Synthetic Study of Keramaphidin B

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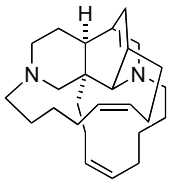

Keramaphidin B (1)

Keramaphidin B (**1**) was isolated from a marine sponge in Kerama island by Kobayashi *et al*. In 1992, Baldwin and Whitehead proposed that **1** was the common intermediate in the Manzamine alkaloids biosynthesis involving an intramolecular Diels-Alder reaction as a key step. According to this hypothesis, Baldwin's group reported total synthesis of **1**. However, Diels-Alder reaction of simple precursor was resulted in low yield. We also synthesized the Diels-Alder precursor using another method, but the Diels-Alder reaction of this compound under various conditions gave same result. We thought that the reason for such a low yield was insufficient tautomerization of imine. Given this factor, the stepwise construction of azabicyclo[2.2.2] ring would be favor than the single step construction found in biosynthesis.

Both compounds **2** and **3** were prepared from the common intermediate by *Z*-selective Horner-Wadsworth-Emmons reaction. Coupling between **2** and **3** under Mitsunobu condition and deprotection of the Ns group and lactamization gave **4**. After transformation of **4** into **5**, Ns group mediated macrocyclization of **5** with DMEAD (0.01M) proceeded in good yields. Conversion to atom transfer radical cyclization precursor **7** was succeeded in 5 steps. Further work to the total synthesis of **1** from **7** via radical cyclization reaction will be discussed.