Synthetic Studies on Peptide—Polyamine Toxin

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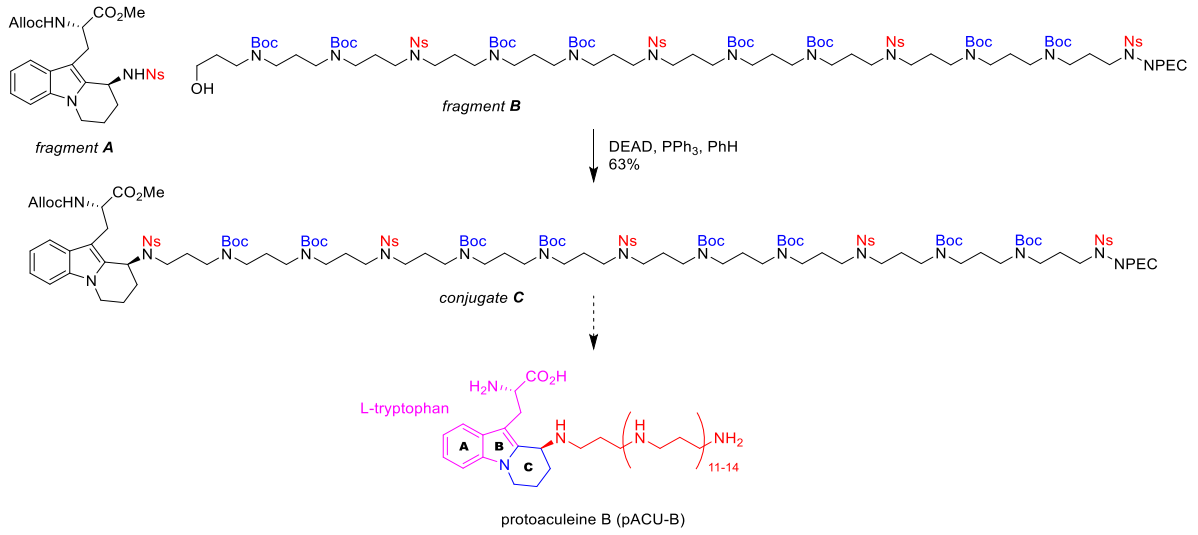
Abstract

Natural products are an attractive source for discovery of biologically functional molecules. Historically, chemical synthesis of such interesting natural product has driven the studies toward biological and medical applications forward strongly. However, the structure of natural product is quite often complex which hampers the synthetic approach. Such "structural complexity" involves three-dimensional complexity, high-density functionalities, and so on.

Protoaculeine B (pACU–B), a polyamine toxin bearing a modified tryptophan, belongs to another class of complex molecule being composed of a hybrid of biogenetically irrelevant fragments. pACU–B and the peptide conjugate aculeine B are toxic to mammalian cells with unique interaction with the plasma membranes, which may be of use to deliver arbitrary molecule into cells. Since its isolation from marine sponge collected in Iriomote, Japan, in 2014,[1] we have been working on the synthesis of pACU–B.

Herein we report our effort toward the chemical synthesis. Starting from tryptophan, the modified tryptophan fragment **A** was synthesized over 16 steps, employing reductive enamide formation from oxime, followed by stereoselective hydrogenation as key steps.[2] To synthesize the polyamine fragment **B** efficiently, we employed Ns strategy. By using photocleavable NPEC protecting group in combination with Ns group, synthesis of suitably protected polyamine fragment **B** was conducted in a convergent manner.[3] Fragment coupling was performed successfully by Mitsunobu reaction to furnish **C**. Out attempts toward completion of the synthesis, as well as some biological profiles of the partial structures will be discussed.

Keywords: NPEC, oxime, protecting group, stereoselective hydrogenation, tryptophan



References

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