Routes to Nine-membered Enediynes: Not such a walk in a park

64th Gordon Research Conference on Natural Products, Andover, NH, USA (26-30 July 2015)

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The kedarcidin and C1027 chromophores are formidable targets for total synthesis. Herein, we describe viable routes to these highly unstable natural products. Over 20-years during our study of these nine-membered enediyne chromophores, several new methods may now be highlighted from the Hirama group: stereoselective epoxyalkyne formation, atropselective Pd/Cu-Sonogashira coupling, 2-deoxy-α-glycosylation, CeX_3-mediated enediyne cyclisation, and SmI_2-based reductive olefination.

Further application of these methods to the biomimetic study of the putative enediyne-precursors of the cyanosporasides, sporolides, and fijiolides are also being finalized in the Natural Products Laboratory at Tohoku University (Sendai, Japan). In particular, we present 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 or cyanosporaside B, respectively. The ionic monochlorination of the cycloaromatized p-benzyne of the C1027 enediyne core to generate the fijiolide aglycon framework will also be presented.

This talk is dedicated to Professor Emeritus Masahiro Hirama both on his retirement and to the continuing challenges of complex and applied total synthesis.