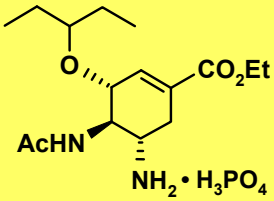
SOCIÉTÉ CHIMIQUE DE GENÈVE

Bird Flu, Swine Flu: En Route to Tamiflu™

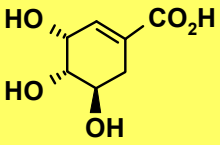
Dr Martin KARPF

F. Hoffmann-La Roche Ltd, Basel

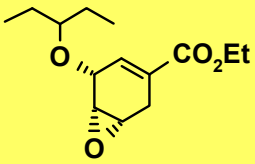
Seasonal influenza is a severe infectious disease affecting millions of people and causing thousands of deaths each winter. The current flu situation is further aggravated by the recent spread of the bird flu virus H5N1 and the swine flu virus of type H1N1. Although the origin of the disease is unclear, after the disastrous pandemics of last century, intensive research uncovering its cause has ultimately lead to the isolation and structural elucidation of the indispensable viral surface protein neuraminidase and paved the way to securing effective inhibitors. Oseltamivir Phosphate **1** was created by the Californian company Gilead and licensed to Roche, entering the market in 1999 under the trade name Tamiflu™ after a fast track co-development effort. In this presentation, the evolution of the synthesis of Tamiflu™ **1** from the discovery chemistry route up to the technical access from (-)-shikimic acid **2** is reviewed. Synthesis and process research investigations towards ascertaining an azide-free conversion of the key intermediate epoxide **3** to **1** are discussed and the search for new routes to **1** independent of shikimic acid **2** are presented.



1
Oseltamivir phosphate
Tamiflu™



2
(-)-Shikimic acid



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