Synthesis of (+)-Asteriscanolide

Significance: Wender and co-workers report the first total synthesis of sesquiterpene lactone (+)-asteriscanolide. Key to their approach is a nickel-catalyzed [4+4]-cycloaddition methodology, which was developed in their group. They successfully establish the first asymmetric synthesis of a cyclooctane-containing terpenoid.

Comment: The synthesis commences with construction of acid F through a Claisen rearrangement. Asymmetric Brinkmeyer reduction of ketone H with LAH in presence of Darvon alcohol (I) as a chiral ligand gives rise to J with excellent enantioselectivity. Tetraene M was accessed by a hydroalumination stannylation sequence followed by lithiation and carboxylation. The key nickel-catalyzed intramolecular [4+4] cycloaddition forged cyclooctadiene N.