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 pentasubstituted 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.