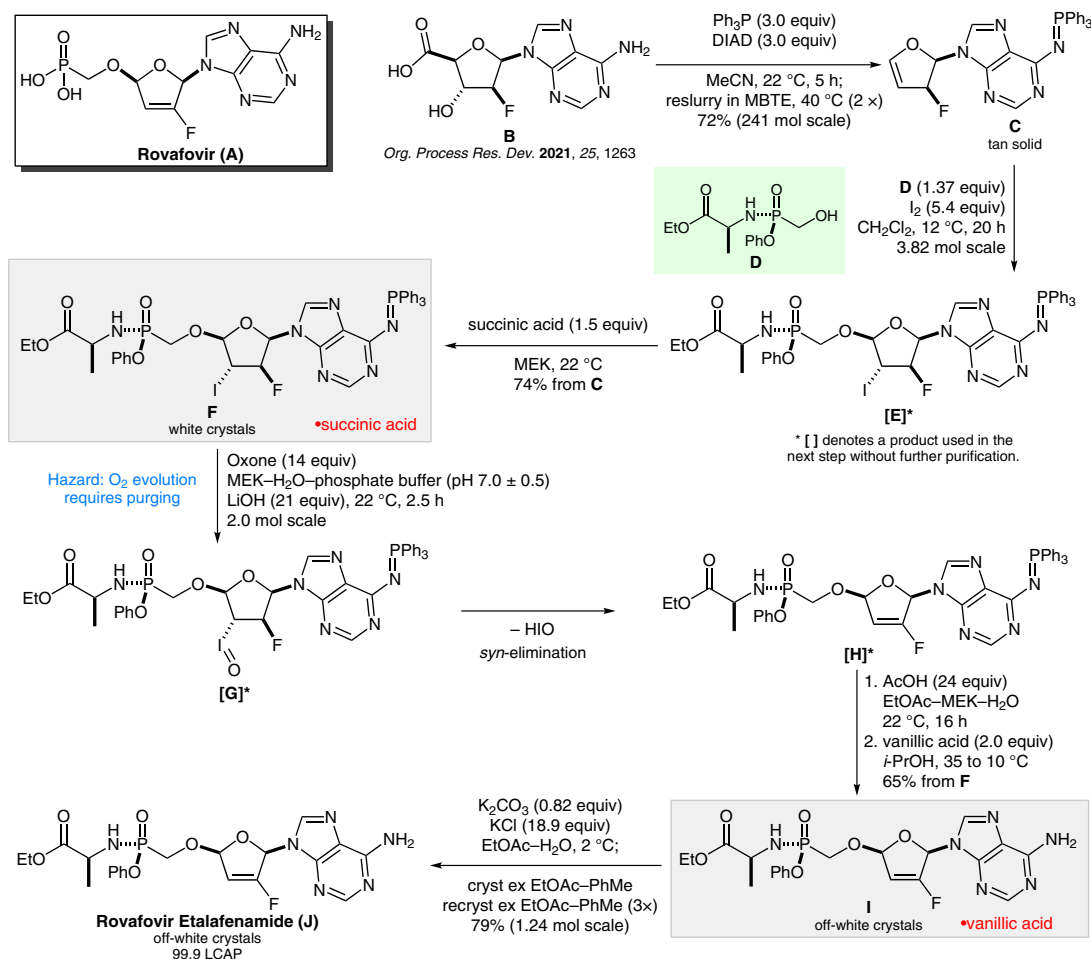


# Synthesis of Rovafovir Etalafenamide



**Significance:** Rovafovir etalafenamide (**J**) is a phosphonamidate prodrug of the nucleotide reverse transcriptase inhibitor rosofovir (**A**) that is under investigation for the treatment of HIV-1 infection. Workers at Gilead describe the development of a manufacturing route to **J** in four parts. Part I (Org. Process Res. Dev. 2021, 25, 1215) deals with the closing stages depicted in which nucleoside **B** is converted to the final product **J**. The key step entails oxidation of the iodo derivative **F** to the iodoso compound **G** that syn-eliminates hypoiodous acid to give the desired fluoroalkene **H** in 65% yield.

**Comment:** Part II (Org. Process Res. Dev. 2021, 25, 1237) gives further details of the key oxidative elimination of iodo derivative **F** to fluoroalkene **H**. Part III (Org. Process Res. Dev. 2021, 25, 1247; Synfacts 2021, 17, 844) focuses on the synthesis of phosphonate **D** and part IV (Org. Process Res. Dev. 2021, 25, 1263; Synfacts 2021, 17, 845) describes the synthesis of nucleoside **B**. In the final step a highly efficient iterative crystallization process was used to purge the product of the *des*-fluoro analogue of **J** (not shown), a mitochondrial toxin, together with other process impurities.