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A General and Scalable Synthesis of Aeruginosin Marine Natural Products Based on Two Strategic C(sp^3)–H Activation Reactions

Synthesis of Aeruginosin Natural Products

Significance: The marine natural products of the aeruginosin family have been shown to possess high in vitro inhibition of serine proteases. In this communication by Baudoin and co-workers, a novel approach for the synthesis of the core structure using an uncommon C(sp^3)–H bond activation is presented, culminating in the efficient total synthesis of aeruginosins 98B and 298A.

Comment: The synthesis of B, used for the pivotal C–H bond activation step, was accomplished from dibromocyclohexene A in two steps. Previously reported conditions (Angew. Chem. Int. Ed. 2012, 51, 10399) gave the cyclization product C in 68% yield. Its elaboration into key precursor D allowed for the installation of the peptide as well as the guanidine side chain of both natural products.