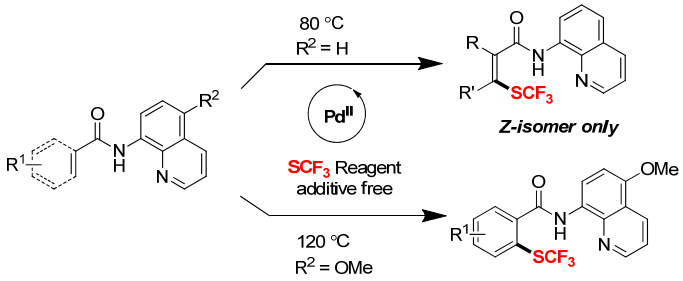
Pd-CATALYZED TRIFLUOROMETHYLTHIOLATION OF ACRYLAMIDES AND AROMATIC AMIDES BY C-H BOND ACTIVATION

Mu-Yi Chen, Qun Zhao, Philippe Jubault and Tatiana Besset

Normandie Univ, INSA Rouen, UNIROUEN, CNRS, COBRA (UMR 6014), 76000 Rouen, France

The organofluorine research has known a very rapid development in the past years.[1] Indeed, the incorporation of a fluorine atom or a fluorinated group on a molecule will modulate the physical and biological activity.[2] Besides, the transition metal catalyzed C-H bond activation is today a great synthetic tool in organic chemistry.[3] The combination of the organofluorine chemistry and transition metal catalyzed C-H bond functionalization constitutes an excellent approach to afford original fluorinated compounds. In this context, a palladium-catalyzed trifluoromethylthiolation of unsaturated derivatives by C-H bond activation was developed.[4] Using amines as the directing group and in the presence of an electrophilic SCF_3 source functionalized acrylamides or aromatic amide derivatives were trifluoromethylthiolated offering a straightforward synthetic pathway to build up the challenging $C(sp^2)$-SCF_3 bond. Mechanism of the transformation and post-functionalization reactions were also studied.



---

[1] For selected reviews, see: (a) X.-X. Shao, F.-C. Xu, L. Lu, Q.-L. Shen, *Acc. Chem. Res.* **2015**, *48*, 1227-1236. (c) T. Besset, C. Schneider, D. Cahard, *Angew. Chem. Int. Ed.* **2012**, *51*, 5048-5050. (d) T. Besset, T. Poisson, X. Pannecoucke, *Chem. Eur. J.* **2014**, *20*, 16830-16845. (e) A. Tlili, T. Billard, *Angew. Chem. Int. Ed.* **2013**, *52*, 6818-6819. (f) T. Besset, T. Poisson, X. Pannecoucke, *Eur. J. Org. Chem.* **2015**, 2765-2789. (g) C.-F. Ni, M.-Y. Hu, J.-B. Hu, *Chem. Rev.* **2015**, *115*, 765-825. (h) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2018**, *37*, 320-330.

[2] D. O'Hagan, *Chem. Soc. Rev.* **2008**, *37*, 308-319.

[3] For selected reviews, see: (a) K. Engle, T.-S. Mei, M. Wasa, J.-Q. Yu, *Acc. Chem. Res.* **2011**, *45*, 788-802. (c) V. Zaitsev, O. Daugulis, *J. Am. Chem. Soc.* **2005**, *127*, 4156-4157. (d) T. M. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147-1169. (e) W. R. Gutekunst, P. S. Baran, *Chem. Soc. Rev.* **2011**, *40*, 1976-1991.(g) K. Murakami, S. Yamada, T. Kaneda, K. Itami, *Chem. Rev.* **2017**, *117*, 9302-9332. (h) M. Wegmann, M. Henkel, T. Bach, *Org. Biomol. Chem.* **2018**, *16*, 5376-5385.

[4] (a) Q. Zhao, T. Poisson, X. Pannecoucke, J.-P. Bouillon, T. Besset, *Org. Lett.* **2017**, *19*, 5106-5109. (b) Q. Zhao, M.-Y. Chen, T. Poisson, X. Pannecoucke, J.-P. Bouillon, T. Besset, *Eur. J. Org. Chem.* **2018**, 6167-6175.