S. ABRECHT, P. HARRINGTON, H. IDING, M. KARPF*, R. TRUSSARDI, B. WIRZ, U. ZUTTER
(F. HOFFMANN-LA ROCHE LTD, BASEL, SWITZERLAND)

The Synthetic Development of the Anti–influenza Neuraminidase Inhibitor Oseltamivir Phosphate (Tamiflu®): A Challenge for Synthesis & Process Research
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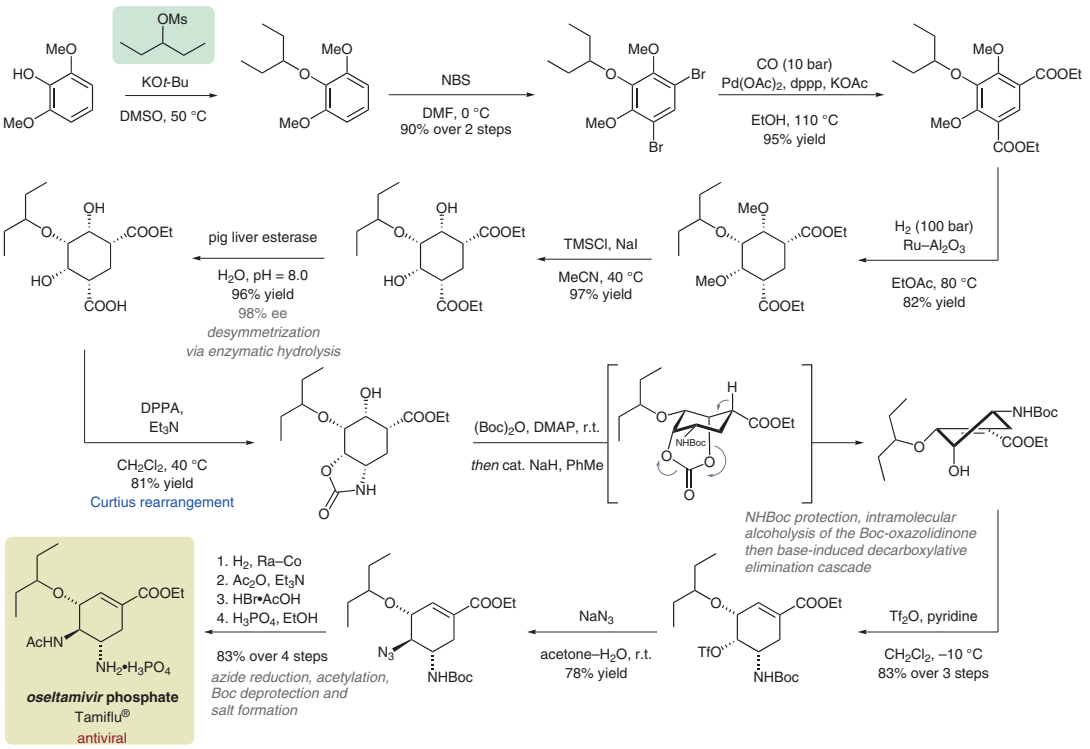
# A Classic Route to the Synthesis of Tamiflu®




**Significance:** Tamiflu®, or oseltamivir, is vital for treating and preventing influenza infections caused by influenza A and B viruses, as it reduces symptom severity and duration when taken within 48 hours of symptom onset. It also serves as a prophylactic measure to prevent influenza in those exposed to the virus and helps in controlling transmission, especially during outbreaks and pandemics. Crucially, Tamiflu® is particularly important for vulnerable populations, such as the elderly and those with underlying health conditions and plays a key role in pandemic preparedness efforts.

**Comment:** The synthesis commences with inexpensive 1,6-dimethoxyphenol. Key steps to the synthesis of oseltamivir rely on an all-*cis* hydrogenation of the electron-rich aryl ring to access five stereocenters in a single step. A desymmetrization enables access to an enantioenriched chiral building block by enzymatic hydrolysis. A key decarboxylative elimination sequence affords the α,β-unsaturated ester in high yield. While there are causes for concern in terms of scalability (i.e. high pressure carbonylations, hydrogenations and the use of azides) this synthesis is arguably a masterclass in the field of synthetic chemistry.

**SYNFACTS Contributors:** Dirk Trauner, Jordan Y. Artzy
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**Category**
Innovative Drug Discovery and Development

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Synfact Classic