

(-)-echinosporin

[2+2] photocycloaddition

palladium catalysis

carbomethoxylation

Davis hydroxylation

dehydrogenation

Parikh–Doering oxidation

Mitsunobu reaction

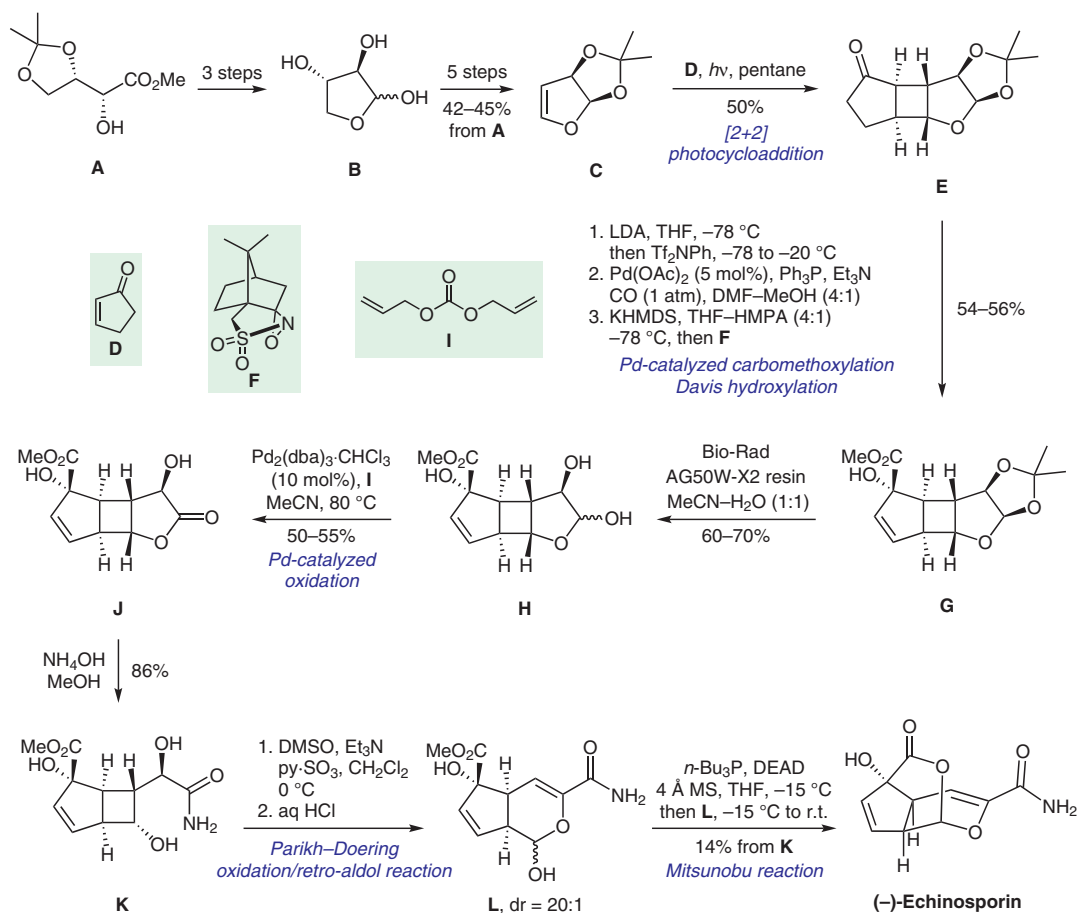
Synfact Classic

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Total Synthesis of Natural (-)-Echinosporin. Determination of the Absolute Configuration

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Synthesis of (-)-Echinosporin



Significance: (-)-Echinosporin is produced by *Streptomyces echinosporus* MK-213, features antibiotic and antitumor activity, and was isolated by Hirayama and co-workers in 1981. In 1989, Smith and co-workers reported the enantioselective synthesis of (-)-echinosporin and determined its absolute configuration. The synthesis relies on an [2+2] photocycloaddition and an oxidation–cyclobutanol fragmentation tactic. Final Mitsunobu lactonization provided (-)-echinosporin.

Comment: Dihydrofuran **C**, obtained from ester **A** in eight steps, was combined with cyclopentenone through a [2+2] photocycloaddition to provide ketone **E**. Pd-catalyzed carbomethoxylation and hydroxylation resulted in α -hydroxy ester **F**. Lactone **I** was subjected to oxidation–fragmentation conditions to give lactol **K** which was converted to (-)-echinosporin via an intramolecular Mitsunobu reaction.