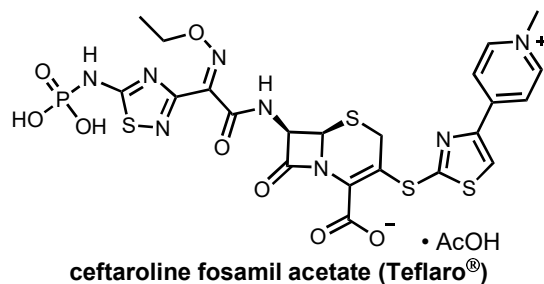
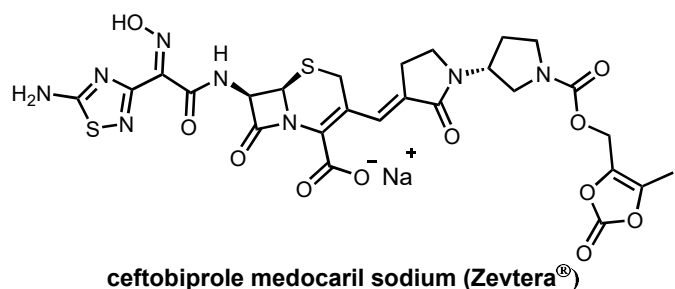


- 5th generation cephalosporin antibiotic active against antibiotic resistant gram-negative bacteria.
- Used to treat urinary tract infections and intra-abdominal infections.
- Administered in combination with the β -lactamase inhibitor tazobactam, used to protect ceftolozane from degradation.



- 5th generation cephalosporin antibiotic active against methicillin-resistant Staphylococcus aureus as well as other Gram-positive bacteria
- Also retains broad spectrum activity against Gram-negative bacteria
- Used to treat community-acquired pneumonia and acute bacterial skin infections



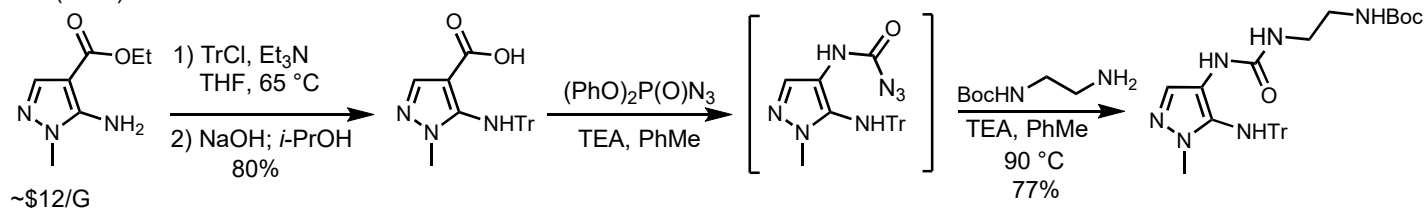
- 5th generation cephalosporin antibiotic also active against methicillin-resistant Staphylococcus aureus as well as other Gram-positive and Gram-negative bacteria
- Used to treat community-acquired pneumonia and acute bacterial skin infections
- Currently available in 12 european countries and is in phase 3 clinical trials in the US

References

1. Huges D. L. *Org. Process Res. Dev.* **2017**, *21*, 430-443.
2. Huges D. L. *Org. Process Res. Dev.* **2017**, *21*, DOI: 10.1021/acs.oprd.7b00143
3. Hebeisen et al. Derivatives of 3-(2-oxo-[1,3'] bipyrolodiny-3-ylidenemethyl)-cephams. U.S. Patent 6,232,306 B1, May 15, 2001.

ceftolozane sulfate (process routes)

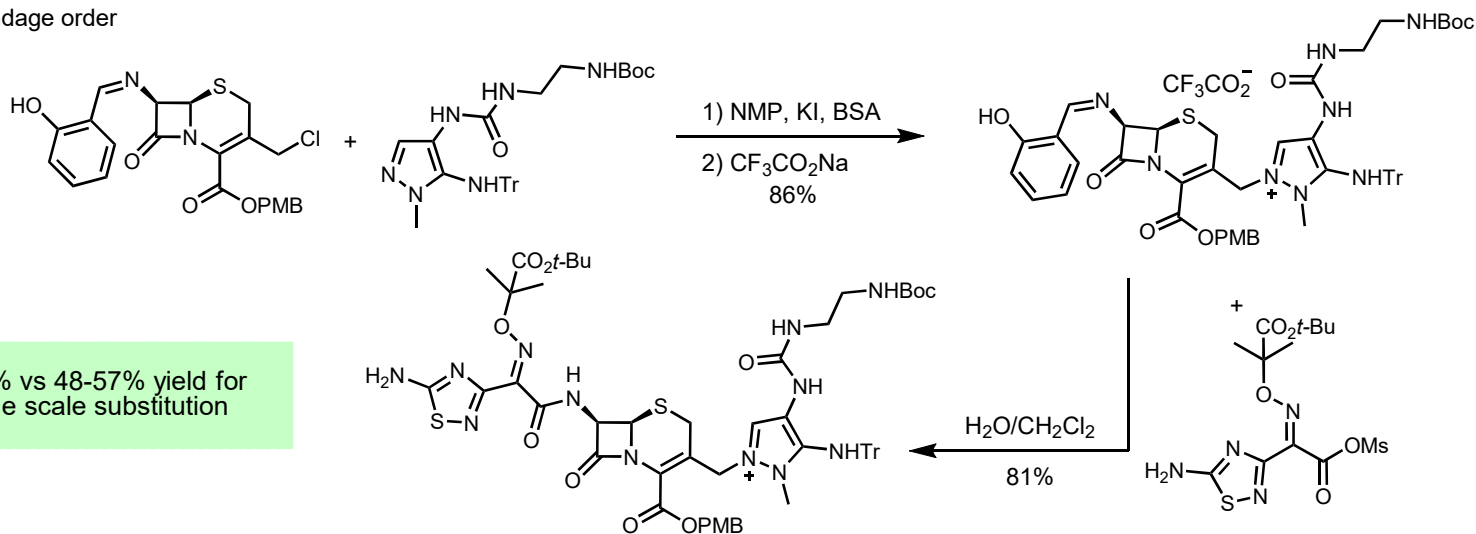
Merck (2016)



- Higher overall yield 61 vs 46%
- No transition metals used
- More time efficient

Reversed appendage order

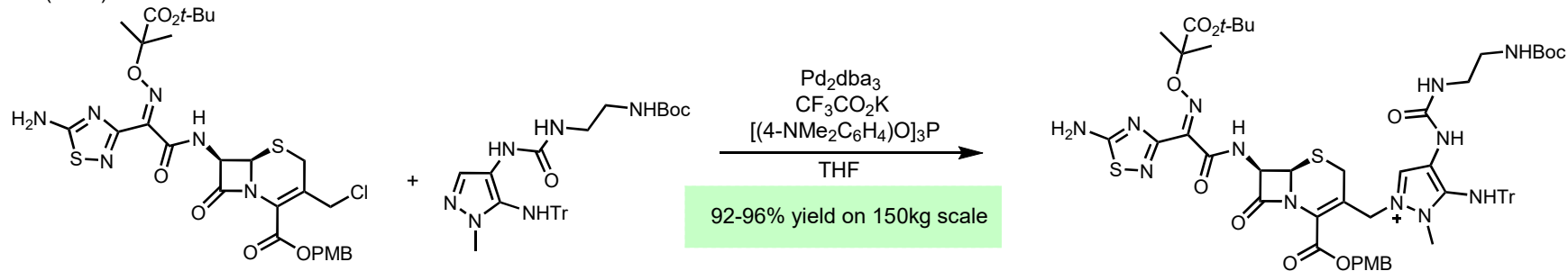
Merck (2015)



- 86% vs 48-57% yield for large scale substitution

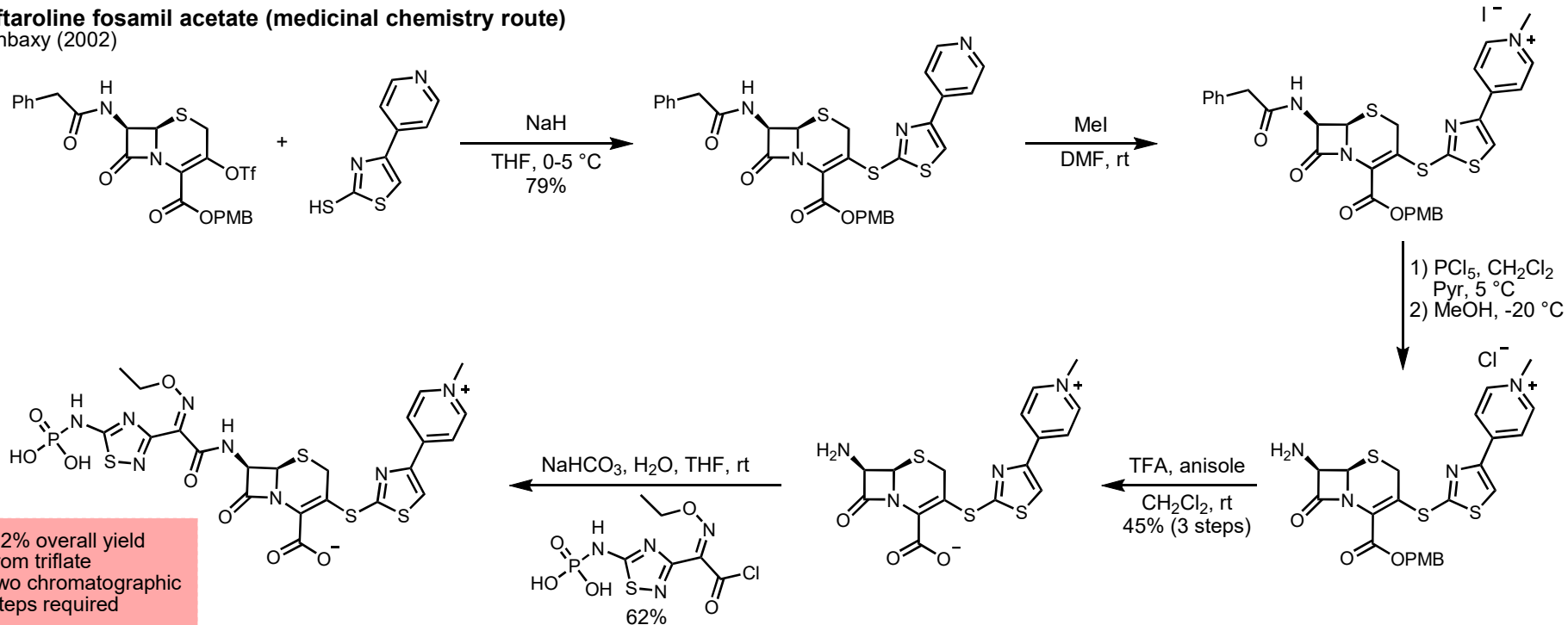
C-N cross coupling

Merck (2016)



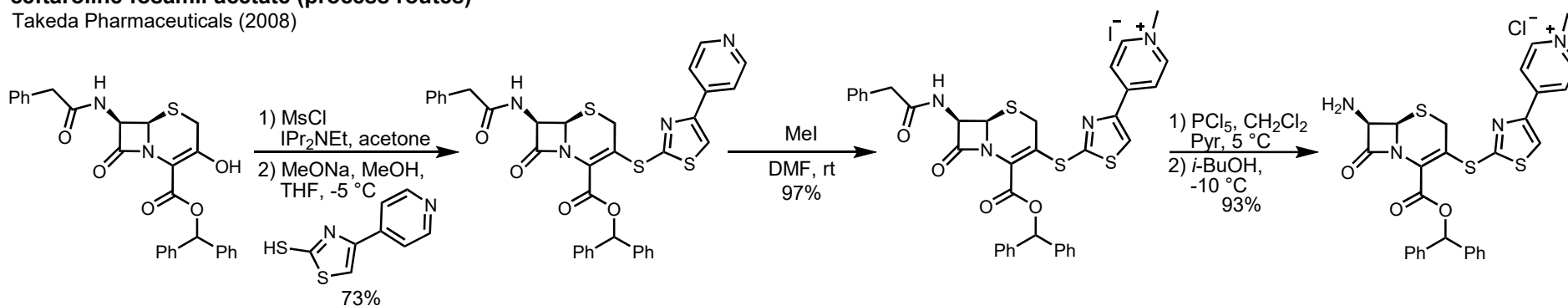
ceftaroline fosamil acetate (medicinal chemistry route)

Ranbaxy (2002)

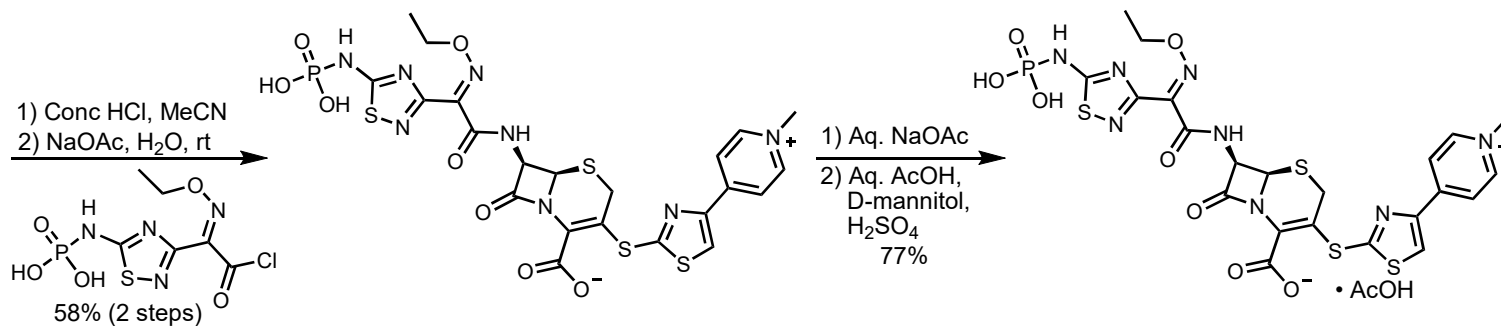


ceftaroline fosamil acetate (process routes)

Takeda Pharmaceuticals (2008)

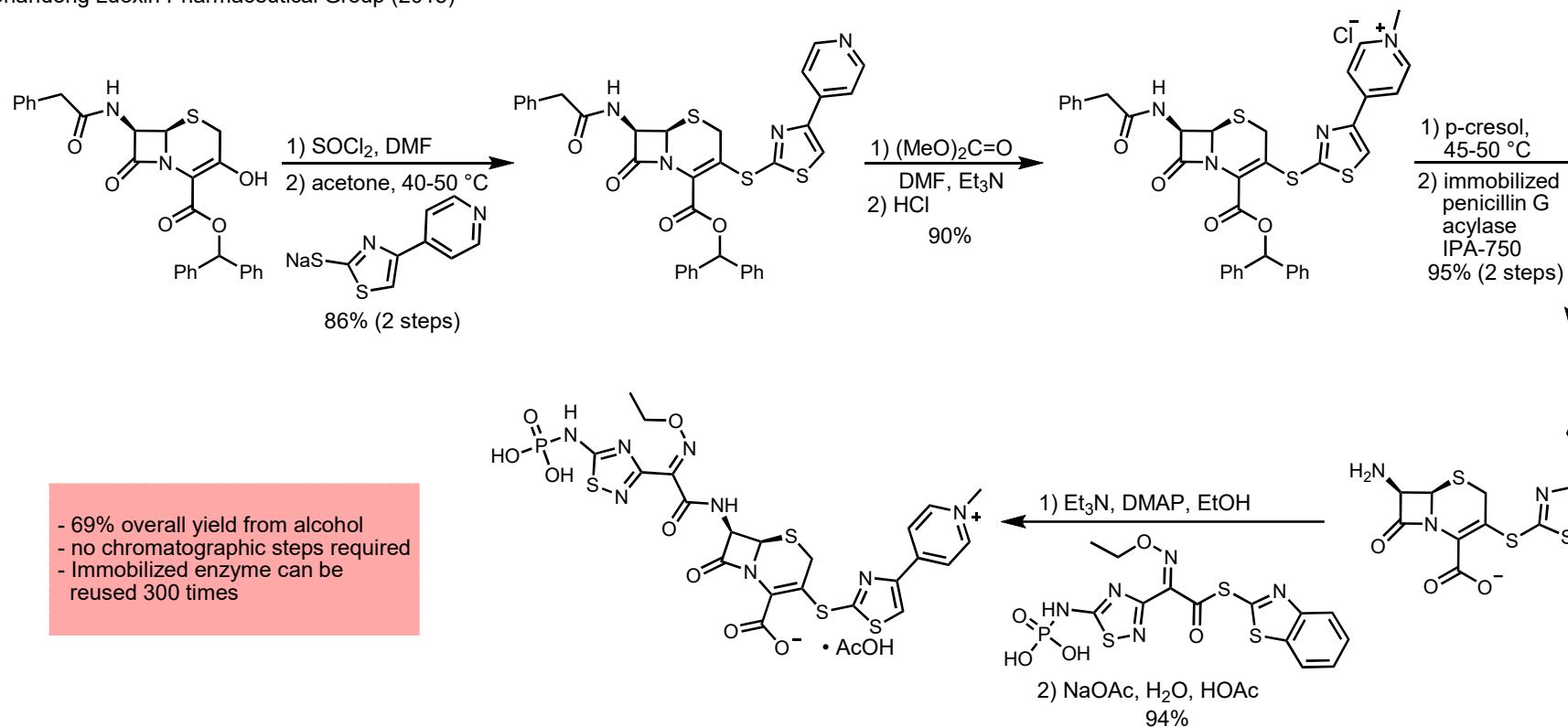


Benzhydryl protection leads to more crystalline intermediates



- 29% overall yield from alcohol
- only one chromatographic step required

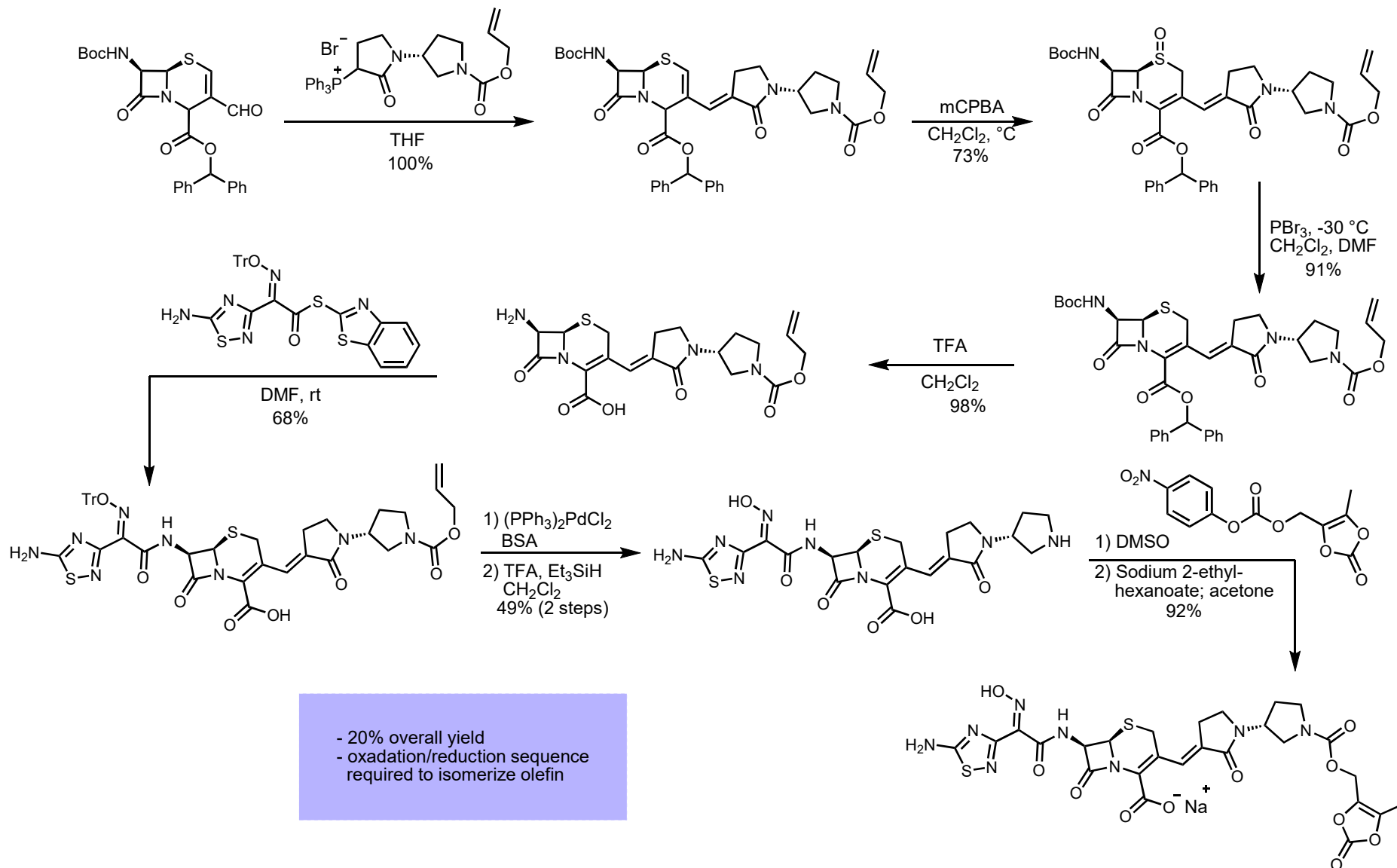
Shandong Luoxin Pharmaceutical Group (2015)



- 69% overall yield from alcohol
- no chromatographic steps required
- Immobilized enzyme can be reused 300 times

ceftobiprole medocartil sodium (medicinal chemistry route)

Hoffmann-La Roche (1999)



ceftobiprole medocartil sodium (process route)

Basilea (2016)

