## Synthesis of ( $\pm$ )-Haouamine A



DCB $=0$-dichlorobenzene

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 $\mathbf{A}$ with electrophilic bromine source $\mathbf{B}$ gave nitrone $\mathbf{C}$ after 5-exo-trig cyclization. Reduction of $\mathbf{c}$ followed by heating induced ring expansion via aziridinium ion E. Prolonged microwave heating of $\mathbf{H}$ induced a pyronealkyne Diels-Alder reaction with concomitant loss of $\mathrm{CO}_{2}$. 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, 23092312.

Synthesis of Natural Products and Potential Drugs

## Key words

aziridinium ion
Stille reaction
Diels-Alder reaction
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