**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.