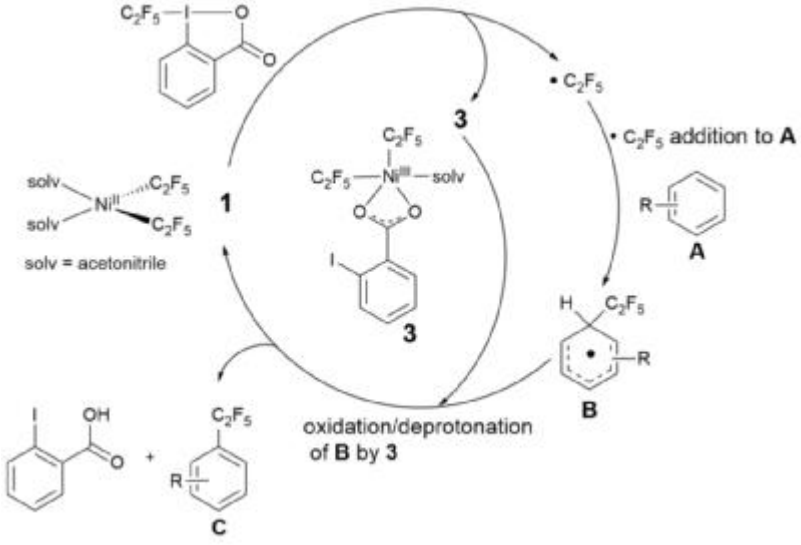
MS13-2-19 Perfluoroalkylation of the arenes by ligand-less Ni catalyst approach: new crystal structures of perfluorinated drug-derived molecules
#MS13-2-19

S. Deolka [1], J. Khusnutdinova [1], E. Khaskin [1], S. Vasylevskyi [1]
[1]OIST, Okinawa Institute of Science and Technology Graduate University Onna-son, Kunigami-gun, Okinawa, Japan, 904-0495 - Okinawa (Japan)

Abstract
The synthetic strategy of perfluoroalkylation of the arenes is important for further improvement of the medical properties of the arene-derived drugs. Incorporation of fluoroalkyl groups can drastically change polarity and thus permeation of the drugs through blood-cell-brain barriers [1]. In addition, perfluoroalkylation enchances a methabolitic half-life by inhibiting drug degradation, resulting in long-lasting drug effects [2]. Nowadays there are only a few examples of perfluoroalkylation of arenes which involves, in rather complex synthetic routes, and the use of expensive metal-based catalysts [3]. Many approaches are energy inefficient for fluoralkylation and normally require a high temperatures 80-130 ºC, strong UV-irradiation, expensive ligands or additives to promote the reaction [4]. Herein we show ligand-free, room temperature, no additional light irradiation requires nickel-catalyzed perfluoalkylation of the arenes with high yields up to 95%. The highly efficient perfluoalkylation mechanism of the reaction will also be discussed, as well as intermediate products (Figure 1). The ligand-free Ni-catalyst is a simple fluoroalkylating Ni-precursor that can be easily prepared and the source of the fluoroalkyls is the commercially available Togni reagent. The single crystal X-Ray structures of the perfluoalkylated arenes with C_2F_5/C_3F_7-groups were obtained for the first time and will be presented at ECM33 (Figure 2).

References
[1]. F. D'Accriscio, P. Borja, N. Saffon-Merceron, M. Fustier-Boutignon, N. Mézailles, N. Nebra, Angewandte Chemie International Edition, **2017**, 56, 12898-12902
[2]. L. Amini-Rentsch, E. Vanoli, S. Richard-Bildstein, R. Marti, G. Vilé, Industrial & Engineering Chemistry Research, **2019**, 58, 10164-10171.
[3]. X. Zhao, D. W. C. MacMillan, Journal of the American Chemical Society, **2020**, 142, 19480-19486.
[4]. S. Zhang, N. Rotta-Loria, F. Weniger, J. Rabeah, H. Neumann, C. Taeschler, M. Beller, Chemical Communications, **2019**, 55, 6723-6726.

Proposed radical pathway for perfluoroalkylation



Substrates obtained by ligand-free Ni-catalyst.