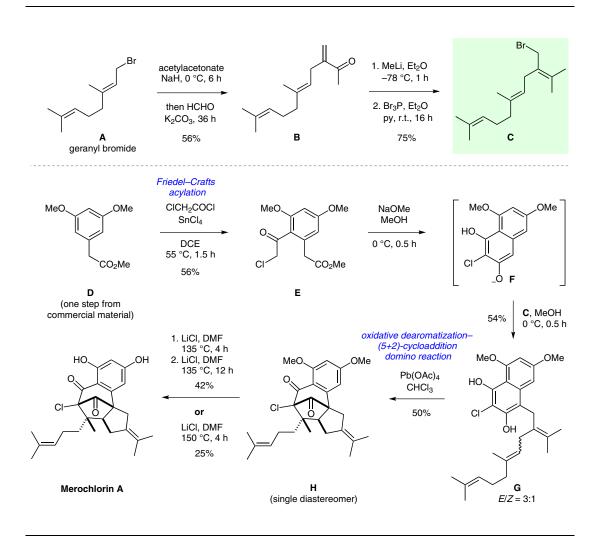
Total Synthesis of (±)-Merochlorin A



Significance: The first total synthesis of (\pm) -merochlorin A, an unusual chlorinated meroterpenoid isolated from the marine bacterium *Streptomyces* sp. strain CNH-189, is reported together with an alternative proposal for its biosynthesis. The natural product, which harbors four contiguous stereogenic centers within a compact bicycle[3.2.1]octanone, exhibits antibiotic activity against several multi-drug resistant *Staphylococcus aureus* strains (MIC = 2-4 µg·mL⁻¹) as well as *Clostridium difficile* (MIC = 0.15 µg·mL⁻¹) and is thus considered an interesting new lead candidate.

SYNFACTS Contributors: Erick M. Carreira, Nikolas Huwyler Synfacts 2013, 9(12), 1257 Published online: 18.11.2013 **DOI:** 10.1055/s-0033-1340125; **Reg-No.:** C07013SF

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Comment: The very concise and potentially biomimetic route towards this natural product as reported by Pepper and George delivers the desired target in a longest linear sequence of only six steps starting from commercially available geranyl bromide and could thus be used to prepare over one gram of this novel antibiotic to date. Thereby, the key element of the synthesis is an oxidative dearomatization–[5+2]-cycloaddition domino reaction that forges the required bicyclic core scaffold as well as all of the four contiguous stereogenic centers in a single step.

Category

Synthesis of Natural Products and Potential Drugs

Key words

merochlorin A

antibiotics

oxidative dearomatization

[5+2] cycloaddition

domino reaction