Phytochemistry xxx (2016) 1–7

Contents lists available at ScienceDirect

Phytochemistry

journal homepage: www.elsevier.com/locate/phytochem

Biotransformation of an africanane sesquiterpene by the fungus *Mucor plumbeus*

Braulio M. Fraga [a, *], Carmen E. Díaz [a, **], Leonardo J. Amador [a], Matías Reina [a], Matías López-Rodriguez [b], Azucena González-Coloma [c]

[a] Instituto de Productos Naturales and Agrobiología, CSIC, Avda. Astrof. F. Sánchez, 3, 38206, La Laguna, Tenerife, Canary Islands, Spain
[b] Instituto Universitario de Bioorgánica "Antonio González", Universidad de La Laguna, Tenerife, Spain
[c] Instituto de Ciencias Agrarias, CSIC, Serrano 113, 28016, Madrid, Spain

ARTICLE INFO

Article history:
Received 9 November 2016
Received in revised form
13 December 2016
Accepted 16 December 2016
Available online xxx

Keywords:
Mucor plumbeus
Biotransformations
Sesquiterpenes
Africanane
Insect antifeedants
Cytotoxic effects

ABSTRACT

Biotransformation of 8β-hydroxy-african-4(5)-en-3-one angelate by the fungus *Mucor plumbeus* afforded as main products 6α,8β-dihydroxy-african-4(5)-en-3-one 8β-angelate and 1α,8β-dihydroxy-african-4(5)-en-3-one 8β-angelate, which had been obtained, together with the substrate, from transformed root cultures of *Bethencourtia hermosae*. This fact shows that the enzyme system involved in these hydroxylations in both organisms, the fungus and the plant, acts with the same regio- and stereospecificity. In addition another twelve derivatives were isolated in the incubation of the substrate, which were identified as the *(2′R,3′R)*- and *(2′S,3′S)*-epoxy derivatives of the substrate and of the 6α- and 1α-hydroxy alcohols, the 8β-*(2′R,3′R)*- and 8β-*(2′S,3′S)*-epoxyangelate of 8β,15-dihydroxy-african-4(5)-en-3-one, the hydrolysis product of the substrate, and three isomers of 8β-hydroxy-african-4(5)-en-3-one 2ξ,3ξ-dihydroxy-2-methylbutanoate. The insect antifeedant effects of the pure compounds were tested against chewing and sucking insect species along with their selective cytotoxicity against insect (Sf9) and mammalian (CHO) cell lines.

1. Introduction

During the past years we have been interested in the study of the biotransformation of diterpenes with different skeleta by the fungus *Mucor plumbeus* (Hoffmann and Fraga, 1993; Fraga et al., 1998, 2001, 2003a, 2003b, 2004, 2010). The aim of these studies has been to develop models to explain the hydroxylation of these compounds by this microorganism, which possesses a broad specificity in the substrate (Arantes and Hanson, 2007; Oliveira-Silva et al., 2013). On the other hand, we have recently investigated the biological activity of africanane sesquiterpenes isolated from transformed root cultures and aerial parts of *Bethencourtia hermosae* (Pit) Kunkel (Asteraceae) (Fraga et al., 2014). To complement these works, in order to study their structure-activity relationship as potential pesticides, we prepared new structural derivatives with this carbon skeleton by biotransformation of 8β-hydroxy-african-4(5)-en-3-one angelate (**1**) (Bohlmann and Zdero, 1978; Fraga et al., 2014) with *M. plumbeus*. In this way, we obtained the following metabolites: 6α,8β-dihydroxy-african-4(5)-en-3-one 8β-angelate (**2**), 1α,8β-dihydroxy-african-4(5)-en-3-one 8β-angelate (**3**), 8β-hydroxy-african-4(5)-en-3-one (**4**), 6α,8β-dihydroxy-african-4(5)-en-3-one 8β-*(2′R,3′R)*-epoxyangelate (**5**), 6α,8β-dihydroxy-african-4(5)-en-3-one 8β-*(2′S,3′S)*-epoxyangelate (**6**), 8β-hydroxy-african-4(5)-en-3-one *(2′S,3′S)*-epoxyangelate (**7**), 8β-hydroxy-african-4(5)-en-3-one *(2′R,3′R)*-epoxyangelate (**8**), 1α,8β-dihydroxy-african-4(5)-en-3-one 8β-*(2′S,3′S)*-epoxyangelate (**9**), 1α,8β-dihydroxy-african-4(5)-en-3-one 8β-*(2′R,3′R)*-epoxyangelate (**10**), 8β,15-dihydroxy-african-4(5)-en-3-one 8β-*(2′S,3′S)*-epoxyangelate (**11**), 8β,15-dihydroxy-african-4(5)-en-3-one 8β-*(2′R,3′R)*-epoxyangelate (**12**) and three diol isomers (**13**–**15**). The insect antifeedant effect of the pure compounds was tested against chewing (*Spodoptera littoralis, Leptinotarsa decemlineata*) and sucking (*Myzus persicae, Rhopalosiphum padi*) insect species along with their selective cytotoxicity against insect (Sf9) and mammalian (CHO) cell lines.

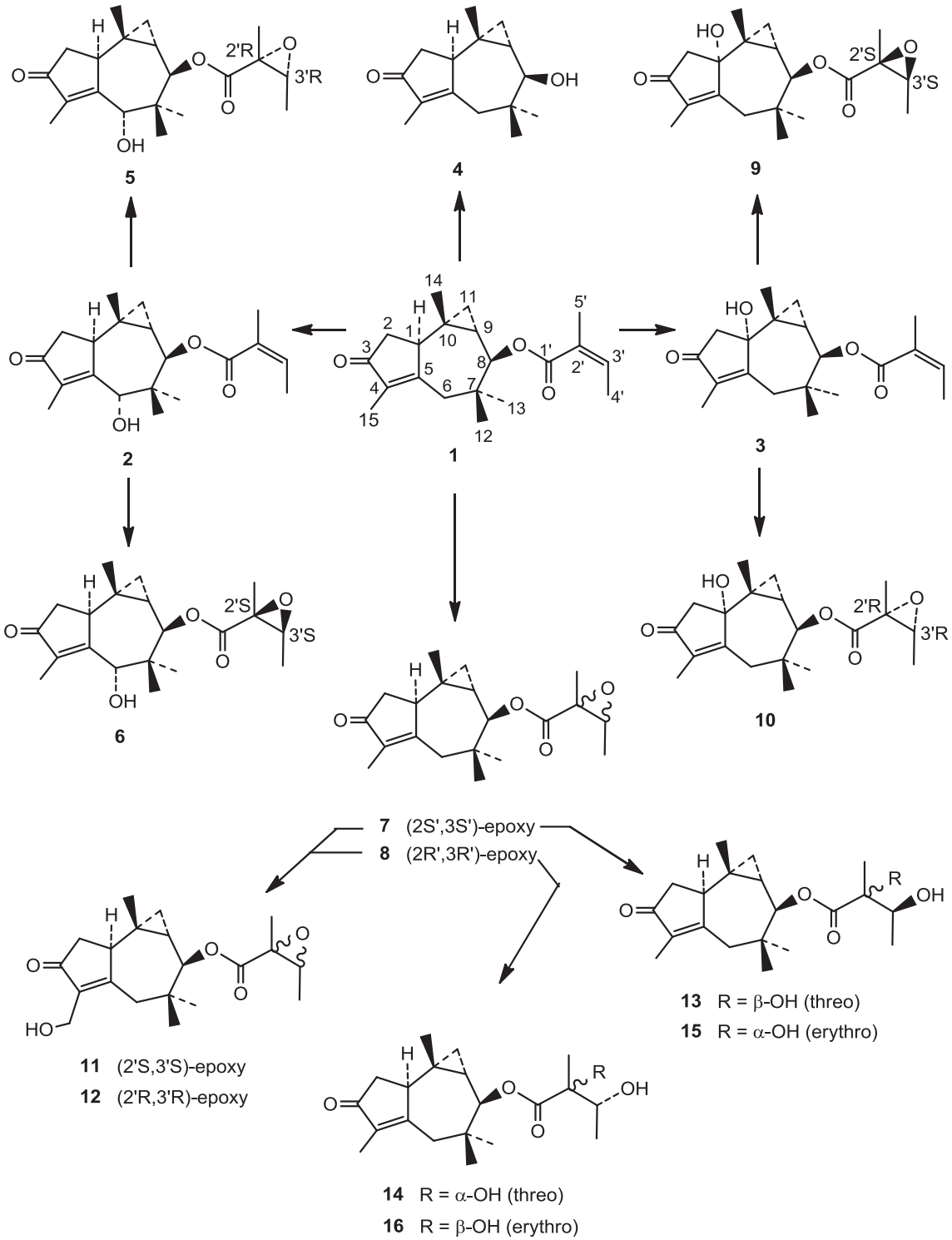
* Corresponding author.
** Corresponding author.
E-mail addresses: bmfraga@ipna.csic.es (B.M. Fraga), celisa@ipna.csic.es (C.E. Díaz).

http://dx.doi.org/10.1016/j.phytochem.2016.12.015
0031-9422/

2. Results and discussion

The incubation of 8β-hydroxy-african-4(5)-en-3-one angelate (**1**) with the fungus *M. plumbeus* led to the isolation of the metabolites **2**–**15** (Scheme 1). Two of them were identified as 6α,8β-dihydroxy-african-4(5)-en-3-one 8β-angelate (**2**) and 1α,8β-dihydroxy-african-4(5)-en-3-one 8β-angelate (**3**), which together with the substrate **1** had been obtained from transformed root cultures of *B. hermosae* (Fraga et al., 2014). Thus, with this biotransformation we have developed a procedure that allows us to obtain compounds **2** and **3** from the major product **1**. Moreover, it should be noted that the isolation of these compounds show that the enzyme system involved in these hydroxylations, in the plant and the fungus, acts with the same regio- and stereospecificity.

The alcohol **4** was also isolated in the biotransformation of the substrate **1**. It had been obtained from the aerial parts of



Scheme 1. Metabolites **2**–**15** obtained by biotransformation of **1** by *Mucor plumbeus*.

Please cite this article in press as: Fraga, B.M., et al., Biotransformation of an africanane sesquiterpene by the fungus *Mucor plumbeus*, Phytochemistry (2016), http://dx.doi.org/10.1016/j.phytochem.2016.12.015