



Transformation of (±)-lavandulol and (±)-tetrahydrolavandulol by a fungal strain *Rhizopus oryzae*

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ABSTRACT

Biotransformation of an irregular monoterpene alcohol, (±)-lavandulol [(±)-5-methyl-2-(1-methylethenyl)-4-hexen-1-ol] (**I**) and its tetrahydro derivative, (±)-tetrahydrolavandulol [(±)-2-isopropyl-5-methylhexan-1-ol] (**II**) were studied using a soil isolated fungal strain *Rhizopus oryzae*. Five metabolites, 2-((3,3-dimethyloxiran-2-yl)methyl)-3-methylbut-3-en-1-ol (**Ia**), 2-methyl-5-(prop-1-en-2-yl)hex-2-ene-1,6-diol (**Ib**), 2-methyl-5-(prop-1-en-2-yl)hexane-1,6-diol (**Ic**), 2-(3-methylbut-2-enyl)-3-methylenbutane-1,4-diol (**Id**), 5-methyl-2-(2-methyloxiran-2-yl)hex-4-en-1-ol (**Ie**) have been isolated from the fermentation medium and characterized with lavandulol as a substrate. When tetrahydrolavandulol used as a substrate, two metabolites 2-isopropyl-5-methylhexane-1,5-diol (**Ila**) and 2-isopentyl-3-methylbutane-1,3-diol (**Ilb**) have been isolated from the fermentation medium. Biotransformation studies with *R. oryzae* clearly indicate that the organism initiates the transformation either by hydroxylation at allylic methyl groups or epoxidation of double bond. GC and GCMS analyses indicated that both (*R*)- and (*S*)-enantiomers of **I** and **II** have been transformed into corresponding hydroxylated or epoxy derivatives, when racemic **I** and **II** were used as substrates.

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1. Introduction

The irregular monoterpene alcohol, lavandulol is a constituent of essential oils and also an important additive in perfumery and cosmetic industry (Schinz and Schappi, 1947; Seino et al., 2008; Simon et al., 1946; Soucek and Dolejs, 1959). Homochiral lavandulol exists naturally in its (*R*)-form in the essential oil of lavender. The esters of both (*R*)- and (*S*)-lavandulol are the segregation pheromones of insects such as *Anthonomus rubi* Herbst (Innocenzi et al., 2001) and *Planococcus ficus*, (Zada et al., 2003, 2008), respectively. (*R*)-lavandulyl-(*S*)-methylbutanoate is a component of female sex pheromone of the hibiscus mealybug (Zhang et al., 2004) whereas (*R*)-lavandulyl acetate is a component of the male sex pheromone of the western flower thrips (Hamilton et al., 2005). (*R*)-lavandulol is being synthesized in nature by the condensation of two molecules of dimethylallyldiphosphate (DMAPP) and the mechanism of formation of (*R*)-lavandulol is well documented (SD, Fig. S1) (Thulasiram et al., 2007). 1'-2 Irregular monoterpene, (*R*)-lavandulol was formed through dissociative electrophilic alkylation of the double bond in

DMAPP by the dimethylallyl carbocation (DMA⁺) to give cyclopropyl carbocation. The cyclopropyl carbocation formed after rearrangement yield lavandulyl carbocation which in turn will be deprotonated to yield lavandulyl diphosphate (SD, Fig. S1) (Thulasiram et al., 2007, 2008). Although considerable work has been carried out on the biosynthesis of lavandulol, very little is known regarding the biotransformation of this irregular monoterpene alcohol. Therefore, it is of great interest to know the mode of biotransformation of lavandulol and tetrahydrolavandulol as they are being used extensively in perfumery and cosmetic industry. This study describes the biotransformation of racemic lavandulol (**I**) and its tetrahydro-derivative (**II**) by a soil isolated fungal strain *Rhizopus oryzae*. In fact, *R. oryzae* is more versatile in its ability to transform lavandulol compared to the fungus tested earlier (Nankai et al., 1997, 1998). Five metabolites for **I** and two metabolites for **II** from fermentation medium were isolated and characterized.

2. Experimental procedures and methods

2.1. Chemicals and reagents

Lavandulol was purchased from Sigma–Aldrich. Media ingredients, salts and acids were purchased from HiMedia Laboratories,

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