

Toward a Total Synthesis of Novel Anti-Cancer Drimentine C

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Drimentines are a novel family of nine alkaloids that exhibit antibiotic, antifungal, anticancer, and anthelmintic activities. Nine forms of drimentines (forms A-H and 3,25-dihydrodrimentine E) have been found in nature; however, only small amounts of drimentines have been isolated from natural sources, and only drimentines A, F, and G have been fully synthesized using synthetic procedures. The purpose of this study was to synthesize the cyclo-L-tryptophan-L-proline portion of drimentine C. This paper details the retrosynthesis design from which the forward synthesis of cyclo-L-tryptophan-L-proline from L-tryptophan and L-proline was developed. The forward synthesis proceeded in a three-step process that included Boc protection of L-tryptophan, esterification of L-proline, and a three-part condensation deprotection sequence to form the cyclo-L-tryptophan-L-proline. Novel purification procedures to purify products are also outlined. A total of 1.7071 g of the cyclo-L-tryptophan-L-proline were successfully produced over four successive syntheses. Future goals include synthesis of the pentacyclic component of drimentine C from the cyclo-L-tryptophan-L-proline using a possible synthesis pathway developed by this author, followed by total synthesis of drimentine C. Once synthesized, the duocyclic section of drimentine C will be combined with the pentacyclic section, using a condensation reaction. Ultimately, drimentine C will be evaluated in vitro against cancer tumor cell lines to determine its effectiveness as an anti-cancer agent.