Asymmetric total synthesis of (+)-cytotrienin A

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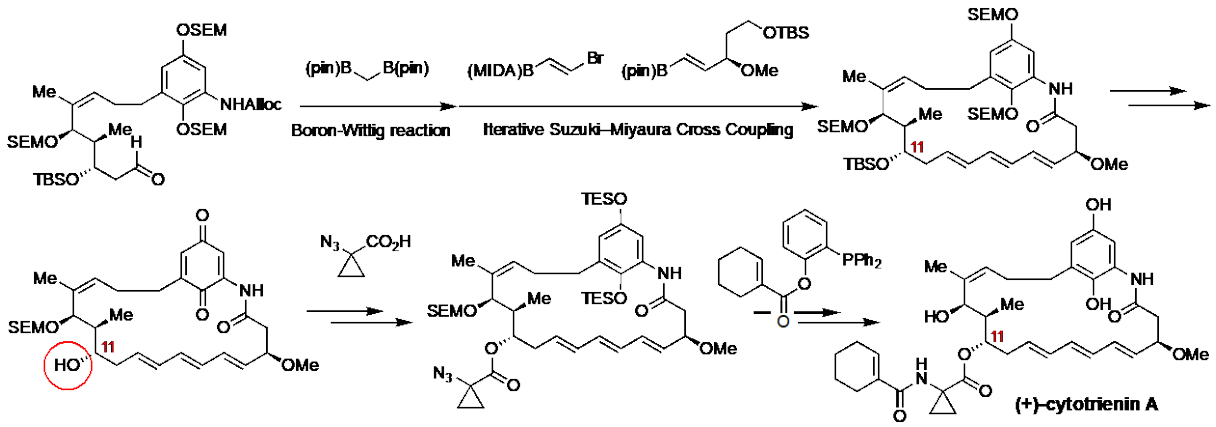
(+)-Cytotrienin A, an ansamycin-class antibiotic, exhibits potent apoptosis-inducing activity and has attracted much attention as a lead compound for anticancer drugs. Herein, we report a new asymmetric synthetic route to (+)-cytotrienin A, employing an unexplored approach involving the late-stage installation of a C11 side chain onto the macrolactam core. In this strategy, we utilized the redox properties of hydroquinone and installed a side chain on the sterically hindered C11 hydroxyl group via the traceless Staudinger reaction. This study also demonstrated that the boron-Wittig/iterative Suzuki–Miyaura cross-coupling sequence was effective for the concise and selective construction of the (*E*,*E*,*E*)-conjugated triene moiety.[1] The developed route should open new opportunities for the structure–activity relationship studies of the side chains of these ansamycin antibiotics and the preparation of other synthetic analogs and chemical probes for further biological studies.



References

1. Tateishi, Y.; Sato, R.; Komatsu, S.; Noguchi, M.; Nagasawa, S.; Sasano, Y.; Kanoh, N.; Iwabuchi, Y.;. *Angew. Chem. Int. Ed.* **2023**, *e202300031*.