S31-1 Three "One-Pot" Synthesis of (-)-Oseltamivir

◯Hayato ISHIKAWA[1], Takaki SUZUKI[1], Aravind APPU[1], Yujiro HAYASHI[1]

[1]Faculty of Engineering, Tokyo University of Science

A great deal of attention has been paid both in the scientific literature and the general media to the high potential risk of a worldwide spread of avian H5N1 influenza virus, the death rate of which is over 50%. Indeed, should this virus acquire the ability to become capable of spreading easily and directly from human to human it could very possibly cause a disastrous pandemic. (–)-Oseltamivir phosphate (Tamiflu), a neuraminidase inhibitor used in the treatment of both type A and type B human influenza, is one of the most promising therapeutics, and many nations have plans to stock a significant amount of this compound in case of a possible influenza outbreak.

An efficient, enantioselective total synthesis of (–)-oseltamivir via separated three one pot operation has been accomplished, demonstrating the power of asymmetric reactions catalyzed by organocatalysts, in particular diphenylprolinol silyl ether. This synthesis requires nine reactions, a total of three separate one-pot operations, and one purification by column chromatography. The total yield of (–)-oseltamivir from nitroalkene is 57%. All the reagents are inexpensive. The metal-based reagents employed in the present total synthesis contain either alkali-metal ions (Na, K, and Cs) or nontoxic Zn. No special care is needed to exclude water or air. Thus, the present procedure is suitable for large-scale preparation.