L. HE, L. ZHAO, D.-X. WANG, M.-X. WANG* (INSTITUTE OF CHEMISTRY, CHINESE ACADEMY OF SCIENCES AND TSINGHUA UNIVERSITY, BEIJING, P. R. OF CHINA)
Catalytic Asymmetric Difunctionalization of Stable Tertiary Enamides with Salicylaldehydes: Highly Efficient, Enantioselective, and Diastereoselective Synthesis of Diverse 4-Chromanol Derivatives
Org. Lett. **2014**, *16*, 5972–5975.

Enantioselective Reaction of Tertiary Enamides with Salicylaldehydes

Significance: Tertiary enamides are related to enamines by replacement of an *N*-alkyl substituent with an electron-withdrawing group. Despite this change, they remain nucleophilic. Taking advantage of this characteristic and of the electrophilicity of the transient iminium, the authors developed a modular titanium(IV)-catalyzed synthesis of 4-chromanol derivatives, by reaction with salicylaldehydes.

Comment: The use of a titanium–(*R*)-BINOL complex enabled the synthesis of diverse 4-chromanol products with good to excellent enantio- and diastereoselectivity. Water was found to have a marked effect on enantioselectivity: under anhydrous conditions, the ee decreased to 50.8%, whereas it was measured at 96.5% in the presence of 20 mol% water, in the model reaction. The exact mechanism remains to be elucidated.

SYNFACTS Contributors: Mark Lautens, Thomas Johnson
Synfacts 2015, 11(1), 0068 Published online: 15.12.2014
DOI: 10.1055/s-0034-1379692; **Reg-No.:** L15814SF

2015 © THIEME STUTTGART • NEW YORK