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Biomimetic Total Synthesis of (±)-Merochlorin A

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Significance: The first total synthesis of (±)-merochlorin A, an unusual chlorinated mero-
terpenoid isolated from the marine bacterium Streptomyces sp. strain CNH-189, is reported to-
gether with an alternative proposal for its biosyn-
thesis. 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 Staphylococ-
cus 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 candi-
date.

Comment: The very concise and potentially bio-
mimetic route towards this natural product as re-
ported 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 re-
action that forges the required bicyclic core scaf-
dold as well as all of the four contiguous stereo-
genic centers in a single step.

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