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The Total Synthesis of Penicillin V
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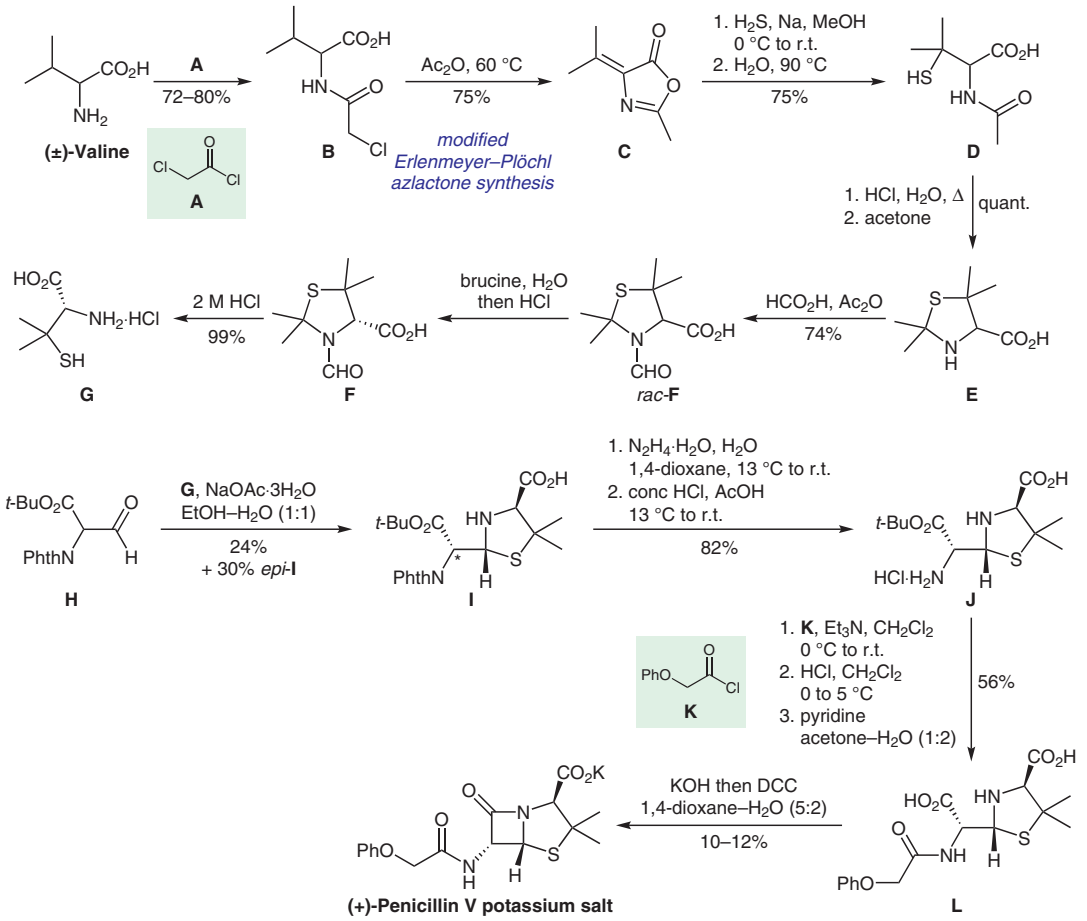
Synthesis of Penicillin V



Significance: The penicillins constitute a family of β-lactam antibiotics which were first discovered in 1928 by Alexander Fleming. The lability of the amide bond is responsible for their remarkable bioactivity. The formation of this bond posed a major challenge in early synthetic studies towards penicillins. Having previously invented carbodiimide coupling agents, Sheehan and co-workers achieved the first total synthesis of penicillin V in 1957.

Comment: Racemic valine was efficiently transformed into *N*-acetylpenicillamine (**D**). Resolution of formamide *rac*-**F** using brucine followed by hydrolysis afforded (–)-penicillamine hydrochloride (**G**). Condensation with aldehyde **H** afforded thiazolidine **I**; side-product *epi*-**I** could be converted into **I** employing pyridine-induced epimerization. Removal of protecting groups and installation of the phenoxyacetyl side chain furnished penicilloic acid **L**. Subsequent construction of the central amide bond was achieved with DCC under basic conditions to give the potassium salt of penicillin V.

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Category

Synthesis of Natural Products and Potential Drugs

Key words

β-lactam antibiotic
penicillamine
penicilloic acid
penicillin V
modified Erlenmeyer–Plöchl azlactone synthesis
carbodiimide coupling