Synthesis of Rovafovir Etalafenamide

**Significance:** Rovafovir etalafenamide (J) is a phosphonamidate prodrug of the nucleotide reverse transcriptase inhibitor rovafovir (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 hypoidous 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.