

## S09-5 Symmetry-Driven Synthesis of Polycyclic Natural Products

○Masayuki INOUE<sup>1</sup>

<sup>1</sup>The University of Tokyo, Grad. Sch. of Pharm. Sci.

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Ryanodine (**1**) is a potent modulator of calcium release channel that is known as the ryanodine receptor. It alters the function of the receptor in a complex manner: submicromolar concentrations lock the channel in a long-lived open state, whereas micromolar or greater concentrations inhibit Ca<sup>2+</sup> release. From a synthetic point of view, the complex molecular architecture of **1**, which includes five rings, eleven stereogenic centers, seven oxygenated carbons, and seven contiguous fully substituted carbons, is a daunting challenge for chemical synthesis.

From our perspective, ryanodine **1** and related structures present an ideal platform to devise efficient strategies for building highly oxygenated multi-cyclic carboskeleton. In addition, development of a flexible synthetic scheme to **1** would enable generation of chemical derivatives with distinct functional properties toward the ryanodine receptors. As an initial phase of this study, we report a concise route to highly substituted skeletons of the ABDE-tetracycle by taking advantage of its embedded symmetric structure.