Total Synthesis of (±)-Salimabromide

Significance: Unlike their terrestrial counterparts, myxobacteria of marine origin have remained underexplored by the scientific community. Recently, the polyketide antibiotic salimabromide was isolated from obligate marine myxobacterium Enhygromyxa salina. Magauer’s team mastered the challenges associated with the preparation of this structurally demanding and biologically potent secondary metabolite. Pivotal in their approach to this bridged tetracycle were a Wagner–Meerwein rearrangement/Friedel–Crafts cyclization, a [2+2] cycloaddition, and a Baeyer–Villiger reaction.

Comment: The authors commenced with the expedient preparation of ketone C from m-anisaldehyde and pinacolone. Following epoxidation and treatment with catalytic acid, Wagner–Meerwein rearrangement and cyclization were effected, furnishing primary alcohol D. This intermediate was further elaborated to amide G. The ketiminium derived from G underwent [2+2] cycloaddition to furnish H in excellent yield. Ultimately, allylic oxidation, Baeyer–Villiger reaction, and dibromination of the arene afforded (±)-salimabromide. An asymmetric route to intermediate D has been devised by the authors as well.