Enantioselective Palladium-Catalyzed Allylic Dearomatization

**Significance:** Chiral α-acyloxy-1-arylethanols are an important class of useful structural motifs (R. S. Bhondwea et al. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 3656). The authors report a palladium catalyzed enantioselective reduction of α-acyloxy-1-arylethanones to access α-acyloxy-1-arylethanols in high enantioselectivities.

**Comment:** The first synthesis of α-acyloxy-1-arylethanols was achieved using a chiral diamine ligand and SnCl₂ (T. Mukaiyama, K. Tomimori, T. Oriyama *Chem. Lett.* **1985**, *1359*). Then, the use of enzymatic methods for their synthesis with excellent enantioselectivities but moderate regioselectivity was reported (A. Manzocchi, A. Fiecchi, E. Santaniello *J. Org. Chem.* **1988**, *53*, 4405; T. Ema, Y. Sugiyama, M. Fukumoto, H. Moriya, J.-N. Cui, T. Sakai, M. Utaka *J. Org. Chem.* **1988**, *63*, 4996; R. Hayakawa, M. Shimizu, T. Fujisawa *Tetrahedron Asymmetry* **1997**, *8*, 3201). With a palladium catalyst and a bisphosphine ligand, the authors were able to show excellent selectivities for a variety of substrates. In addition, catalyst loadings could be lowered to 0.2 mol% without affecting enantioselectivity.

Selected examples:

- R = HO
  - >99% conversion 92% ee
- R = Cl
  - >99% conversion 83% ee
- R = MeO
  - >99% conversion 86% ee
- R = S
  - >99% conversion 96% ee

Pd(OCOCF₃)₂ (2 mol%) ligand (2.4 mol%) H₂ (30 bar) EtOH–TFE (4:1, 0.1 M) 0 °C, 24 h up to >99% conversion up to 97% ee 20 examples

**SYNFACTS Contributors:** Mark Lautens, Zafar Qureshi

*SYNFACTS* 2014, 10(1), 0064 Published online: 13.12.2013
DOI: 10.1055/s-0033-1340444; Reg-No.: L15413SF