Asymmetric Total Synthesis of (+)-Fusarisetin A via the Intramolecular Pauson–Khand Reaction


Significance: Isolated in 2011 from the soil fungus Fusarium sp. FN080326, fusarisetin A has gained considerable attention because of its unprecedented molecular structure and its striking bioactivity. Fusarisetin A exhibits a complex 6,6,5,5,5-fused pentacyclic ring system containing ten stereocenters. Moreover, this natural product displays potent inhibition of acinar morphogenesis, cell migration, and invasion in MDA-MB-231 breast cancer cells, without apparent cytotoxicity. Li, Yang, and co-workers report a total synthesis of (+)-fusarisetin A based on a stereoselective intramolecular Pauson–Khand reaction for the construction of the 6,6,5-tricyclic moiety.

Comment: After screening of conditions, the authors identified the $\text{Co}_2(\text{CO})_8$-mediated Pauson–Khand reaction as the most efficient method for the stereoselective formation of cyclopentenone B. Stereoselective reduction of B proved to be challenging. Thus, installation of a mesylate group followed by desilylation was crucial to access ketone C with the correct configuration at C6 and C7. Carboxylative esterification afforded ester D, which was further elaborated into amide E. Finally, Dieckmann condensation followed by hemiacetalization furnished (+)-fusarisetin A along with the separable diastereoisomer F (dr = 3:2).