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A Synthetic Antibiotic Class Overcoming Bacterial Multidrug Resistance

Nature **2021**, 599, 507–512, DOI: 10.1038/s41586-021-04045-6.

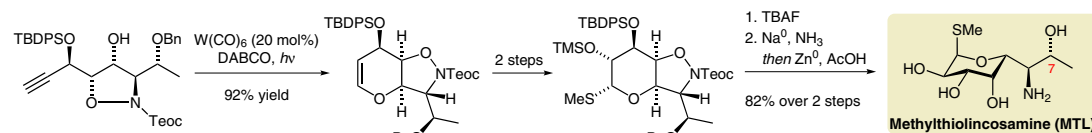
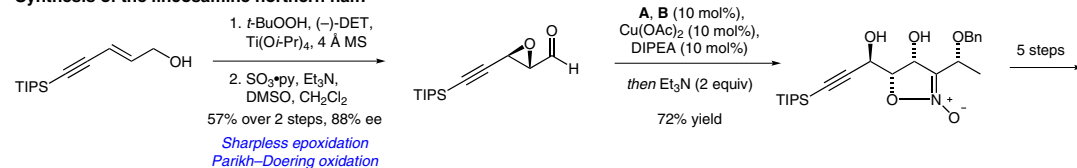
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A Practical, Component-Based Synthetic Route to Methylthiolincosamine Permitting Facile Northern-Half Diversification of Lincosamide Antibiotics

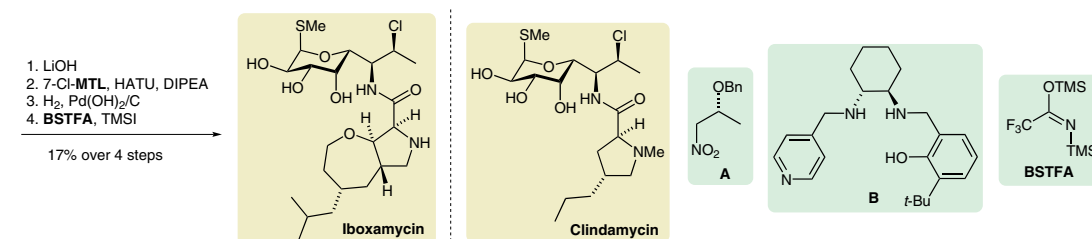
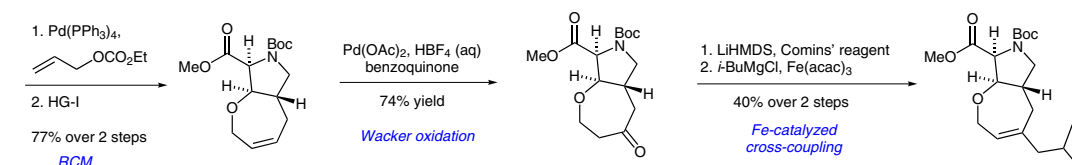
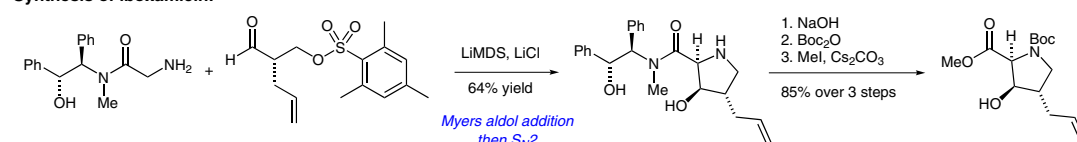
J. Am. Chem. Soc. **2021**, 143, 6829–6835, DOI: 10.1021/jacs.1c03536.

The Next Generation Lincosamide: Iboxamycin

Synthesis of the lincosamine northern half:



Synthesis of iboxamicin:



Significance: The lincosamides are a class of antibiotics that acts by inhibition of the bacterial ribosome. 50 years after the semisynthetic derivative clindamycin was approved by the FDA, Myers and co-workers published their component-based total synthetic platform, which resulted in a new, highly potent lincosamide analogue: **iboxamycin**. It acts in Gram-positive, Gram-negative, and resistant strains.

Comment: The lincosamine northern half was accessed from an epoxy aldehyde and a nitro compound **A**. The diastereoselective Henry reaction between both building blocks was followed by an epoxide opening that established a cyclic nitronate. Hydroxyproline analogues of the southern half were accessed using the Myers' pseudoephanamine auxiliary.

SYNFACTS Contributors: Dirk Trauner, Klaus-Peter Ruehmann

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Key words

antibiotics

Sharpless
epoxidation

pseudoephanamine
auxiliary

ring-closing
metathesis

Wacker oxidation

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