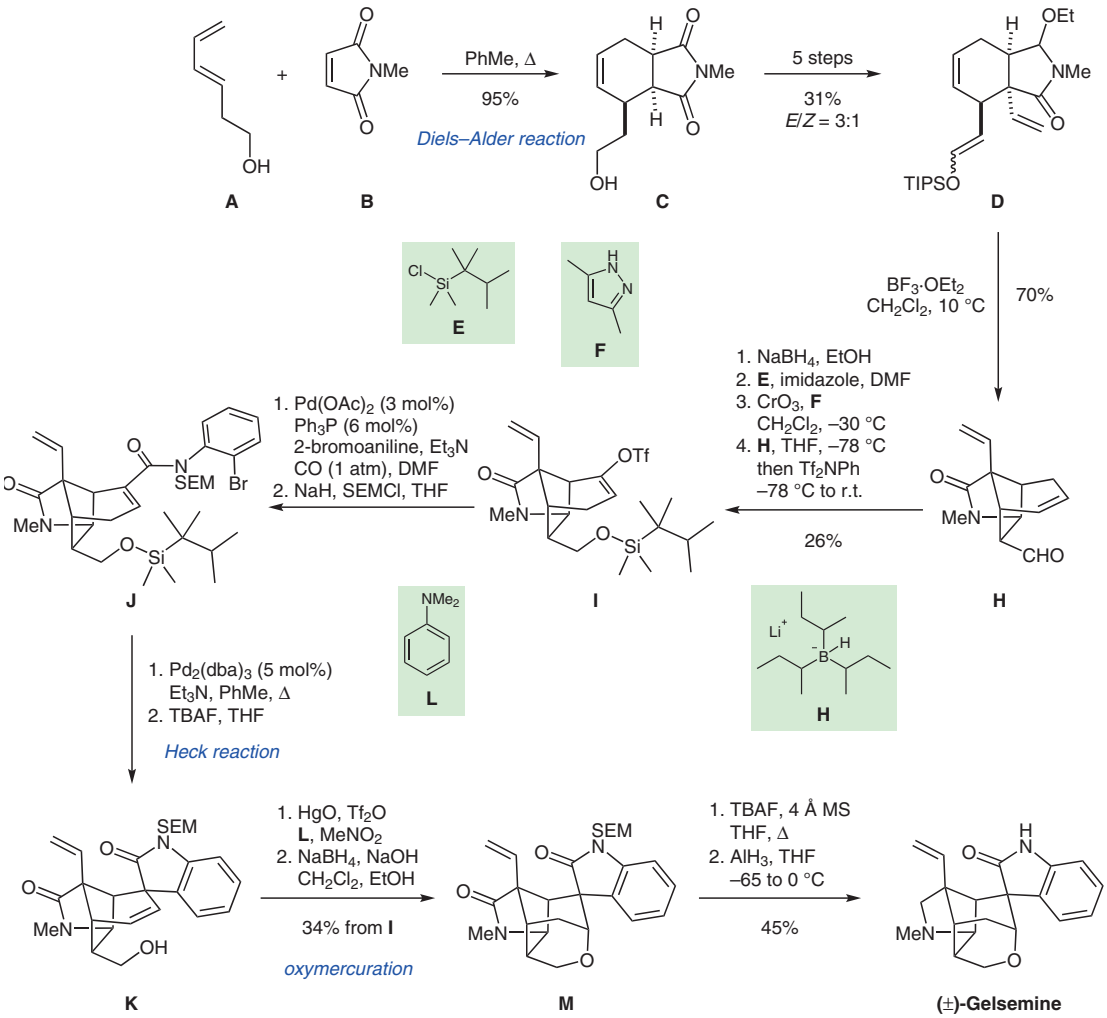
N. J. NEWCOMBE, F. YA, R. J. VIJN, W. H. HIEMSTRA, N. SPECKAMP* (UNIVERSITY OF AMSTERDAM, THE NETHERLANDS)

The Total Synthesis of (±)-Gelsemine
J. Chem. Soc., Chem. Commun. **1994**, 767–768, DOI: 10.1039/C39940000767.

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.

SYNFACTS Contributors: Erick M. Carreira, Sven M. Papidocha
Synfacts 2024, 20(05), 0453 Published online: 15.04.2024
DOI: 10.1055/s-0043-1763717; **Reg-No.:** C03524SF

Category
Synthesis of Natural Products

Key words
(±)-gelsemine
oxindole alkaloid
Diels–Alder reaction
Heck reaction
oxymercuration