SYNTHETIC STUDIES TOWARD THE 11-DEOXYFISTULARIN-3 NATURAL PRODUCT

Ashton T. Hamme II\textsuperscript{1}, Prasanta Das\textsuperscript{1}, Erick D. Ellis\textsuperscript{1} and Edward J. Valente\textsuperscript{2}

\textsuperscript{1}Department of Chemistry & Biochemistry, Jackson State University, Jackson, Mississippi, USA
\textsuperscript{2}Department of Chemistry, University of Portland, Portland, Oregon, USA

Abstract: A series of natural products isolated from the sponge of \textit{Verongida} have been intensively studied due to the presence of alkaloids with one, or more bromotyrosine residues. Many of these alkaloid metabolites show interesting bioactivity and cytotoxic properties in tumor cell lines. 11-deoxyfistularin-3 is cytotoxic against human breast carcinoma cell line MCF-7. The purpose of this project was to find a synthetic methodology that will be applied towards the total synthesis of the 11-deoxyfistularin-3 and other spirocyclic isoxazolines. Aromatic ring and ester containing nitrile oxides reacted with disubstituted geminal alkenes in a 1,3-dipolar fashion to afford the analogous 5,5-isoxazolines which were then used to construct the corresponding spiroisoxazolines through an intramolecular cyclization/methylation reaction in one reaction vessel. Due to the fact that the methylation process yields two regioisomeric spiroisoxazolines, other methods were investigated to selectively methylate one enolate oxygen over the other. Subsequent bromination of the spiroisoxazoline affords a product that is a few steps away from the natural product core. The synthesis, mechanistic details, and isolated yields for the reported spirocyclic isoxazoline compounds will be discussed.

Keywords: Natural Products, Heterocycles, Cycloaddition

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