

# Plant-Mediated Stereoselective Biotransformation of Phenylglyoxylic Acid Esters

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*This work is dedicated to the memory of Prof. Agnieszka Mironowicz (1939–2012).*

Enantioselective reduction of the carbonyl group of three phenylglyoxylic acid esters (methyl, ethyl, and *n*-propyl esters, **2–4**) was conducted using blended plant materials (roots of carrot, beet-root, celeriac and parsley; apple). All used biocatalysts transformed these esters to the corresponding mandelic acid esters with high yield, preferably into the respective *R*-enantiomer. Butanedione addition improved the enantioselectivity of the reaction.

**Key words:** Biotransformation, Butanedione, Mandelates

## Introduction

The biological activity of chiral compounds used as agrochemicals, pharmaceuticals or flavouring substances often depends on the configuration of the chiral centre. The market value of chiral compounds reached around 2.7 billion US dollars in 2007 with an average annual growth rate of 10.8% (Ghanem, 2007). For this reason, stereo- and regioselective synthesis is one of the most important issues in organic synthesis.

Mandelic acid (MA) is used as an antibacterial agent as well as a skin exfoliant, effective for acne treatment. The mixture of this acid and benzilic acid [hydroxy(diphenyl)acetic acid] with 0.5% salicylic acid (SA) displays significant skin oil-reducing properties as well as a favourable tolerability profile. MA causes lower discomfort than glycolic acid, the traditionally used alpha hydroxy acid (AHA) in skin care (Draelos, 2009). It also has a long history of use in the treatment of urinary tract infections associated with urethral catheterization (van Putten, 1979).

Due to their bifunctional properties, hydroxy esters are particularly useful synthons in organic synthesis. MA enantiomers are employed for the resolution of racemic alcohols and amines (Yadav and Sivakumar, 2004). They are also the starting material for the syn-

thesis of 1,4-diketones, which are important and valuable precursors of substituted cyclopentenones, such as jasmones, cuparenones, and prostaglandins, and of five-membered heterocyclic compounds (Blay *et al.*, 2006). The *R*-(–)-enantiomer of MA is a precursor of semi-synthetic penicillin, cephalosporin, and antiobesity agents (Fulenmeier *et al.*, 1976; Mills *et al.*, 1983; Yamamoto *et al.*, 1991; Takahashi *et al.*, 1995). The *S*-(+)-enantiomer has been used in the synthesis of the commercial nonsteroidal anti-inflammatory drugs celecoxib (Celebrex®) and deracoxib (Deramaxx®) (Blay *et al.*, 2006; Mateo *et al.*, 2006) and many others such as (–)-utenon A and (–)-carbovir, a potentially useful antiretroviral agent (Saravanan and Singh, 1998). MA esters are also used in artificial flavours and perfumes (Yadav and Sivakumar, 2004).

Usually MA enantiomers are obtained by hydrolytic resolution of MA esters or esterification catalyzed by lipases (Dakin, 1903; Dąbkowska and Szewczyk, 2009; Liu *et al.*, 2010a; Shangguan *et al.*, 2012; Yadav and Sivakumar, 2004; Yadav *et al.*, 2008; Yao *et al.*, 2013). Various microorganisms catalyze the enantioselective reduction of phenylglyoxylic acid esters or their substituted derivatives to the corresponding (*R*)-isomers with high optical purity. This method provides a high yield of the product, but the substrate concentra-

tion is limited, and the reaction time is quite long (Guo *et al.*, 2010).

Recently, whole plant cells, as well as plant cell cultures, microorganisms, and enzymes have been explored as potential catalytic agents in organic chemistry. Plant roots have been used as sources of enzymes for the conversion of simple compounds. Amongst different plants, the potential of *Daucus carota* L. root (carrot) as biocatalyst has been studied most extensively (Baldassarre *et al.*, 2000; Blanchard and van de Weghe, 2006; Bruni *et al.*, 2002; Ferraz *et al.*, 2008; Liu *et al.*, 2010b; Mączka and Mironowicz, 2002, 2004a, b, 2007; Scarpi *et al.*, 2005; Yadav *et al.*, 2001, 2007; Yang *et al.*, 2008). Generally, differentiated plant cells, *i.e.* tissues or organs, were found to express higher activity towards the studied compounds than undifferentiated ones, *i.e.* cell cultures.

The aim of this work was to obtain the enantiomers of mandelates using the enzymatic system of blended plant parts. The method used in our laboratory has some advantages compared to other biotechnological methods, for example very low cost, common availability of the material, and simple reaction work-up.

## Experimental

### Analytical methods

$^1\text{H}$  NMR spectra were recorded in  $\text{CDCl}_3$  on a Bruker Avance DRX 300 MHz spectrometer (Karlsruhe, Germany). Chemical shifts were referenced to the residual solvent signal ( $\delta_{\text{H}} = 7.26$  ppm). IR spectra were recorded on a Thermo-Nicolet IR300 FT-IR spectrometer (Madison, WI, USA). Optical rotations were determined on an Autopol IV automatic polarimeter (Rudolph Research, Flanders, NJ, USA) in  $\text{CHCl}_3$ , and concentrations were denoted in g/100 mL. Analytical thin-layer chromatography (TLC) was performed on Merck Kieselgel 60 F254 plates (Darmstadt, Germany) with mixtures of *n*-hexane and acetone in various ratios. Compounds were detected by spraying the plates with 1%  $\text{Ce}(\text{SO}_4)_2$  and 2%  $\text{H}_3[\text{P}(\text{Mo}_3\text{O}_{10})_4]$  in 10%  $\text{H}_2\text{SO}_4$  or 20% ethanolic  $\text{H}_2\text{SO}_4$ , containing 0.1% of anisaldehyde, followed by heating. Preparative column chromatography (CC) was performed on silica gel (Kieselgel 60, 230–400 mesh ASTM; Merck) with mixtures of *n*-hexane and acetone in various ratios. Gas chromatography (GC) analysis was carried out on a Hewlett-Packard 6890N instrument (Palo Alto, CA, USA) with a flame ionization detector (FID) and  $\text{H}_2$  as carrier

gas at 2 mL/min. The following capillary columns were used: HP-5 (Hewlett-Packard)-crosslinked 5% phenylmethylsiloxane (25 m  $\times$  0.32 mm  $\times$  0.52  $\mu\text{m}$ ), to control the reaction progress during the synthesis of substrates and product standards (temperature program, 100  $^\circ\text{C}$  for 2 min, at 20  $^\circ\text{C}/\text{min}$  to 200  $^\circ\text{C}$ , at 40  $^\circ\text{C}/\text{min}$  to 300  $^\circ\text{C}$ , hold for 1 min; injector temperature, 150  $^\circ\text{C}$ ; detector temperature, 300  $^\circ\text{C}$ ), and BETA DEX<sup>TM</sup> 225 fused silica (Supelco, Bellefonte, PA, USA) (30 m  $\times$  0.25 mm  $\times$  0.25  $\mu\text{m}$ ), to determine the percentage of substrate conversion [ $\text{mandelate}/(\text{mandelate} + \text{ketoester}) \cdot 100$ ] and the enantiomeric excess of the products [ $\text{ee} = (|(S)\text{-mandelate} - (R)\text{-mandelate}|)/((S)\text{-mandelate} + (R)\text{-mandelate}) \cdot 100$ ] (temperature program, 113  $^\circ\text{C}$  for 2 min, at 0.1  $^\circ\text{C}/\text{min}$  to 116  $^\circ\text{C}$ , at 30  $^\circ\text{C}/\text{min}$  to 200  $^\circ\text{C}$ , hold for 2 min; injector temperature, 150  $^\circ\text{C}$ ; detector temperature, 200  $^\circ\text{C}$ ).

### Biocatalysts

Fresh plant materials used in the biotransformations were roots of *Daucus carota* L. (carrot), *Petroselinum sativum* Hoffm. (parsley), *Apium graveolens* L. var. *rapaceum* (celeriac), and *Beta vulgaris* L. (beetroot), as well as apples, *Malus pumila* L. cv. "Gloster", which were all purchased in a local market.

### Synthesis of substrates

The phenylglyoxylic acid esters **2**, **3**, and **4** (Fig. 1) were obtained according to the same procedure: Phenylglyoxylic acid (**1**) (1.5 g, 0.010 mol) and 1.36 g (0.010 mol) of  $\text{KHSO}_4$  were dissolved in 30 mL of benzene together with 0.027 mol of the corresponding alcohol. The mixture was refluxed for 3 h. Progress of the reaction was monitored by TLC. When the reaction was completed, the mixture was diluted with diethyl ether, washed with water and brine, and dried over  $\text{MgSO}_4$ . Next, the solvent was evaporated *in vacuo*, and the crude product was purified by CC [*n*-hexane/acetone (3:1, v/v)] giving the ester.

**Phenylglyoxylic acid methyl ester (2)**: Yield: 1.29 g (79%). –  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta = 3.98$  (s, 3H,  $\text{OCH}_3$ ), 7.52, 7.67, 8.00 (three m, 5H,  $\text{C}_6\text{H}_5$ ). –  $^{13}\text{C}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta = 52.818$ , 128.940, 130.123, 135.026, 164.075, 186.090. – IR (KBr):  $\nu = 2957$  (s), 1740 (s), 1691 (s), 1208 (s), 688  $\text{cm}^{-1}$  (s).

**Phenylglyoxylic acid ethyl ester (3)**: Yield: 1.47 g (83%). –  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.43$  (t,

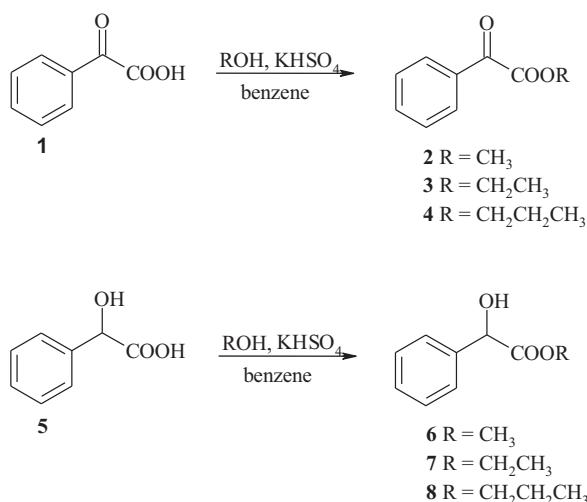


Fig. 1. The synthesis of substrates **2–4** and product standards **6–8**.

$J = 7.14$  Hz, 3H, OCH<sub>2</sub>CH<sub>3</sub>), 4.45 (q,  $J = 7.14$  Hz, 2H, OCH<sub>2</sub>CH<sub>3</sub>), 7.52, 7.66, 8.00 (three m, 5H, C<sub>6</sub>H<sub>5</sub>). – <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 14.146$ , 62.375, 128.922, 130.066, 134.926, 163.868, 186.460. – IR (KBr):  $\nu = 2984$  (s), 1735 (s), 1688 (s), 1201 (s), 688 cm<sup>–1</sup> (s).

*Phenylglyoxylic acid n-propyl ester (4)*: Yield: 1.64 g (85%). – <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 1.01$  (t,  $J = 7.14$  Hz, 3H, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.81 (m,  $J = 7.14$  Hz, 2H, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 4.35 (t,  $J = 6.7$  Hz, 2H, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 7.51, 7.66, 8.00 (three m, 5H, C<sub>6</sub>H<sub>5</sub>). – <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 10.334$ , 21.923, 67.813, 128.929, 130.043, 134.916, 164.048, 188.538. – IR (KBr):  $\nu = 2971$  (s), 1735 (s), 1690 (s), 1200 (s), 688 cm<sup>–1</sup> (s).

#### Chemical synthesis of the products

The MA esters **6**, **7**, and **8** (Fig. 1) were obtained according to the same procedure as used above: In 30 mL of benzene and 0.052 mol of the corresponding alcohol 3 g (0.020 mol) of MA (**5**) and 2.7 g (0.020 mol) of KHSO<sub>4</sub> were dissolved. The mixture was refluxed for 3 h. When the reaction was completed (monitored by TLC, GC), the mixture was treated as above. The crude product was purified by CC [*n*-hexane/acetone (3:1, v/v)].

*Mandelic acid methyl ester (6)*: Yield: 2.35 g (72%). – <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 3.50$  (s, 1H, OH), 3.76 (s, 3H, OCH<sub>3</sub>), 5.18 (s, 1H, CH),

7.35–7.44 (m, 5H, C<sub>6</sub>H<sub>5</sub>). – <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 53.108$ , 72.940, 126.639, 128.587, 128.682, 138.208, 174.211. – IR (KBr):  $\nu = 3445$  (sb), 2952 (s), 1741 (s), 1205 (s), 697 cm<sup>–1</sup> (s).

*Mandelic acid ethyl ester (7)*: Yield: 2.96 g (85%). – <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 1.23$  (t,  $J = 7.15$  Hz, 3H, OCH<sub>2</sub>CH<sub>3</sub>), 3.50 (s, 1H, OH), 4.22 (q,  $J = 7.15$  Hz, 2H, OCH<sub>2</sub>CH<sub>3</sub>), 5.15 (s, 1H, CH), 7.26–7.44 (m, 5H, C<sub>6</sub>H<sub>5</sub>). – <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 15.237$ , 63.014, 72.860, 126.521, 128.485, 128.594, 138.202, 174.101. – IR (KBr):  $\nu = 3481$  (sb), 2983 (s), 1733 (s), 1184 (s), 698 cm<sup>–1</sup> (s).

*Mandelic acid n-propyl ester (8)*: Yield: 3.70 g (97%). – <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 0.82$  (t,  $J = 7.2$  Hz, 3H, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.60 (m,  $J = 7.2$  Hz, 2H, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.54 (s, 1H, OH), 4.13 (m,  $J = 7.2$  Hz, 2H, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 5.17 (s, 1H, CH), 7.31–7.45 (m, 5H, C<sub>6</sub>H<sub>5</sub>). – <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 10.120$ , 21.851, 67.745, 72.894, 126.535, 128.411, 128.563, 138.522, 173.837. – IR (KBr):  $\nu = 3481$  (sb), 2969 (s), 1734 (s), 1184 (s), 698 cm<sup>–1</sup> (s).

#### Transformation conditions

The experiments were carried out according to the procedure worked out by Mączka and Mironowicz (2002). Healthy roots were blended for 5 min in an electric mixer, and 20 mL of plant pulp (1.0–1.5 g of dry weight) were placed in Erlenmeyer flasks with 50 mL of 0.1 M phosphate buffer [pH 5.9 (beetroot and apple), 6.2 (celeriac), 6.5 (carrot and parsley)]. After the addition of 20 mg of substrate dissolved in 0.5 mL acetone, the suspensions were shaken (120 rpm) for 48 h at room temperature. Then the mixtures were extracted with 3 × 50 mL of CHCl<sub>3</sub>. After evaporation of the solvent in a vacuum rotary evaporator, extracts were dissolved in 2 mL of acetone. The course of biotransformation was controlled by means of TLC and chiral GC (1  $\mu$ L injection volume).

Substrates in the buffer solution were stable under these conditions. At least three repetitions of each biotransformation experiment were performed.

## Results and Discussion

### General

The first step of our investigation was the synthesis of methyl, ethyl, and *n*-propyl esters of phenylgly-

Table I. Composition (in % according to GC) of the crude extract after 48 h of biotransformation of phenylglyoxylic acid esters **2–4** by means of blended plant materials.

Substrate	Biocatalyst	Product (corresponding mandelate)	
		Conv. (%)	ee (%)
Phenylglyoxylic acid methyl ester ( <b>2</b> )	<i>Daucus carota</i> L.	100	0
	<i>Petroselinum sativum</i> Hoffm.	98	53 <i>R</i> -(–)
	<i>Apium graveolens</i> L.	100	17 <i>R</i> -(–)
	<i>Beta vulgaris</i> L.	100	0
	<i>Malus pumila</i> L.	8	33 <i>R</i> -(–)
Phenylglyoxylic acid ethyl ester ( <b>3</b> )	<i>Daucus carota</i> L.	100	26 <i>R</i> -(–)
	<i>Petroselinum sativum</i> Hoffm.	100	47 <i>R</i> -(–)
	<i>Apium graveolens</i> L.	100	0
	<i>Beta vulgaris</i> L.	100	28 <i>R</i> -(–)
	<i>Malus pumila</i> L.	18	70 <i>R</i> -(–)
Phenylglyoxylic acid <i>n</i> -propyl ester ( <b>4</b> )	<i>Daucus carota</i> L.	100	26 <i>S</i> -(+)
	<i>Petroselinum sativum</i> Hoffm.	100	0
	<i>Apium graveolens</i> L.	100	43 <i>S</i> -(+)
	<i>Beta vulgaris</i> L.	100	43 <i>R</i> -(–)
	<i>Malus pumila</i> L.	7	76 <i>R</i> -(–)

oxylic acid, **2–4**, and MA, **6–8**, respectively, which were used as substrates and product standards, respectively, in the GC analysis. Structures of all compounds were confirmed by spectroscopic methods.

Based on our previous experience, we decided to use the most economical and ecological biotransformation method, *i. e.* the enzymatic systems provided by fruit and vegetable pulp. The choice of the *Daucus carota* root (carrot) as biocatalyst was based on the very good results previously obtained in the reduction of simple carbonyl compounds (Baldassarre *et al.*, 2000; Blanchard and van de Weghe, 2006; Bruni *et al.*, 2002; Ferraz *et al.*, 2008; Liu *et al.*, 2010b; Mączka and Mironowicz, 2002, 2004a, b; Scarpi *et al.*, 2005; Yadav *et al.*, 2001, 2007). Roots of *Apium graveolens* and *Petroselinum sativum* were chosen, because these plants belong to the same family as carrot. We wished to compare the transformation efficacy within the Apiaceae family. The choice of the other plants was based on their wide availability and low cost.

#### Biotransformation of phenylglyoxylic acid methyl ester (**2**)

Phenylglyoxylic acid methyl ester (**2**) was transformed by all five plant systems to methyl mandelate (**6**) with varying enantioselectivity, depending on the biocatalyst (Fig. 2, Table I). The ester bond of the substrates did not undergo hydrolysis during biotransformation.

The four root systems were more efficient than the apple, for which only 8% conversion was ob-

tained. The best enantiomeric excess was achieved with parsley root as biocatalyst, amounting to approximately 53% enantiomeric excess of the *R*-(–)-enantiomer of **6** with a high degree of substrate conversion (98%). Carrot, as the only of the umbelliferous species, transformed the substrate to the racemic mixture, which was quite surprising considering the literature data on transformation of various ketones by this biocatalyst (Baldassarre *et al.*, 2000; Blanchard and van de Weghe, 2006; Bruni *et al.*, 2002; Ferraz *et al.*, 2008; Liu *et al.*, 2010b; Mączka and Mironowicz, 2002, 2004a, b; Scarpi *et al.*, 2005; Yadav *et al.*, 2001, 2007).

Preliminary identification of the obtained products was carried out by means of GC and comparison with appropriate chemical standards.

To assign the specific configuration of isomers of **5** to individual peaks on gas chromatograms, phenylglyoxylic acid methyl ester (**2**) was transformed using *Petroselinum sativum* Hoffm. as a biocatalyst. Following purification of the transformation products by means of CC, their specific rotation was measured. Based on the literature data, the rotation sign (–) was assigned to the *R*-enantiomer of **5**:  $[\alpha]_{\text{D}}^{29} = -53.44$  (*c* 1.20, CHCl<sub>3</sub>, ee 53%) [Chen *et al.* (2007):  $[\alpha]_{\text{D}}^{20} = -135.60$  (*c* 1.00, methanol, ee 95%)].

#### Biotransformation of phenylglyoxylic acid ethyl ester (**3**)

Preparative biotransformation (Fig. 2) of phenylglyoxylic acid ethyl ester (**3**) with *Petroselinum sativum*

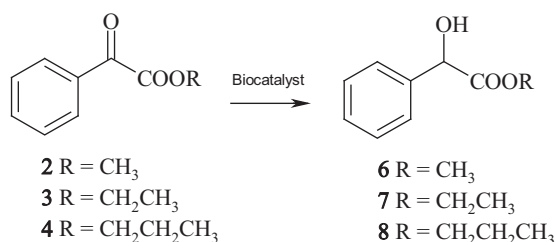


Fig. 2. Biotransformation by means of blended plant material of phenylglyoxylic acid methyl ester (**2**), phenylglyoxylic acid ethyl ester (**3**), and phenylglyoxylic acid *n*-propyl ester (**4**) to methyl mandelate (**6**), ethyl mandelate (**7**), and *n*-propyl mandelate (**8**).

Hoffm. was performed with this substrate to assign the GC peaks to the respective isomers. According to literature data, the negative (−) rotation was assigned to the *R*-enantiomer of **7**:  $[\alpha]_{\text{D}}^{28} = -19.44$  (*c* 0.9, CHCl<sub>3</sub>, ee 47%) [Weng *et al.* (2013):  $[\alpha]_{\text{D}}^{32} = -125.68$  (*c* 1.00, CHCl<sub>3</sub>)].

As in the case of the first substrate **2**, the ketoester **3** was completely transformed by all used root biocatalysts (Table I). Surprisingly, the celeriac system transformed the substrate to the racemic mixture of **7**. The other systems favoured the product with *R*-configuration, and the enantiomeric excess amounted to 26–47%. The most effective biocatalyst in terms of enantioselectivity was the apple system (ee 70% *R*), but substrate **3** conversion was low.

#### Biotransformation of phenylglyoxylic acid *n*-propyl ester (**4**)

Phenylglyoxylic acid *n*-propyl ester (**4**) was completely transformed by all biocatalysts, again with the exception of apple (Fig. 2, Table I). Like with the other two esters, the parsley system transformed the substrate **4** to the racemic mixture of **8**, while the highest enantiomeric excess of **8** was obtained again with apple as biocatalyst (ee 76% *R*), however the process efficiency was only 7%. The celeriac and beetroot systems transformed the substrate **4** with the same enantiomeric excess of **8**, but with opposite configuration: the celeriac system favoured the *S*-isomer of **8**, the beetroot system the *R*-isomer of **8**. The carrot system reduced the *n*-propyl ester to the *S*-isomer of **8**, while the methyl and ethyl esters **2** and **3** were transformed to the racemic mixture of **2** and the *R*-isomer of **3**.

It is interesting that in contrast to transformations of substrates **2** and **3** by carrot and celeriac, *n*-propyl mandelate (**8**) was obtained with an excess of the *S*-(+)-enantiomer. It is worth noting that the beetroot enzymatic system transformed *n*-propyl ester **4** from all substrates with the highest excess of the *R*-(−)-enantiomer of **8**.

To assign the specific rotation values of enantiomers to individual peaks in the gas chromatograms, phenylglyoxylic acid *n*-propyl ester (**4**) was transformed using blended roots of *Beta vulgaris* L. After comparison of the specific rotation values of the obtained product

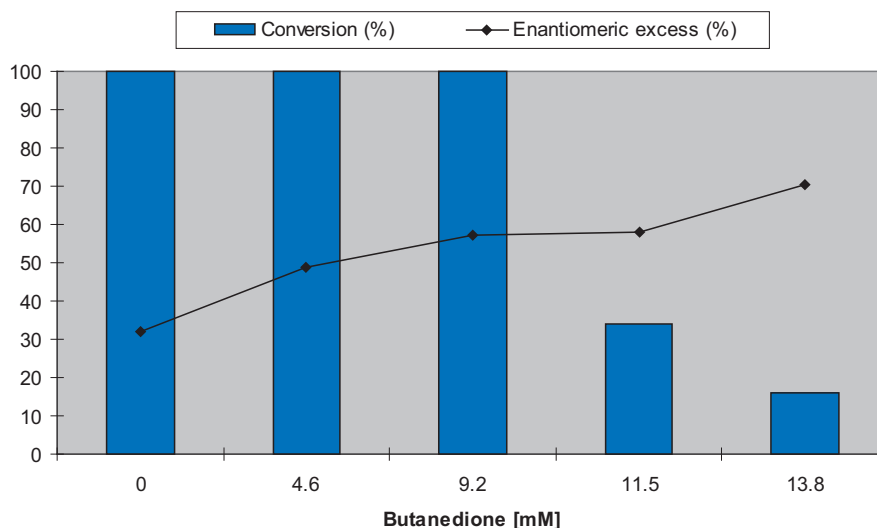


Fig. 3. Effect of butanedione on phenylglyoxylic acid ethyl ester (**3**) reduction by the carrot system.



with the literature data, the negative (–) sign was assigned to the *R*-enantiomer of **8**:  $[\alpha]_{\text{D}}^{25} = -28.86$  (*c* 1.1, CHCl<sub>3</sub>, ee 43%) [Alamsetti and Sekar (2010):  $[\alpha]_{\text{D}}^{30} = -67.90$  (*c* 1.00, CHCl<sub>3</sub>, ee 91%)].

### Improvement of enantioselectivity

The very low enantiomeric excess obtained in the biotransformations, made us search for methods to improve the reaction stereoselectivity.

Reduction of the carbonyl group can be catalyzed by alcohol dehydrogenases (ADH) or reductases (Kroutil *et al.*, 2004). Application of pyrazole as a specific ADH inhibitor (Anderson *et al.*, 1981) was unsuccessful, because we obtained racemic mixtures of hydroxyesters, regardless of the pyrazole dose (concentration of 5.9–17.7 mM). As reductase inhibitor, butanedione (diacetyl) was selected (Ishihara *et al.*, 2000). The results are shown in Fig. 3.

Increasing concentrations of the inhibitor (4.6–13.8 mM) caused an increasing enantiomeric excess of ethyl mandelate (**7**). Butanedione at 11.5 mM caused a dramatic decrease in the degree of substrate conversion, *i. e.* from 100% to about 30%. The best result was obtained for 9.2 mM of butanedione, which enhanced the enantioselectivity of the reaction to about 60%, while maintaining 100% substrate conversion.

### Conclusions

Several blended plant materials catalyzed the reduction of phenylglyoxylic acid methyl (**1**), ethyl (**2**),

and *n*-propyl esters (**4**), respectively, to the corresponding mandelates **6–8**, which are important chiroins in the asymmetric synthesis of various biologically active compounds.

It is worth noting that in the case of plants from the Apiaceae family the synthesis of propyl mandelate occurred contrary to the Prelog rule, when the attack of the hydrogen anion from the *se* carbonyl group forced the synthesis of the *S*-enantiomer (Prelog, 1964).

There are many reports on the individual transformation of phenylglyoxylic acid methyl or ethyl esters (**2** and **3**), but only few reports provided information on the transformation of **2** and **3** by the same biocatalyst. The alcohol chain length of the ester had no effect on yield and enantioselectivity of ester biotransformation by *Saccharomyces cerevisiae* (Zeror *et al.*, 2010). To the best of our knowledge, there is no information in the literature on any transformation of phenylglyoxylic acid *n*-propyl ester (**4**).

Addition of the reductase inhibitor butanedione improved the enantioselectivity of the biotransformation, while another inhibitor, pyrazole, did not affect the process enantioselectivity.

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