Total Synthesis of Garsubellin A and Further Progress

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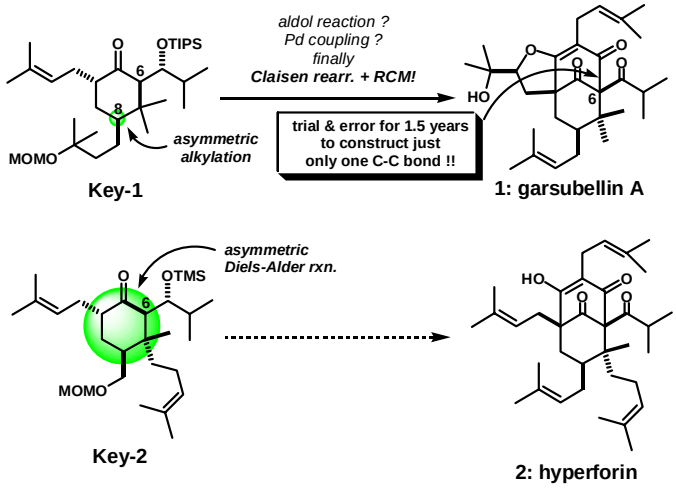
PPAPs (polycyclic polyprenylated acylphloroglucinols) have attracted recent attention from synthetic and medicinal points of view due to their structural complexity and interesting biological activities. Among them, garsubellin A (**1**) has neurotrophic activity through choline acetyltransferase (ChAT) induction. Structurally, it has a bicyclo[3.3.1] moiety bearing quaternary carbons at both of the two bridgeheads. We have recently achieved total synthesis of garsubellin A. In the process of the research, there were many dropped-out strategies, such as aldol reaction and Pd-catalyzed coupling reaction strategies to construct the central framework, bicyclo[3.3.1] moiety. Above all, we found Claisen rearrangement and RCM as key reactions to complete the total synthesis[1].

Another interesting compound is hyperforin (**2**), which is an antidepressant element of St. John's wort. For an easy access to the compound with other PPAPs including garsubellin A, we developed a powerful catalytic asymmetric Diels-Alder reaction with highly functionalized substrates[2]. To evaluate the efficiency of the methodology, we are now challenging the asymmetric total synthesis of hyperforin.



[1] Kuramochi, A.; Usuda, H.; Yamatsugu, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2005**, *127*, 14200.

[2] Usuda, H.; Kuramochi, A.; Kanai, M.; Shibasaki, M. *Org. Lett.* **2004**, *6*, 4387.