Synthetic studies aiming structural elucidation of (-)-parviestemoamide

Gilmar A. Brito Jr. and Ronaldo A. Pilli*
Instituto de Química, Unicamp, Campinas, São Paulo, Brasil
*pilli@iqm.unicamp.br

Keywords: alkaloid, silyloxyfuran, Michael addition

INTRODUCTION

The alkaloid parviestemoamide was isolated from the roots of Stemona parviflora. The chemical structure of this compound was firstly proposed by Xu¹ and coworkers (1a), but in a different work², another structure (1b) was suggested by the same authors, as showed in figure 1.

![Figure 1: Chemical structures proposed for the parviestemoamide alkaloid](image)

Our retrosynthetic analysis of parviestemoamide was based on the cyclization of aminoester 2, providing the parviestemoamide skeleton 1a (Scheme 1).

![Scheme 1: Retrosynthetic analysis of parviestemoamide 1a](image)

Aminoester 2 could be obtained by Michael addition of nitroester 4 onto benzylcarbamate 7 derived from aldehyde 3, followed by a Nef reaction. We decided to start the synthesis of this alkaloid on a racemic approach. Based on MacMillan’s strategy³ of silyloxyfuran addition onto conjugated aldehydes, we were able to prepare racemic aldehyde 3, using an achiral organocatalyst. This aldehyde was submitted to reductive carbamoylation, resulting in protected primary amine 7 (Scheme 2).

![Scheme 2: Synthesis of carbamate 7 by Mukaiyama-Michael addition and reductive carbamoylation](image)

RESULTS AND DISCUSSION

After removing the nitrogen protecting group we expected to form the lactam 10 under acid or basic conditions. Unfortunately, only degradation products were obtained.

Future work will focus on a selective methyl ester hydrolysis and after removal of the carboxybenzyl group, aminoacid 11 would be obtained. Classical methods of peptide synthesis will be employed to prepare lactam 10 that could be converted to 1a, after further modifications (Scheme 4).

![Scheme 3: Sequential Michael addition and Nef reaction toward the synthesis of advanced intermediate 9](image)

![Scheme 4: Proposed final steps aiming to the total synthesis of (+/-)-1a](image)

CONCLUSION

In this work, we were able to prepare an advanced intermediate toward the parviestemoamide skeleton. At present, methyl ester hydrolysis conditions are under study and next, the peptide synthesis methods will be employed, aiming the structural elucidation of this alkaloid.

ACKNOWLEDGEMENTS

The authors are grateful to Fapesp and CNPq for financial support.

REFERENCES
