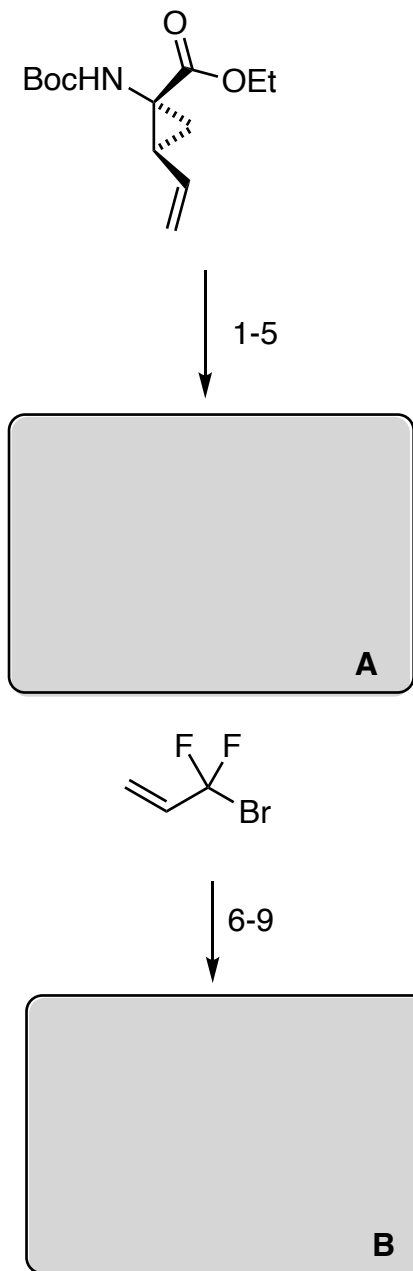


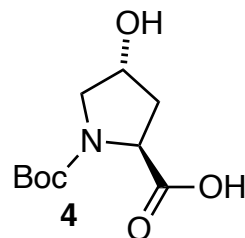
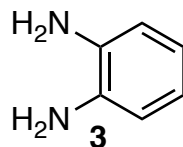
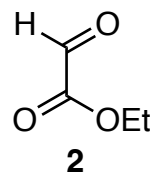
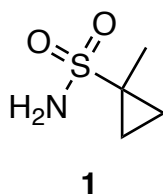
# Development of the Enabling Route for Glecaprevir via Ring-Closing Metathesis

Russell D. Cink, Kirill A. Lurkin, *et. al.*

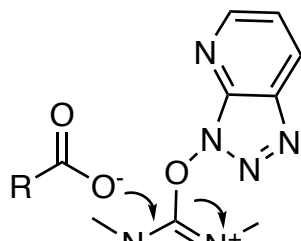
*OPRD* 2020, 24, 183–200.



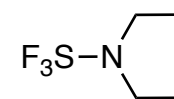
- 1) BOC<sub>2</sub>O, DMAP
- 2) OsO<sub>4</sub>, NaIO<sub>4</sub>
- 3) DAST, 2,6-Lutidine
- 4) HATU, DMAP, **1**
- 5) HCl



- 6) **2**, Indium, THF/Water
- 7) T3P, DMSO, *then* **3**, NEt<sub>3</sub>, AcOH
- 8) SOCl<sub>2</sub>, DMF, heat
- 9) **4**, NaOtBu, *then* HCl, MeOH

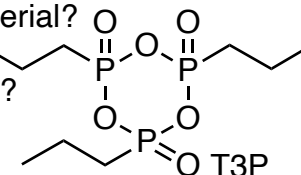


- 2) *Hint*: Only one Boc Remains
- 3) What is the structure of DAST?

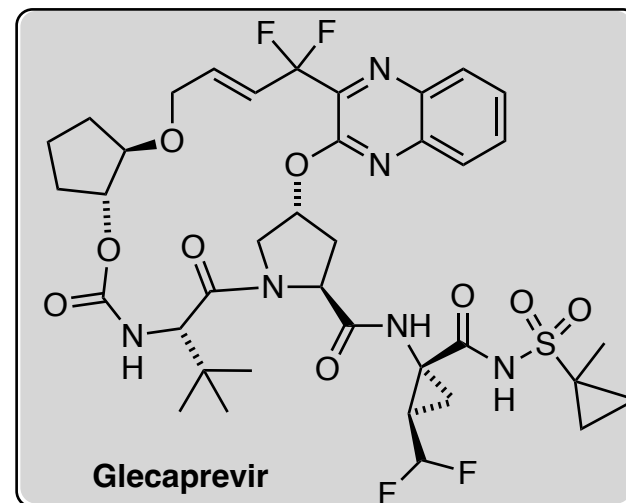


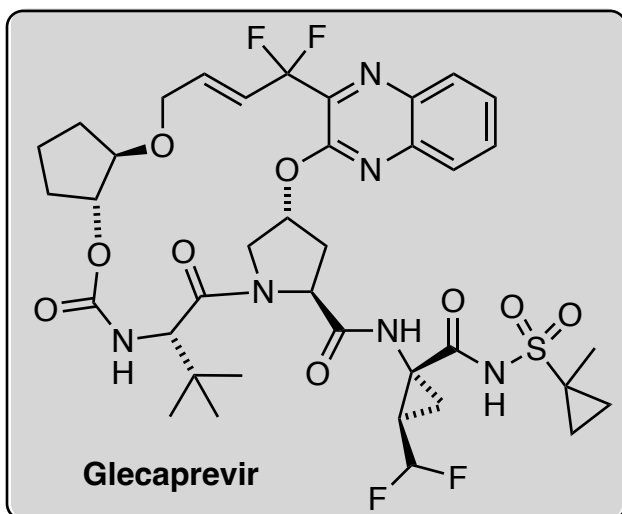
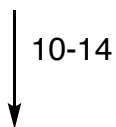
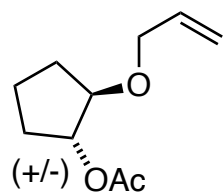
- 6) How would you prepare the alkene starting material?

- 7) Structure of T3P?

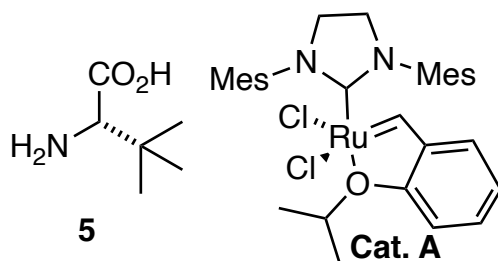


- 9) How would you make **4**?

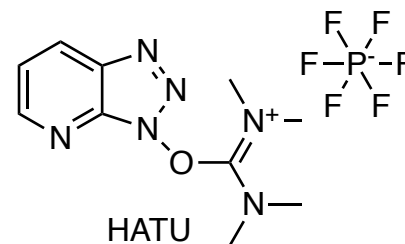




- 10) Novozym 435, phosphate buffer, then triphosgene, 2,6-lutidine, then **5**, NaOH, water  
 11) **B**, HATU, DIPEA  
 12) **Cat. A**, 40 °C  
 13) NaOH  
 14) **A**, EDAC, HOPO, TEA



- 10) Hint: enantioselective enzymatic functional group cleavage.  
 11) Structure of HATU? Provide a general mechanism of a HATU coupling



- 12) Compare **Cat. A** to a Grubbs catalyst what's the difference? Name some reasons this may be a better catalyst.

