Progress Towards the Total Synthesis of Maoecrystal Z

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Historically, many natural products, like Taxol, Penicillin, Morphine, etc, have proven to show anti-cancer, anti-bacterial activities and greatly improved the human health condition. Maoecrystal Z, a natural product recently isolated, showed anti-cancer activity towards several cell lines such as K562 (leukemia), MCF7 (breast), and A2780 (ovarian) cell. Despite the enormous potential use of this molecule, the limited amount available from the natural source severely restricts further investigation. At best, 1.1 kg of dried, powdered *Isodon eriocalyx* leaves yield only 8 mg of Maoecrystal Z (0.00073% by mass). The inefficiency of natural acquisition demands an innovative synthetic method to produce this molecule and the designing a scalable synthesis is difficult because of its strained carbocyclic core and its 7 stereogenic centers. The short term goal of this research is to develop a concise, efficient total synthesis of maoecrystal Z and the strategy should be applicable to its structurally related diterpenes such as macrocalyxoformin E. Here, we report a convergent, enantioselective synthesis route to the common precursor of both maoecrystal Z and macrocalyxoformin E, employing a Nozaki-Hiyama-Kishi coupling reaction followed by Nazarov cyclization as key stereogenic and ring forming steps.