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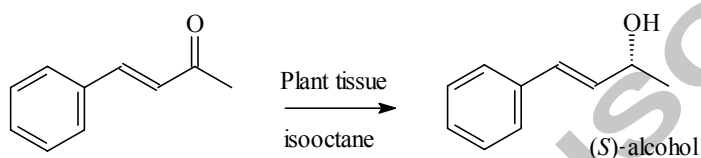
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Graphical Abstract

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ABSTRACT

(*S*)-*trans*-4-Phenylbut-3-en-2-ol has been obtained in excellent yields and with high enantiomeric excess in the reduction of *trans*-4-phenylbut-3-en-2-one using the comminuted roots of carrot (*Daucus carota* L.), celeriac (*Apium graveolens* L. var. *rapaceum*) and beetroot (*Beta vulgaris* L. subsp. *Vulgaris*) in isooctane. This is the first report of this bioreduction with plant tissue in an organic solvent.

Keywords:

trans-4-phenylbut-3-en-2-one
(*S*)-*trans*-4-phenylbut-3-en-2-ol
isooctane
plants

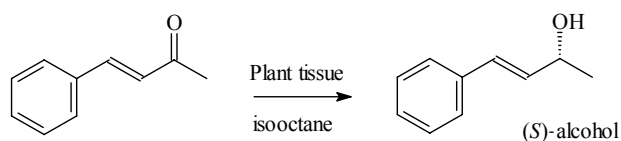
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Chemical reactions using intact parts of miscellaneous plants as biocatalysts have received significant attention. This growing interest is due to the wide biotechnological potential of enzymatic reactions. Biocatalytic transformations using plants can be applied in bioreduction of ketones,¹ enzymatic lactonization,² hydrolysis of esters,^{1c,3} bioreduction of nitro compounds,^{4,5} and hydroxylation and oxidation reactions.⁴ Usually, healthy roots of common vegetables, that can be obtained in all seasons, are used. The application of comminuted tissue of ripe vegetable roots in biotransformations has the advantages of low cost and short reaction times of ca. 48 hours, the procedure is very simple and represents an alternative to Baker's yeast owing to the easy availability of plants, the use of water without a carbon source and the simple work-up because no emulsion is formed.

Enantiomerically pure allylic alcohols are an important class of versatile building blocks for organic synthesis. They permit a wide range of subsequent transformations, including carbon-carbon bond formation reactions, in addition to numerous possibilities for the manipulation and introduction of functional groups, and they may serve as useful chiral auxiliaries in many stereoselective transformations.⁶

The enantiomeric allylic alcohols (*S*)-(-) and (*R*)-(+)-*trans*-4-phenylbut-3-en-2-ol are frequently used as chiral building blocks for numerous biologically active compounds, and they are used for studies of reaction mechanisms.⁷ Therefore, it is desirable that both enantiomers of this chiral starting material are available in high enantiomeric purity. Optically active *trans*-4-phenylbut-3-en-2-ol may be obtained via the lipase-catalyzed transesterification of (*R*, *S*)-*trans*-4-phenylbut-3-en-2-ol using vinyl acetate⁸ or dimethyl malonate⁷ as an acyl donor, or by ruthenium⁹ or enzyme-catalyzed asymmetric reduction of *trans*-4-phenylbut-3-en-2-one.¹⁰ The lipase-catalyzed transesterification of the racemic alcohol using isopropenyl acetate as an acyl donor in toluene is an efficient method for the preparation of enantiomerically pure (*S*)-alcohol,¹¹ whereas the (*R*)-alcohol may be obtained by lipase-catalyzed enantioselective hydrolysis of the corresponding racemic acetate.¹¹

In this paper the regio- and stereoselective reduction of *trans*-4-phenylbut-3-en-2-one with various plants is described as a convenient and simple procedure for the gram-scale preparation of (*S*)-*trans*-4-phenylbut-3-en-2-ol (Scheme 1) with high enantiomeric excess.



Scheme 1.

The biotransformation of *trans*-4-phenylbut-3-en-2-one into *trans*-4-phenylbut-3-en-2-ol using plant tissue, has already been observed in the reaction catalyzed by the beans of *Vigna unguiculata*.⁵ In this case, the double bond was mainly reduced, resulting in the formation of 4-phenylbutan-2-one. The product of the exclusive reduction of the C=O bond was observed in only trace amounts (3%). On the other hand, reduction of cinnamaldehyde with coconut juice occurred selectively at the carbonyl group to yield the corresponding alcohol (84%) without affecting the double bond.¹²

Healthy and ripe roots of carrot (*Daucus carota* L.), celeriac (*Apium graveolens* L. var. *rapaceum*) and beetroot (*Beta vulgaris* L. subsp. *Vulgaris*) were selected for this biotransformation. These vegetables are accessible in all seasons and have the advantage of low cost. The reaction procedure is very simple: to a stirred suspension of comminuted plant tissue (330 g) in isooctane (600 ml), *trans*-4-phenylbut-3-en-2-one (1.5 g) was added at 25 °C. Aliquots were withdrawn periodically and the progress of the reaction was monitored by means of TLC and GC. After three days, we observed the maximum percentage yield and the plant residue was filtered off. The organic phase was dried over MgSO₄, the isooctane was evaporated and the crude residue was purified by flash column chromatography. The structure of the product was confirmed by ¹H NMR and FT-IR.¹³ The enantiomeric excesses of the products were determined by measuring specific rotations and calculated as follows:

$$ee (\%) = ([\alpha]_{\text{observed}} / [\alpha]_{\text{maximum}}) \times 100$$

The biotransformation of *trans*-4-phenylbut-3-en-2-one was also carried out in polar solvents such as water and acetonitrile (Table 1). A water-miscible organic solvent was thought to aid in the solubility by the phenomenon of co-solvency, however, water-immiscible organic solvents aid by forming a biphasic reaction mixture. In the cases of water and acetonitrile no reaction was observed, probably due to the insolubility of the substrate in polar solvents.

Table 1. Reduction of *trans*-4-phenylbut-3-en-2-one with plant tissue^a

Plant	Solvent	S-Alcohol	
		Yield (%) ^b	ee (%)
carrot	H ₂ O	-	-
carrot	MeCN	-	-
carrot	isooctane	96	>99
celeriac	H ₂ O	-	-
celeriac	MeCN	-	-
celeriac	isooctane	78	98
beetroot	H ₂ O	-	-
beetroot	MeCN	-	-
beetroot	isooctane	71	72

^a Reduction over 3 days.

^b Determined by GC analysis.

Whole cell biocatalysis in an organic solvent has a limitation due to the toxic effect of the solvent on the enzyme activity. On the other hand, organic solvents may absorb inside the cell membrane leading to a change in membrane fluidity and ease in substrate uptake resulting in activity retention.

The bioreductions in isooctane in the presence of carrot (*Daucus carota* L.), celeriac (*Apium graveolens* L. var. *rapaceum*) and beetroot (*Beta vulgaris* L. subsp. *Vulgaris*) proceeded in good to excellent yields. The highest yield was achieved with carrot (96%), and were lower with celeriac (78 %) and beetroot (71%).

All the selected plants reduced *trans*-4-phenylbut-3-en-2-one to (*S*)-*trans*-4-phenylbut-3-en-2-ol with high enantioselectivity (Table 1). The reduction occurred only at the carbonyl group. Bioreduction of the carbonyl group by carrot and celeriac enzyme systems is well documented¹ and proceeds enantioselectivity, following Prelog's rule, which results in the formation of (*S*)-alcohols predominantly.

In conclusion, the regio- and stereoselective reduction of *trans*-4-phenylbut-3-en-2-one with comminuted roots of the popular vegetables such as carrot, celeriac and beetroot in isooctane can be viewed as a further useful tool for organic chemists by virtue of the simplicity. The encouraging results obtained here may offer new possibilities for the reduction of selected α,β -unsaturated carbonyl compounds that are insoluble in water, as a critical step in a synthetic organic pathway, specifically avoiding the use of non-sustainable, hydride reducing agents.

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- Analytical methods:

Gas chromatography – Shimadzu GC-17, capillary column: Inert Cap WAX (30 m x 0.25 mm), flame ionisation detector temp. 250 °C, split injector temp 250 °C, column temp. 40 °C/ min, gradient 15 °C/min to 230 °C, carrier gas: N₂ at 1 ml/min, retention time (min): ketone 13.18, alcohol 14.59

(*S*)-*trans*-4-phenylbut-3-en-2-ol:

¹H NMR (500 MHz, CDCl₃): 7.23-7.39 (m, 5H, aromatic), 6.55 (d, *J* = 15.5 Hz, 1H), 6.27 (dd, *J* = 15.5, 6.5 Hz, 1H), 4.50 (m, 1H), 2.77 (s, 1H, OH), 1.38 (d, 3H, CH₃)

FT-IR (CH₂Cl₂): ν = 3600 cm⁻¹ (OH)

Polarimetry ATAGO AP-300: carrot, (*S*)-alcohol > 99% ee: [α]_D²⁰ -19.8 (c 1, CHCl₃), [lit. [α]_D²⁰ -19.9 (c 1, CH₂Cl₂) >99% ee]; celeriac, (*S*)-alcohol 98% ee: [α]_D²⁰ -19.52 (c 1, CHCl₃); beetroot, (*S*)-alcohol 72% ee: [α]_D²⁰ -14.32 (c 1, CHCl₃)