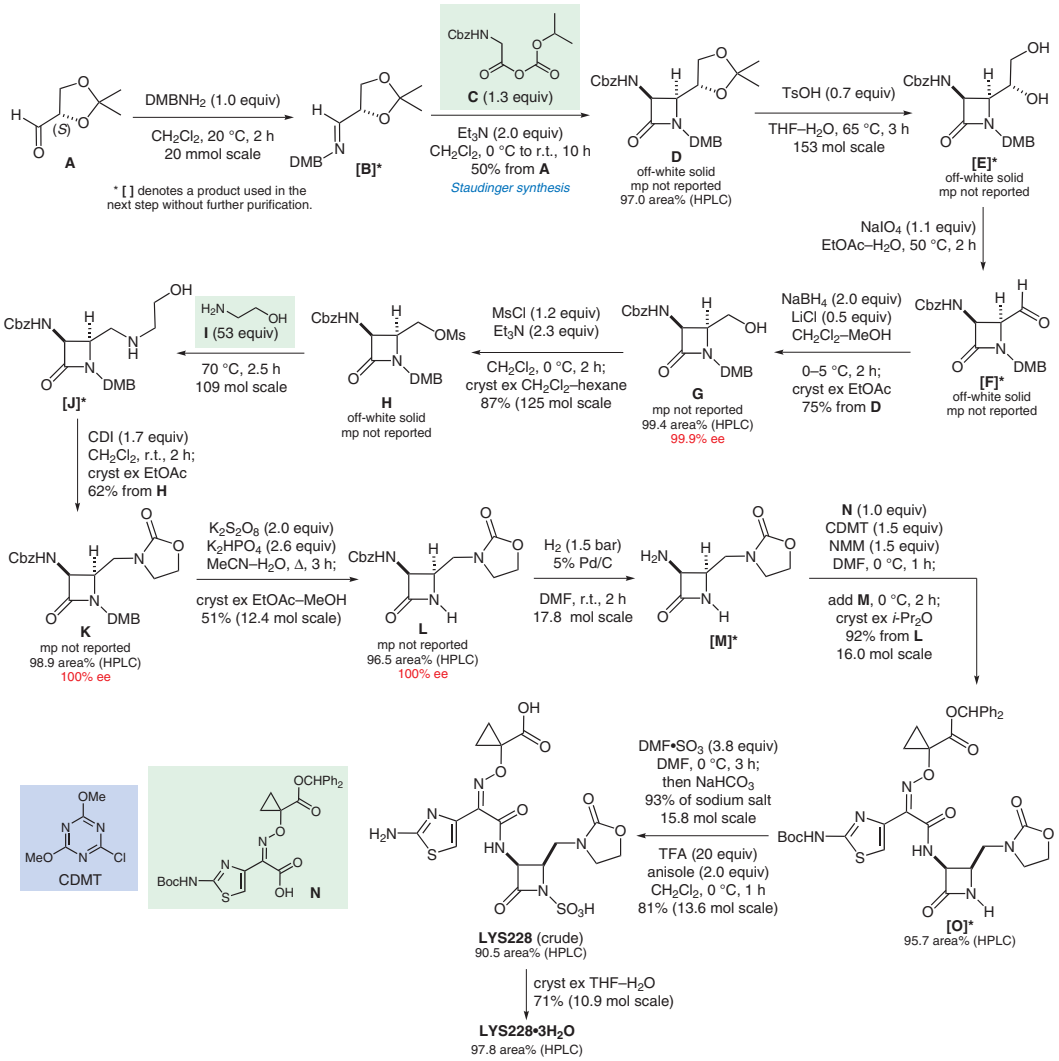
C. M. CHEUNG* ET AL. (SUZHOU NOVARTIS PHARMA TECHNOLOGY CO. LTD., CHANGSHU, P. R. OF CHINA)

Process Development for the Synthesis of a Monobactam Antibiotic – LYS228
Org. Process Res. Dev. **2020**, *24*, 363–370.

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.

SYNFACTS Contributors: Philip Kocienski
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Synthesis of Natural Products and Potential Drugs

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[2+2] cycloaddition
Staudinger β-lactam synthesis

Synfact of the Month

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