

Mechanism for biotransformation of geraniol and nerol catalyzed by *Candida albicans*

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Abstract

Biotransformation of geraniol to (*R*)-citronellic acid (90% conversion, 70% e.e.) catalyzed by *C. albicans* was carried out after 7 days. In order to study the mechanism of the reaction, the biotransformation of the intermediates were performed and it indicates the stereoselectivity obtained is due to isomerization of geraniol to nerol which results in both (*R*)- and (*S*)-citronellic acid.

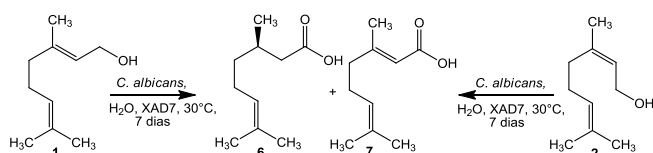
Introduction

Monoterpenes are commonly found in the volatile essence of flowers and plants oils. Some are commonly used as food additives and fragrance components, and are of great interest of food, pharmacy and cosmetic industries.^{1,2}

In a previous work performed by our group, *Candida albicans* has shown great potential to oxidize geraniol to (*R*)-citronellic acid with good e.e., which has not yet been reported. Therefore, the aim of this work was to study the mechanism of the oxidation of geraniol catalyzed by *C. albicans* in order to understand how the (*R*)- and (*S*)-citronellic acids are obtained.

Results and Discussion

Biocatalysis of 50 mg of geraniol (**1**) with *C. albicans* (CCT 0776) resulted in 90% of conversion to (*R*)-citronellic acid (**6**) with 70% e.e. ($[\alpha]_D^{20} = +2^\circ$, lit. $[\alpha]_D^{20} = +8,4^\circ$)³, and 10% of the geranic acid (**7**). Notably, the same products were obtained for the biotransformation of nerol (**2**) in a similar reaction, with 80% of conversion to (*R*)-**6** with 66% e.e. and 20% of conversion to **7** (Scheme 1).



Scheme 1

The intermediates geraniol (**3**), nerol (**4**) and citronellol (**5**) were observed in the biotransformation of **1** and **2** with *C. albicans* (Figure 1). The presence of the aldehydes **3** and **4** suggested an isomerization during the reaction. Based on these intermediates we proposed that the mechanism for

biotransformation of **1** and **2** includes the oxidation of the alcohols to **3** and **4** followed by isomerization, biohydrogenation and reduction of both to **5**.

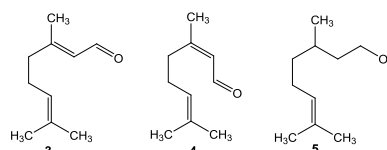


Figure 1. Reaction intermediates

Biotransformations of **3** and **4** with *C. albicans* indicated isomerization of **3** to **4** and **4** to **3**. After 7 days of biocatalysis of **4**, only (*R*)-**6** and (*S*)-**6** were obtained with 53% and 47% (35% e.e.) of conversion, respectively. The chiral product (*R*)-**6** was formed with lower e.e. for the reaction with **4** compared to the biocatalysis of **3**, 100% conversion and 58% e.e. Hence, we assume that the biohydrogenation of **3** leads to the formation of (*R*)-**5** while (*S*)-**5** is formed by **4**.

After 24 hours of reaction the oxidation of racemic **5** leads to the (*S*)-citronellic acid with 53% e.e. However, after 7 days, by the completion of the reaction, there was a racemic mixture of (*R*)- and (*S*)-citronellic acid. Consequently, the rate of oxidation of (*S*)-**5** to (*S*)-**6** is faster than the oxidation of (*R*)-**5** to (*R*)-**6**. These results correlate to the increase of the e.e. of citronellic acid during the biotransformation of **1** to (*R*)-**6**.

Conclusion

During the biotransformation of geraniol (**1**) by *C. albicans*, there is isomerization of the geraniol and nerol aldehydes. The oxidation rate of (*S*)-citronellol **5** is faster than the oxidation of (*R*)-citronellol **5**. An alternative to increase stereoselectivity would be to inhibit isomerization of geraniol **3** to nerol **4** resulting in only (*R*)- or (*S*)-citronellic acid **6**.

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¹Lee, S.-Y., Kim, S.-H., Hong, C.-Y., Park, S.-Y. & Choi, I.-G; *J. Microbiol* **2015**, 53, 462.

²Leleti, R. R.; Hu, B.; Prashad, M.; Repic, O. *Tetrahedron Lett.* **2007**, 48, 8505.

³Flachsbarth, Birte *Chemistry & Biodiversity* **2009**, 6, 1-37.