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Enantioselective Synthesis of (+)-Cortistatin A, a Potent and Selective Inhibitor of Endothelial Cell Proliferation
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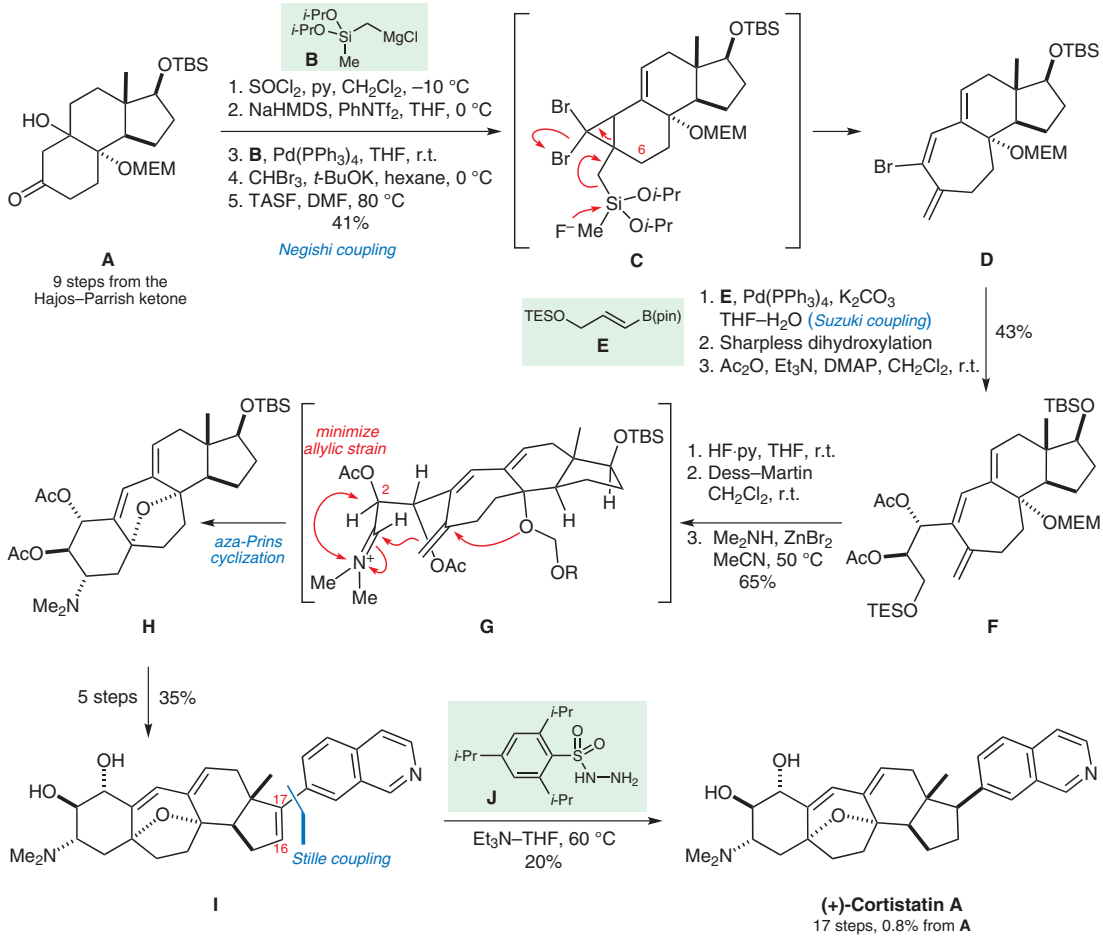
# Synthesis of (+)-Cortistatin A




**Significance:** Cortistatin A was isolated together with structurally related molecules from the sponge *Corticium simplex*. It shows potent anti-angiogenetic activity with a high selectivity towards several human and murine cancer cell lines. The focal step of the synthesis is a highly stereoselective aza-Prins cyclization to complete the steroid-like carbon framework (**G** → **H**).

**Comment:** Thermal loss of bromide from **C** and cyclopropyl opening followed by fluoride-induced desilylation of the resulting pentadienyl cation leads to vinyl bromide **D**. Using the less electrophilic TMS group gave a cycloheptadiene via deprotonation at C6 by fluoride. Hydrogenation of the C16/C17 double bond in **I** could only be achieved in low yield using diimide generated from **J**.

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