

Total Synthesis and Stereochemistry of (+)-Dragmacidin D

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Dragmacidin D is a complex deep-sea marine heterocyclic natural product whose stereochemical identity has remained unclear since its isolation. This bis(indole) pyrazinone alkaloid contains a single stereocenter, whose configuration was proposed based on stereochemistry of another congener, dragmacidin F. Recently, Capon and Jia revised the assignment to 6''R based on total synthesis, the first enantioselective preparation of dragmacidin D in 26 steps. We developed an effective direct asymmetric alkylation of arylacetic acids, which enabled the synthesis of (+)-dragmacidin D in 10 steps. Curiously, our own effort confirmed the originally proposed assignment as 6''S. We also determined that dragmacidin D undergoes a slow racemization in aqueous solution at pH 6.8, essentially complete within 16 days at room temperature.

