Synthesis of (–)-7-Deacetoxyalcyonin Acetate

Significance: The eunicellin diterpenes feature a synthetically challenging tricyclic ring system, including a hydroisobenzofuran and oxonane subunit. MacMillan and Overman reported in 1995 the first synthesis of a member of this natural product family in asymmetric fashion, confirming the relative and absolute configuration proposed by the isolation team. Highlights of this synthesis include use of a Prins–pinacol rearrangement to access the hydroisobenzofuran core as well as a photolytic deformylation of a β,γ-desaturated aldehyde.

Comment: The synthesis commences with regioselective opening of A, which was converted into aldehyde E in three steps. Dienyl iodide F was accessed in three steps starting with (S)-carvone. Fusing the two fragments set the stage for Prins–pinacol rearrangement, affording I as a single stereoisomer. Deprotection and photolytic deformylation afforded intermediate J. The final oxonane ring was constructed using Nozaki–Hiyama–Kishi coupling, the natural product in two additional steps.