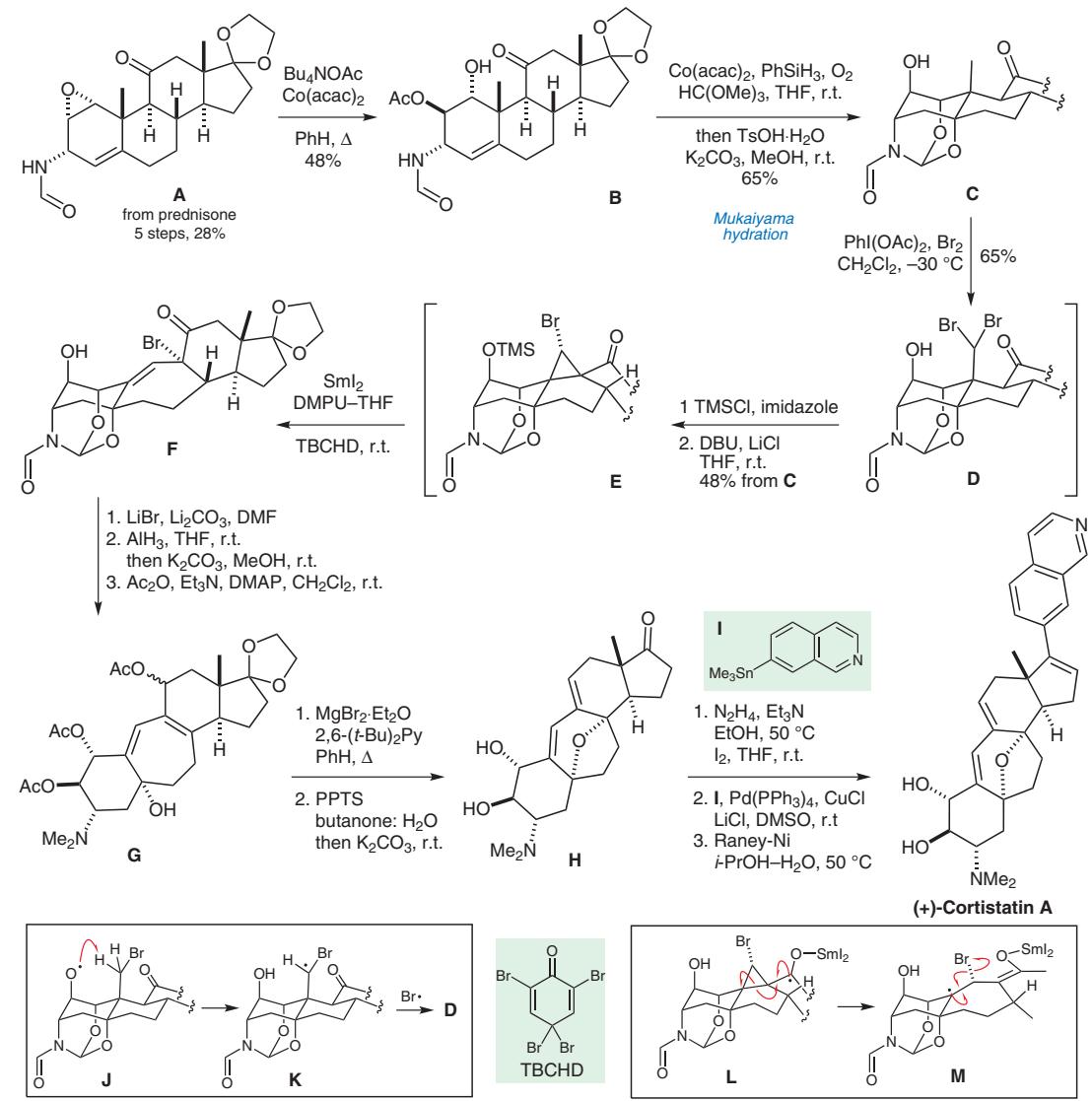


Synthesis of (+)-Cortistatin A



Significance: (+)-Cortistatin A inhibits the proliferation of human umbilical vein endothelial cells (HUVECs, $\text{IC}_{50} = 1.8 \text{ nM}$) without showing any toxicity. This synthesis utilizes a novel hydroxyl-directed dibromination of a methyl group (**C** → **D**) using AcOBr generated in situ.

Comment: Dibromination was achieved by a $\text{S}_{\text{H}}2$ reaction of the transient O-centered radical (**C** → **J** → **K** → **D**). A Sml_2 -mediated radical opening of the cyclopropane **E** led to the formation of a dienolate via intermediates **L** and **M**, which then reacted with TBCHD to give the α -bromoketone **F**.