Enantioselective Synthesis of Oseltamivir Phosphate (Tamiflu) via the Iron-Catalyzed Stereoselective Olefin Diazidation


Significance: Xu and co-workers report a gram-scale synthesis of the neuraminidase inhibitor oseltamivir phosphate (Tamiflu®), in which the trans-diamino moiety was installed through an iron-catalyzed, diastereoslective diazidation of enantiopure olefin E to give the 1,2-trans-diazide H in 70% yield (dr > 20:1). Electronically deactivated substrates, that have been otherwise problematic, are tolerated.

Comment: Mechanistic studies revealed that both the iron catalyst and the complex substrate cooperatively modulate the stereoselectivity of the diazidation. Process safety assessment using both differential scanning calorimetry and the drop weight test indicate that the diazidation reaction can be performed on large scale.