



HAL
open science

Chemo-Enzymatic Synthesis of alpha amino acids by acylases (amidases) and aminooxydases

Valérie Rolland, Nicolas Haroune, Marie-Louise Roumestant, Jean Martínez

► **To cite this version:**

Valérie Rolland, Nicolas Haroune, Marie-Louise Roumestant, Jean Martínez. Chemo-Enzymatic Synthesis of alpha amino acids by acylases (amidases) and aminooxydases. 26th European Peptide Synthesis, Jean Martinez; Jean-Alain Fehrentz, Sep 2000, Montpellier, France. pp.343-344. hal-04715103

HAL Id: hal-04715103

<https://hal.science/hal-04715103v1>

Submitted on 30 Sep 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Chemo-Enzymatic Synthesis of α -Aminoacids by Acylases (Amidases) and Aminooxydases

Valérie Rolland, Nicolas Haroune, Marie-Louise Roumestant, Jean Martinez

Laboratoire des Aminoacides, Peptides et Protéines, UMR CNRS 5810,
Université Montpellier 2, Place E. Bataillon, 34095 Montpellier Cedex 5, France

Introduction

Even if alkylations or diastereoselective reprotonations were tried in our laboratory with 2-hydroxypinan-3-one as chiral auxiliary, (S) 7-Azatryptophane, a fluorescent probe, was prepared only by enzymatic resolution [1]. In front of the success of this method most of our strategies were adapted with at the last step an hydrolysis by enzymatic resolution [2]. In this communication we describe the different ways to access to : (S) 1,2-pyrazolylalanine **3a**, (S) 1,2,4-triazolylalanine **3b** with hypoglycemic properties, (S) 7-azaindolylalanine **3c**, isostere of the fluorescent probe (S) 7-Azatryptophane, (S) quisqualic acid which is the preferential agonist of NMDA receptors (Figure 1) [3], and finally γ -hydroxyisoleucine isomers with potent antidiabetic properties (Figure 2).

The first efficient synthesis has been performed on solid support and can be applicable in combinatorial chemistry [4].

Results and discussion

For the synthesis of β -heterocyclic aminoacids, the commercially available starting material, N-Acetyl-dehydroalanine methyl ester, is convenient to obtain optically pure α -aminoacids by enzymatic resolution by *Aspergillus genus* acylase in excellent yields (Figure 1) :

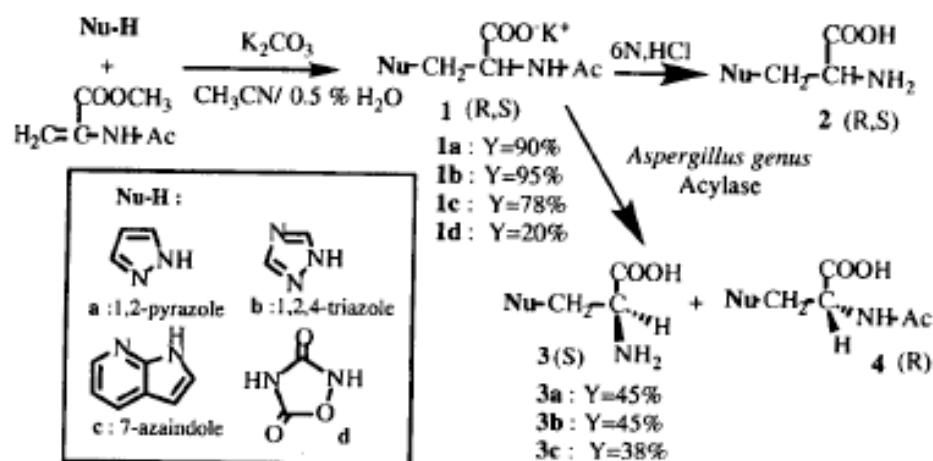


Figure 1. The strategy used to obtain β -heterocyclic aminoacids

At the first step 0.5% water in CH₃CN are sufficient to carried out one pot Michael addition and esterolysis, giving directly the free carboxyl group of the N-acetylaminoacid, substrate of this acylase. The Quisqualic acid synthesis is in progress ; the synthesis of the heterocycle oxadiazolidinedione d and the Michael addition gave low yields [6].

Because N-Ac-hydroxyaminoacids are not common acylase substrates, we investigated an other strategy for the synthesis of γ -hydroxyaminoacids (Figure 2) and we describe here only the final enzymatic step carried out by penicillin amidase G immobilized on Eupergit C called PAG C ((Y=35%). The five steps before have been described for enantioselective synthesis of γ -hydroxynorvaline [5].

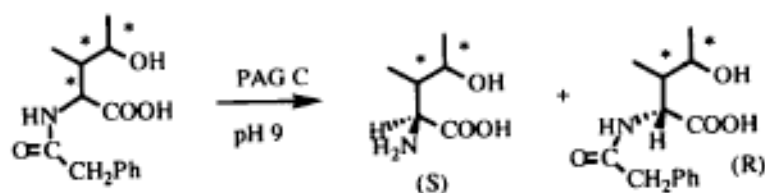


Figure 2. The enzymatic step for γ -hydroxyaminoacid synthesis

Aminooxydases being efficient biocatalysis in optically pure hydroxynorvaline preparation, commercially available (D) aminooxydase from *hog kidney* (DAAO) and (L) aminooxydase from *Crotalus adamanteus* (LAAO) have been used in γ -hydroxyisoleucine isomers synthesis, but without success.

The procedure using immobilized penicillin acylase is in progress and for the natural γ -hydroxyisoleucine synthesis, it is the best result obtained at this day.

References

1. Lecoite L., Rolland-Fulcrand V., Roumestant M.L., Viallefont Ph., Martinez J. *Tetrahedron Asym.*, 1998, 9, 1753-1758.
2. L.Pappalardo, J.M. Receveur, V. Rolland, Y. Vidal, M.L. Roumestant, Ph. Viallefont, 1999, *Recent Res. Devel. Synth. Organic Chem.*, 2: 35-47.
3. Rolland V., Haroune N., Roumestant M.L., Martinez J. *Tetrahedron: Asym.* 2000, in preparation.
4. Barbaste M., Rolland-Fulcrand V., Roumestant M.L., Viallefont Ph., Martinez J., *Tetrahedron Lett.* 1998, 39, 6287-6290.
5. M.Jacob, M.L.Roumestant, Ph Viallefont, J. Martinez, *Synlett*, 1997, 6, 691-692.
6. P. Renault, D. Thomas, F.D. Bellamy, *Synthesis*, 1991, 265-266.