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Ligand-Controlled Selectivity in Palladium(0)-Catalyzed Barbier-Negishi Cross-Couplings of Secondary Alkyl Bromides

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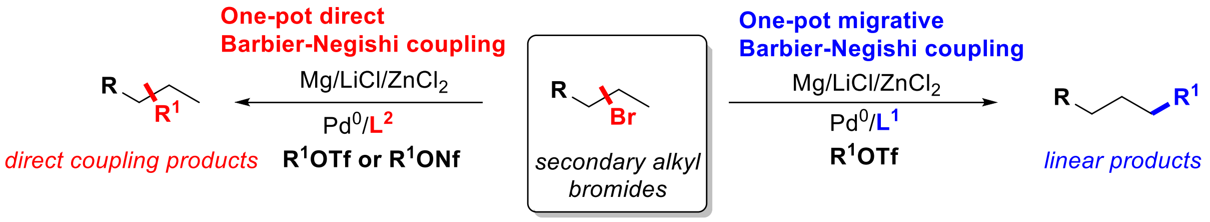
Palladium-catalyzed C(sp^2)-C(sp^3) cross-coupling reactions are particularly valuable tools in synthetic chemistry and hence a great deal of interests has emerged in this area.[1] Although great progress has been made over the last decades, important challenges still exist, such as the preformation of organometallic species prior to the cross-coupling step and the control of the coupling site-selectivity due to competing β-H elimination.[2,3] Herein, an operationally simple and mild Barbier-Negishi coupling of secondary alkyl bromides is described. Whereas the newly developed sterically hindered phosphine ligands favour the direct cross-coupling, more flexible phosphine ligands induce migrative couplings through a β-H elimination/rotation/reinsertion sequence. [4]



- ***Ligand-controlled site-selectivity***
  Remote functionalization of alkyl chains by chain-walking mechanism
  Divergent access to synthetically useful organic intermediates

[1] (a) R. Jana, T. P. Pathak, M. S. Sigman, *Chem. Rev.*, **2011**, *111*, 1417-1492; (b) O. Baudoin, *Chimia* **2016**, *70*, 768-772.

[2] Representative examples: (a) C. Han, S. L. Buchwald, *J. Am. Chem. Soc.* **2009**, *131*, 7532-7533; (b) C. Valente, S. Çalimsiz, K. H. Hoi, D. Mallik, M. Sayah, M. G. Organ, *Angew. Chem. Int. Ed.* **2012**, *51*, 3314-3332.

[3] For leading articles: (a) A. Renaudat, L. Jean-Gérard, R. Jazzar, C. E. Kefalidis, E. Clot, O. Baudoin, *Angew. Chem. Int. Ed.* **2010**, *49*, 7261-7265. (b) S. Aspin, Anne-S. Goutierre, P. Larini, R. Jazzar, O. Baudoin, *Angew. Chem. Int. Ed.* **2012**, *51*, 10808-10811. (c) A. Millet, P. Larini, E. Clot, O. Baudoin, *Chem. Sci.* **2013**, *4*, 2241-2247. (d) A. Millet, D. Dailler, P. Larini, O. Baudoin, *Angew. Chem. Int. Ed.* **2014**, *53*, 2678-2682.

[4] (a) S. Dupuy, K.-F. Zhang, A.-S. Goutierre, O. Baudoin, *Angew. Chem. Int. Ed.* **2016**, *55*, 14793-14797. (b) K.-F. Zhang, F. Christoffel, O. Baudoin, *Angew. Chem. Int. Ed.* **2018**, *57*, 1982-1986.