Total Synthesis of (+)-Zaragozic Acid C

Significance: Johnson and co-workers present a rapid synthesis of (+)-zaragozic acid C, a highly oxygenated polyketide featuring a dioxabicyclo[3.2.1]octane bearing six contiguous stereocenters. The natural product, also known as squalestatin 1, is a potent inhibitor of the squalene synthase which is responsible for cholesterol production.

Comment: 1,2-Addition of vinyl Grignard \( B \) to silyl glyoxylate \( A \) triggers a controlled trimerization which is terminated with the addition of ketene acetal \( E \) into glyoxylate \( C \). This sequence is highly efficient. Triacetate \( L \) is thus promptly accessed, enabling the synthesis of (+)-zaragozic acid C.