Synthesis of Actinophyllic Acid

Significance: Actinophyllic acid is a highly congested, polycyclic indole alkaloid found in Alstonia actinophylla. It is a potent inhibitor in the coupled enzyme assay TAFIa/hippuricase. Chen and co-workers report a 13-step total synthesis of the title compound based on a desymmetrization strategy.

Comment: Nitrile oxide cycloaddition with dibromooxime C under basic conditions gave isoxazoline D. Two more steps led to isoxazole E, which was subjected to a deprotection/palladium-catalyzed aminoaarylation sequence. Indole synthesis followed by acetal formation completed the total synthesis of actinophyllic acid.