azomethine ylides

Key words

JAPAN) Total Synthesis of (-)-Lycoposerramine-S

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Total Synthesis of (-)-Lycoposerramine-S

N. SHIMADA, Y. ABE, S. YOKOSHIMA, T. FUKUYAMA* (THE UNIVERSITY OF TOKYO,

A steps 37%

B OTBS C TBSO D TBS

Intramolecular 1,3-dipolar cycloaddition

1. Red-Al, PhMe 2. H₂, Pd(OH)₂/C, Boc₂O, EtOAc

3. methoxyacetyl chloride, TMEDA, PhMe then ClCH₂SO₂Cl, TMEDA then K₂CO₃, MeOH,
$$\Delta$$

69%

1. PhOCSCI, DMAP, MeCN 2. I, TMS₃SiH, PhMe

3. PhSH, Cs₂CO₃, TBAI, DMF

3. PhSH, Cs₂CO₃, MeCN then aq HCOH, NaBH(OAc)₃

OH 4. TFA, CH₂Cl₂

J 35%

(-)-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.

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