Concise Total Synthesis of (−)-Bipolarolide D

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Total Synthesis of (−)-Bipolarolide D

Significance: Lu and co-workers report the first total synthesis of the sesterpenoid (−)-bipolarolide D. The natural product, which was isolated from the fungus Bipolaris sp. TJ403-B1, is biosynthetically related to the ophiobolin class. The synthesis of the natural product with its 5/5/5/5-tetracyclic skeleton and three contiguous quaternary centers hinges on enantioselective [6+2] cycloaddition, enolate alkylation, and Heck reaction.

Comment: Pentafulvene aldehyde A was converted into ketone C by enantioselective [6+2] cycloaddition and ketal hydrolysis. Alkylation followed by Heck reaction and hydrolysis gave rise to triene G. Installation of the side chain from diketone J was achieved through Grignard addition and Suzuki reaction, furnishing the pentacyclic hemiketal N. Elimination followed by global deprotection afforded (−)-bipolarolide D.

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