DESIGN OF A CHEMO-ENZYMATIC PROCESS FOR STEREOSELECTIVE PRODUCTION OF SYNTHETIC (α and β) AMINO ACIDS

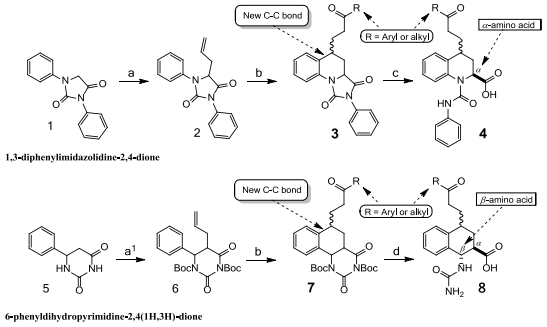
Israel Montes de Oca Nava, Luis Germán López-Valdez*
Universidad Politécnica del Valle de Toluca, División de Ingeniería en Biotecnología
Km. 5.6 carretera Toluca - Almoloya de Juárez, calle loma bonita s/n. Santiaguito Tlalcilalcali, Almoloya de Juárez, Estado de México. C.P. 50900.
Email: luis.lopez@upvt.edu.mx , lgermanlv@gmail.com

Key words: hydantiones, biotransformation, free radicals.

Introduction. To develop new technologies based on *α* and *β* amino acids is of primordial importance, specially developing new synthetic drugs, exploring new proteins, as cheap raw materials, used in asymmetric synthesis and as components of biodegradable polymers. *β*-amino acids are being studied as new compounds to avoid the resistance of several microorganisms to the antibiotics.(i) The synthesis of *β*-amino acids optically actives, is still a challenge in organic synthesis. In recent years, has been reported a series of different mechanisms of synthesis to obtain *β*-amino acids and derivatives efficiently. Nevertheless, few of them are based on using chemo-enzymatic process. Indeed, several methodologies has been developed to produce *α* and *β* amino acids optically actives, among them are: kinetic resolutions with synthetic catalyst, bio-catalytic process using transaminases, lipases, aminopeptidases and aminomutases which isomerize *α* to *β* amino acids.(ii) In an effort to contribute to this area (biotransformations in organic chemistry), here in, we report a new methodology to produce not-natural, optically actives *α* and *β* amino acids with structural diversity and complexity, though reactions of alkylation, radical addition cyclization(iii) and enzymatic hydrolysis using hydantoinases from legumes.

Methods. We used the Hydantiones **1** and **5** as skeleton base and raw materials of *α* and *β* amino acids, which after alkylation in *α* position with allyl bromide, followed by a radical cascade addition cyclization, afforded tricyclic Hydantoines **3** y **7**. These tricyclic compounds were submitted to the enzymatic condition described by Morin,(iv) to obtain the hydrolyzed products *α* and *β* amino acids precursors **4** and **8**, (Fig. 1).

Results.



Conditions reaction: **a**) K_2CO_3, TBAI (PTC), CH_3CN, allyl bromide, **a**[1]) i) $(Boc)_2O$, Et_3N, ii) NK_2CO_3, TBAI (PTC), CH_3CN, allyl bromide, **b**) EtOC(S)SR, AcOEt reflux, DLP, **c**)D-hydantoinase from *legumes*. **d**) i. TFA, CH_2Cl_2, ii) D-hydantoinase from *legumes*.

Fig. 1. General scheme of the methodology.

Table 1. Hydantoins enzymatic resolution.

Entry	Hydantoine	R	d. r.	Yield
1	**3**	CH_3-	**4** (2:1)	18
2	**7**	CH_3-	**8** (1.5:1)	21

Conclusions. The bio-catalytic asymmetric synthesis of *α* and *β*-amino acids starting from simple and cheap starting materials and using sustainable biocatalysts remains an important challenge. Here, we have demonstrated the catalytic activity of the hydantoinase from legumes, on the hydantoins prepared via a free radical addition cyclization process. This is the preliminary work of a new methodology to produce synthetic *α* and *β* amino acids.

Acknowledgements. We thank PROMEP (UPVT-PTC-024) for financial support. Helpful comments from Professor Erick Cuevas-Yañez (UAEM) and the collaboration with Centro Conjunto de Investigación en Química Sustentable UAEM-UNAM (CCIQS).

i . a) Weiner, B.; Szymanski, W.; Janssen, D. B.; Minnaard, A. J.; Feringa, B. L. (2010), *Chem. Soc. Rev.* (39), 1656–1691. b) Gross, R. A.; Kalra, B. (2002), *Science*. (*5582)*, 803–807. c) *Enantioselective synthesis of beta amino acids*, 2nd Ed.; Juaristi, E., Soloshonok, V. A., Eds.; (2005), Wiley-VCH Verlag GmbH: Weinheim,
ii . Maeve O'Neill, Bernhard Hauer, Nina Schneider, Nicholas J. Turner, (2011), ACS Catal. (1), 1014–1016
iii . *Radical Reactions in Organic Synthesis*, Samir Z. Zard (2003), Oxford University Press
iv. André Morin, (1993), *Enzyme Microbiol. Technol.* (15), 208-214.