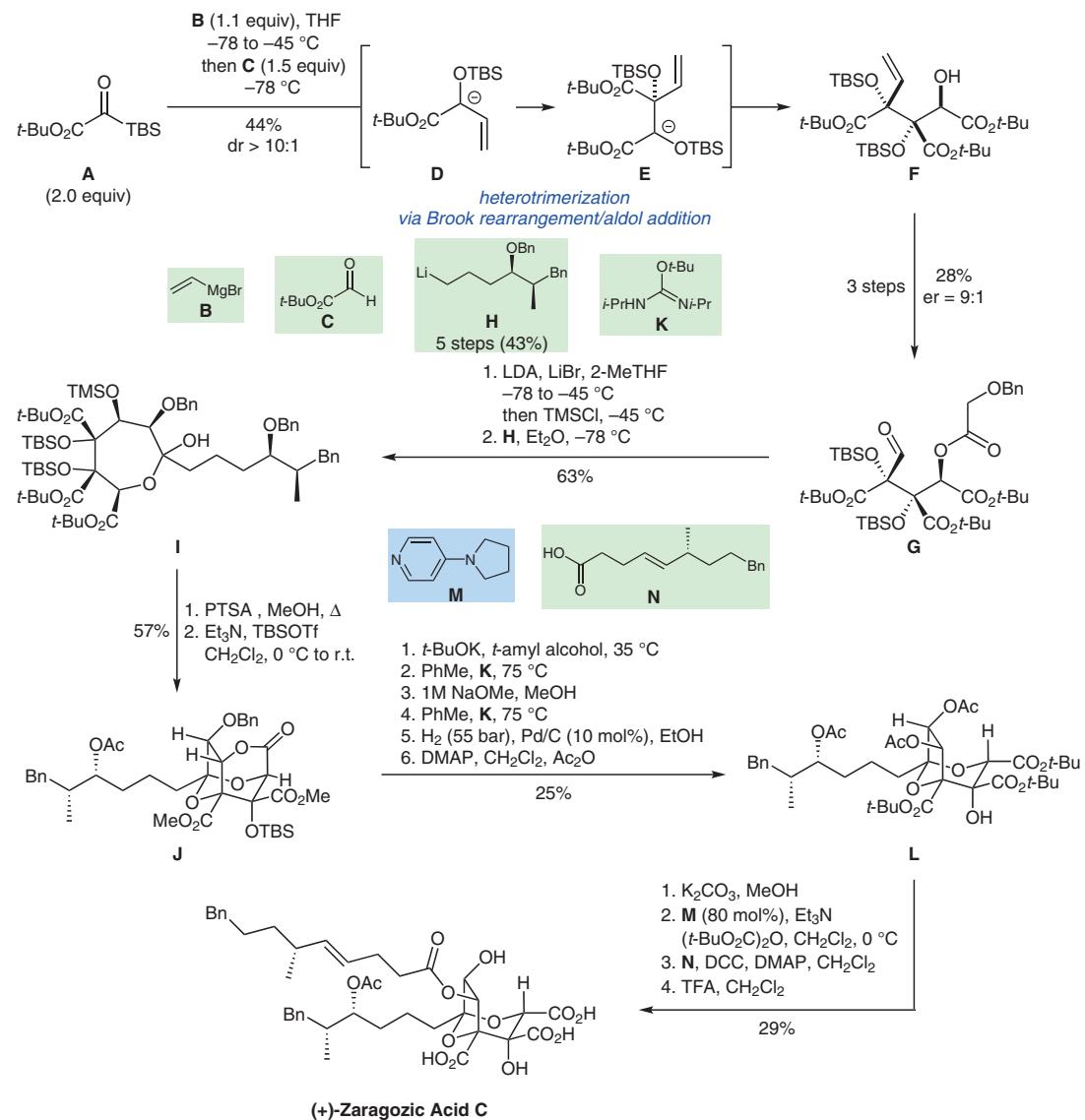


Total Synthesis of (+)-Zaragozic Acid C



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.