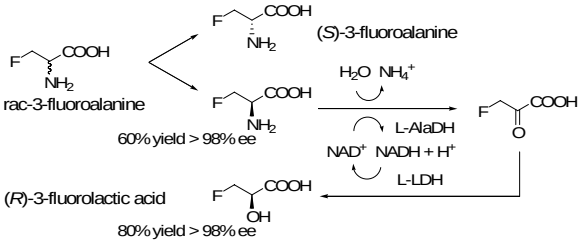
Enzyme and Microbial Production of Amino and Hydroxy Acids

O. A. C. Antunes

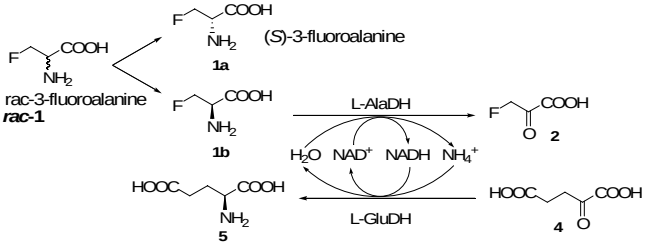
Instituto de Química, UFRJ, CT Bl A, Lab 641, Cidade Universitária, Rio de Janeiro, RJ 21945-970, Brazil

For the past years our group has been involved in the design and synthesis of inhibitors of aspartic and serine proteases. Our targets have been simple peptide mimetic compounds derived of simple scaffolds. Our firs and main interest have been the synthesis of HIV protease inhibitors, although some efforts have been done in Dengue, Hepatitis and West Nile Fever Viruses that share related serine proteases. Due to that we have been involved in the development of new protocols to produce alpha-, beta- and gamma-amino acids that can be scaled up.

In the course of our research programme, we envisaged that biotechnological related process could be useful in industrial bases due to mainly the favorable mild process conditions and, in general, low environmental impact. Although water consumption in these cases should eventually be a drawback, its recovery, normally, do not require big investments. We started our efforts in the enzymic side looking for simple *cascade* systems to the production of alpha-amino acids in which NADH or NAD^+, the co-enzymes used in these processes would be recycled. Systems based on oxidation of diols, to recycle NAD^+, or in the (aminative) reduction of keto acid derivatives were (kinetically) studied and proved to be useful, so can be generalized (schemes 1 and 2).



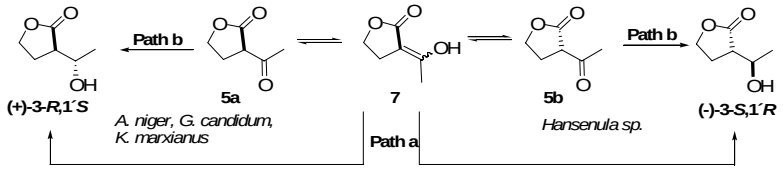
Scheme 1



Scheme 2

In parallel, we started working on hydrolases as D-hydantoinase, easily obtained from japaneses bean or from black beans.This enzyme is a very good since it allows the development of dynamic kinetic resolution processes since at pH 10, the optimum reaction pH, epimerization of hydantoins occur so allowing 100% conversion. Other enzymes have also been studied, including acylase I and several lipases. In addition several processes to immobilize these enzymes have been developed as well as their uses under super critical CO_2.

In the microbial side, we started with very simple systems so we became able to produce enantioenriched beta-hydroxy acids which allow us to go further. Therefore, we were able to discover simple enzymatic systems capable to carry out enantioselective/ diastereoselective reduction of alpha-substituted-beta-keto-lactones (scheme 3) and of the other alpha- and beta-keto-esters.



Scheme 3

Other microbial and enzymatic processes including oxidation are presently under investigation.

Acknowledgements: To CAPES, CNPq and FAPERJ (Brazilian Agencies) for financial support and to IQ-UFRJ, NPPN-UFRJ and FarManguinhos-FIOCRUZ (Brazilian Research Facilities) for analytical support.