Synthesis of IPI-926

Significance: Cyclopamine (A) is a teratogenic alkaloid isolated from the corn lily (*Veratrum californicum*). IPI-926 is a Hedgehog signalling pathway antagonist derived from cyclopamine that was evaluated for the treatment of cancer. The key step in the synthesis depicted is the robust and scalable Simmons–Smith cyclopropanation of B followed by an acid-catalyzed carbocation rearrangement.

Comment: For the large-scale Simmons–Smith reaction, a series of new safe and soluble iodo-methylzinc bis(aryl)phosphate reagents (e.g., C) were prepared under mild conditions that were stable during the course of the reaction. Note the rare application of an Oppenauer oxidation (I → J).