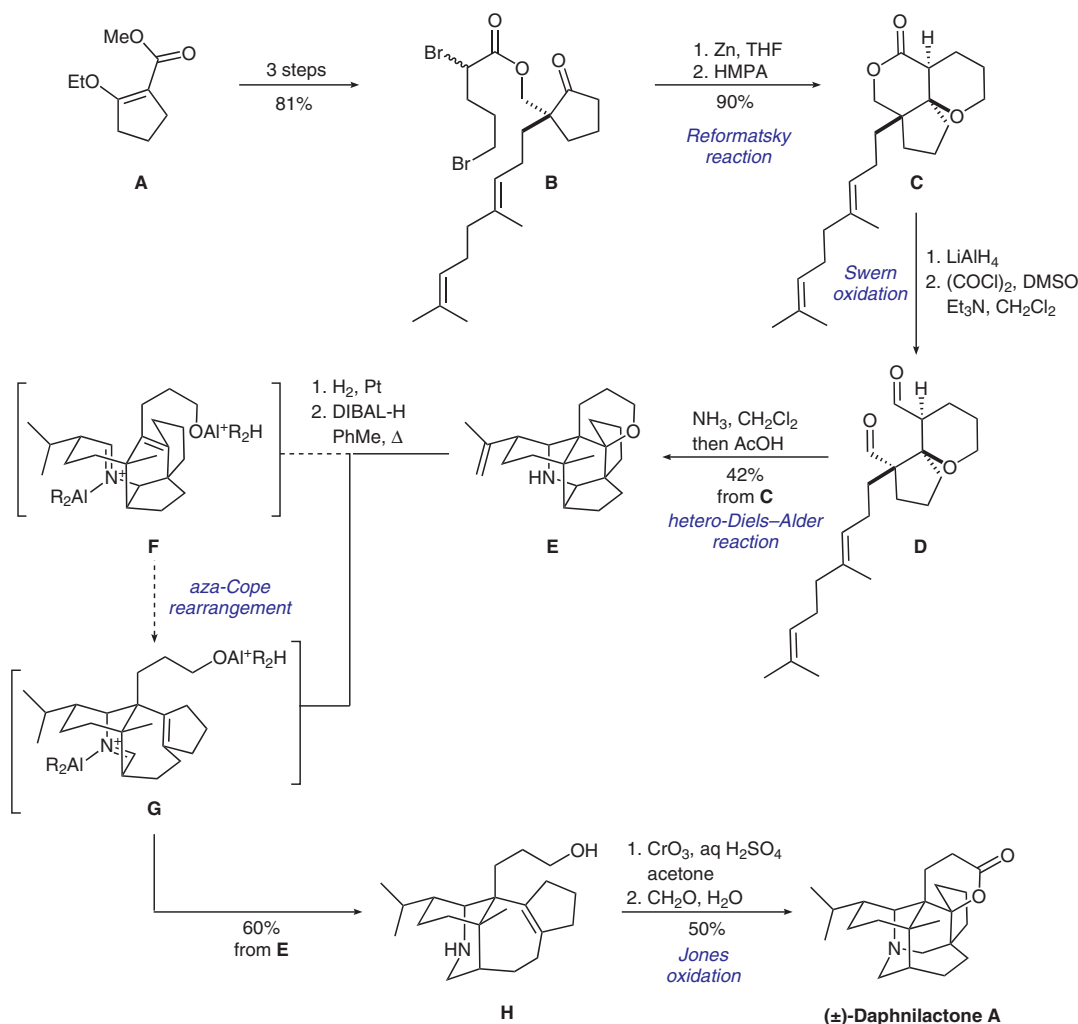


Synthesis of (±)-Daphnilactone A



Significance: In 1989, Heathcock and co-workers reported the first total synthesis of (±)-daphnilactone A through a key fragmentation reaction. The natural product is unique among the *daphniphyllum* alkaloids, because it features 23 carbons, thereof one not derived from squalene.

Comment: Reformatsky reaction and alkylation of bromoester **B** yielded **C**. Hetero-Diels-Alder reaction followed by Prins cyclization rapidly forged aminoether **E**. The key fragmentation reaction after reduction of **E** gave rise to single product **H**. This reaction could proceed either via intermediate **F** followed by aza-Cope rearrangement to less strained iminium **G** or by direct C–C cleavage to **G**.