

MICROBIAL TRANSFORMATION REACTIONS OF STEROIDS AND SESQUITERPENES

ABSTRACT

The biotransformation of steroids and sesquiterpenes by a plethora of fungi is described. A multifaceted group of proteins, known as the cytochrome P450 enzymes, is involved in a vast array of biological processes and reactions. Some of these reactions and the mechanistic pathways by which these processes occur are highlighted.

The current research focuses on the biotransformation of eight steroids by the fungus *Aspergillus ochraceus* ATCC 18500. For most, the 11 α hydroxyl analogue of the parent substrate was isolated almost exclusively, with the exception of pregnenolone and dehydroepiandrosterone, which produced a variety of previously reported analogues. A cursory examination of the triangular relationship that exists between the two binding sites of the substrate and the point of hydroxylation observed in the metabolites explains the dominance of 11 α hydroxylation in the results obtained. The steroids estrone and sarsasapogenin failed to produce any metabolites.

The ability of five fungi to transform the sesquiterpenes cedrol and cedrene was explored. These were *Aspergillus ochraceus* ATCC 18500, *Calonectria decora*

ATCC 14767, *Cunninghamella echinulata* var. *elegans* ATCC 8688a, *Curvularia lunata* ATCC 12017 and *Penicillium decumbens* ATCC 10436. Of the five, only *C. lunata* and *C. echinulata* var. *elegans* showed any promise. A total of five metabolites were isolated in this project, all of which were obtained from the substrate cedrol. A discussion on the genesis of the differences in conversion rates between cedrol and cedrene is also included.

Isolation, biotransformation and synthesis of analogues of cembranes from the plant *Cleome spinosa* are detailed. While isolation of the cembranes was relatively straightforward, synthesis and biotransformation of several analogues was unsuccessful. The cembranes obtained were shown to be active against human carcinoma cell lines.

Keywords: Biotransformation, cembranes, Cleome spinosa, sesquiterpenes, steroids, Aspergillus ochraceus ATCC 18500, *Calonectria decora* ATCC 14767, *Cunninghamella echinulata* var. *elegans* ATCC 8688a, *Curvularia lunata* ATCC 12017, *Penicillium decumbens* ATCC 10436, Nadya-Kaye Kamay Phillips.