Total Synthesis and Biomimetic Studies of Nine-Membered Enediyynes

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The kedarcidin and C1027 chromophores are formidable targets of total synthesis. During our 20-year study of these nine-membered enediyne chromophores, several powerful, yet chemoselective methods have been developed: stereoselective epoxyalkyne formation, atropselective Pd/Cu-Sonogashira coupling, 2-deoxy-α-glycosylation, CeX₃-mediated enediyne cyclisation, and SmI₂-based reductive olefination. Besides their total syntheses, application of these methods to the biomimetic study of the putative enediyne-precursors of the cyanosporasides, sporolides, and fijiolides will be presented. In particular, we disclose biomimetic evidence of a p-benzyne diradical species reacting in either a radical mode (hydrogen abstraction) or ionic mode (chloride attack) at the same sterically exposed site, leading to either monochlorinated cyanosporaside A/F or cyanosporaside B–E, respectively. The ionic monochlorination of the cycloaromatized p-benzyne of the C1027 enediyne core to generate the fijiolide aglycon framework will also be presented.

* Dedicated to the lasting contributions of Professor Emeritus Masahiro Hirama to Total Synthesis