

Nouvelles voies d'accès à des molécules portant des groupements fluorés innovants.

Applications à l'imagerie médicale.

New strategies to synthesize molecules with innovative fluorinated groups.

Applications to Medical imaging.

Fluorinated compounds have played, these last years, a growing role to become, at this day, "essential" molecules for everyday life. The fluorine atom is then a key constituent of about 20% of recently approved pharmaceuticals. Its prevalence gradually increases since its first appearance in an organic molecule in the 1950s. Better resistance to metabolism, increased lipophilicity, enhanced activity, modifications of physico-chemical properties can partly explain the positive effect of this atom. Beyond the world of life sciences, its introduction has also allowed major progress in materials, polymers science or in the domain of energy.

It is noteworthy that all benefits brought by the fluorine atom are enhanced when this latter belongs to a more elaborated entity. Recently, new concepts have emerged from the association of fluorinated moieties and heteroatoms. This led to the development of new molecules with particular physico-chemical properties.

Our group have recently developed several new efficient reagents to easily introduce CF_3S , CF_3Se and CF_3O groups onto organic molecules.

The objective of this PhD thesis will be to continue to develop efficient methods to introduce onto organic molecules various innovative fluorinated groups associated to heteroatoms. In particular, metal-free "green" methods to perform coupling reactions with arenes and heteroarenes will be studied. Furthermore, asymmetric approaches, which have been scarcely studied to this day, will be also developed.

Finally, thanks to the fluorine-18 isotope, the fluorinated molecules can also be used in medical imaging (PETscan). Our group is also well involved in this thematic. Consequently, the previously developed methods will be also extended to radiolabeling of selected molecules for medical imaging applications.

Some references:

1. Q. Glenadel, E. Ismalaj, T. Billard, *Org. Lett.* **2018**, *20*, 56-59.
2. C. Ghiazza, V. Debrauwer, T. Billard, A. Tlili, *Chem. Eur. J.* **2018**, *24*, 97-100.
3. Q. Glenadel, C. Ghiazza, A. Tlili, T. Billard, *Adv. Synth. Catal.* **2017**, *359*, 3414-3420.
4. C. Ghiazza, T. Billard, A. Tlili, *Chem. Eur. J.* **2017**, *23*, 10013-10016.
5. L. J. C. Bonazaba-Milandou, H. Carreyre, S. Alazet, G. Greco, A. Martin-Mingot, C. Nkounkou-Loumpangou, J.-M. Ouamba, F. Bouazza, T. Billard, S. Thibaudeau, *Angew. Chem. Int. Ed.* **2017**, *56*, 169-172.
6. A. Tlili, F. Toulgoat, T. Billard, *Angew. Chem. Int. Ed.* **2016**, *55*, 11726-11735.
7. E. Ismalaj, D. Le Bars, T. Billard, *Angew. Chem. Int. Ed.* **2016**, *55*, 4790-4793.
8. J. Colomb, G. Becker, S. Fieux, L. Zimmer, T. Billard, *J. Med. Chem.* **2014**, *57*, 3884-3890.
9. S. Alazet, L. Zimmer, T. Billard, *Angew. Chem. Int. Ed.* **2013**, *52*, 10814-10817.
10. F. Baert, J. Colomb, T. Billard, *Angew. Chem. Int. Ed.* **2012**, *51*, 10382-10385.