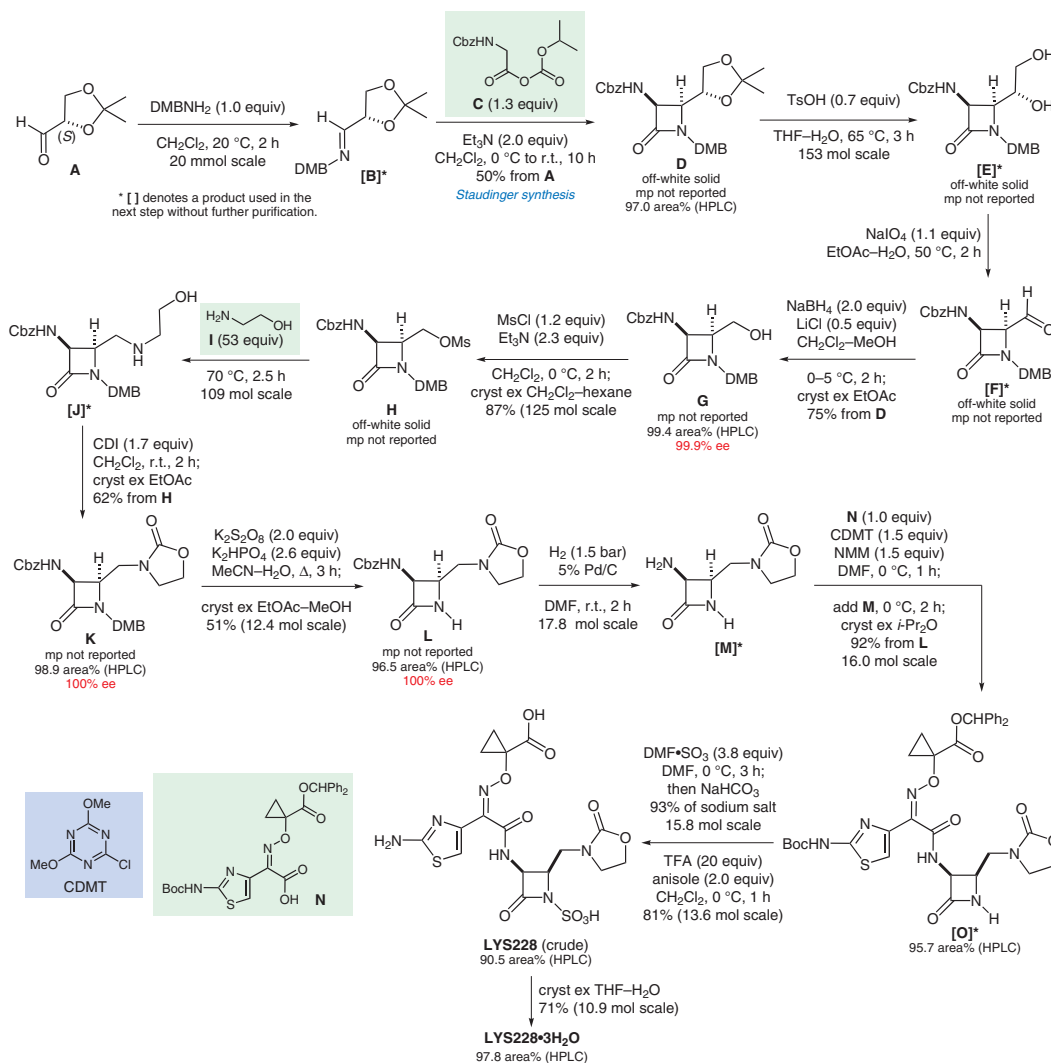


Synthesis of Monobactam Antibiotic LYS228



Significance: LYS228 is a monobactam antibiotic that inhibits cell-wall synthesis in Gram-negative bacteria through covalent modification of the active-site serine of penicillin-binding protein 3. It is active in vitro and in vivo against *Enterobacteriaceae*, and it is stable to most serine-β-lactamases and all metallo-β-lactamases profiled to date.

Comment: The key step in the manufacturing process for LYS228 depicted is the asymmetric Staudinger β-lactam synthesis involving a [2+2] cycloaddition of a ketene derived from **C** with aldimine **B** derived from (*S*)-glyceraldehyde acetonide **A** (C. Hubschwerlen, J.-L. Specklin *Org. Synth.* 1995, 72, 14). For the discovery synthesis, see: *Bioorg. Med. Chem. Lett.* 2018, 28, 7748.