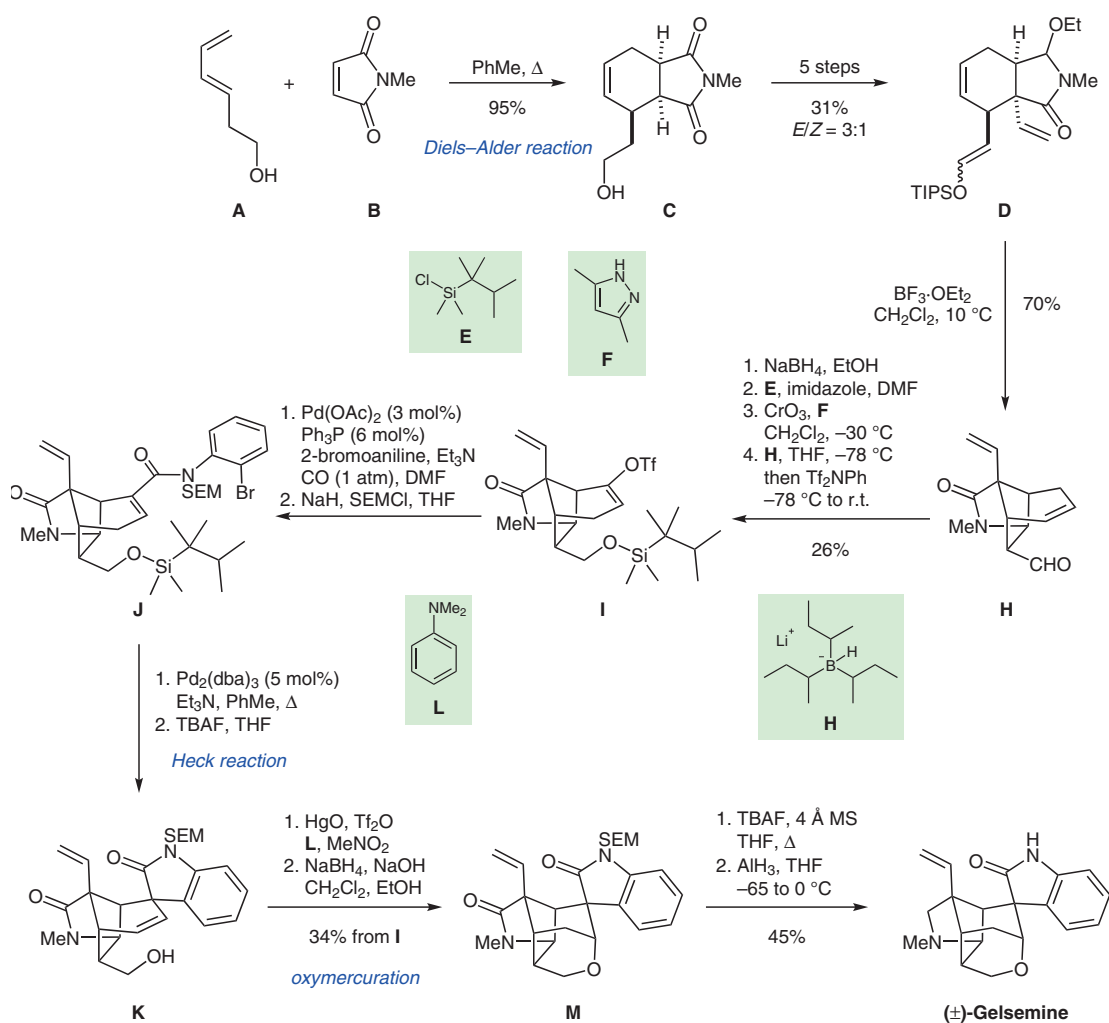


Synthesis of (±)-Gelsemine



Significance: Speckamp, Hiemstra, and co-workers present the first total synthesis of gelsemine, an oxindole alkaloid isolated from *Gelsemium sempervirens* in 1870. Investigation of the biological activity identified gelsemine as a potent glycine receptor agonist, which exhibits significantly higher binding affinity for some of these receptors than their native agonist, glycine. Hence, gelsemine is a highly toxic substance and to this day no antidote has been found.

Comment: Adduct **C** is readily accessed through an *endo*-selective Diels–Alder reaction of diene **A** and malimide **B**. Intramolecular *N*-acyliminium cyclization forges the bridged tricyclic core in **H**. Pd-mediated carbonylative coupling of vinyl triflate **I** and 2-bromoaniline paves the way for a subsequent Heck cyclization to install the quaternary spirocenter in **K**. Hg(OTf)₂-promoted oxymercuration and organomercurial reduction followed by global deprotection conclude the synthesis of (±)-gelsemine.