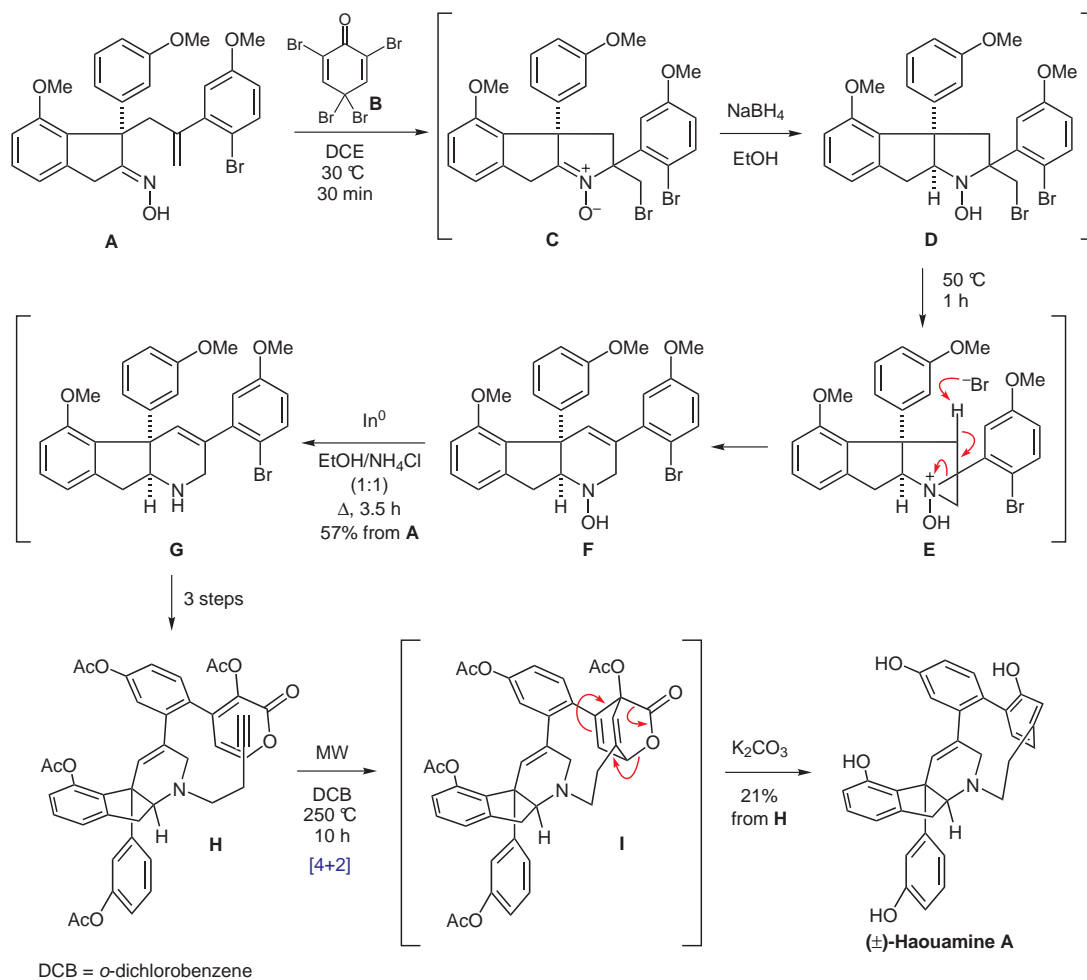


Synthesis of (±)-Haouamine A



Significance: Isolated from the tunicate *Aplidium haouarianum*, haouamine A exhibits selective activity against human colon cancer. Haouamine A exists as an inseparable mixture of isomers due to inversion of the nitrogen in the tetrahydropyridine ring. In addition, the highly strained paracyclophane moiety contains a bent aromatic ring.

Comment: Treatment of oxime **A** with electrophilic bromine source **B** gave nitron **C** after 5-*exo-trig* cyclization. Reduction of **C** followed by heating induced ring expansion via aziridinium ion **E**. Prolonged microwave heating of **H** induced a pyrone-alkyne Diels–Alder reaction with concomitant loss of CO₂. Subsequent deacetylation gave haouamine A. For an alternative approach based on a 1,3-dipolar cycloaddition strategy, see: J. H. Jeong, S. M. Weinreb *Org. Lett.* **2006**, 8, 2309-2312.