ketone^[7]. At the turn of century,

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*Address for correspondence

E-mail: ehsancontact@kmu.ac.ir

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reports on the use of whole plant cells to reduce prochiral ketones began to appear^[8]. *Daucus carota* has been the plant most frequently used to convert prochiral ketones to relevant chiral alcohols until now^[9-11].

Progressive studies on the use of biocatalysts in chemicals and pharmaceuticals to obtain important optically active alcohols show the great value of this method. The objective of the current study was to explore the asymmetric reduction of some important prochiral ketones (fig. 1). For this purpose, five plants (*D. carota*, *Brassica rapa*, *Brassica oleracea*, *Pastinaca sativa*, and *Raphnus sativus*) and five microorganisms (*Aspergillus foetidus*, *Penicillium citrinum*, *Saccharomyces carlbergensis*, *Pichia fermentans*, and *Rhodotrula glutinis*) were chosen because of their efficiency and availability. In this paper, we report our results in the bioreduction of important prochiral ketones (fig. 2) from different categories using the aforementioned biocatalysts.

MATERIALS AND METHODS

Optical rotations were measured with a Kruss P8100. The ¹H NMR spectra was obtained with an Avance III Bruker 400 MHz instrument using TMS

as the internal standard. Bioreduction reactions were monitored by GC-MS analysis (compound 1a-7a) equipped with an HP-5 Agilent capillary column (30 m×0.25 mm; 0.25 μm) and a CP-Chirasil-DEX CB Varian GC column. HPLC analysis (compound 8a, 9a) was carried out in a Knauer HPLC pump 1000, UV detector 2500 Knauer, and a 7725 injection valve with a 20 μl loop equipped with a Nucleocell Delta (4.6 mm×250 mm×5 μm) Macherey-Nagel, Germany. Preparative TLC was carried out on Silicagel 60 F₂₅₄ Merck (Darmstadt, Germany).

The substrate 3-chloropropiophenone (6a) was purchased from Acros Organics. Other substrates were purchased from Merck.

Biocatalysts:

Fresh carrots (*D. carota*), turnips (*Brassica rapa*), cabbages (*Brassica oleracea*), parsnips (*Pastinaca sativa*), and radishes (*Raphnus sativus*) were obtained from a local market. Freeze-dried *Aspergillus foetidus* (PTCC 5099), *Penicillium citrinum* (PTCC 5304), *Saccharomyces carlbergensis* (PTCC 5051), *Pichia fermentans* (PTCC 5296), and *Rhodotrula glutinis* (PTCC 5256) were bought from the Persian Type Culture Collection (Iranian Research Organization for Science and Technology).

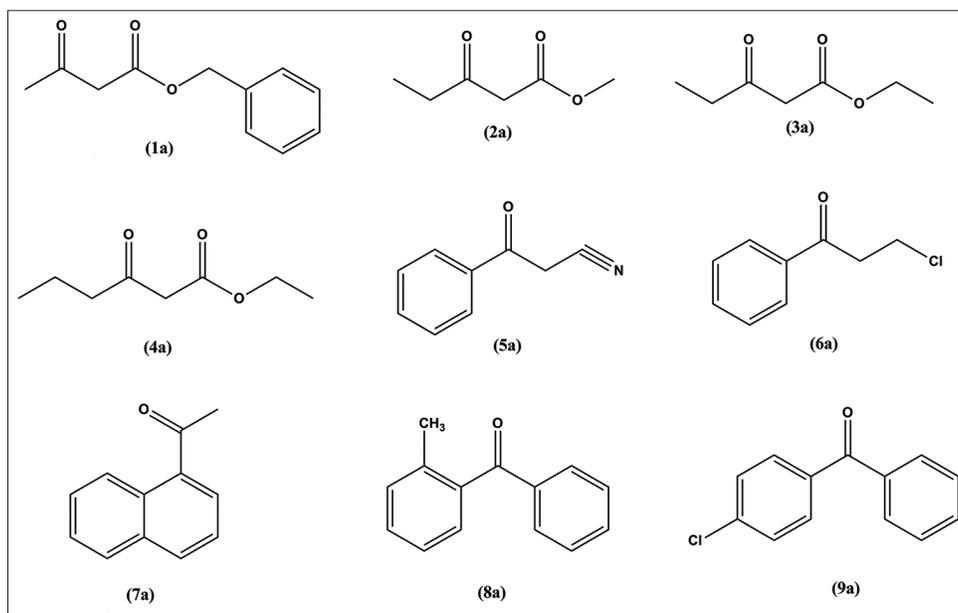


Fig. 1: Prochiral ketones used as substrates.

(1a): Benzyl acetoacetate, (2a): methyl 3-oxopentanoate, (3a): ethyl 3-oxopentanoate, (4a): ethyl butyrylacetate, (5a): benzoyl acetonitrile, (6a): 3-chloropropiophenone, (7a): 1-acetyl naphthalene, (8a): 2-methyl benzophenone, (9a): 4-chloro benzophenone.

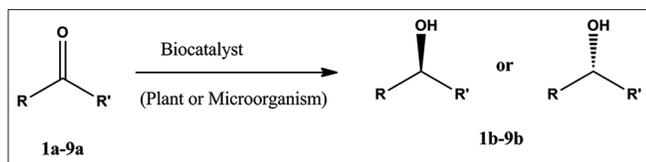


Fig. 2: Asymmetric reduction of prochiral ketones catalyzed by plants or microorganisms.

Benzyl-3-hydroxybutyrate (1b), methyl 3-hydroxypentanoate (2b), ethyl 3-hydroxypentanoate (3b), ethyl 3-hydroxyhexanoate (4b), 3-hydroxy-3-phenylpropanenitrile (5b), 3-chloro-1-phenylpropan-1-ol (6b), 1-(1-naphthyl) ethanol (7b), (2-methylphenyl)(phenyl) methanol (8b), (4-chlorophenyl)(phenyl)methanol (9b).

General procedure for the asymmetric reduction of ketones with plants:

The plant roots of *D. carota*, *B. rapa*, *R. sativus*, *P. sativa*, and *B. oleracea* were excised. Their surfaces were disinfected with 70% EtOH for 5 min and 20% NaClO for 10 min, and then they were rinsed thoroughly with sterile distilled water. Roots were cut and put in 500 ml Erlenmeyer flasks (75 g per each). The substrate (50 mg) was dissolved in 5 ml of absolute ethanol, and then the solution was added to each Erlenmeyer flask. Incubation was continued for 144 h (6 days). Each experiment was repeated at least three times.

General procedure for the asymmetric reduction of ketones with microorganisms:

The stock cultures were maintained on a Sabouraud dextrose agar medium at 4° and freshly sub-cultured before being used in transformation experiments. Ten 500 ml Erlenmeyer flasks, each containing 100 ml of Sabouraud broth medium, were inoculated with freshly obtained cells and incubated at 25° in a rotary shaker (150 rpm). The cultures were allowed to reach a constant cell density (detected by optical density or dry cell weight). The substrate (50 mg) was dissolved in 5 ml of absolute ethanol, and then solution was added to each Erlenmeyer flask. A higher concentration of substrate resulted in lower conversion and a decrease in yield. Incubation was continued for 144 h (6 days). Each experiment was repeated at least three times.

General procedure for preparation of racemic alcohols:

Compounds 1a-9a were reduced to the corresponding racemic alcohol with NaBH₄ in MeOH^[12]. The reduced products were purified by preparative TLC, and their chemical structures were confirmed by ¹H NMR.

Benzyl-3-hydroxybutyrate (1b): ¹H NMR (400 MHz, CHCl₃): δ 7.47-7.38 (m, 5H, CH-Ar), 5.18 (s, 2H,

CH₂O), 4.14-4.03 (m, 1H, CH), 3.58 (br s, 1H, OH), 2.58-2.54 (dd, 1H, CH₂), 2.49-2.44 (dd, 1H, CH₂), 1.20-1.18 (d, 3H, CH₃).

Methyl 3-hydroxypentanoate (2b): ¹H NMR (400 MHz, CHCl₃): δ 3.84-3.80 (m, 1H, CH), 3.71 (s, 3H, CH₃), 3.55 (br s, 1H, OH), 2.52-2.48 (dd, 1H, CH₂), 2.33-2.29 (dd, 1H, CH₂), 1.48-1.45 (m, 2H, CH₂), 0.85-0.79 (t, 3H, CH₃).

Ethyl 3-hydroxypentanoate (3b): ¹H NMR (400 MHz, CHCl₃): δ 4.14-4.11 (q, 2H, CH₂O), 3.89-3.85 (m, 1H, CH), 3.58 (br s, 1H, OH), 2.55-2.52 (dd, 1H, CH₂), 2.31-2.28 (dd, 1H, CH₂), 1.48-1.43 (m, 2H, CH₂), 1.27-1.23 (t, 3H, CH₃), 1.2-1.1 (t, 3H, CH₃).

Ethyl 3-hydroxyhexanoate (4b): ¹H NMR (400 MHz, CHCl₃): δ 4.17-4.13 (q, 2H, CH₂O), 3.91-3.85 (m, 1H, CH), 3.58 (br s, 1H, OH), 2.57-2.54 (dd, 1H, CH₂), 2.29-2.26 (dd, 1H, CH₂), 1.47-1.44 (m, 2H, CH₂), 1.33-1.29 (m, 2H, CH₂), 1.27-1.24 (t, 3H, CH₃), 1.1-0.9 (t, 3H, CH₃).

3-Hydroxy-3-phenylpropanenitrile (5b): ¹H NMR (400 MHz, CHCl₃): δ 7.34-7.19 (m, 5H, CH-Ar), 4.99-4.95 (m, 1H, CH), 3.19 (br s, 1H, OH), 2.70-2.69 (m, 2H, CH₂).

3-Chloro-1-phenylpropan-1-ol (6b): ¹H NMR (400 MHz, CHCl₃): δ 7.30-7.18 (m, 5H, CH-Ar), 4.89-4.86 (m, 1H, CH), 3.7-3.6 (m, 2H, CH₂-Cl), 3.66 (br s, 1H, OH), 2.21-2.13 (m, 1H, CH₂), 2.06-1.98 (m, 1H, CH₂).

1-(1-Naphthyl) ethanol (7b): ¹H NMR (400 MHz, CHCl₃): δ 7.72-7.27 (m, 7H, CH-Ar), 5.44-5.39 (q, 1H, CH), 2.44 (br s, 1H, OH), 1.47-1.45 (d, 3H, CH₃).

(2-Methylphenyl)(phenyl)methanol (8b): ¹H NMR (400 MHz, CHCl₃): δ 7.41-7.02 (m, 9H), 5.85 (s, 1H, CH), 2.21 (br s, 1H, OH), 2.13 (s, 3H, CH₃).

(4-Chlorophenyl)(phenyl)methanol (9b): ¹H NMR (400 MHz, CHCl₃): δ 7.26-7.17 (m, 9H, CH-Ar), 5.79-5.77 (m, 1H, CH), 2.23 (br s, 1H, OH).

Conversion rate analysis:

After 2 and 4 days of incubation, biomass was separated from the media by filtration (plants) or centrifugation (microorganism). The media was

extracted with EtOAc ($\times 3$). The solvent was dried over anhydrous Na_2SO_4 and removed in vacuo. The samples were analyzed by GC-MS (1a-7a) or HPLC (8a and 9a). The methods were established prior to sample analysis by use of racemic alcohols.

Enantiomeric excess analysis:

For the reduction of (1a-7a), enantiomeric separation was achieved on a Chirasil-Dex CB Varian GC column. For the reduction of (8a and 9a), enantiomer separation was achieved on a Nucleocell delta MN column (4.6mm \times 250mm, 5 μ m) *n*-Hexan/2-propanol 95/5 flow: 0.5 ml/min.

Assignment of absolute configuration for alcohols:

Optical rotations of the purified alcohols (1b-9b) obtained by bioreductions were measured and compared with the literature: Benzyl (*S*)-(+)-3-hydroxybutyrate (1b) $[\alpha]_D^{25} = +29.0$ (CHCl_3 , $c=1$)^[13]; methyl (*R*)-(-)-3-hydroxypentanoate (2b) $[\alpha]_D^{25} = -35.7$ (CHCl_3 , $c=1$)^[14]; ethyl (*R*)-(-)-3-hydroxypentanoate (3b) $[\alpha]_D^{25} = -34.6$ (CHCl_3 , $c=5$)^[14]; ethyl (*R*)-(-)-3-hydroxyhexanoate (4b) $[\alpha]_D^{25} = -24.3$ (CHCl_3 , $c=0.7$)^[15]; (*S*)-(-)-3-hydroxy-3-phenylpropanenitrile (5b) $[\alpha]_D^{20} = -57.0$ (EtOH, $c=1.1$)^[16]; (*R*)-(+)-3-chloro-1-phenylpropan-1-ol (6b) $[\alpha]_D^{22} = +24.3$ (CHCl_3 , $c=1$)^[17]; (*S*)-(-)-1-(1-naphthyl)ethanol (7b) $[\alpha]_D^{20} = -78.0$ (MeOH, $c=1$)^[18]; (*S*)-(+)-(2-methylphenyl) (phenyl) methanol (8b) $[\alpha]_D^{22} = +6.38$ (CHCl_3 , $c=0.9$)^[19]; (*S*)-(+)-(4-chlorophenyl) (phenyl)methanol (9b) $[\alpha]_D^{22} = +22$ (CHCl_3 , $c=0.48$)^[20]

RESULTS AND DISCUSSION

Among the plants tested, *B. oleracea*, *D. carota*, and *P. sativa* reduced benzyl acetoacetate (1a) with a high conversion rate, and all plants produced benzyl (*S*)-(+)-3-hydroxybutyrate (*S*-1b). *B. oleracea* achieved the highest stereoselectivity (>99% *ee*) (Table 1). All microorganisms except *P. citrinum* could produce (*S*)-alcohol with a high conversion rate; using *S. carlbergensis* and *A. foetidus* as biocatalysts resulted in a higher optical purity. (*R*)-Alcohol was not produced in any bioreduction.

B. oleracea, *R. sativus*, and *P. sativa* could reduce methyl 3-oxopentanoate (2a) when it was used as the substrate. The stereoselectivity of bioreduction with *B. oleracea* was quite good (>76% *ee* *S*-2b), although the conversion rate was highest with *R. sativus*. All microorganisms except *P. citrinum* managed to reduce

TABLE 1: RESULTS FOR BIOREDUCTION OF BENZYL ACETOACETATE (1a)

Compound 1a	Biocatalyst	Time (days)	% conversion	Enantiomeric excess%
Plants and microorganisms	<i>D. carota</i>	2	91	38 (S)
		4	93	70 (S)
	<i>B. oleracea</i>	2	98	>99 (S)
		4	100	>99 (S)
	<i>P. sativa</i>	2	45	70 (S)
		4	100	70 (S)
	<i>S. carlbergensis</i>	3	84	>99 (S)
		6	100	96 (S)
	<i>P. fermentans</i>	2	100	75 (S)
		4	100	75 (S)
	<i>R. glutinis</i>	2	85	76 (S)
		4	85	76 (S)
<i>P. citrinum</i>	2	13	73 (S)	
	4	13	73 (S)	
<i>A. foetidus</i>	2	96	73 (S)	
	4	96	>99 (S)	

Absolute configuration is in parenthesis. *D. carota*: *Daucus carota*, *B. oleracea*: *Brassica oleracea*, *P. sativa*: *Pastinaca sativa*, *S. carlbergensis*: *Saccharomyces carlbergensis*, *P. fermentans*: *Pichia fermentans*, *R. glutinis*: *Rhodotrula glutinis*, *P. citrinum*: *Penicillium citrinum*, *A. foetidus*: *Aspergillus foetidus*

2a to (*R*-2b) with high yield and stereoselectivity (Table 2).

R. sativus and *P. sativa* could accomplish the bioreduction of ethyl 3-oxopentanoate (3a), but the stereoselectivity was achieved with *P. sativa* rather than *R. sativus*. Almost all microorganisms could reduce 3a to (*R*-3b) with high yield and stereoselectivity (Table 3).

For the compound ethyl butyrylacetate (4a), only *R. sativus* could produce 4b in high optical purity and yield. All microorganisms except *R. glutinis* accomplished the bioreduction with high optical purity and yield, and all produced (*R*-4b, Table 4).

Among plants and microorganisms, only *R. glutinis* and *A. foetidus* could reduce benzoyl acetonitrile (5a). Using *R. glutinis* as the biocatalyst resulted in an outstanding conversion yield and optical purity with (*S*)-(-)-3-hydroxy-3-phenyl propanenitrile (*S*-5b) as the main product, which is a useful precursor in the synthesis of (*S*)-fluoxetine, the active form of fluoxetine (Table 5).

In the case of 3-chloropropiophenone (6a), the plants *D. carota* and *P. sativa* could reduce the ketone with low yield but high optical purity. Among microorganisms, *S. carlbergensis*, *P. citrinum*, and *R. glutinis* were capable of producing 3-chloro-1-

TABLE 2: RESULTS FOR BIOREDUCTION OF METHYL 3-OXOPENTANOATE (2a)

Compound 2a	Biocatalyst	Time (days)	% conversion	Enantiomeric excess %
Plants and microorganisms	<i>B. oleracea</i>	2	44	-
		4	52	76 (S)
	<i>R. sativus</i>	2	0	-
		4	91	34 (R)
	<i>P. sativa</i>	2	71	<2
		4	73	low
	<i>S. carlbergensis</i>	2	79	-
		4	100	92 (R)
	<i>P. fermentans</i>	2	100	99 (R)
		4	100	99 (R)
	<i>R. glutinis</i>	2	100	72 (R)
		4	100	72 (R)
	<i>A. foetidus</i>	2	100	98 (R)
		4	100	98 (R)

Absolute configuration is in parenthesis. *B. oleracea*: *Brassica oleracea*, *R. sativus*: *Raphanus sativus*, *P. sativa*: *Pastinaca sativa*, *S. carlbergensis*: *Saccharomyces carlbergensis*, *P. fermentans*: *Pichia fermentans*, *R. glutinis*: *Rhodotrula glutinis*, *A. foetidus*: *Aspergillus foetidus*, *P. citrinum*: *Penicillium citrinum*

TABLE 3: RESULTS FOR BIOREDUCTION OF ETHYL 3-OXOPENTANOATE (3a)

Compound 3a	Biocatalyst	Time (days)	% conversion	Enantiomeric excess %
Plants and microorganisms	<i>R. sativus</i>	2	0	-
		4	100	6 (R)
	<i>P. sativa</i>	2	65	82 (S)
		4	80	82 (S)
	<i>S. carlbergensis</i>	2	100	95 (R)
		4	100	95 (R)
	<i>P. fermentans</i>	2	100	99 (R)
		4	100	99 (R)
	<i>R. glutinis</i>	2	100	72 (R)
		4	100	72 (R)
	<i>P. citrinum</i>	2	100	98 (R)
		4	100	98 (R)
	<i>A. foetidus</i>	2	100	98 (R)
		4	100	98 (R)

Absolute configuration is in parenthesis. *R. sativus*: *Raphanus sativus*, *P. sativa*: *Pastinaca sativa*, *S. carlbergensis*: *Saccharomyces carlbergensis*, *P. fermentans*: *Pichia fermentans*, *R. glutinis*: *Rhodotrula glutinis*, *A. foetidus*: *Aspergillus foetidus*, *P. citrinum*: *Penicillium citrinum*, *R. glutinis*: *Rhodotrula glutinis*

phenyl propanol (6b). *R. glutinis* could produce (S)-(-)-3-chloro-1-phenylpropanol, a useful precursor for the synthesis of (S)-fluoxetine, with acceptable yield (70%) and high optical purity (93% *ee*). As could be expected, elimination and dehalogenation products such as propiophenone, 1-phenyl-1-propanol, and phenyl vinyl ketones were also observed in the reduction of (6a) (Table 5).

For compound (7a), the conversion rate when using plants as the biocatalysts was very low and

TABLE 4: RESULTS FOR BIOREDUCTION OF ETHYL BUTYRYLACETATE (4a)

Compound 4a	Biocatalyst	Time (days)	% conversion	Enantiomeric excess %
Plants and microorganisms	<i>B. oleracea</i>	2	0	-
		4	17	-
	<i>R. sativus</i>	2	30	64 (R)
		4	100	90 (R)
	<i>P. sativa</i>	2	72	14 (S)
		4	72	14 (S)
	<i>S. carlbergensis</i>	2	100	98 (R)
		4	100	98 (R)
	<i>P. fermentans</i>	2	100	>99 (R)
		4	100	>99 (R)
	<i>P. citrinum</i>	2	100	>99 (R)
		4	100	>99 (R)
<i>A. foetidus</i>	2	100	99 (R)	
	4	100	99 (R)	

Absolute configuration is in parenthesis. *R. sativus*: *Raphanus sativus*, *P. sativa*: *Pastinaca sativa*, *S. carlbergensis*: *Saccharomyces carlbergensis*, *P. fermentans*: *Pichia fermentans*, *A. foetidus*: *Aspergillus foetidus*, *B. oleracea*: *Brassica oleracea*, *P. citrinum*: *Penicillium citrinum*

TABLE 5: RESULTS FOR BIOREDUCTION OF BENZOYL ACETONITRILE (5a) AN 3-CHLOROPROPIOPHENONE (6a)

	Biocatalyst	Time (days)	% conversion	Enantiomeric excess %	
Compound 5a	Microorganisms	<i>R. glutinis</i>	2	99	96 (S)
			4	99	96 (S)
	<i>A. foetidus</i>	2	15	-	
		4	70	7 (S)	
Compound 6a	Plants and microorganisms	<i>D. carota</i>	2	0	>99 (S)
			4	25	
	<i>P. sativa</i>	2	30	90 (S)	
		4	32	90 (S)	
	<i>S. carlbergensis</i>	2	29	65 (S)	
		4	29	65 (S)	
	<i>R. glutinis</i>	2	70	93 (S)	
		4	70	93 (S)	
	<i>P. citrinum</i>	2	40	40 (S)	
		4	40	40 (S)	

Absolute configuration is in parenthesis. *P. citrinum*: *Penicillium citrinum*, *P. sativa*: *Pastinaca sativa*, *D. carota*: *Daucus carota*, *A. foetidus*: *Aspergillus foetidus*, *S. carlbergensis*: *Saccharomyces carlbergensis*, *R. glutinis*: *Rhodotrula glutinis*

insignificant. Among microorganisms, only *R. glutinis* could produce optically active alcohol (S-7b) with high yield (94%) and stereoselectivity (>96%). (S)-(-)-1-1-(naphthyl)ethanol (S-7b) is an important intermediate in the synthesis of mevinic acid which has an HMG-Co-A reductase inhibitory effect (Table 6).

Diaryl ketones like 2-methyl benzophenone (8a) and 4-chloro benzophenone (9a) are

important prochiral ketones for the production of diarylmethanols which are important intermediates for the synthesis of pharmaceutically interesting molecules, such as (*S*)-cloprastine, (*S*)-carbinoxamine, (*R*)-orphenadrine, (*R*)-neobenodine. Among plants and microorganisms, only *R. glutinis* could produce the relevant chiral alcohol (*S*-8b) for compound (8a) with 45% conversion rate and more than 99% optical purity. In the case of compound (9a), only *S. carlbergensis* and *R. glutinis* could produce chiral alcohol (*R*-9b). The conversion rate (>99%) and optical purity (>99% *ee*) were very high when *R. glutinis* was used as the biocatalyst (Table 7).

In view of these results, it can be concluded that plant and microbial biocatalysis is an efficient, easy, green procedure and an alternative to chemical methods for the production of enantiopure chiral alcohols. Overall, our results show the superiority

TABLE 6: RESULTS FOR BIOREDUCTION OF 1-ACETYL NAPHTHALENE (7a)

Compound 7a	Biocatalyst	Time (days)	% conversion	Enantiomeric excess %
Plants and microorganisms	<i>D. carota</i>	2	6	>99 (S)
		4	3	>99 (S)
	<i>B. rapa</i>	2	3	>99 (S)
		4	3	>99 (S)
	<i>B. oleracea</i>	2	3	>99 (S)
		4	3	>99 (S)
	<i>P. sativa</i>	2	3	>99 (S)
		4	3	>99 (S)
	<i>S. carlbergensis</i>	2	5	>99 (S)
		4	5	>99 (S)
	<i>R. glutinis</i>	2	25	96 (S)
		4	94	96 (S)

Absolute configuration is in parenthesis. *D. carota*: *Daucus carota*, *B. rapa*: *Brassica rapa*, *B. oleracea*: *Brassica oleracea*, *P. sativa*: *Pastinaca sativa*, *S. carlbergensis*: *Saccharomyces carlbergensis*, *R. glutinis*: *Rhodotrula glutinis*

TABLE 7: RESULTS FOR BIOREDUCTION OF 2-METHYL BENZOPHENONE (8a) AND 4-CHLOROBENZOPHENONE (9a)

Compound	Biocatalyst	Time (days)	% conversion	Enantiomeric excess %
Compound 8a	Micoorganisms <i>R. glutinis</i>	2	38	>99 (S)
		4	45	>99 (S)
Compound 9a	Micoorganisms <i>S. carlbergensis</i>	2	26	>99 (R)
		4	34	>99 (R)
	<i>R. glutinis</i>	2	100	>99 (R)
		4	100	>99 (R)

Absolute configuration is in parenthesis. *S. carlbergensis*: *Saccharomyces carlbergensis*, *R. glutinis*: *Rhodotrula glutinis*

of microorganisms over plants in the bioreduction of prochiral ketones. This may be attributed to the presence of more dehydrogenases in microbes than in plants. However, in some cases and in the production of a special enantiomer, some plants were more successful. Among microorganisms, *R. glutinis* showed a noteworthy performance and could reduce nearly all prochiral ketones with high conversion rates and optical purity. Thus, *R. glutinis* can be recommended as a promising microorganism for yeast mediated stereoselective production of the aforementioned chiral alcohols.

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There are no conflicts of interest.

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