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Total synthesis of Cephalosporolide E via a tandem radical/polar crossover reaction.

Cortezano-Arellano, O.; Quintero, L. *J. Org. Chem.* **2015**, **ASAP**
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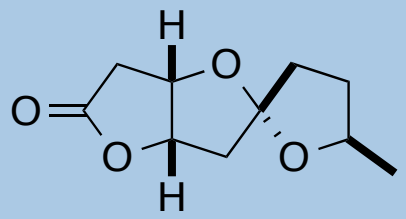
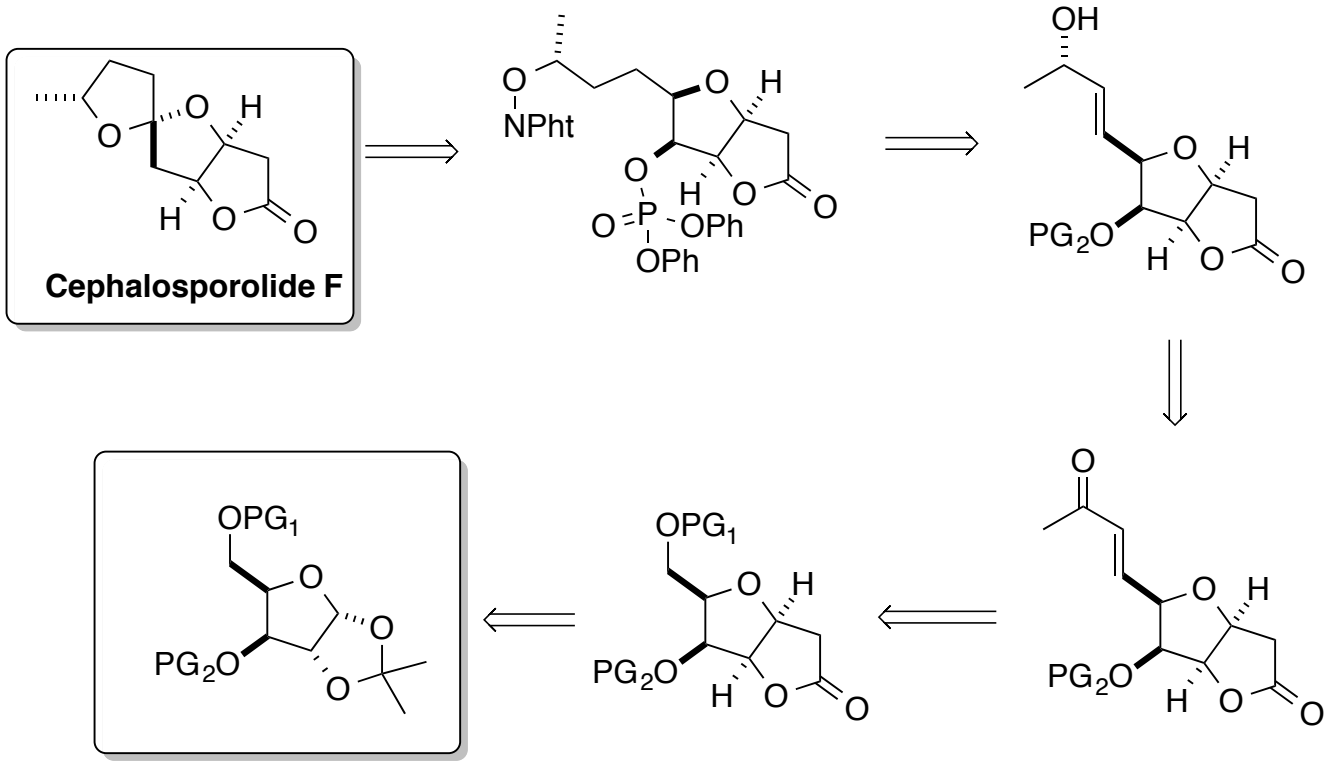


Nicolas Volkoff
19/02/2015

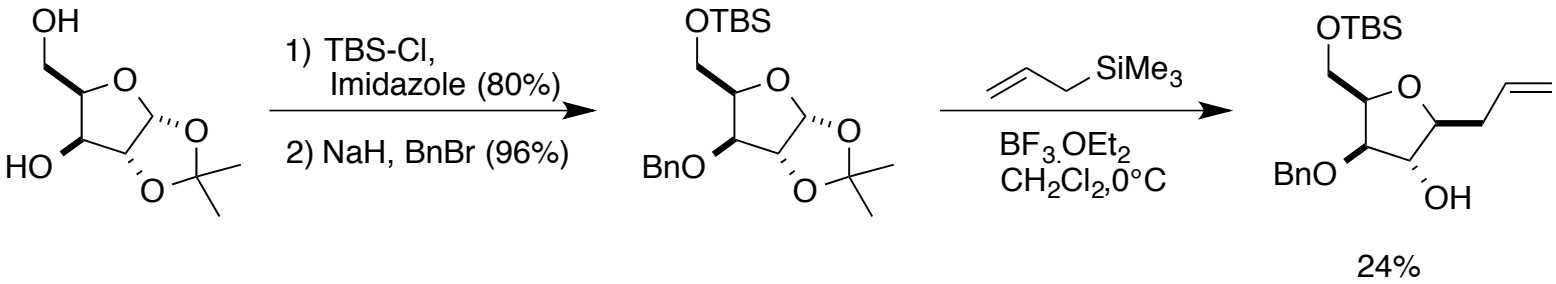
Introduction

- Extracted from *cephalosporium aphidicola* in 1985 by J. R. Hanson
- At least 6 previous synthesis
- They claimed to be the first direct diastereoselective synthesis

Retrosynthetic Approach

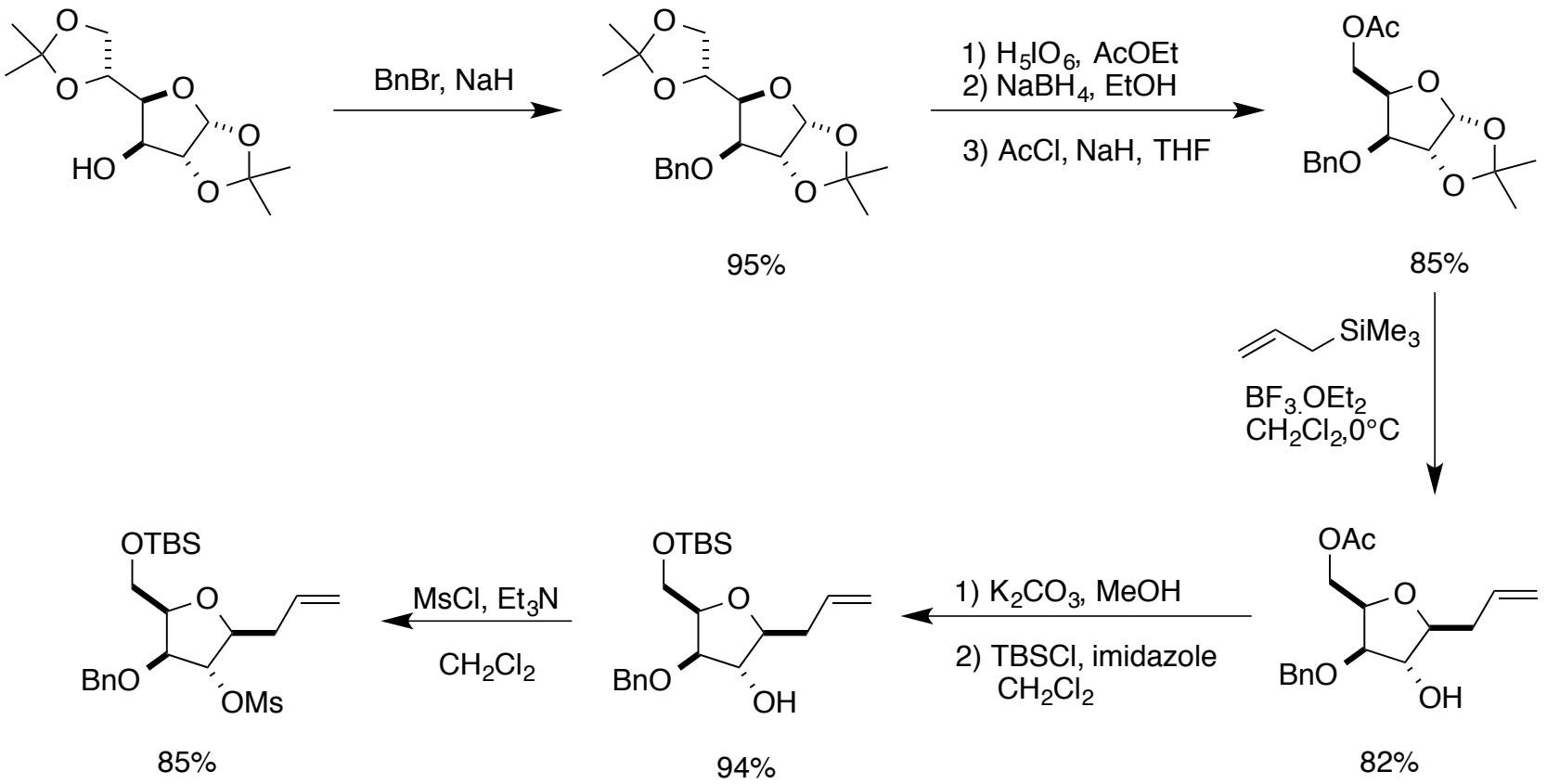


Synthesis

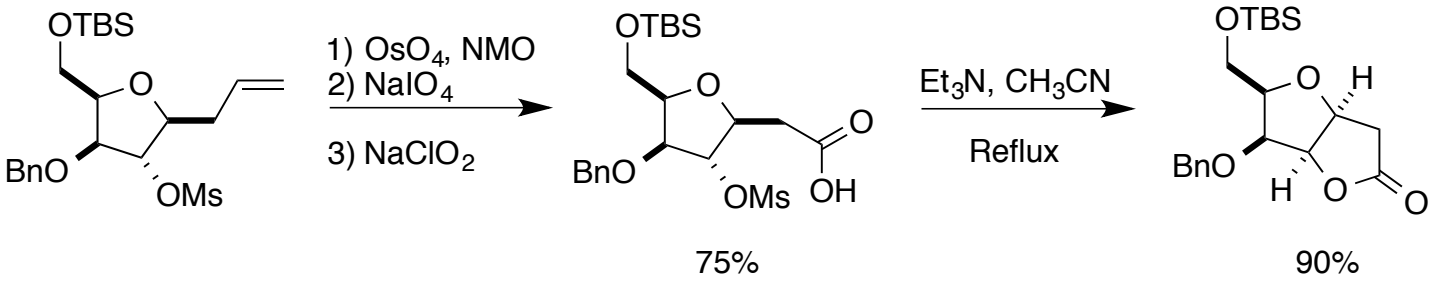


> Low yield : deprotection of the hydroxyl group

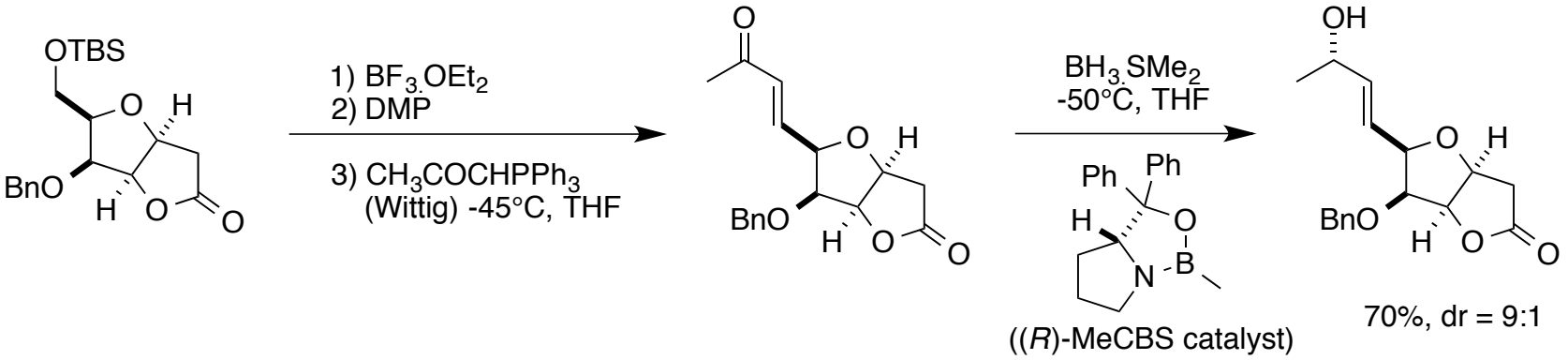
Precursor for the lactonization



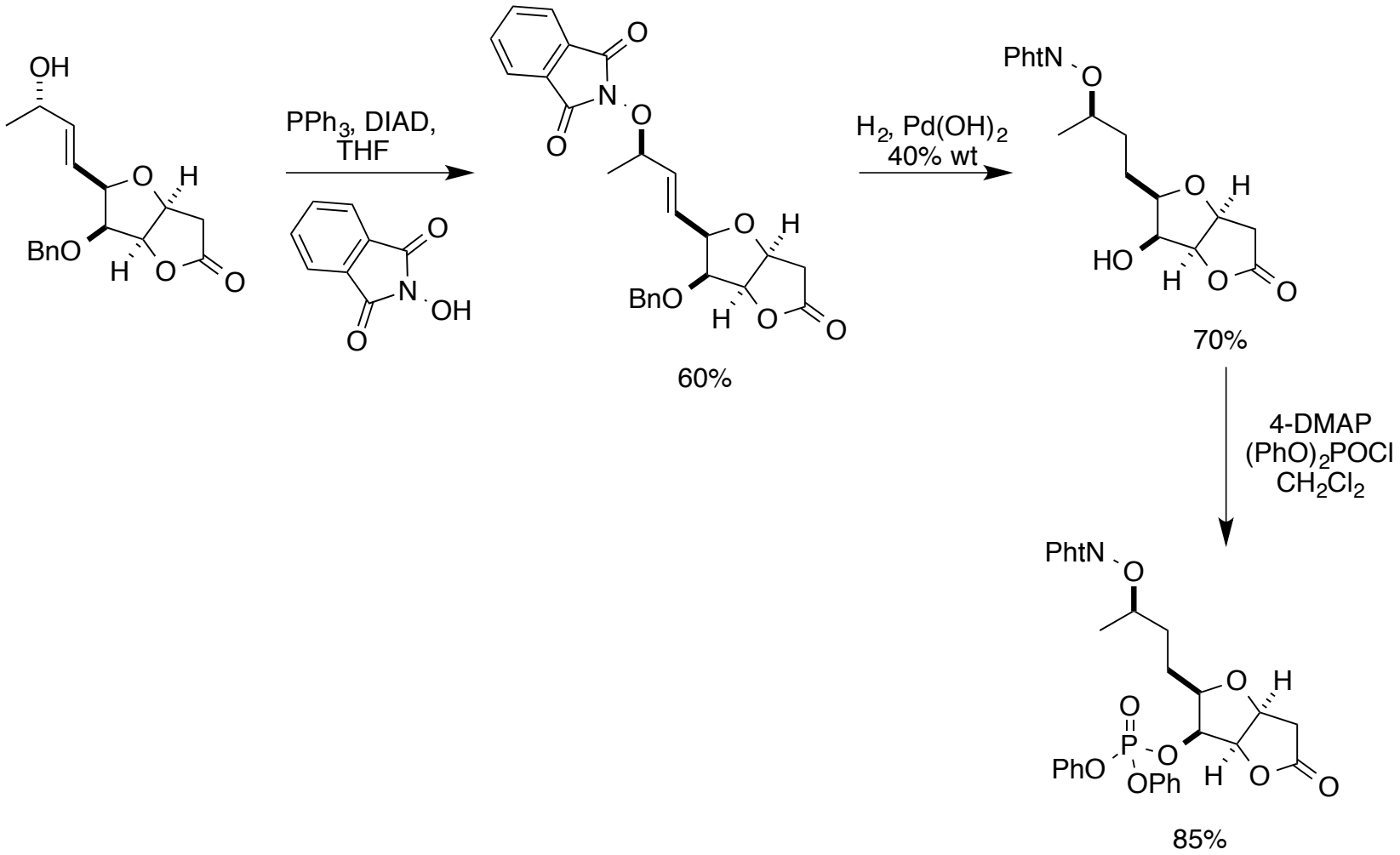
Lactonization



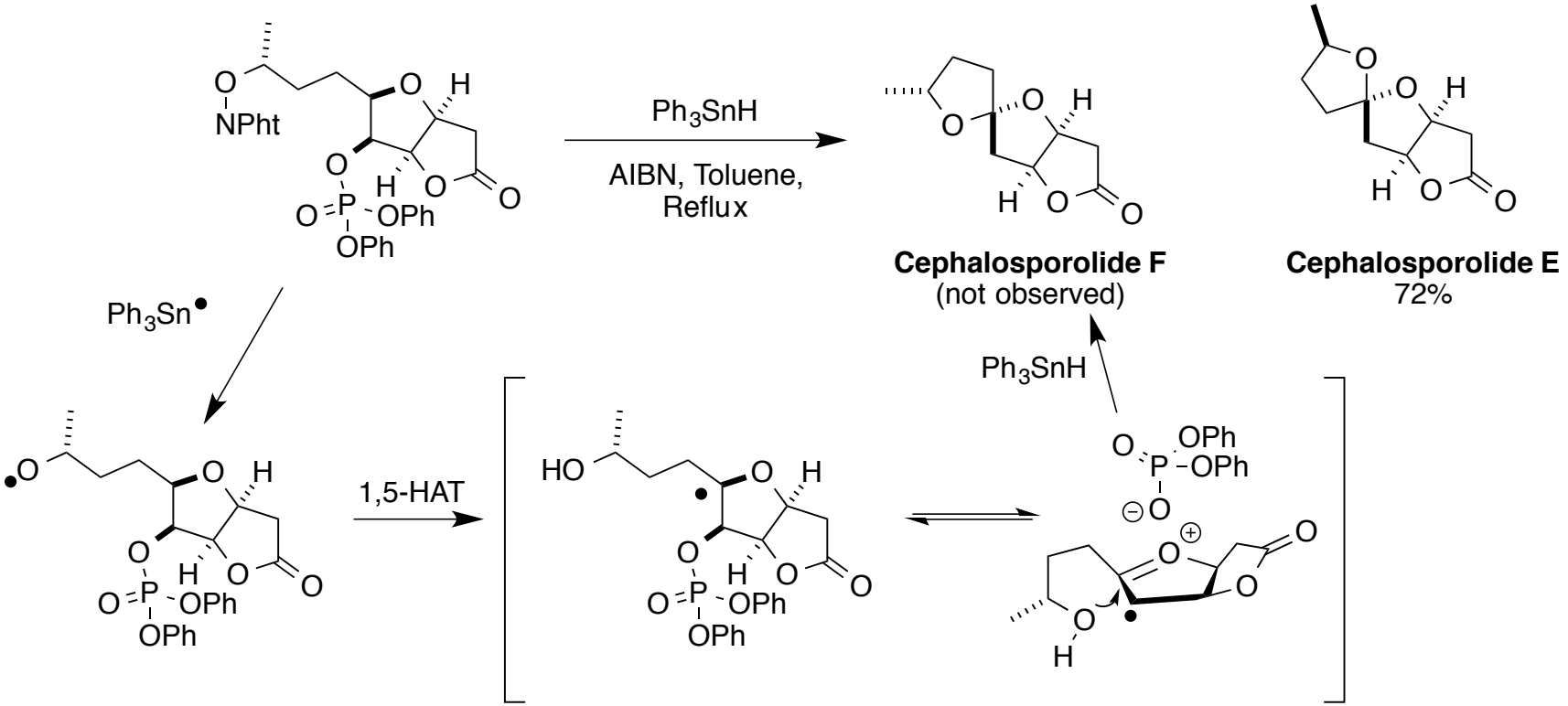
Corey-Bakshi-Shibata Reduction



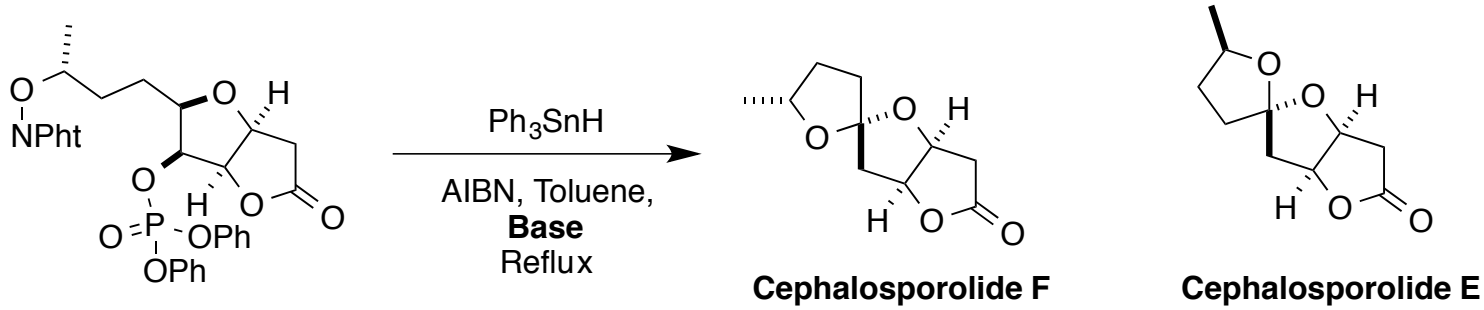
Preparation of the radical precursor



Spirocyclization



Spirocyclization



Cephalosporolide F **Cephalosporolide E**

Base (equiv.)	Cephalosporolide E/F (NMR ratio)
Et_3N (3)	85/15
Et_3N (6)	76/24
Et_3N (8)	75/25
Imidazole (6)	53/47
Imidazole (8)	51/49

Conclusion

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- Diastereoselective synthesis of Cephalosporolide E
- 20 steps and 4% overall yield starting from comercially available di-O-isopropylidene-α-D-glucofuranose
- The use of radical cation under non oxidative conditions

Thank you for your attention