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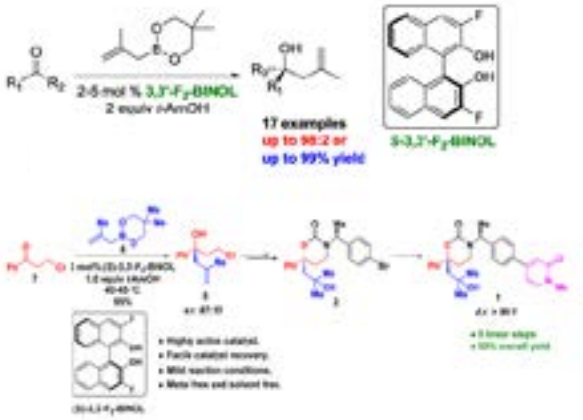
Yongda Zhang

Boehringer Ingelheim Pharmaceuticals Inc., USA

Asymmetric methallylation of ketones catalyzed by a highly active organocatalyst 3,3'-F2-BINOL and its application in synthesis of 11-β-HSD inhibitor

(S)-3,3'-F2-BINOL has been synthesized for the first time and demonstrated as a highly active organocatalyst for asymmetric methallylation of ketones. Up to 98:2 enantioselectivity and 99% yield were obtained with 5 mol% catalysts loading. The catalyst (S)-3,3'-F2-BINOL could be easily recovered and reused. Based on the methodology, an efficient asymmetric synthesis of 11-β-HSD inhibitor 1 has been accomplished in five linear steps and 53% overall yield, starting from the readily available 3-chloro-1-phenylpropan-1-one. The key feature of the synthesis includes an asymmetric methallylation of 3-chloro-1-phenylpropan-1-one catalyzed by the highly effective organocatalyst (S)-3,3'-F2-BINOL.



Biography

Yongda Zhang received his BA degree in Chemistry from Hangzhou University in 1994. He earned his PhD in Organic Chemistry at Fudan University under the guidance of Professor Dawei Ma (Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences) and Professor Fenggang Tao (Fudan University) in 2000. After his Post-doctoral research with Professor Alan J Kennan and additional Post-doctoral training with Professor Tomislav Rovis at Colorado State University, he joined Boehringer Ingelheim Pharmaceuticals Inc., in Ridgefield, CT; where, currently, he is a Principal Scientist. His research interests include design and development of innovative and practical processes for large-scale production of active pharmaceutical ingredients and synthetic methodology.

Yongda.zhang@boehringer-ingelheim.com

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