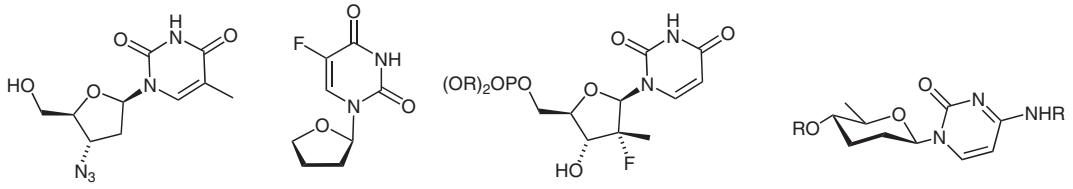
B. M. TROST*, S. XU, E. U. SHARIF (STANFORD UNIVERSITY, USA)

New Catalytic Asymmetric Formation of Oxygen Heterocycles Bearing Nucleoside Bases at the Anomeric Carbon
J. Am. Chem. Soc. **2019**, *141*, 10199–10204.

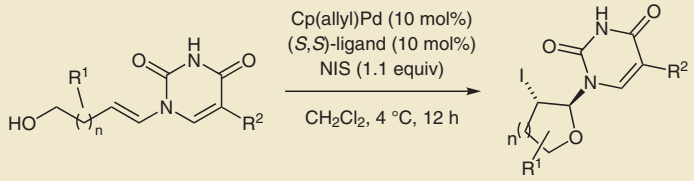
Palladium-Catalyzed Synthesis of Pyrimidine Nucleoside Analogs

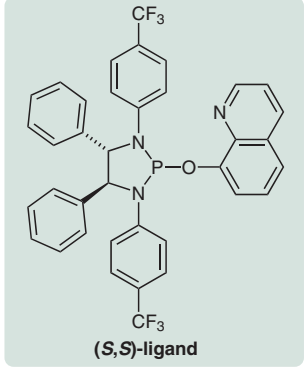
Biologically important pyrimidine nucleoside derivatives:



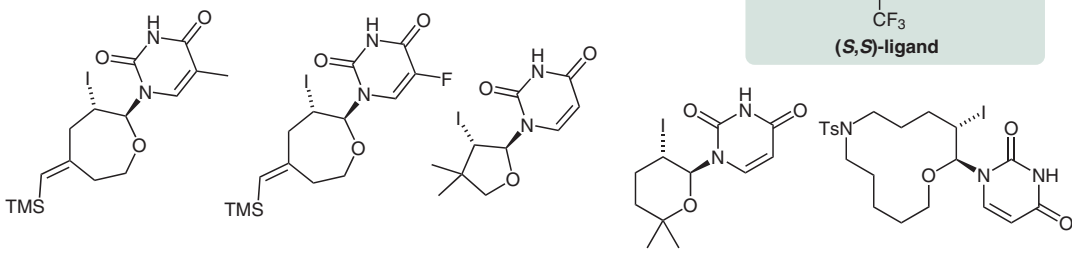
AZT (antiviral activity) | Tegafur (anticancer activity) | Sovaldi (antiviral activity) | Amicetin (antibiotic activity)

General reaction conditions:



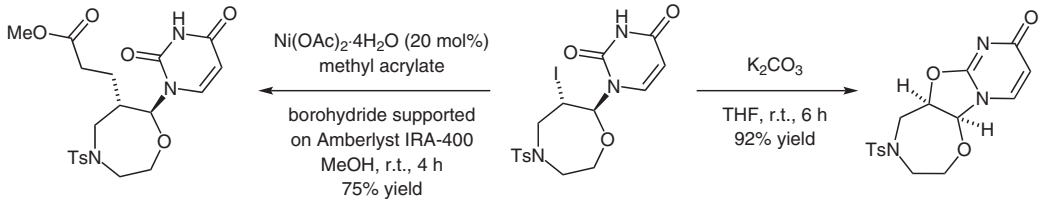


Substrate scope:



90% yield, 90% ee | 91% yield, 91% ee | 96% yield, 99% ee | 94% yield, 99.5% ee | 84% yield, 99.5% ee

Derivatization reactions:



Significance: Many FDA approved antiviral and anticancer drugs contain nucleoside analogs. The biologically active nucleosides are synthesized either by derivatization of an intact nucleoside or by coupling a nitrogenous base with a modified sugar (glycolsylation reaction). However, all previous methods suffered from poor yields and low diastereoselectivities.

Comment: Trost and co-workers reported a new Pd-catalyzed synthesis of pyrimidine nucleoside analogs bearing an iodide substituent. This process occurs in high yields as well as excellent enantio- and diastereoselectivity (dr >20:1). The products can be transformed into a variety of new pyrimidine nucleoside analogs. According to the proposed mechanism, the reaction proceeds through a Pd(IV) species, which undergoes reductive elimination to form a C–I bond.

SYNFACTS Contributors: Dirk Trauner, Andrej Shemet
Synfacts 2019, 15(09), 1059 Published online: 20.08.2019
DOI: 10.1055/s-0039-1690600; **Reg-No.:** T07319SF

Category

Chemistry in Medicine and Biology

Key words

pyrimidine nucleoside analogs

oxygen heterocycles

iodoetherification

Synfact of the Month