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One-Pot Evolution of Ageladine A through a Bio-Inspired Cascade towards Selective Modulators of Neuronal Differentiation

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Abstract

© 2016 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim A bio-inspired cascade reaction has been developed for the construction of the marine natural product ageladine A and a de novo array of its N1-substituted derivatives. This cascade features a 2-aminoimidazole formation that is modeled after an arginine post-translational modification and an aza-electrocyclization. It can be effectively carried out in a one-pot procedure from simple anilines or guanidines, leading to structural analogues of ageladine A that had been otherwise synthetically inaccessible. We found that some compounds out of this structurally novel library show a significant activity in modulating the neural differentiation. Namely, these compounds selectively activate or inhibit the differentiation of neural stem cells to neurons, while being negligible in the differentiation to astrocytes. This study represents a successful case in which the native biofunction of a natural product could be altered by structural modifications.

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Keywords

2-aminoimidazole, ageladine A, natural products, neural differentiation, one-pot synthesis