

Synthetic studies on aculeine B, a peptide–polyamine hybrid marine toxin

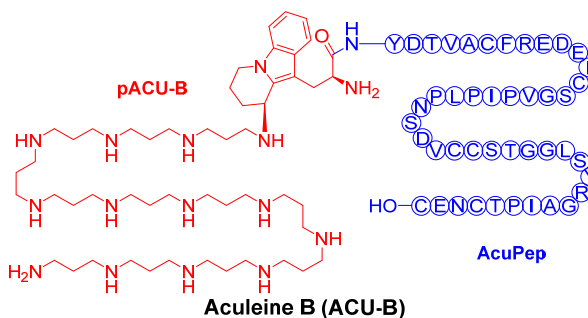
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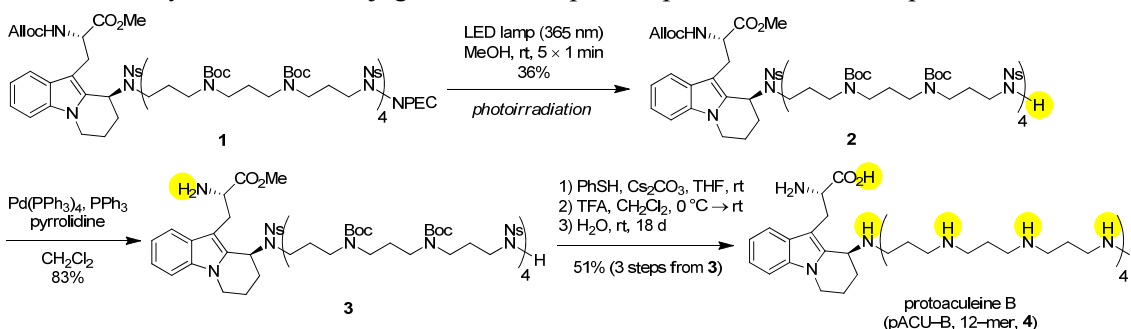
Keywords: Natural Product; Aculeine; Polyamine; Structure–Activity Relationships; Total Synthesis

Aculeine B (ACU–B) is a peptide–polyamine conjugate isolated from a marine sponge collected in Iriomote, Okinawa, Japan.¹⁾ ACU–B is toxic to cultured cancer cells, and it has been suggested that the toxicity is based on specific interactions between the long-chain polyamine moiety and cell surface molecules.



Since ACU–B may be of use for 1) development of a new anticancer drug, and/or 2) delivery of drugs into cells, we have started functional analyses of ACU–B based on synthetic organic chemistry. Herein we report our efforts toward total synthesis of pACU–B, which is the *N*-terminal partial structure of ACU–B.²⁾

First, the NPEC group of the fully protected pACU–B **1**, synthesized by Mitsunobu coupling of heterotricyclic and polyamine moieties,³⁾ was removed by photoirradiation.⁴⁾ The Alloc group was then deprotected with palladium catalyst to give **3**. Finally, Ns group, Boc group, and methyl ester were sequentially removed in three steps to furnish pACU–B (**4**). Synthesis and bioactivity of artificial conjugates of AcuPep with spermine will be also presented.



1) S. Matsunaga, M. Jimbo, M. B. Gill, L. L. Lash-Van Wyhe, M. Murata, K. Nonomura, G. T. Swanson, R. Sakai, *ChemBioChem* **2011**, *12*, 2191–2200. 2) S. Matsunaga, R. Kishi, K. Otsuka, M. Fujita, M. Oikawa, R. Sakai, *Org. Lett.* **2014**, *16*, 3090–3093. 3) H. Shiozaki, M. Miyahara, K. Otsuka, K. Miyako, A. Honda, Y. Takasaki, S. Takamizawa, H. Tukada, Y. Ishikawa, R. Sakai, M. Oikawa, *Org. Lett.* **2018**, *20*, 3403–3407. 4) M. Miyahara, H. Shiozaki, H. Tukada, Y. Ishikawa, M. Oikawa, *Tetrahedron Lett.* **2018**, *59*, 4197–4278.