30.11.2017

Problem Session

Oseltamivir (Tamiflu[®]) is an antiviral medication listed on the WHO list of essential medicines. The emergence of the avian influenza in the 2000's gave rise to an urgent need for a high yielding and robust route to orally effective oseltamivir phosphate. Intensive efforts of the chemical community have been devoted to the development of efficient preparation of this drug, with >60 synthesis reported to this date. Corey published a short enantioselective synthesis in 2006, and chose not to patent the procedure:



1) Determine the structure of intermediates 3-12

2) Provide a plausible mechanism for the bromoacetamidation of **9** to **10**.

Problem Session

More recently, a 60-minute one-pot total synthesis has been reported by Y. Hayashi. This 5-step synthesis relies on the use of an organocatalyst and a domino Michael / Horner-Wardworth-Emmons reaction.



- 1) Determine the structure of **13** & **14**, and give a plausible mechanism.
- 2) Provide an explanation for the role of TMSCl in the protonation step of nitronate **14** to **15**.