SYNTHESIS OF TETRAHYDROFURAN RINGS AS CHIRAL BUILDING BLOCKS FOR THE SYNTHESIS OF C-NUCLEOSIDES AND OTHER NATURAL PRODUCTS VIA ENANTIOSELECTIVE BAUER-VILLIGER BIOOXIDATIONS

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Enantioselective biooxidations using Baeyer-Villiger monoxygenases (BVMOs) offer a "green chemistry" method for the preparation of chiral lactones, which represent key intermediates for the synthesis of a large number of natural products and highly active pharmaceutical compounds.\(^1\)

Natural products containing tetrahydrofurans have been of special interest due to their widespread occurrence and diverse biological activities. In this work we present the chiral synthesis of the epoxy ester 6 and the halobicyclic-lactones 8 as valuable precursors for the enantioselective synthesis of modified C-nucleosides and several other tetrahydrofuran natural products.

Our synthetic strategies towards 6 and 8 start with the acquisition of prochiral bicyclo-ketone 3 by traditional chemical synthesis using compounds 1 and 2 as starting materials by a sonochemical strategy. The following transformation of ketone 3 to lactone 4 was carried out by direct enantioselective Baeyer-Villiger biooxidation by CPMO expressing cells, generating two stereogenic centers in >95% ee. Oxidation of 4 with m-chloroperoxybenzoic acid at room temperature provided the epoxylactone 5 diastereoselectively. The epoxylactone 5 was opened with methanolic potassium carbonate to give the epoxyester 6. On the other hand, the synthesis of compounds 8 was carried out by hydrolysis of lactone 4 followed by a halolactonization strategy. In summary, we achieved a short and completely stereocontrolled synthesis of the highly functionalized tetrahydrofuran rings 6 and 8. Further applications of this strategy to the synthesis of structurally related natural products are currently in progress.