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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 a [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.

**Key words**
(-)-echinosporin  [2+2] photocycloaddition  palladium catalysis  carbomethoxylation  Davis hydroxylation  dehydrogenation  Parikh–Doering oxidation  Mitsunobu reaction

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