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Nature goes natural: A novel chemo-enzymatic one-pot cascade for the synthesis of fragrance & flavor aldehydes

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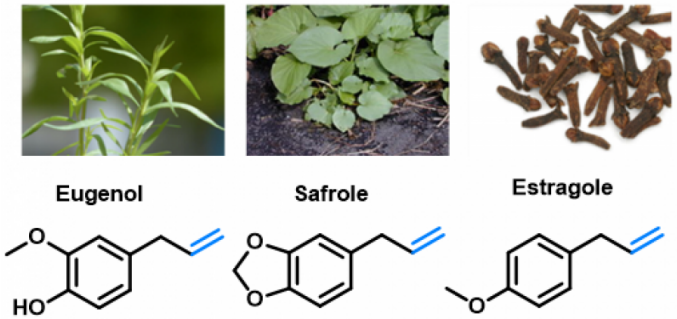
PURPOSE OF THE ABSTRACT

The effective utilization of naturally occurring compounds is of the most importance when the sustainability of the chemical industry needs to be increased. However, due to the multitude of different compound classes with varying usability for chemical applications combined with difficult and inefficient transformation strategies, most natural resources lie fallow for the chemical industry. To tackle this problem a proof of concept for two novel methods was developed that allows the conversion of naturally occurring phenylpropene derivatives (e.g., eugenol and safrole, Figure 1) to valuable aromatic aldehydes (e.g., vanillin and piperonal). Both methods utilize a common approach where a chemical transformation is coupled to whole-cell biocatalysis in a one-pot fashion (Figure 2). The first method (Strategy A) - the “shortcut” approach - involves a palladium-catalyzed isomerization of the terminal olefinic bond of a phenylpropene derivative followed by an enzymatic oxidative cleavage performed by a coenzyme-free aromatic dioxygenase (ADO)[1]. On the other hand, the second strategy (Strategy B), couples a Wacker-oxidation[2] to a three-step enzymatic cascade involving the combination of a Baeyer-Villiger monooxygenase (TmCHMO or PAMO)[3], an esterase (pfe I)[4], and an alcohol dehydrogenase (AlkJ)[5] To demonstrate the scope of these transformations eight phenylpropene derivatives were chosen. Strategy A allowed for the synthesis of one of the desired aldehydes (vanillin) due to limitations in the substrate profile of ADO. Strategy B on the other hand allowed for the transformation of all of the tested phenylpropene derivatives resulting in the formation of seven of the desired aldehydes with yields of up to 42 % after 4 reaction steps (80% for each step).

FIGURES



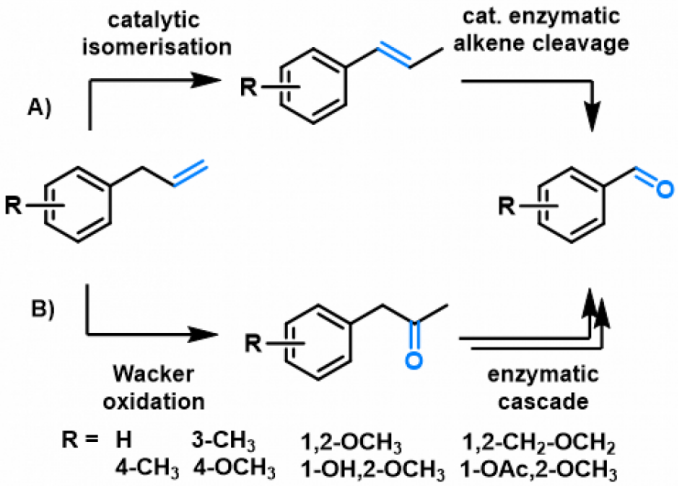


FIGURE 1

Natural occurring phenylpropenes and their natural source

Eugenol from Clove[6].(Image adapted from Brian Arthur (CC BY-SA 4.0)) Safrole from Makulan[7]. (Image: Forest & Kim Starr (CC BY 3.0)) Estragole from Estragon[8].

FIGURE 2

Reaction sequence overview

Two different concepts, exploiting oxidation bio/chemistry for the synthesis of fragrance and flavor aldehydes.

KEYWORDS

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