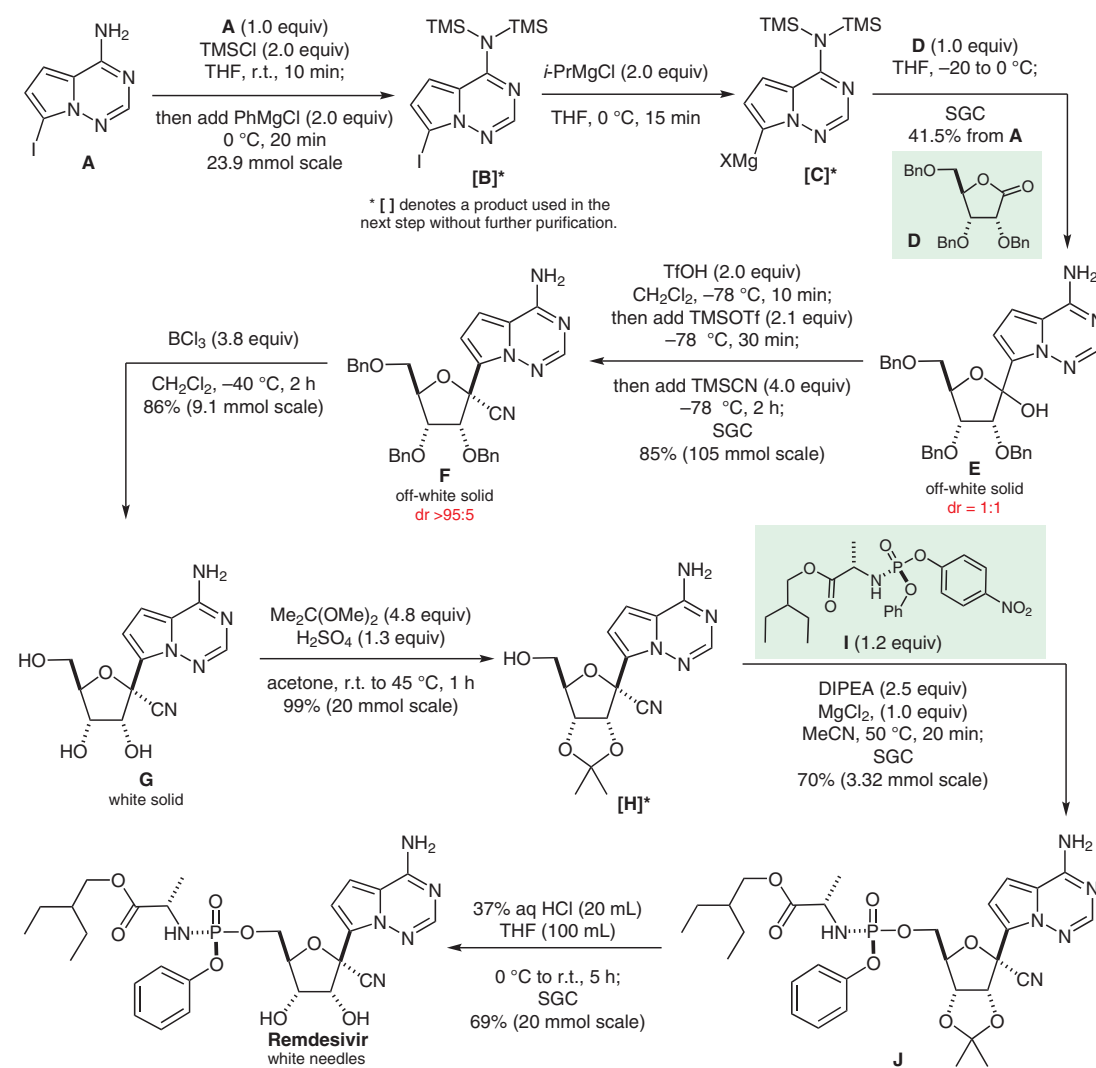


Synthesis of Remdesivir (GS-5734) – A Candidate for the Treatment of Ebola and COVID-19 Infections



Significance: Remdesivir (GS-5734) is a C-nucleoside phosphoramidate prodrug of an adenosine analogue discovered by workers at Gilead, that is of intense interest for the treatment of Ebola virus disease, COVID-19, and other lethal viruses. It is an RNA-dependent RNA polymerase inhibitor.

Comment: The key step in the short synthesis depicted entails the construction of 1'-cyano C-glycoside **F** by reaction of *O,O*-acetal **E** with trimethylsilylcyanide (dr > 95:5). The presence of the 1'-cyano modification was critical in providing selectivity toward viral polymerases. See also: D. Siegel et al. *J. Med. Chem.* 2017, 60, 1648.