Difluorocyclopropanes for drug discovery

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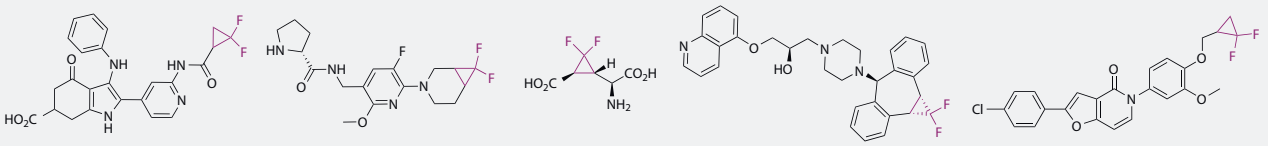
Introduction and Aim

Up to 20% of all modern marketed drugs and even 30% of all agrochemicals are fluorine-containing organic compounds.[1] Difluorocyclopropane-containing compounds also gained popularity in drug discovery in recent years. In 2011, Prakash reported that the combination CF_3TMS/NaI efficiently converted the non-activated alkenes into the *gem*-difluorocyclopropanes.[2] Herein, we aim to use this procedure to convert the functionalized non-activated alkenes - amines, esters, nitriles, ethers and ketals - into the functionalized difluorocyclopropanes: novel building blocks for drug discovery.[3]



Anti-cancer agent
WO 2016/202755
Bayer Pharm

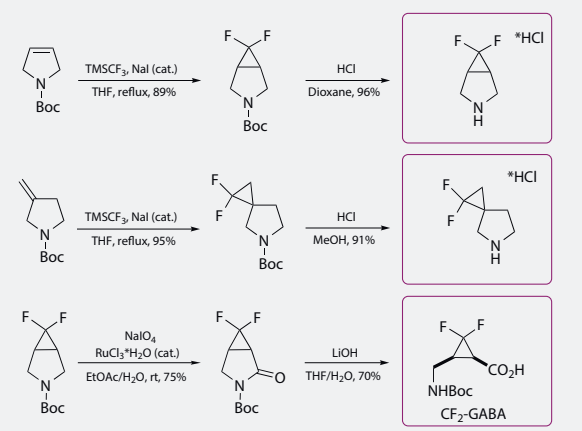
Agonist of the 5-HT2C receptor
WO 2017/50807
AbbVie

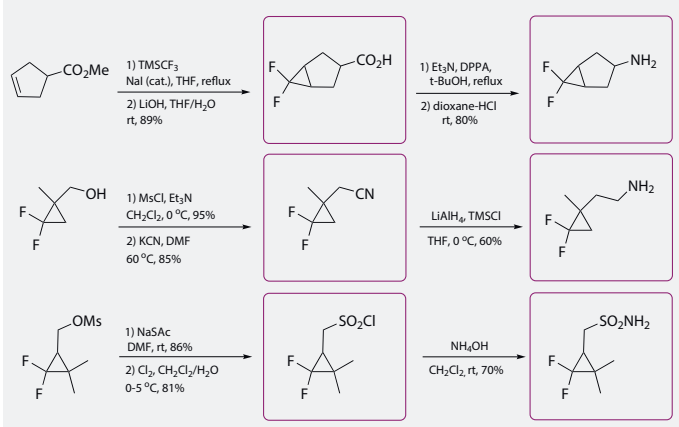
Selective mGluR2 agonist
J. Med. Chem. **2004**, 47, 456

Zosuquidar
antineoplastic drug
Eli Lilli

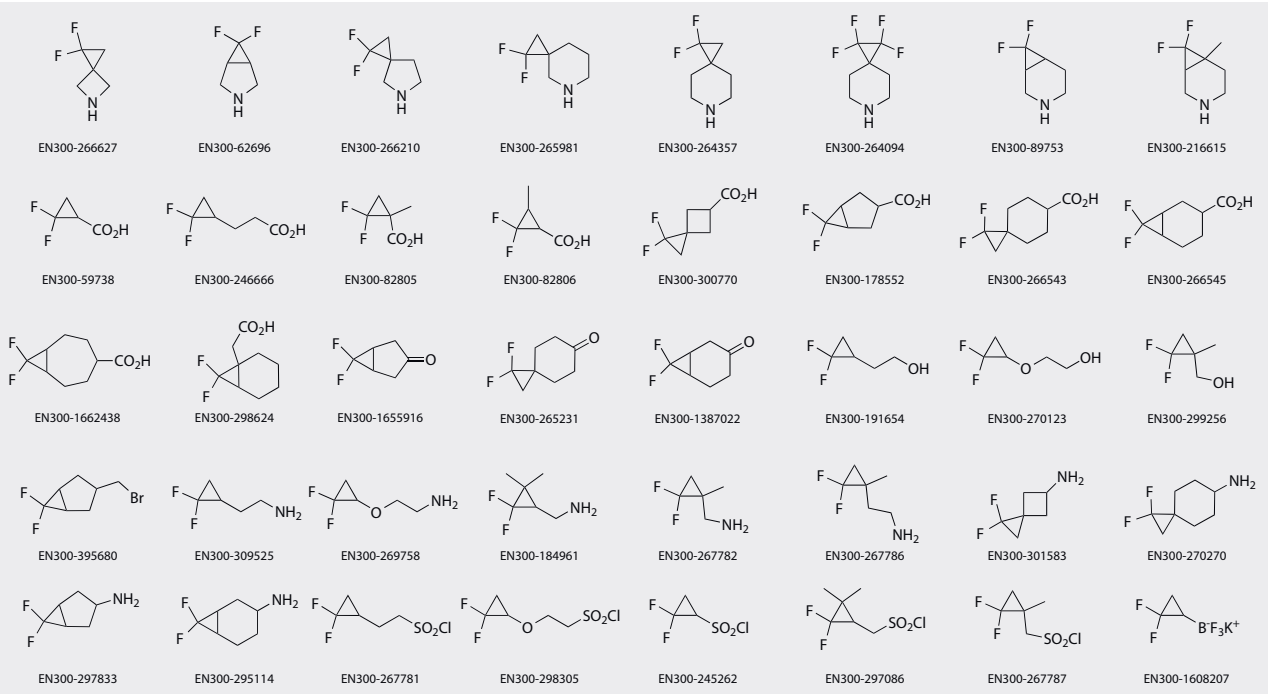
Agent to treat obesity
EP 2015/2848622
Takeda Pharm

Synthesis





Results



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References

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2. F. Wang et al. *Angew. Chem. Int. Ed.* **2011**, 7153.
3. R. M. Bychek et al. *Chem. Eur. J.* **2018**, *in press*.