

Y. S. POLIKANOV\*, A. G. MYERS\* ET AL. (UNIVERSITY OF ILLINOIS AT CHICAGO AND HARVARD UNIVERSITY, CAMBRIDGE, USA)

A Synthetic Antibiotic Class Overcoming Bacterial Multidrug Resistance

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

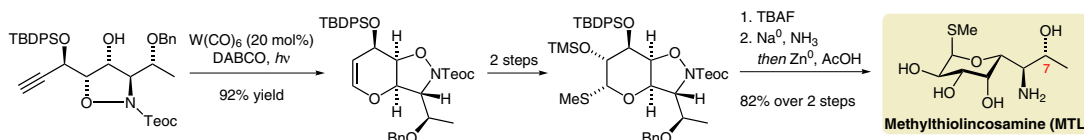
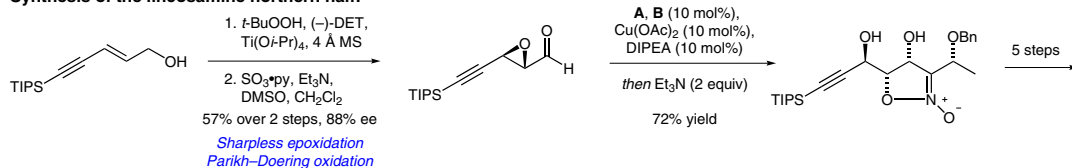
M. J. MITCHELTREE, J. W. STEVENSON, A. PISIPATI, A. G. MYERS\* (HARVARD UNIVERSITY, CAMBRIDGE, USA)

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

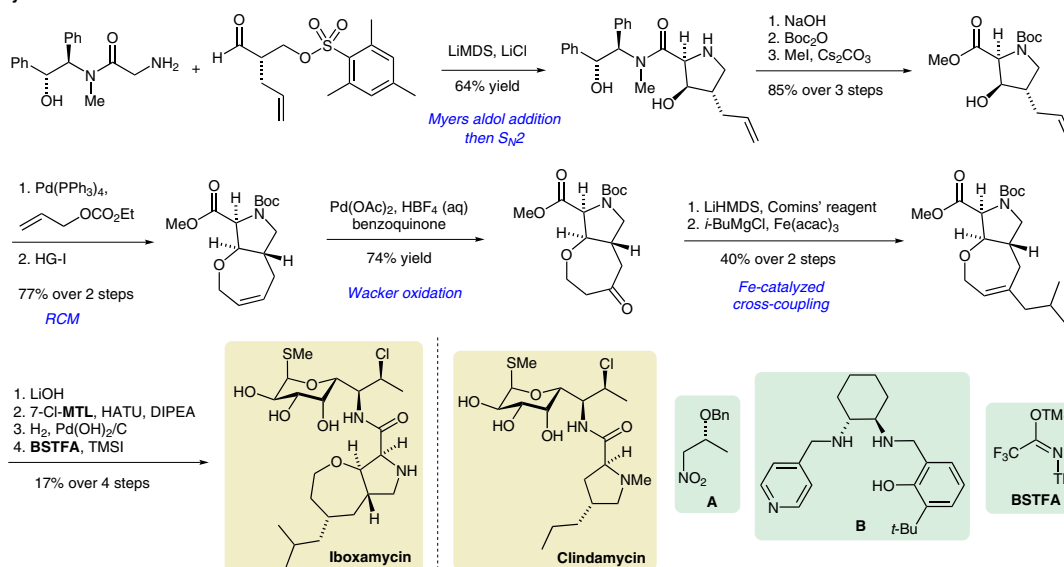
*J. Am. Chem. Soc.* **2021**, 143, 6829–6835, DOI: 10.1021/jacs.1c03536.

## 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' pseudoephedrine auxiliary.

**SYNFACTS Contributors:** Dirk Trauner, Klaus-Peter Ruehmann

Synfacts 2022, 18(01), 0085 Published online: 17.12.2021

DOI: 10.1055/s-0041-1737169; Reg-No.: T00822SF

Category

Chemistry in  
Medicine and  
Biology

Key words

antibiotics

Sharpless  
epoxidation

pseudoephedrine  
auxiliary

ring-closing  
metathesis

Wacker oxidation

Synfact  
of the  
Month