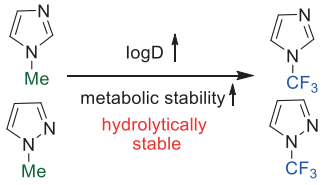
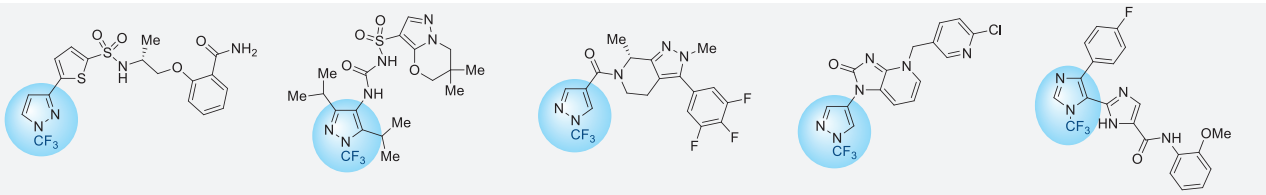
# Practical scalable synthesis of *N*-$CF_3$ substituted heterocycles

I. Denysenko, V. Kozlyk, A. Boretskyi, S. Trofymchuk, A. A. Tolmachev, P. K. Mykhailiuk

## Introduction and Aim

*N*-$CF_3$ azoles are very promising and valuable targets for medicinal chemistry. Recently, Schiesser and coworkers from *AstraZeneca* showed that *N*-$CF_3$ azoles possess high hydrolytic, chemical and metabolic stability.[1] Moreover, *N*-$CF_3$ azoles are considered as stable and more lipophilic surrogates for popular *N*-$CH_3$ azoles in medicinal chemistry. Limited utilization of *N*-$CF_3$ azoles is mainly due to the lack of scalable methods to prepare them.[2,3] Herein we report on an alternative and scalable method for the preparation of *N*-$CF_3$ azoles by fluorination of the corresponding *N*-$CF_2Br$ substituted precursors using $AgBF_4$ under mild conditions.[4]



Glucocorticoid receptor modulator
US2009/0093485, A1
*AstraZeneca*

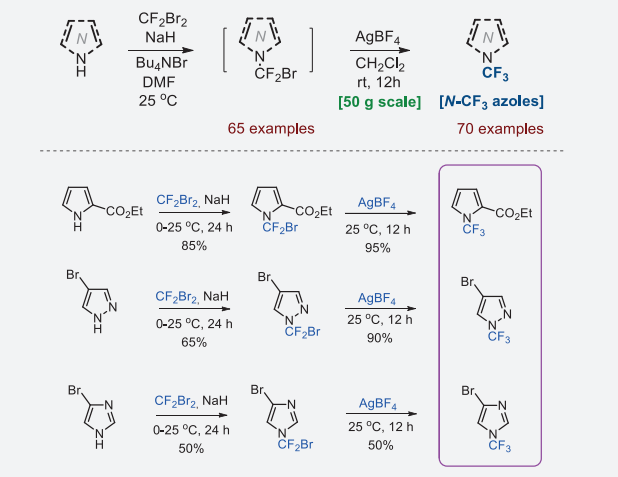
Inhibitors of interleukin-1 activity
WO2020/18970, A1
*Genentech*

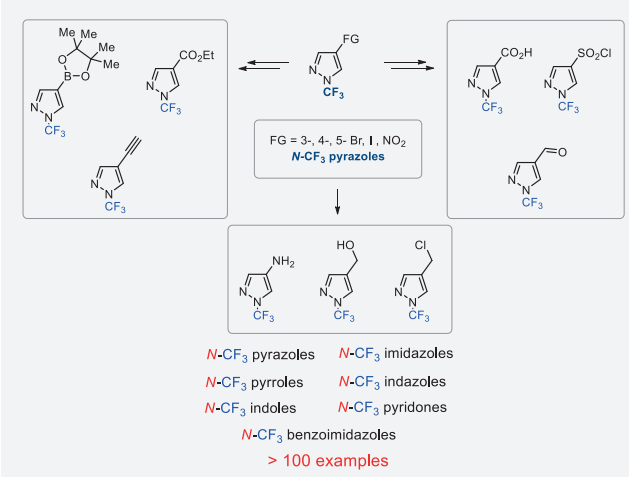
Monoacylglycerol lipase modulator
WO2020/65613, A1
*Janssen Pharm.*

Crop protection
WO2020/30503, A1
*Syngenta*

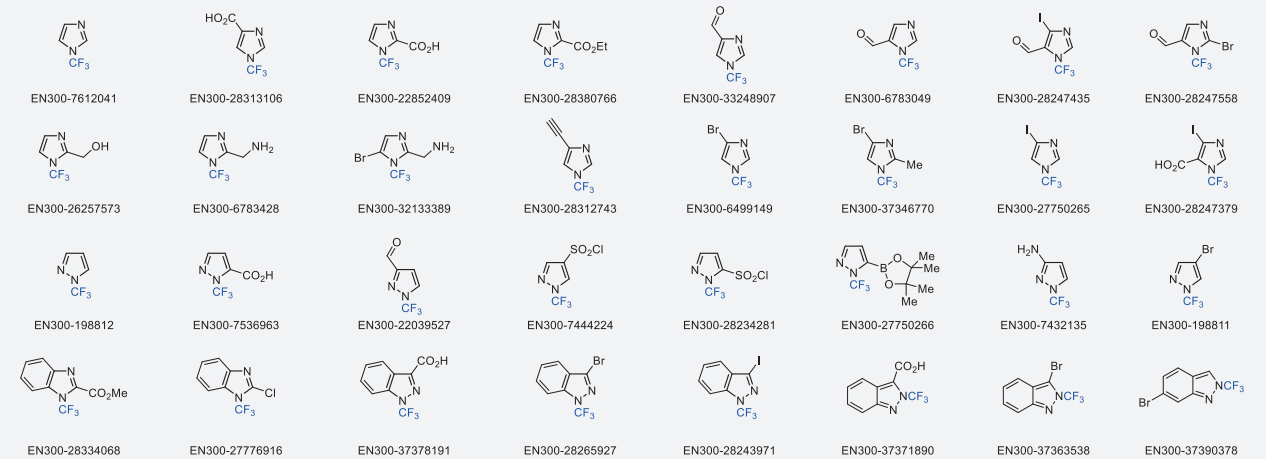
Kinase Inhibitor
US2020/0270231, A1
*Insilico Medicine*

## Synthesis and modification




## Results




## Contact

Iryna Denysenko, PhD
i.denysenko@mail.enamine.net,
Enamine Ltd, www.enamine.net
78 Chervonotkatska St, 02660 Kyiv, Ukraine

## References

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2. R. Z. Zhang et al. *Angew. Chem. Int. Ed.* **2022**, **61**, e202110749.
3. T. M. Sokolenko et al. *Chem. Heterocycl. Comp.* **2009**, *945*, 430–435.
4. I. Denysenko, V. Kozlyk, P. Mykhailiuk. *Under preparation.*