Rhodium-Catalyzed Enantioselective Hydrogenation of Tetrasubstituted α-Acetoxy β-Enamido Esters

J. Am. Chem. Soc. **2014**, *136*, 16120–16123

Asymmetric hydrogenation of polysubstituted enamides has become one of the most powerful strategies for the stereocontrolled synthesis of non-racemic chiral amines, amino acids and their derivatives, and has important practical applications in the pharmaceutical industry. However, due to the strong steric hindrance, the hydrogenation of tetrasubstituted enamides is very challenging and only a few special tetrasubstituted enamides have been effectively obtained in an enantioselective manner (for references see ref. 18 in the original article). Therefore, development of an efficient method for synthesizing multifunctionalized chiral amines via hydrogenation of tetrasubstituted enamides is highly desirable.

The group of Professor Xumu Zhang at Wuhan University (P. R. of China) has a strong ongoing interest in developing economic and environmentally friendly routes to synthesize chiral non-racemic molecules with strong biological activities. Recently, as a result of a research effort directed by Professors Hui Lv and Xumu Zhang, the group successfully developed a very effective catalytic enantioselective hydrogenation of tetrasubstituted enamides to biologically important α-hydroxy-β-amino acids. Professor Zhang said: "The synthesis of enantiomerically pure chiral α-hydroxy-β-amino acid moieties drew our interest because of the unique properties of these compounds.[1] Although there are many approaches to the synthesis of α-hydroxy-β-amino acid derivatives, a straightforward synthesis of chiral α-hydroxy-β-amino acid derivatives through asymmetric hydrogenation of α-acetoxy β-enamido esters had not been reported prior to this work."

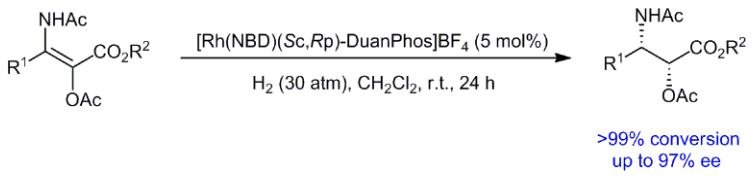
"By employing the Rh-DuanPhos catalytic system developed in our lab, we have achieved asymmetric hydrogenation of tetrasubstituted α-acetoxy β-enamido esters under mild conditions," explained Professor Zhang, who added: "This new methodology has several advantages over existing methodologies: (1) the reaction allows the synthesis of structurally diverse α-hydroxy-β-amino acid derivatives with excellent yields and excellent enantioselectivities, which is more atom-economic and more practical than previous synthetic routes.[2] (2) The reaction has a broad substrate scope and potential applications in total synthesis or drug synthesis. Moreover," concluded Professor Zhang, "the methodology can be used for a very direct synthesis of the C13 side chain of paclitaxel."

Matteo Zanda

REFERENCES

(1) (a) H. Suda, T. Takita, T. Aoyagi, H. Umezawa *J. Antibiot.* **1976**, *29*, 600. (b) T. Aoyagi, H. Tobe, F. Kojima, M. Hamada, T. Takeuchi *J. Antibiot.* **1978**, *31*, 636.

(2) (a) P. Dziedzic, P. Schyman, M. Kullberg *Chem. Eur. J.* **2009**, *15*, 4044. (b) Y. Jiang, X. Chen, Y. Zheng, Z. Xue, C. Shu, W. Yuan, X. Zhang *Angew. Chem. Int. Ed.* **2011**, *50*, 7304.



SYNFORM, 2015/03
Published online: 16.02.2015, **DOI**: 10.1055/s-0034-1380014

About the authors

Q. Wang

Qingli Wang was born in Heilongjiang Province (P. R. of China) in 1985. She received her Bachelor's degree (2009) and Master's degree (2012) from the Wuhan Institute of Technology (P. R. of China). In 2012 she joined Professor Xumu Zhang's research group and is currently a PhD student in the College of Chemistry and Molecular Sciences, Wuhan University. Her research interests focus on asymmetric hydrogenation.

Prof. H. Lv

Hui Lv obtained his BSc degree in 2003 from Xiangtan University (P. R. of China) and PhD in 2010 from the Institute of Chemistry, Chinese Academy of Sciences (ICCAS, Beijing, P. R. of China). He continued his research as a postdoctoral associate at Nanyang Technological University (Singapore) from 2010 to 2012. He began his academic career at Wuhan University in 2013 in Professor Xumu Zhang's group. His research focuses on asymmetric hydrogenation and the application of transition-metal complexes of N-heterocyclic carbenes.

Prof. X. Zhang

Xumu Zhang received his BS degree in chemistry (1982) from Wuhan University and MS in chemistry (1985) from the Chinese Science Academy, Fuzhou (P. R. of China), under the supervision of Professor Jiaxi Lu. After a short stay at UC San Diego (USA), he received his PhD in chemistry in 1992 from Stanford University (USA) under the guidance of Professor James P. Collman. He then carried out postdoctoral work at Stanford University for two years. In 1994, he joined the Department of Chemistry at The Pennsylvania State University (USA) as an assistant professor of chemistry. In 2003, he was promoted to Full Professor. In 2007, he moved to The State University of New Jersey (USA) and was appointed as Distinguished Professor. In 2011, he joined Wuhan University as the winner of the "Thousand Talent Program." His research interests include the development of chiral phosphine ligands for asymmetric catalysis, the investigation of asymmetric hydrogenation and carbon–carbon bond-forming reactions, the synthesis of biologically active compounds, and the discovery of new synthetic methods.

SYNFORM, 2015/03
Published online: 16.02.2015, **DOI**: 10.1055/s-0034-1380014