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Enantioselective Total Synthesis of (+)-Lithospermic Acid

Synthesis of (+)-Lithospermic Acid

Significance: This elegant synthesis of the HIV integrase inhibitor lithospermic acid features (1) an enantioselective intramolecular oxa-Michael reaction; (2) an oxidative ring contraction of the chromanone \( F \); and (3) an intermolecular palladium-catalyzed C–H olefination used to append acrylate ester \( K \) to \( J \).

Comment: The enantiomeric ratio of \( F \) improved to 99:1 after one recrystallization. The presence of the two electronegative bromine atoms on chromanone \( F \) were essential for the success of the oxidative ring contraction mediated by phenyl-iodonium bis(trifluoroacetate).