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Chemoenzymatic synthesis of enantioenriched (R)- and (S)- aryloxyalkanoic herbicides

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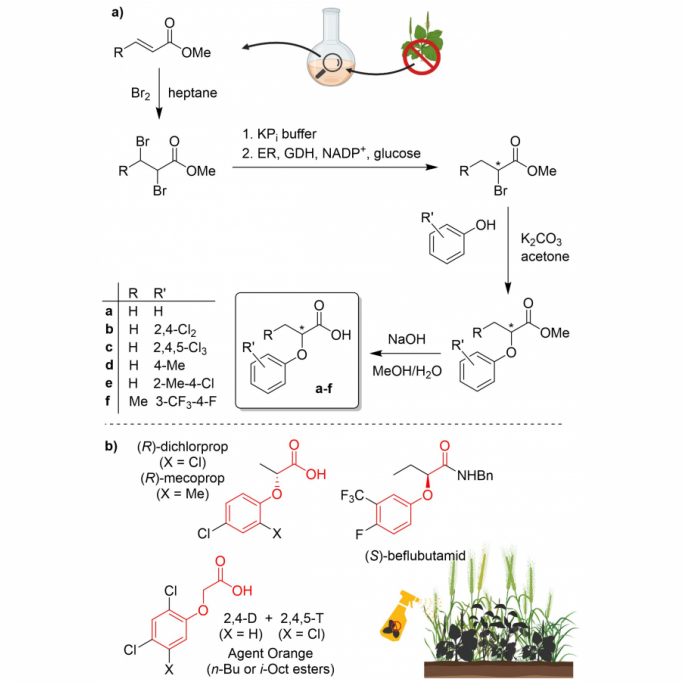
PURPOSE OF THE ABSTRACT

Aryloxyalkanoic herbicides are a class of agrochemicals of widespread use for the protection of cereals and monocotyledonous crops from broad-leaf weeds. The production method of this class of herbicides changed a lot during the past decades. Indeed, chemical industry and in particular the agrochemical sector, has been subjected to a consistent and urgent pressure to develop and adopt more sustainable manufacturing processes, with particular regard to the reduction of greenhouse gas emission, waste output and replacement of toxic and dangerous reagents [1]. The extensive chemical development led to aryloxy alkanoic acids and derivatives with decreased toxicity and environmental hazard, and these molecules are currently sold as mixture of both (R) and (S) enantiomers although usually one of the two is more active than the other. Dichloroprop and mecoprop are sold as racemate but only the (R)-enantiomer is responsible for the biological activity, conversely herbicide (S)-beflubutamid is 1000 time more active than its corresponding (R)-enantiomer. The stereoselectivity of an enzymatic transformation in this context appear as an elite strategy for the synthesis of the more active enantiomer [2,3]. In this work, starting from simple and commercially available materials, the combination of a biocatalytic asymmetric C=C reduction with a simple sequence of chemical transformations was implemented in a new chemo enzymatic synthesis of various substituted Aryloxyalkanoic acids (Figure 1) [4]. Stereoselective bioreduction is mediated by ene-reductases (ERs) belonging to the family of Old Yellow Enzymes (OYEs), versatile biocatalysts for the enantiospecific reduction of C=C double bonds activated by electron withdrawing groups [5]. By careful selection of the biocatalyst, either enantiomer of the product could be obtained in good yield and moderate to good ee without chromatographic purifications and by using crude enzyme preparations [4].

FIGURES



	R	R'
a	H	H
b	H	2,4-Cl_2
c	H	2,4,5-Cl_3
d	H	4-Me
e	H	2-Me-4-Cl
f	Me	3-CF_3-4-F

FIGURE 1

Figure 1

(a) Chemoenzymatic synthesis of enantioenriched aryloxyalkanoic herbicides.

(b) Representative examples of commercial chiral aryloxyalkanoic herbicides in their most active enantiomeric form (the common phenoxy-acetic acid skeleton is shown in red).

FIGURE 2

KEYWORDS

Chemo-enzymatic catalysis | Enzymes | Green chemistry | Industrial Biocatalysis

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