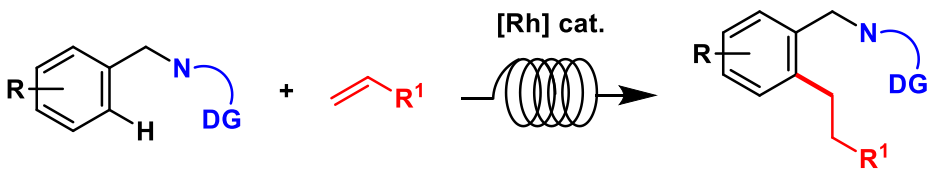
Rh(I)- and Rh(II)-Catalyzed C-H Alkylation of Benzylamines with Alkenes and its Application in Flow

(*Faculty of Engineering, Osaka University*) ○Amrita Das, Naoto Chatani

Keywords: Rhodium Catalyst; Carbon-Hydrogen Bond Cleavage; Benzylamine; Alkylation; Flow Chemistry

The Rh-catalyzed C-H alkylation of benzylamines with alkenes using a picolinamide derivative as a directing group is reported. Having significant utility of benzylamine derivatives in various biologically active compounds and natural products,[1] the functionalization of benzylamine derivatives via C-H bond activation strategies is one of the more important areas in organic chemistry.[2] Given our continuous interest in C-H alkylation reactions,[3] we were strongly motivated to investigate the *ortho*-alkylation of benzylamines with alkenes as an alkyl source. In recent years flow transformation reactions have found their way into academic research laboratories.[4] To this context, a flow set up was designed to successfully mimic this process under flow. Several examples are presented under flow conditions and its advantage over a batch process was confirmed.



1) (a) Zhang, Z.; Mccormick, D. B. *Proc. Natl. Acad. Sci. USA*, **1991**, *88*, 10407. (b) Choi-sledeski, Y. M.; Becker, M. R.; Klein, S. I.; Ewing, W. R.; Pauls, H. W.; Spada, A. P.; Mikol, V. *J. Med. Chem.*, **2000**, *43*, 3226.

2) (a) Orito, K.; Horibata, A.; Nakamura, T.; Ushito, H.; Nagasaki, H.; Yuguchi, M.; Yamashita, S.; Tokuda, M. *J. Am. Chem. Soc.*, **2004**, *126*, 14342. (b) Cai, G.; Fu, Y.; Li, Y.; Wan, X.; Shi, Z. *J. Am. Chem. Soc.*, **2007**, *129*, 7666. (c) Zhao, Y.; Chen, G. *Org. Lett.* **2011**, *13*, 4850.

3) (a) Aihara, Y.; Chatani, N. *J. Am. Chem. Soc.*, **2013**, *135*, 5308. (b) Rouquet G.; Chatani, N. *Chem. Sci.*, **2013**, *4*, 2201. (c) Shibata, K.; Chatani, N. *Org. Lett.*, **2014**, *16*, 5148. (d) Shibata, K.; Yamaguchi, T.; Chatani, N. *Org. Lett.*, **2015**, *17*, 3584. (e) Chatani, N. *Bull. Chem. Soc. Jpn.*, **2018**, *91*, 211.

4) (a) Webb, D.; Jamison, T. F. *Chem. Sci.*, **2010**, *1*, 675. (b) Porta, R.; Benaglia, M.; Puglisi, A. *Org. Process Res. Dev.*, **2016**, *20*, 2. (c) Plutschack, M. B.; Gilmore, K.; Seeberger, P. H. *Chem. Rev.*, **2017**, *117*, 11796. (d) Santoro, S.; Ferlin, F.; Ackermann, L.; Vaccaro, L. *Chem. Soc. Rev.*, **2019**, *48*, 2767.

© The Chemical Society of Japan