http://www.biocis.u-psud.fr/?-Molecules-Fluorees-et-Chimie-

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Keywords **: peptidomimetics, peptides, Prot-Prot interactions, bioactive compounds, fluorous chemistry, fluorous phase**

Principal Investigators : Dr. B. Crousse, Pr. S. Ongeri

Synthesis of fluorinated peptidomimetics

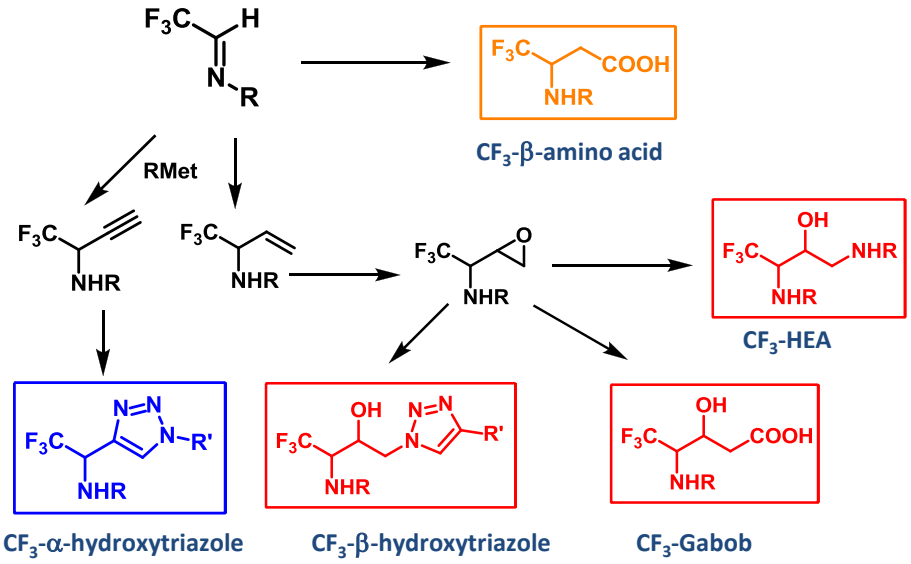
Method: From trifluoromethylaldimines, trifluorocrotonate, trifluoroacetoacetate

Competitors: S. Fustero (Spain), S. Funabiki (Japan), Enamine (Ukraine)

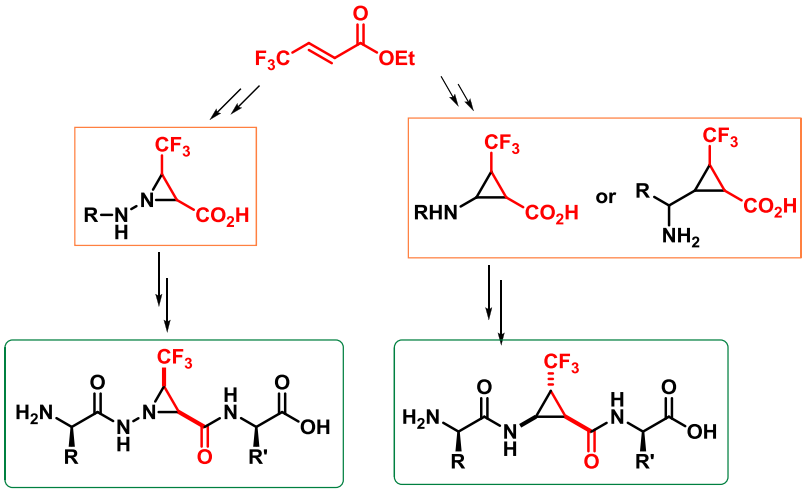
Background: *Bioorg. & Med. Chem. Lett.*, **2009**, *19*, 83; *Eur. J. Org. Chem.* **2009**, 5215; *Org. Biol. Chem.* **2010**, *8*, 3025; *Tetrahedron* **2012**, 68 (35), 7028; *Tetrahedron* **2013**, 69, 3308; *Beilstein J. Org. Chem.* **2013**, *9*, 2387; *Org. Biomol. Chem.* **2014**, 6345; *Tetrahedron Lett.* **2014**, *55*, 6339; *Eur. J. Org. Chem.* **2014**, 3072.

Collaborations: O. Lequin (UPMC), V. Soloshonok (Spain)

CF_3-aldimines as platform to CF_3-peptidomimetics



Constrained fluorinated peptidomimetics



Synthesis of CF_3-N-amino aziridines and CF_3 cyclopropanes. Both derivatives allowed the access to novel constrained pseudopeptides .

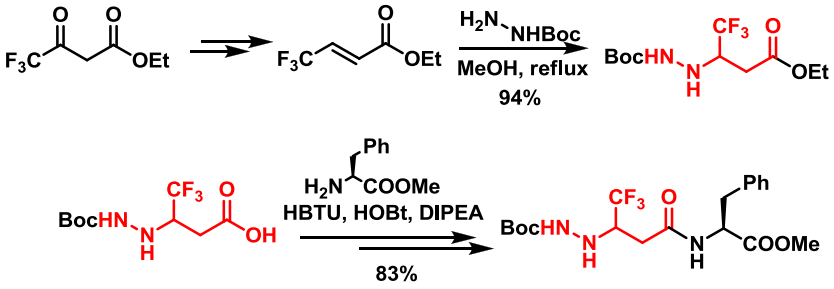
Bioactive molecules

Method: *Synthesis of fluorinated inhibitors of proteasome, Design and synthesis of inhibitors of carbapenemases.*
^{19} F NMR studies of ligand/protein interactions and « Spy » molecule : FAXS and FABS

Competitors: Beate Kosch (Germany)

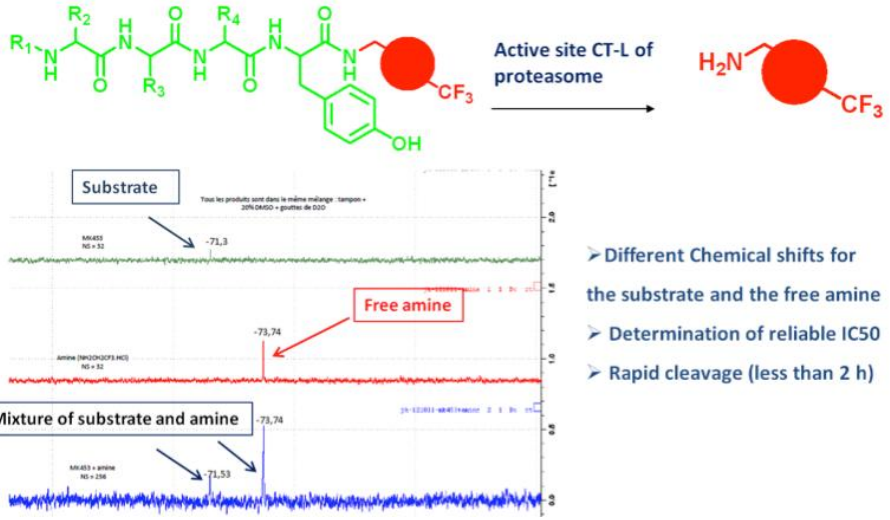
Background: *Org. Biomol. Chem.* **2014**, 4576; *J. Med. Chem.* **2012**, *55 (15)* 6762; *J. Fluorine Chem.* **2012**, *134*, 136; *Bioorg. & Med. Chem. Lett.*, **2009**, *19*, 83.

Fluorinated Inhibitors of proteasome



Inhibitors of proteasome

Development of fluorinated substrates to monitor the proteolytic activity of the proteasome by ^{19}F NMR



- Different Chemical shifts for the substrate and the free amine
- Determination of reliable IC50
- Rapid cleavage (less than 2 h)

Fluorous phase, fluorinated alcohols, supramolecular associations

Aims : multicomponent reactions, clean and selective reactions

Method: reaction in fluoroalkyl alcohols, hydrogen and halogen bond associations

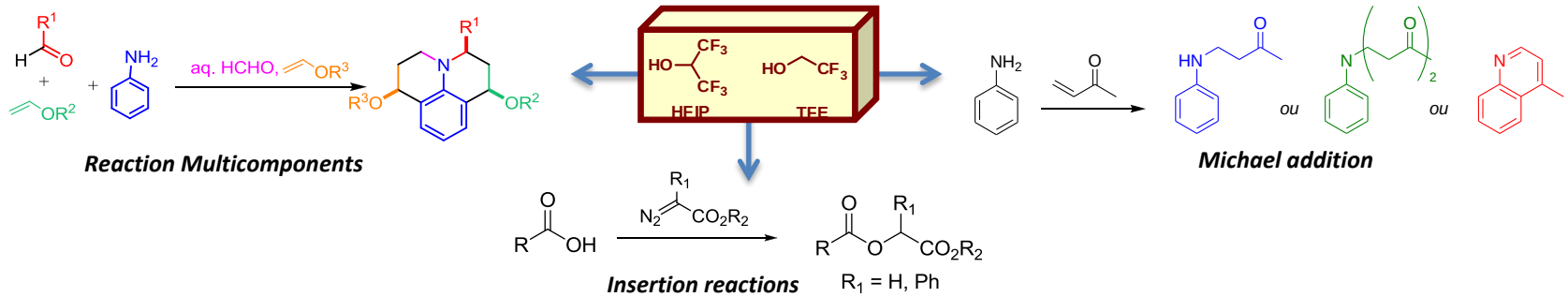
Competitors: *G. Resnati, P. Metrangolo (Italia), B. Linclau (UK)*

Background: *Polymer*, **2013**, *54*, 3757; *Catalysis Science & Technology* **2012**, *2* (*5*), 934, *J. Fluorine Chem.* **2011**, *132* (*10*), 811, *Org. Lett.* **2011**, *13*, 692, *J. Org. Chem.* **2011**, *76*, 1126, *Org. Biol. Chem.* **2011**, *9* (*2*), 347.

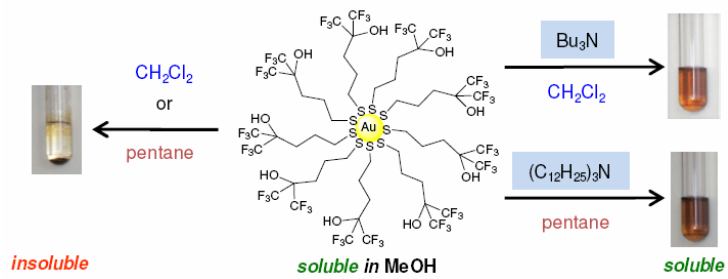
Collaboration: A. Slawin (St Andrews), S. Chandrasekaran (India)

Some examples in fluoroalkyl solvents

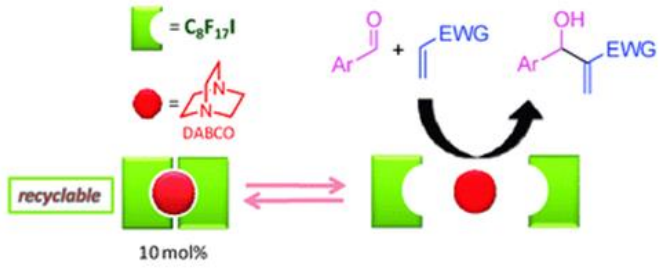
Fluoroalkyl alcohols TFE and HFIP possessed particular properties (acidity, polarity, high H-Bond donor, …), and allowed to perform clean and selective reactions without externe promotor (Lewis acid, or Brönsted acid).



Supramolecular associations



Solubility « Switch » of HFIP-AuNPs by supramolecular association with amines



DABCO catalyst recovered through halogen bond (RfI---N), application in Baylis Hillman reaction