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Daphniphyllum Alkaloids. Part 5. Total Synthesis of (±)-Daphnilactone A: A Novel Fragmentation Reaction J. Am. Chem. Soc. 1989, 111, 1530-1531.

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 daphniphyllium 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**.

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Synthesis of Natural Products and **Potential Drugs**

Key words

(±)-daphnilactone A

aza-Cope rearrangement

Reformatsky reaction

daphniphyllum alkaloids

Swern oxidation

Jones oxidation

hetero-Diels-Alder reaction

Prins cyclization

