Solid phase synthesis of two biologically important natural products

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Keywords: *Biosurfactants, 2,5-diketopiperazines, Solid phase synthesi, Wang resin.*

Abstract

Synthesis of peptides a difficult pathway, mostly because of the change of energy involving the process. Solid phase peptide synthesis can overcome these reaction bottle necks. 2,5-diketopiperazines (2,5-DKP) are small cyclopeptides involved in biological activity and quorum-sensing. Biosurfactants (BS) are organic and amphiphilic molecules with activity on interfaces. This work aimed to synthesize cyclo(L-Pro-L-Leu), a 2,5-DKP and Surfactin, a BS and characterize them with MS and NMR.

Introduction

The peptide bond formation by direct condensation of two amino acids is an energetically disfavored process[1].

Solid phase peptide synthesis can overcome this drawback, allowing the production of peptides from two to ten amino acids.

2,5-DKPs are cyclopeptides produced by many microorganisms, displaying important biological activity. DKPs are also present in intra and interspecies communication (quorum-sensing)[2].

BS are amphiphilic compounds responsible for hydrophobic and hydrophilic properties, changing interfacial conditions. Surfactin (Figure 1) is a class of surfactants composed by a cyclic chain of amino acids and a long chain of β-hydroxy-fatty acid[3].

Herein we demonstrate the solid phase peptide synthesis of cyclo(L-Pro-L-Leu) and surfactin.

Results and Discussion

For the synthesis of both natural products the resin chosen was Wang's resin and the strategy Fmoc (Fluorenylmethyloxycarbonyl)[4] was selected.

The first amino acid already comes coupled to the resin, being only necessary the disprotection of the amino terminal part and plug of the new amino acid using coupling reactants diisopropylcarbodiimide (DIC) and 1-Hydroxybenzotriazole (HOBt).

The adding of acidic reactants like trifluoroacetic acid (TFA) and scavengers like triisopropylsilane (TIS) and water, cleaves the peptides from the resin.

Synthetic cyclo(L-Pro-L-Leu) (Figure 2) was characterized by EI-MS and ^{1}H and ^{13}C NMR including 2D NMR. The data were compared with literature.

Surfactin structure confirmation was made by ESI(+)MS and ^{1}H and ^{13}C NMR including 2D NMR.

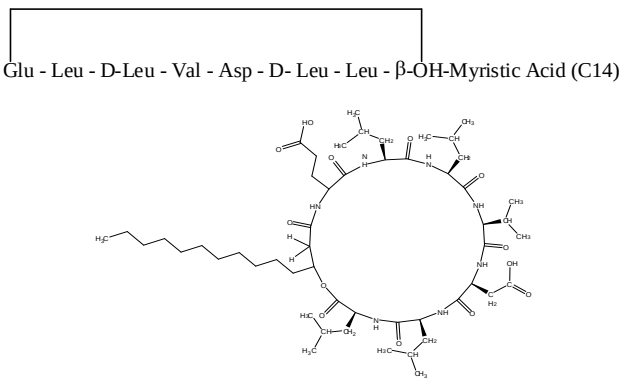

Figure 1. Representation and structure of surfactin

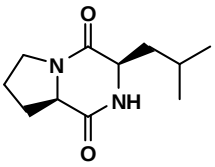

Figure 2. Cyclo(L-Pro-L-Leu)

Conclusions

The solid phase synthesis proved to be an easy pathway for syntheses of biologically active peptides, overcoming problems of common condensation reactions. Spectroscopic and spectrometric data confirmed the structures synthesized of cyclo(L-Pro-L-Leu) and surfactin.

Acknowledgements

CAPES, CNPq, Petrobrás (Proj. 4955), FAPESP (Proj. 2010/51278-0).

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