Trifluoromethyl vinamidinium salt – the promising precursor for fused pyridine-contained heterocycles

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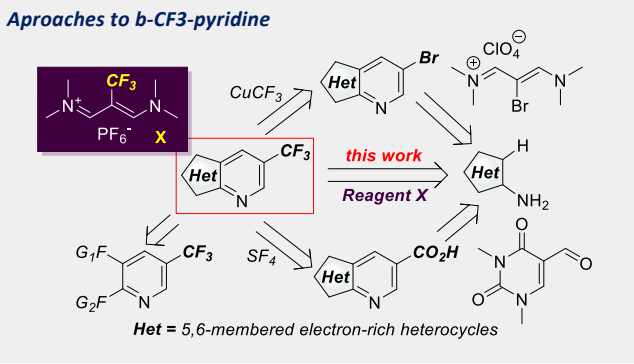
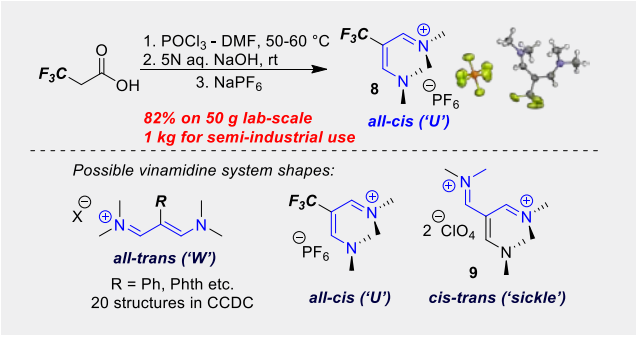
Background and synthetic strategy

Background of the work:
- extreme importance of fluorine for medicinal and agrochemistry;
- the presence of fluorine riches ~20% among all marketed drugs;
- application of fluorine in drug discovery supported by ^{19}F NMR technique;
- underrepresentation of fused pyridines bearing CF_3-label in β-position compared to the α- and γ-derivatives caused by poor diversity abilities of the existing methods.



Research Results & Representative Examples

Elaborated method towards the trifluoromethyl vinamidinium salt:



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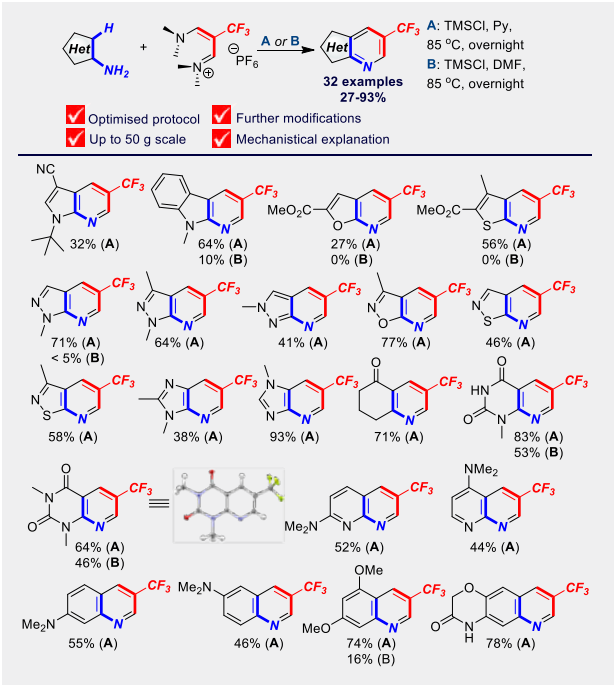
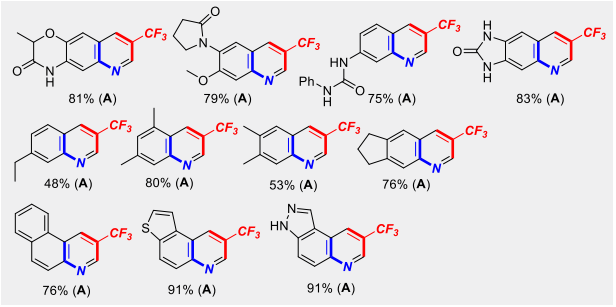
Achievements of the project:
- an **efficient multigram scale synthetic protocol** for preparing functionalized fused b-CF_3 pyridines by Combes-type cyclization was devised;
- the **scope of the substrates** was investigated and determined;
- the **alternative ways** of the reaction were disclosed;
- the **cyclization direction depends on the value of C- over N-nucleophilicity** of ambident amine substrates;
- the **mini-library of potential fragments** for ^{19}F NMR-based fragment-based drug discovery was synthesized.

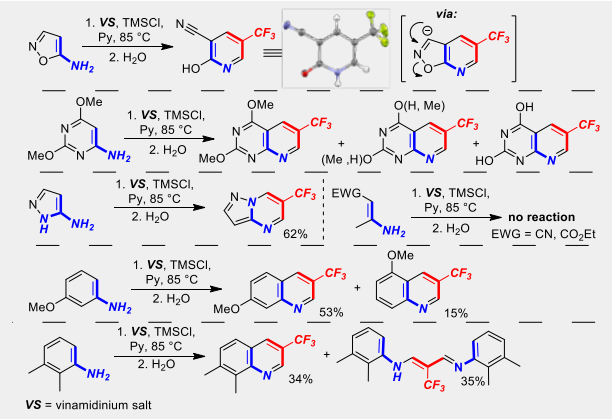


Results have been published as

Trifluoromethyl Vinamidinium Salt as a Promising Precursor for Fused β-Trifluoromethyl Pyridines. *J. Org. Chem.* **2023**, *88* (5), 2961-2972. https://doi.org/10.1021/acs.joc.2c02684



Scope and Limitations of the Method



Functionalization

- the obtained products are easily able to further transformations leading to functionalized derivatives