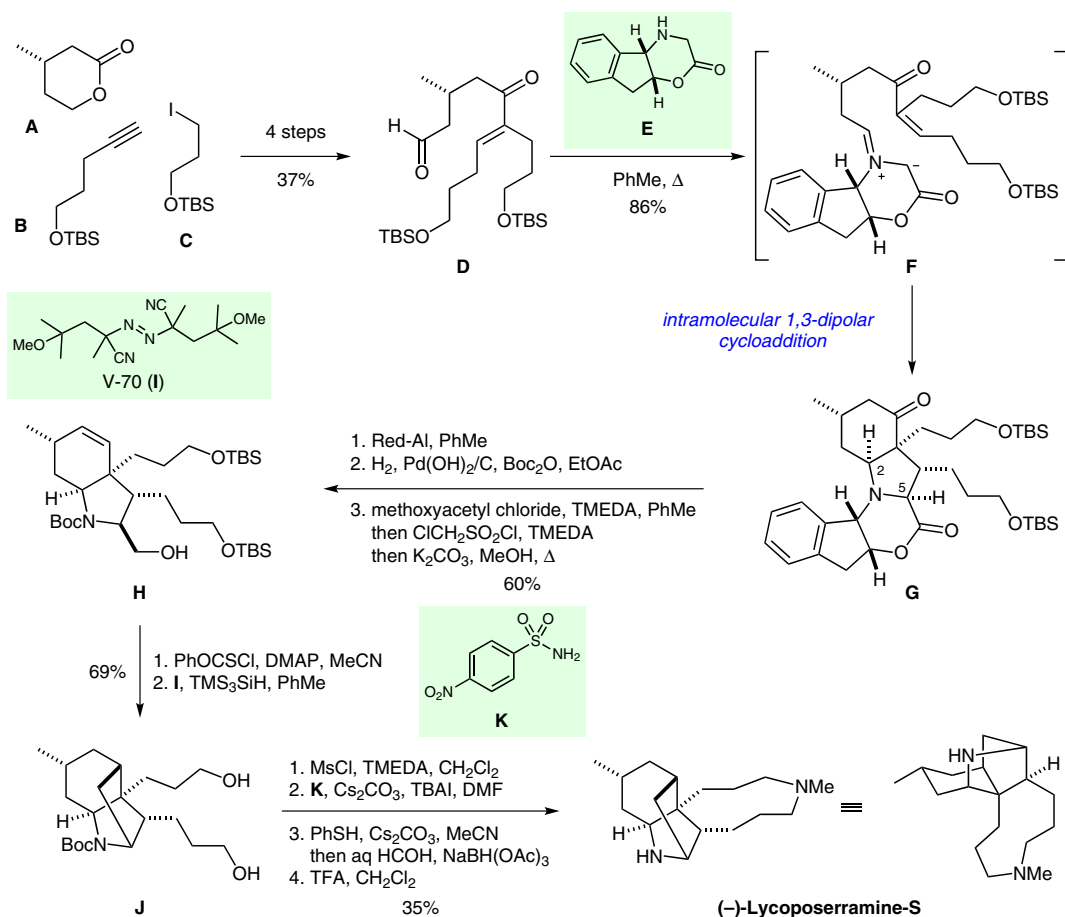


Total Synthesis of (–)-Lycoposerramine-S



Significance: Fukuyama and co-workers report the first total synthesis of the caged tetracyclic *Lycopodium* alkaloid (–)-lycoposerramine-S. The enantioselective synthesis is centered around an impressive 1,3-dipolar cycloaddition which diastereoselectively constructs the central penta-substituted pyrrolidine ring utilizing a chiral morpholinone. A radical cyclization and alkylative ring closure of the nine-membered ring using a 4-nitrobenzenesulfonyl amide leads to the synthesis of the natural product in only 14 steps.

Comment: In a striking intramolecular 1,3-dipolar cycloaddition, condensation of aldehyde **D** with morpholinone **E** led to the diastereoselective formation of pyrrolidine **G** containing four newly constructed contiguous stereocenters in excellent yield. The formation of the 2,5-*cis* relationship is thought to arise from preferential formation of *Z*-azomethine ylide **F**. Exhaustive reduction, selective elimination of the resulting secondary alcohol followed by a radical annulation led to tricycle **J**. Finally, the medium-sized ring was assembled by use of alkylative nosyl amide chemistry previously developed by the Fukuyama group.