P266 IS THE AROMA COMPOUND γ-DECALACTONE PRODUCED BY YEAST IN RESPONSE TO A MEMBRANE-RIGIDIFYING STRESS INDUCED BY THE BIOTRANSFORMATION MEDIUM?

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The peach-like aroma compound γ-decalactone is produced biotechnologically through the biotransformation of ricinoleic acid (RA) by some yeast species. In order to better understand the interactions occurring during the process between the lactone and the yeast cells, the influence of the lactone on the physical properties of cell membranes and model phospholipids has been studied. The producing yeast *Yarrowia lipolytica* was used as a model cell in this study. γ-Decalactone strongly increased membrane fluidity *in vivo* and decreased in a concentration-dependent manner, the phase transition temperature (*T*m) of the deuterated phospholipid DMPC-d27 (ref.[1–3]). This indicates that the lactone exhibits an important membrane-fluidizing action. On the other hand, the hydroxylated C18 fatty acid (RA) used as the precursor of the biotransformation, increased the *T*m of DMPC-d27, i. e. it rigidified the phospholipid bilayers. These observations bring about the hypothesis that the production of the lactone, a compound that is presently considered as a secondary metabolite, in fact could be stimulated in order to enable a homeoviscous adaptation of cell membranes and so to permit an optimal cell development in the medium. From this point of view, new strategies may be elaborated to improve γ-decalactone production yields.

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P267 GLYCOMIMETICS AS SELECTIVE TOOLS FOR ENZYME INHIBITION

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Sugar mimetics have shown to be inhibitors of enzyme-promoted hydrolysis of C-O glycosidic bonds exhibiting interesting applications as antibacterial, antiviral and anticancer agents. Among them, 1,4-dideoxy-1,4-iminoalditols (hydroxylated pyrrolidines) constitute an important type of compounds with a well-known importance as glycosidase inhibitors[1]. However, in many instances they are not selective presenting a wide range of enzymatic inhibition.

The selectivity in enzyme inhibition can be improved by providing the iminosugar with some information of the structure of the glycosyl moiety that is cleaved in the enzymatic hydrolysis and of the aglycon itself. Therefore, the introduction of additional groups in the iminosugar joined by hydrolytically stable C-C links could led to new more potent, more selective and hydrolytically stable enzyme inhibitors. Lipophilic moieties are important structural features because they, additionally, have the advantage of their permeability through membranes, which is an important requirement for a compound to become a useful drug.

We have found that diamines of type **1** with aryl(alkyl)-aminomethyl chains can be higly selective and competitive inhibitors of α-mannosidases and we have reported[2] a quick combinatorial approach for their preparation.

In this commuincation we report on the influence on the enzymatic activity of three stereogenic centers in the pyrrolidine ring and the influence of the methylene spacer between the nitrogen of the pyrrolidine ring and of the aminoalkyl chain. To achieve this goal, we describe the synthesis and enzymatic evaluation of derivatives of (2*S*,3*R*,4*S*), (2*R*,3*R*,4*S*), (2*R*,3*S*,4*R*) and (2*S*,3*S*,4*R*)-2-alkyl(aryl)aminoethyl-3,4-dihydroxypyrrolidines **(3-6)** and of (2*S*,3*R*,4*S*)-2-(*N*-alkyl(aryl)-aminomethyl-3,4-dihydroxypyrrolidines **(2)**.

Enzymatic inhibitory studies of diamines **2-6** indicate that the activity and selectivity in enzyme inhibition are influenced by the absolute configuration of the stereogenic centers in the pyrrolidine. Thus, (2*S* and 2*R*, 3*R*, 4*S*)-2-alkyl(aryl)aminoethyl **3** and **5** and (2*S* and 2*R*, 3*R*, 4*S*)-2-alkyl(aryl)aminomethyl **1** and **2** have shown to be moderate-to-good inhibitors of β-mannosidases, while derivatives **4** and **6** of configuration (2*R* and 2*S*, 3*S*, 4*R*) were inactive towards those enzymes presenting good inhibitory values towards β-galactosidases