BOS 2012 TALLINN

International Conference on Organic Synthesis

July 1-4, 2012
Tallinn, Estonia

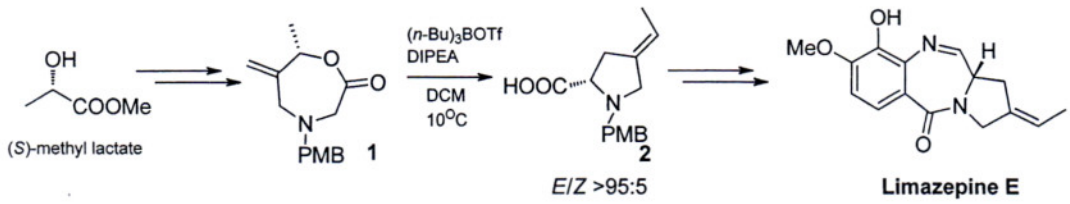
Balticum Organicum Syntheticum

Program and Abstracts

STEREOSELECTIVE SYNTHESIS OF LIMAZEPINE E *VIA* A BORON ENOLATE IRELAND-CLAISEN REARRANGEMENT

Gints Smits[1,2], Ronalds Zemribo[2] *
[1]Riga Tehnical University, Azenes 14/24, Riga, Latvia,
[2]Latvian Institute of Organic Synthesis, Latvia, Riga, Aizkraukles 21
gintssmits@osi.lv, ronalds @osi.lv

Pyrrolo[1,4]benzodiazepines (PDBs) are a well known, yet still growing class of natural products possessing antitumor antibiotic properties due to their ability to covalently bind the minor groove of DNA[1]. The latest isolated members of PBDs are Limazepines (A-E), reported in 2009[2]. Limazepine E, as well as known PBDs prothracarcine and tomaymycine possess an *E*-ethylidene substituent at 2-position. Although several total syntheses of these natural products have been reported, efficient control of the olefin geometry has not been achieved.



The key building block for the total syntheses of ethylidene group containing PDBs is a proline derivative **2**, possesing both elements of stereochemistry – an (*S*)- chiral center and an *E*- olefin.

Herein we disclose an efficient, stereoselective synthesis of (*S*,*E*) ethylidene proline derivatives **2** via a boron enolate Ireland-Claisen rearrangement of 7-membered lactone **1**, and the further elaboration of this building block into Limazepine E. The synthesis of 7-membered lactone **1** from (*S*)-methyl lactate, the optimization studies of the key transformation – the Ireland-Claisen rearrangement and the completion of total synthesis will be presented.

1. For a recent review see: Cipolla, L.; Araújo, A.C; Airoldi, C.; Bini, D. *Anti Canc. Agents Med. Chem.*, **2009**, *9*, 1-31.
2. Fotso, S; Zabriskie, M; Proteau, P; Flatt, P; Santosa, D, A; Mahmud, S; Mahmud, T. *J. Nat. Prod*, **2009**, *72*, 690-695.