

Synthesis of the rosette-inducing factor RIF-1 and analogs.

Beemelmans C, Woznica A, Alegado RA, Cantley AM, King N, Clardy J (2014) Synthesis of the rosette-inducing factor RIF-1 and analogs. *J. Am. Chem. Soc.* 136(29), 10210-10213.

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Abstract

Studies on the origin of animal multicellularity have increasingly focused on one of the closest living relatives of animals, the choanoflagellate *Salpingoeca rosetta*. Single cells of *S. rosetta* can develop into multicellular rosette-shaped colonies through a process of incomplete cytokinesis. Unexpectedly, the initiation of rosette development requires bacterially produced small molecules. Previously, our laboratories reported the planar structure and femtomolar rosette-inducing activity of one rosette-inducing small molecule, dubbed rosette-inducing factor 1 (RIF-1), produced by the Gram-negative Bacteroidetes bacterium *Algoriphagus machipongonensis*. RIF-1 belongs to the small and poorly explored class of sulfonolipids. Here, we report a modular total synthesis of RIF-1 stereoisomers and structural analogs. Rosette-induction assays using synthetic RIF-1 stereoisomers and naturally occurring analogs defined the absolute stereochemistry of RIF-1 and revealed a remarkably restrictive set of structural requirements for inducing rosette development.

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