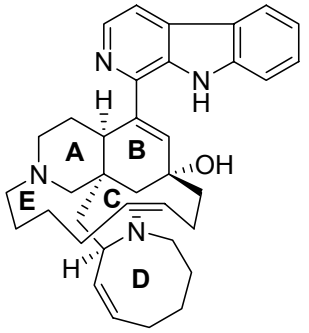
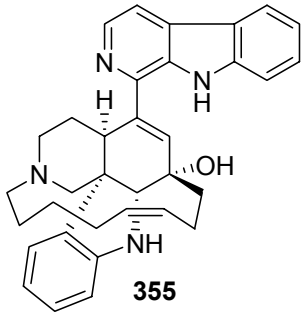
Summary

Manzamine A **1** (Scheme 1) is an indole alcaloid discovered and isolated in 1986 by T. Higa and Coworkers[1] from marine sponges of the genus *Pellina* and *Haliclona*. Manzamine A displays interesting antitumour and antibacterial activities. The unique structure of Manzamine A **1**, coupled with its biological proprieties - and its rarity – has provided a major impetus towards its total synthesis. During initial studies in our laboratory, we were able to access new tetracyclic structures, analogues of the core of the Manzamines, by a novel anionic polycyclisation strategy. Following this success, we have decided to take advantage of this new methodology to complete the synthesis of an indolic analogue **355**.

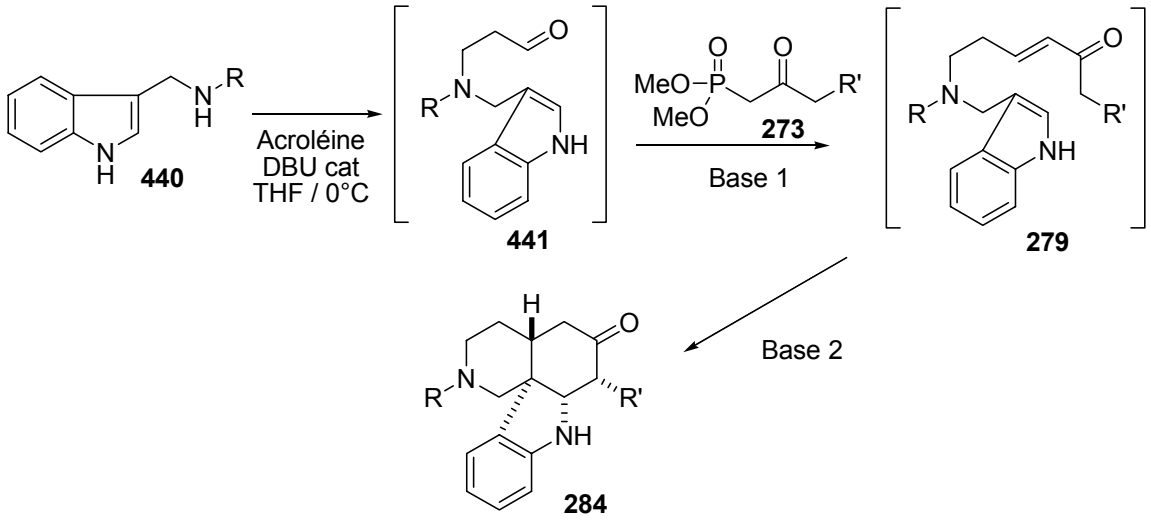


Manzamine A **1**



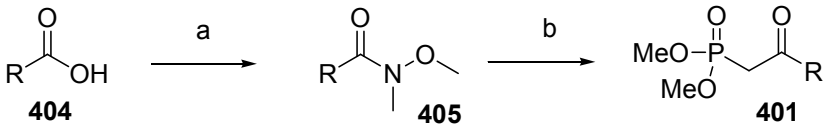
355

At first, we have studied in more detail our anionic polycyclisation strategy. Some intermediates of our on pot procedure were isolated or observed. This allowed us to propose a detailed reaction pathway and to explain the diastereoselectivity of the isolated tetracycles **284**.



440 **441** **273** **279** **284**

We also have developed a general and efficient method in order to synthesise varied β-kéto-phosphonates **401** from the corresponding acids **404**.



404 **405** **401**

(a) CDI (1,1 éq), DCM puis MeOMeNH.HCl (1,1 éq), Et_3N (2,2 éq) (b) $(MeO)_2P(O)CH_2Li$ (1,5 éq), THF, -78°C

Our following goal was to obtain the 13 membered ring. To do so, five different approaches were studied. Whilst the desired macrocyclic derivative has never been obtained, many key-intermediates were synthesised by short and efficient routes, showing the versatility of our method.

Finally, we have performed some fonctional transformations on the obtained tetracyclic compounds. The corresponding aziridines and diones were isolated in good yields.