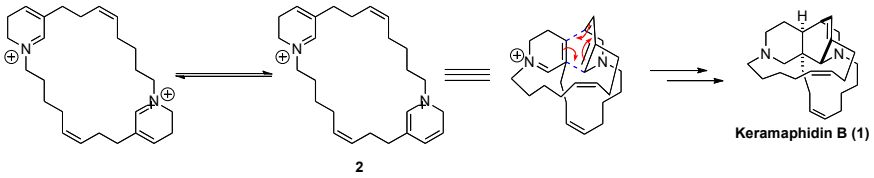
Synthetic Studies on Keramaphidin B

Yuuki Sakai

Department of Medicinal Sciences, Graduate School of Pharmaceutical Sciences

Keramaphidin B (**1**) was isolated by Kobayashi *et al*. from Okinawan Marine Sponge (*Amphimedon* sp.). Since **1** was considered as a precursor of Manzamine alkaloids, **1** has been attracted much attension of many synthetic chemists. In 1992, Baldwin and Whitehead proposed that biosynthesis of **1** would be accomplished by intramolecular Diels-Alder reaction. According to this hypothesis, Baldwin *et al.* completed total synthesis of **1**, however Diels-Alder reaction of simple precursor (**2**) was finished in low yield. Given this factor, I considered stepwise construction of azabicyclo[2,2,2] ring that single step construction in biosynthesis. We started synthetic study of **1**, by through of the intermediate **3**.



Compounds **4**, **5** was prepared from common intermediate using *Z*-selective Horner-Wadsworth-Emmons reaction. Coupling of **4** and **5** under Mitsunobu condition and deprotection of the Ns group and lactamization gave **6**. Conversion to macrocyclization precursor **7** by 2 steps. Ns group mediated macrocyclization of **7** was achieved using DMEAD (0.01M) good yields. Deprotection and iodination gave atom transfer radical cyclization precursor **9**. Further work to the total synthesis of **1** from **3** via radical cyclization will be discussed.