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.