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

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

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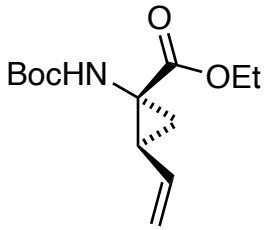
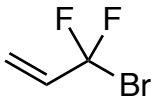


1-5

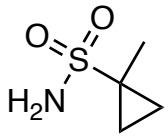
A



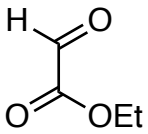
6-9

B

1) BOC_2O, DMAP
2) OsO_4, $NaIO_4$
3) DAST, 2,6-Lutidine
4) HATU, DMAP, **1**
5) HCl



1



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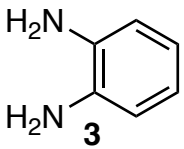

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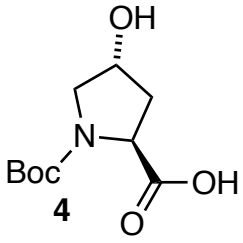


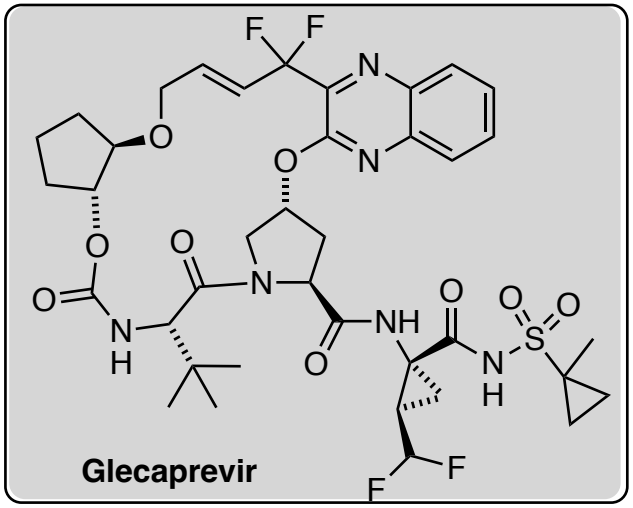
4

6) **2**, Indium, THF/Water
7) T3P, DMSO, *then* **3**, NEt_3, AcOH
8) $SOCl_2$, DMF, heat
9) **4**, NaO*t*Bu, *then* HCl, MeOH

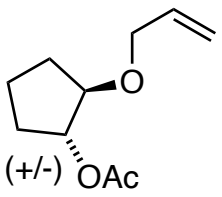
1) What is the structure of DAST?

2) *Hint:* Only one Boc Remains

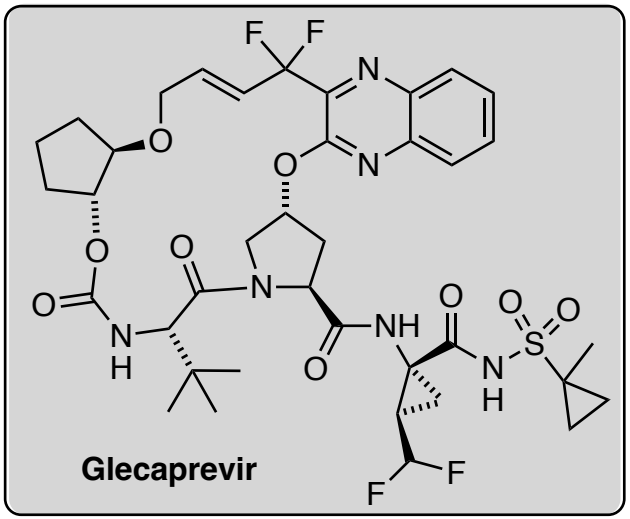
6) How would you prepare the alkene starting material?
7) Structure of T3P?
9) How would you make **4**?



Glecaprevir

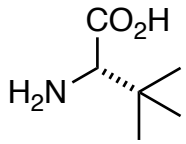


10-14



Glecaprevir

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



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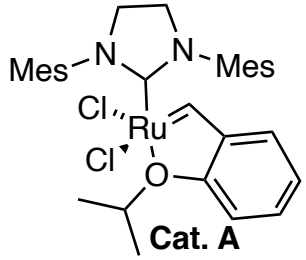

Cat. A

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 whats the difference? Name some reasons this may be a better catalyst.