A New Sulfoximine Scaffold for the Generation of Fluorinated Radicals in Photoredox Catalysis

Gabriel Goujon[1], Bruce Pégot[1], Elsa Anselmi[1,2], Emmanuel Magnier[1]

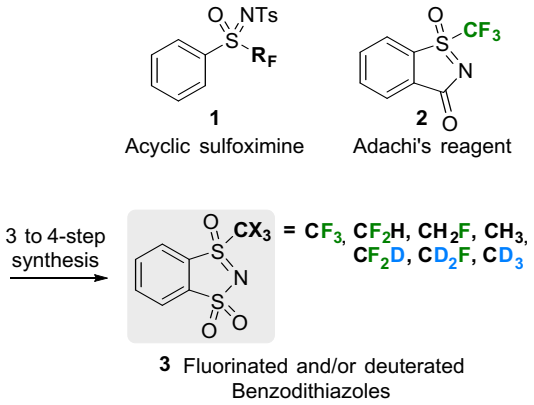
[1]Université Paris-Saclay, UVSQ, CNRS, UMR 8180, Institut Lavoisier de Versailles, 78000, Versailles, France.

[2]Université de Tours, Faculté des Sciences et Techniques, 37200 Tours, France.

E-mail: gabriel.goujon-laisney@uvsq.fr

Fluoromethyl groups are of high interest for modifying electronic properties of molecules, and are especially relevant for improving drug efficacy. Insertion of -CF_3 group is well described in the literature, and a lot of FDA-approved drugs today contain this motif. Recognizing the importance of fluorine in medicinal chemistry but hampered by the recent controversy surrounding PFAS, reactions for the insertion of non-PFAS fluorinated motifs have emerged, such as the -CF_2H moiety. N-tosylated sulfoximines have demonstrated their effectiveness in these reactions **1**,[1-3] though little research has been conducted on monofluoromethylation, or on combining fluorine and deuterium chemistry in novel functional groups.

Inspired by the cyclic sulfoximine **2** described by Adachi and Ishihara,[4] we are presenting herein the multi-gram scale synthesis of a new cyclic sulfoximine scaffold **3** capable of generating in photoredox catalysis all of the fluorinated methyl radicals (from •CF_3 to •CH_2F) with an improved reactivity compared to acyclic sulfoximines. This scaffold also has the critical advantage to be able to generate the scarcely described •CH_3 radical, to be usable in flow chemistry, and recyclable after use.[5] Moreover, easy deuteration of these benzodithiazoles enables them to react as •CF_xD_y donors, forming unique functional groups.



References

[1]Zhang, W.; Wang, F.; Hu, J. N-Tosyl-S-difluoromethyl-S-phenylsulfoximine: A New Difluoromethylation Reagent for S-, N-, and C-Nucleophiles. *Org. Lett*. **2009**, *11*, (10), 2109-2112.

[2]Noto, N.; Koike, T.; Akita, M. Visible-Light-Triggered Monofluoromethylation of Alkenes by Strongly Reducing 1,4-Bis(diphenylamino)naphthalene Photoredox Catalysis. *ACS Catal*. **2019**, *9*, (5), 4382-4387.

[3]Pégot, B.; Urban, C.; Bourne, A.; Le, T. N.; Bouet, S.; Marrot, J.; Diter, P.; Magnier, E. Difluoromethyl and Chlorofluoromethyl Sulfoximines: Synthesis and Evaluation as Electrophilic Perfluoroalkylating Reagents. *Eur. J. Org. Chem*. **2015**, 3069.

[4]Adachi, K., Ishihara, S. *Japan Tokkyo Kokai Patent*, **2005,** 145917.

[5]Wu, P., Goujon, G., Pan, S., Tuccio, B., Pégot, B., Dagousset, G., Anselmi, E., Magnier, E., Bolm, C. Cyclic Sulfoximines as Methyl and Perdeuteromethyl Transfer Agents and Their Applications in Photoredox Catalysis. *Adv. Synth.Catal.* **2023**, 365, 2392-2399.