Deoxofluorination of Aliphatic and (Hetero)aromatic Acids

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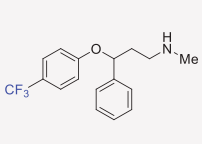
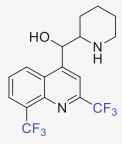
Introduction and Aim

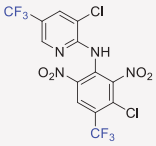
Modern medicinal chemistry and agrochemistry are tightly bound to organofluorine chemistry, because around 20% of all pharmaceuticals and up to 30% of agrochemicals are organic compounds that contain at least one fluorine atom. Trifluoromethyl group, in particular, is a part of the structure of more than seventy approved drugs. Carboxylic acids are amongst the most available chemical compounds classes, and it would have been desirable to have a practical method to converting them into the trifluoromethyl-substituted derivatives.[1] Herein we report on a mild fluorination of aliphatic and aromatic carboxylic acids with sulfur tetrafluoride.[2,3]



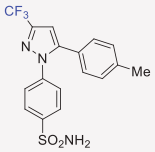
Fluoxetine (Prozak)
antidepressant



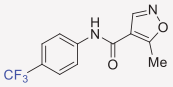
Mefloquine (Lariam)
antimalarial drug



Fluazinam
fungicide



Celecoxib (Celebrex)
antiinflammatory drug



Leflunomide (Avara)
antirheumatic drug

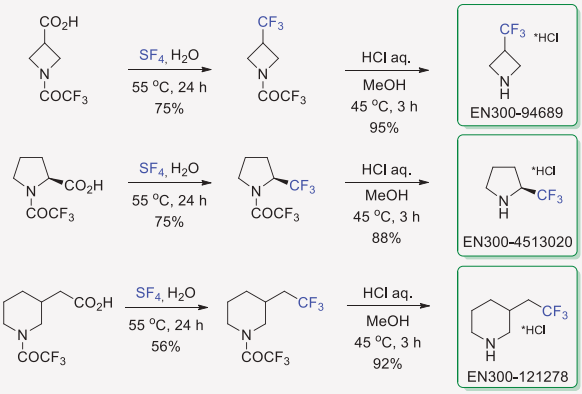
Synthesis

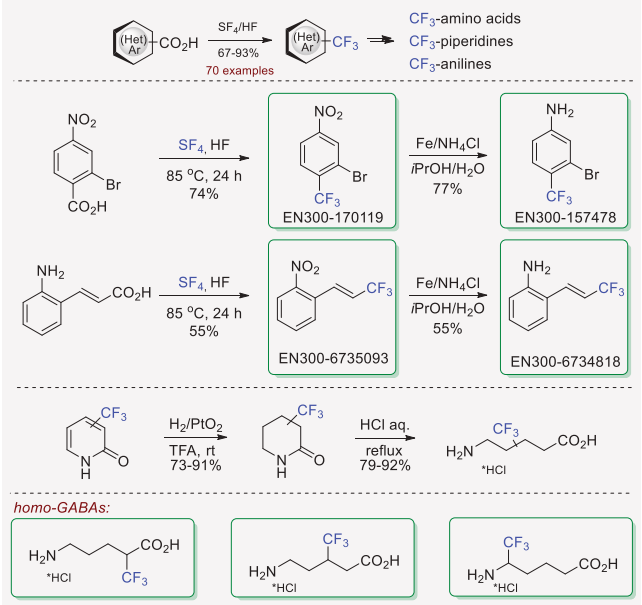
Alk-CO_2H
1°, 2°, and 3° aliphatic acids

SF_4, H_2O
55 °C
43 examples

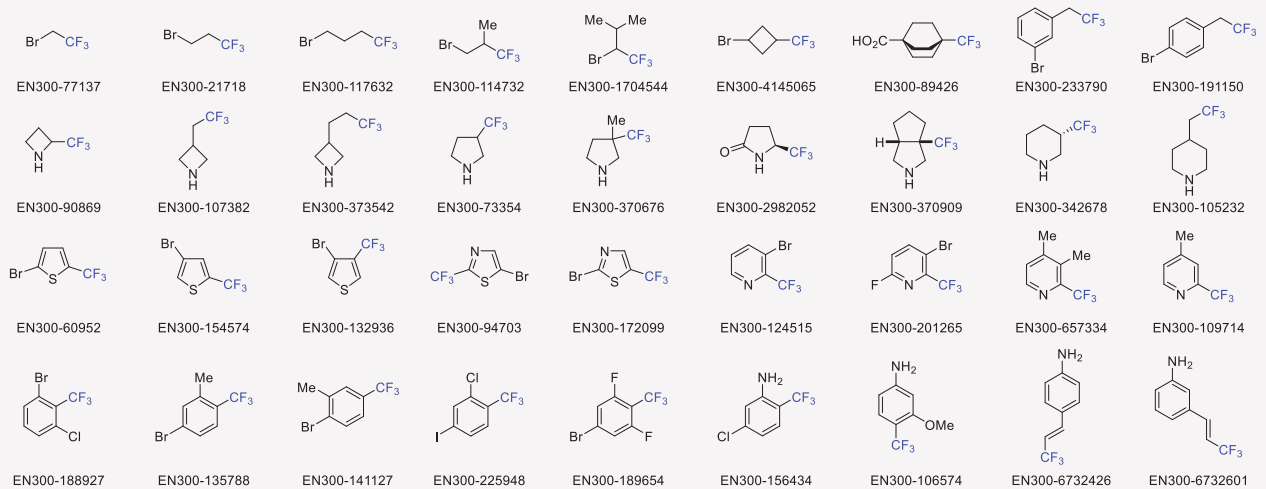
Alk-CF_3
retention of stereo- and absolute configuration

CF_3-Amines





Results



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References

1. W. A. Engelhardt at al. *J. Am. Chem. Soc.* **1960**, *82*, *3*, 543.
2. M. Bugera at al. *J. Org. Chem.* **2019**, *84*, *24*, 16105.
3. S. Trofymchuk at al. *J. Org. Chem.* **2020**, (minor revision).