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ABSTRACTS

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Application of Ireland-Claisen Rearrangement in the Total Syntheses Pumiliotoxins

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I. Introduction

Pumiliotoxins **1** (figure 1) are biologically active [1], lipid-soluble alkaloids, which were isolated from amphibian skin [2]. Although several total syntheses have been reported in the literature, formation of stereochemically defined exocyclic double bond as well as 2 stereogenic centers, still posseses a considerable synthetic challenge. Recently we have reported a novel approach to double bond geometry control using the Ireland-Claisen rearrangement [3]. Herein we report an extension of this methodology towards the synthesis of pumiliotoxins.

II. Results and Discussions

The key step in our total syntheses of pumiliotoxins is a stereoselective Ireland – Claisen rearrangement of a ketene acetal **2**, derived from 8-membered lactone **1**.

The necessary lactone **1** was obtained by a 3 step sequence starting from readily available building blocks. The Ireland – Claisen rearrangement proceeds with high degree of stereoselectivity, both in respect to the newly generated double bond and the chiral center. The acid derivative **3** was converted to the target pumiliotoxin by a simple reduction sequence.

III. Conclusions

A stereoselective Ireland – Claisen 27earrangement was as a key step for the total syntheses or pumiliotoxins.

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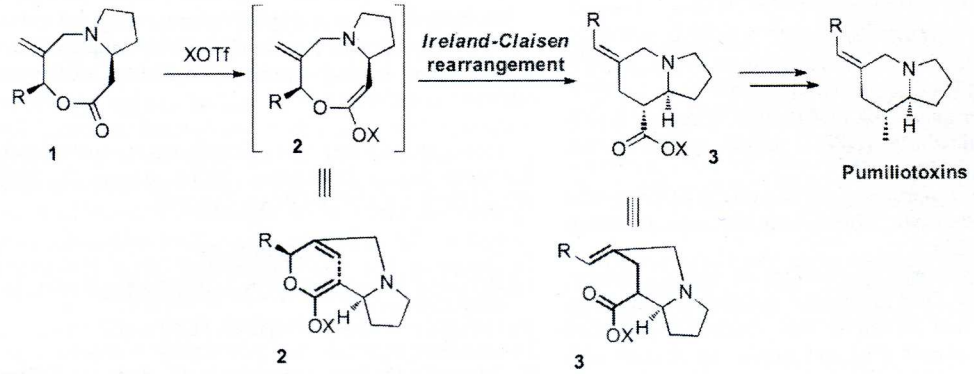

Figure 1. Total syntheses of pumiliotoxins.