Total Synthesis and Study of 6-deoxyerythronolide B by Late-stage C—H Oxidation

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A late-stage C—H oxidation strategy will be presented in the total synthesis of 6-deoxyerythronolide B (6-dEB), the aglycone precursor to the erythromycin antibiotics. An advanced linear alkenoic acid intermediate is cyclized to the 14-membered macrocyclic core of 6-dEB using a late-stage (step 19 of 22) C—H oxidative macrolactonization reaction that proceeds with high regio-, chemo-, and diastereoselectivity (>40:1). A chelate-controlled model for macrolactonization was used to predict the stereochemical outcome of C—O bond formation and led to the discovery of conditions for synthesizing the first diastereomeric 13-epi-6-dEB precursor. Overall, this C—H oxidation strategy affords a highly efficient and stereochemically versatile synthesis of the erythromycin core.