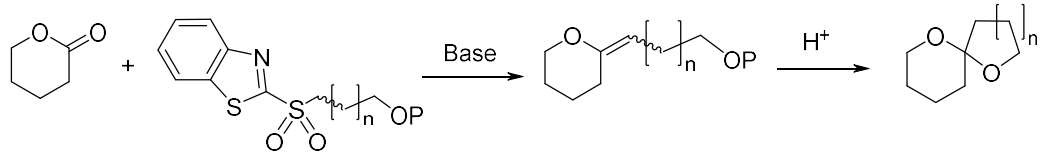
UMR 5246 - «Institut de Chimie et Biochimie Moléculaires et Supramoléculaires » (ICBMS) Laboratoire de Chimie Organique 2 – Glycochimie

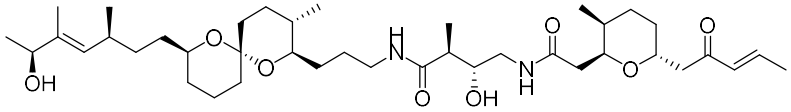
Total synthesis of spiroketal natural products via the Mukaiyama aldol on exocyclic enol ethers

Directors: Dr. David Gueyrard, Pr. Peter Goekjian.

The stereoselective synthesis of exocyclic enol ethers by the extension of the modified Julia Reaction to the synthesis of enol ethers from lactones has been extensively studied in our group.[1] Based on this reaction, we developed an original method to provide spiroketals through an acid catalyzed cyclization of exo-enol ethers.[2]

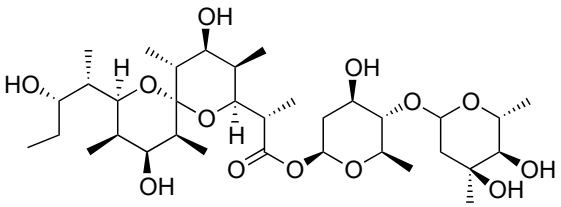


We applied this methodology for the total synthesis of Bistramide A and others spiroketals isolated from natural sources.[3]



Bistramide A

An alternative approach involves a stereoselective Mukaiyama aldol reaction, followed by an *in situ* cyclization, which would allow us to control the two centers adjacent to the spirocyclic carbon. Current studies on the scope, relative diastereoselection, and induction will provide new routes to this essential class of natural products such as the antibiotic Enteridinine A.[4]



[1] a) D. Gueyrard, R. Haddoub, A. Salem, N. Said Bacar, P. G.Goekjian, Synlett 2005, 520; b) B. Bourdon, M. Corbet, P. Fontaine, P. G. Goekjian, D. Gueyrard, Tetrahedron Lett. 2008, 49, 747.

[2] M. Corbet, B. Bourdon, D. Gueyrard, P. G. Goekjian, Tetrahedron Lett. 2008, 49, 750

[3] a) L. Tomas, D. Gueyrard, P. G. Goekjian, Tetrahedron Lett., 2010, 51, 4599. b) L. Tomas, G. Boije Af Gennas, M. A. Hiebel, P. Hampson, D. Gueyrard, B. Pelotier, J. Yli-Kauhaluoma, O. Piva, J. M. Lord, P. G. Goekjian, Chem. Eur J., 2012, 18, 7452. c) L. Tomas, B. Bourdon, J. C. Caille, D. Gueyrard, P. G. Goekjian, Eur. J. Org. Chem., 2013, 915.

[4] Rezanka, Tomas; Dvorakova, Radmila; Hanus, Lumir O.; Dembitsky, Valery M. Phytochemistry 2004, 65, 455.