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Total Synthesis of Caprazol, a Core Structure of the Caprazamycin Antituberculosis Antibiotics
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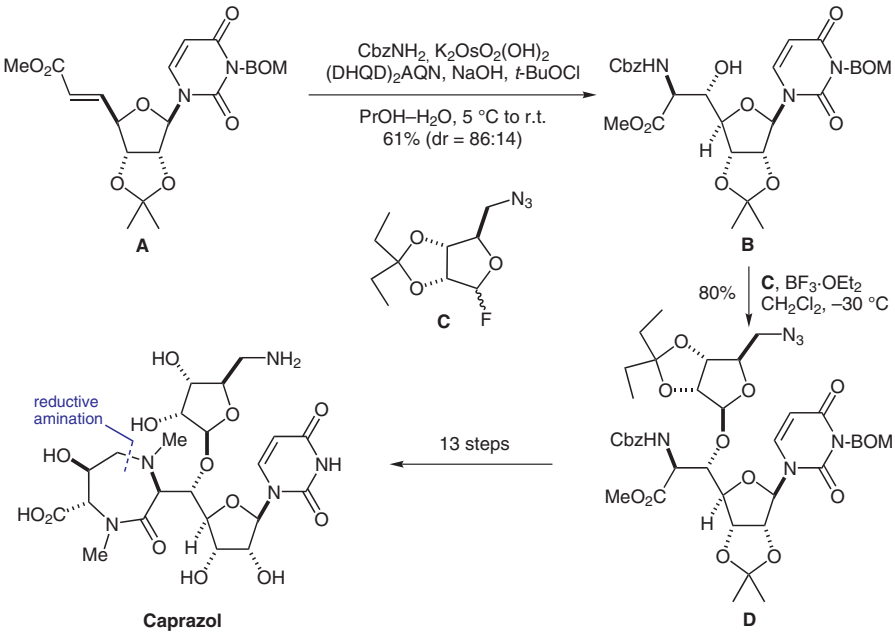
Total Synthesis of Caprazol



Significance: Caprazol is the core structure of the Caprazamycin antibiotics. The Caprazamycins are isolated from *Streptomyces* sp MK730-62F2. They inhibit Mra Y, a key enzyme in peptidoglycan synthesis in *Mycobacterium tuberculosis*. They have no significant toxicity to mice.

Comment: Key steps in the 18-step synthesis of Caprazol were (a) a Sharpless asymmetric amino-hydroxylation reaction which converts **A** to **B**; glycosylation using a 5-aminoribosyl fluoride **C**; and (c) a reductive amination to create the diazepanone ring. The stereochemistry of the difficult glycosylation depended strongly on the steric bulk of the 3-pentylidene protecting group and the Lewis acid activator. With $BF_3{\cdot}OEt_2$ at –30 °C, the anomeric ratio was $\alpha{:}\beta$ = 4:96.

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Category
Synthesis of Natural Products and Drugs

Key Words
Sharpless asymmetric amino-hydroxylation
glycosylation
glycosyl fluoride