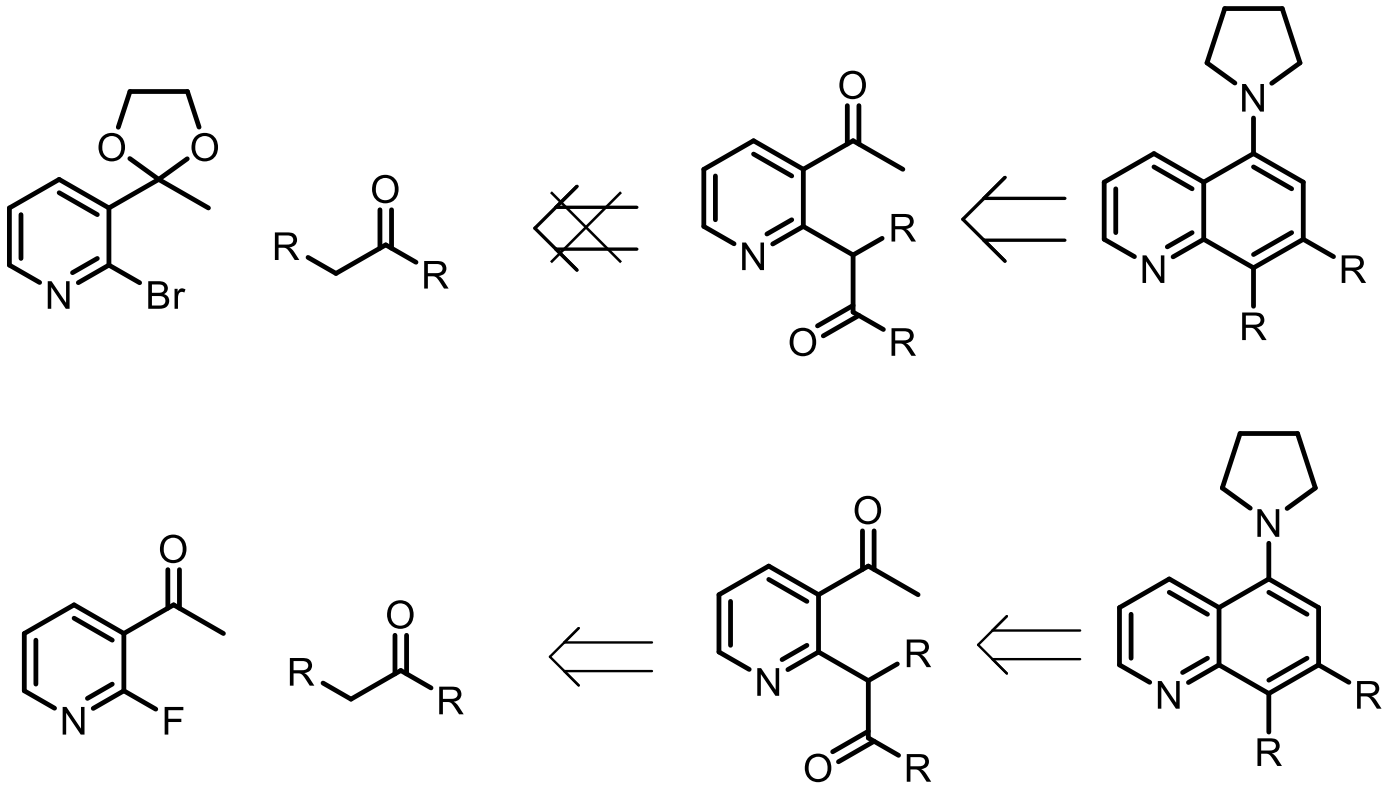
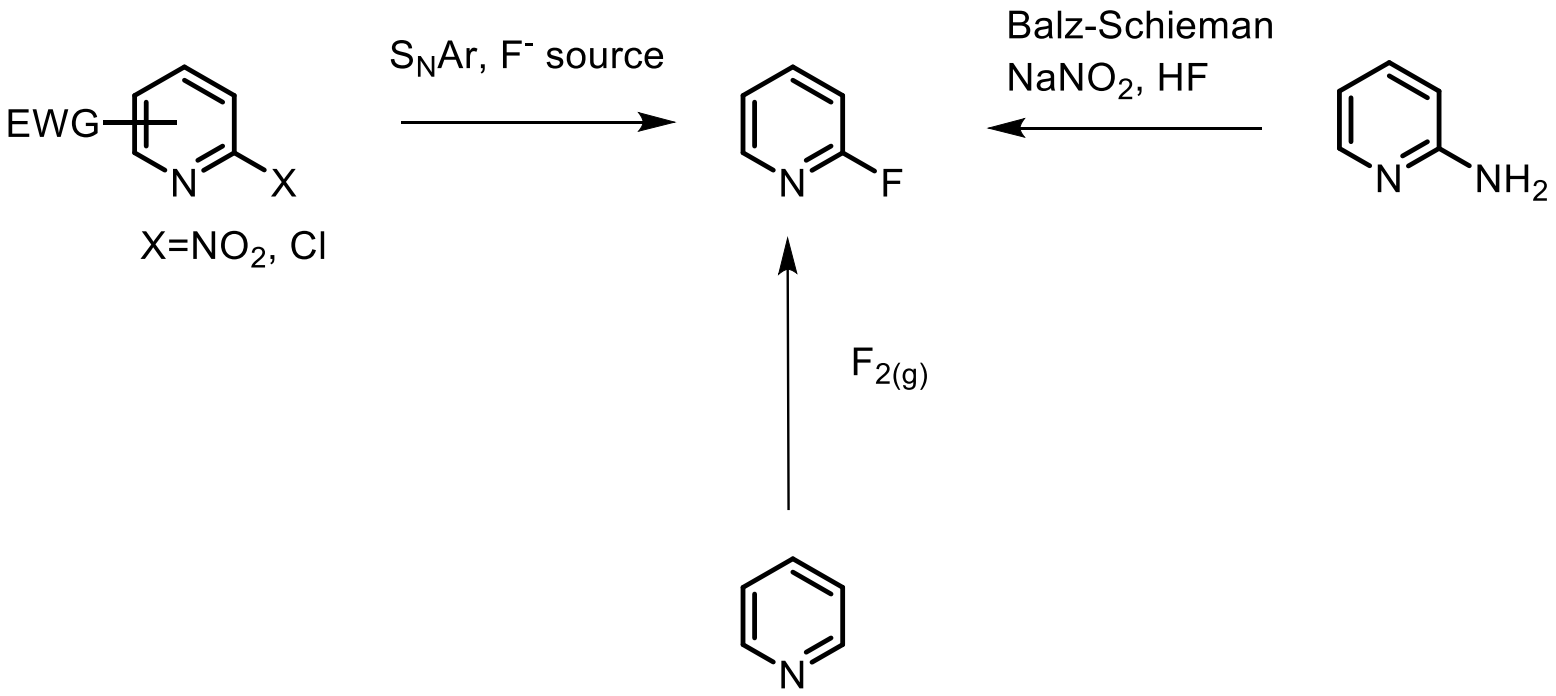
Literature Presentation
20/01/2014

1. Synthesis of isoquinolines



2. C2-Fluorination of pyridine



Selective C-H Fluorination of Pyridines and Diazines Inspired by a Classic Amination Reaction

Patrick S. Fier and John F. Hartwig*

Fluorinated heterocycles are prevalent in pharmaceuticals, agrochemicals, and materials. However, reactions that incorporate fluorine into heteroarenes are limited in scope and can be hazardous. We present a broadly applicable and safe method for the site-selective fluorination of a single carbon-hydrogen bond in pyridines and diazines using commercially available silver(II) fluoride. The reactions occur at ambient temperature within 1 hour with exclusive selectivity for fluorination adjacent to nitrogen. The mild conditions allow access to fluorinated derivatives of medicinally important compounds, as well as a range of 2-substituted pyridines prepared by subsequent nucleophilic displacement of fluoride. Mechanistic studies demonstrate that the pathway of a classic pyridine amination can be adapted for selective fluorination of a broad range of nitrogen heterocycles.

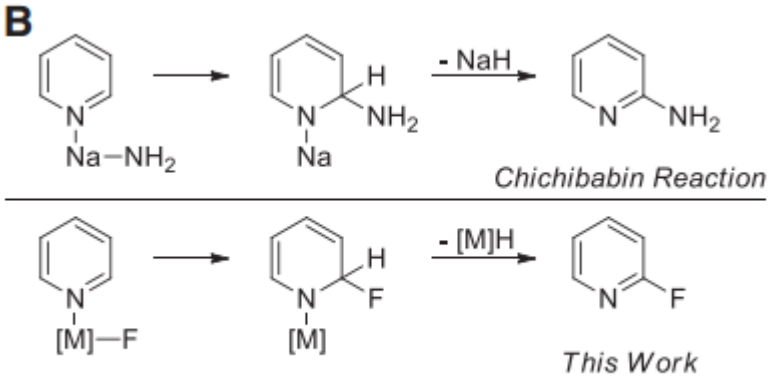


Fig. 1. Toward a milder pyridine fluorination.

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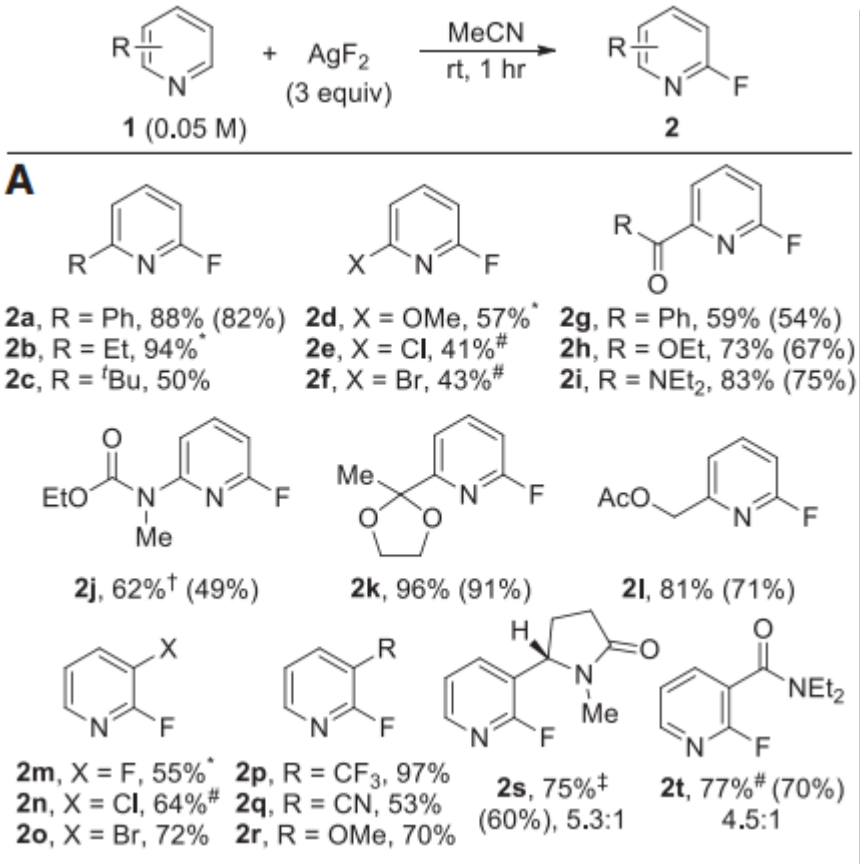
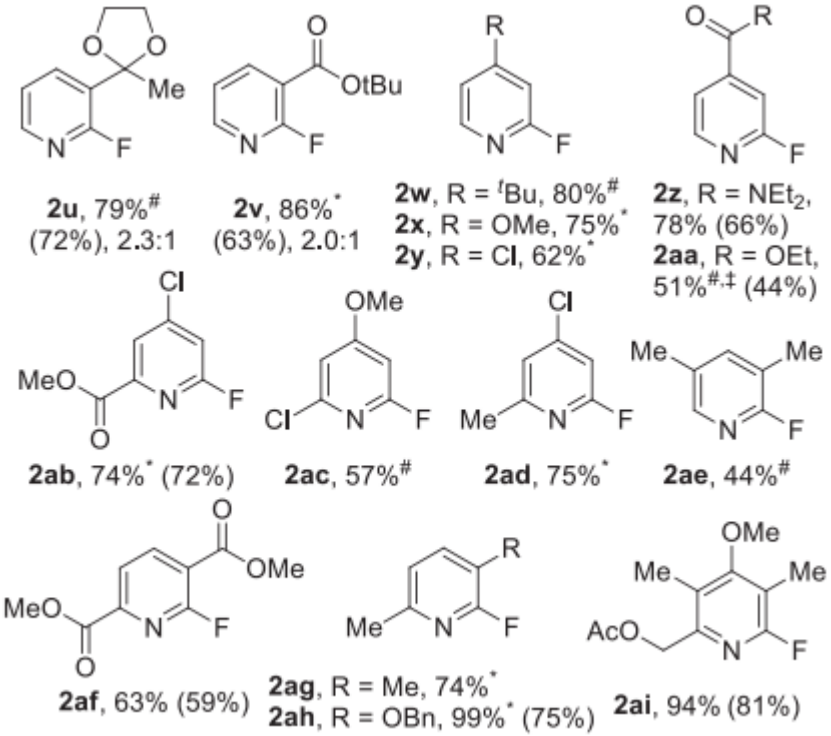
3. Substrate scope 1





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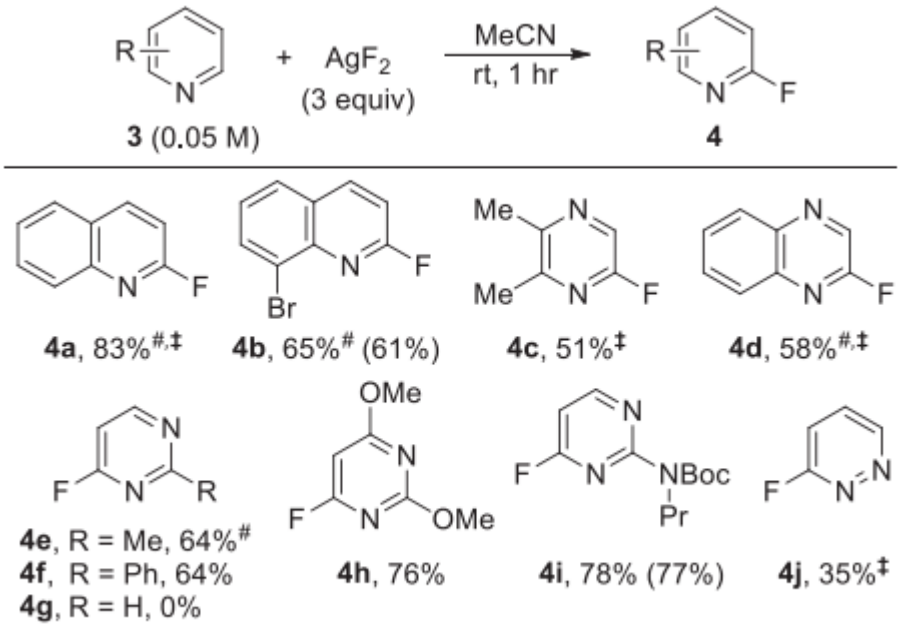
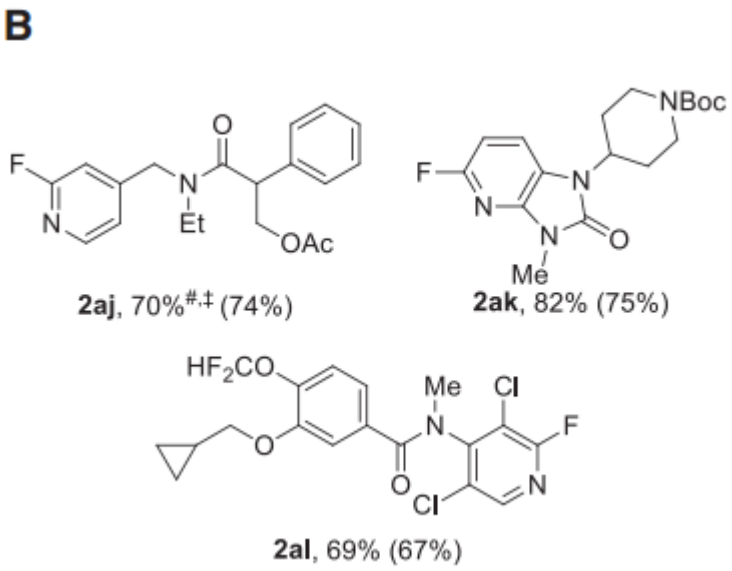
3. Substrate scope 2





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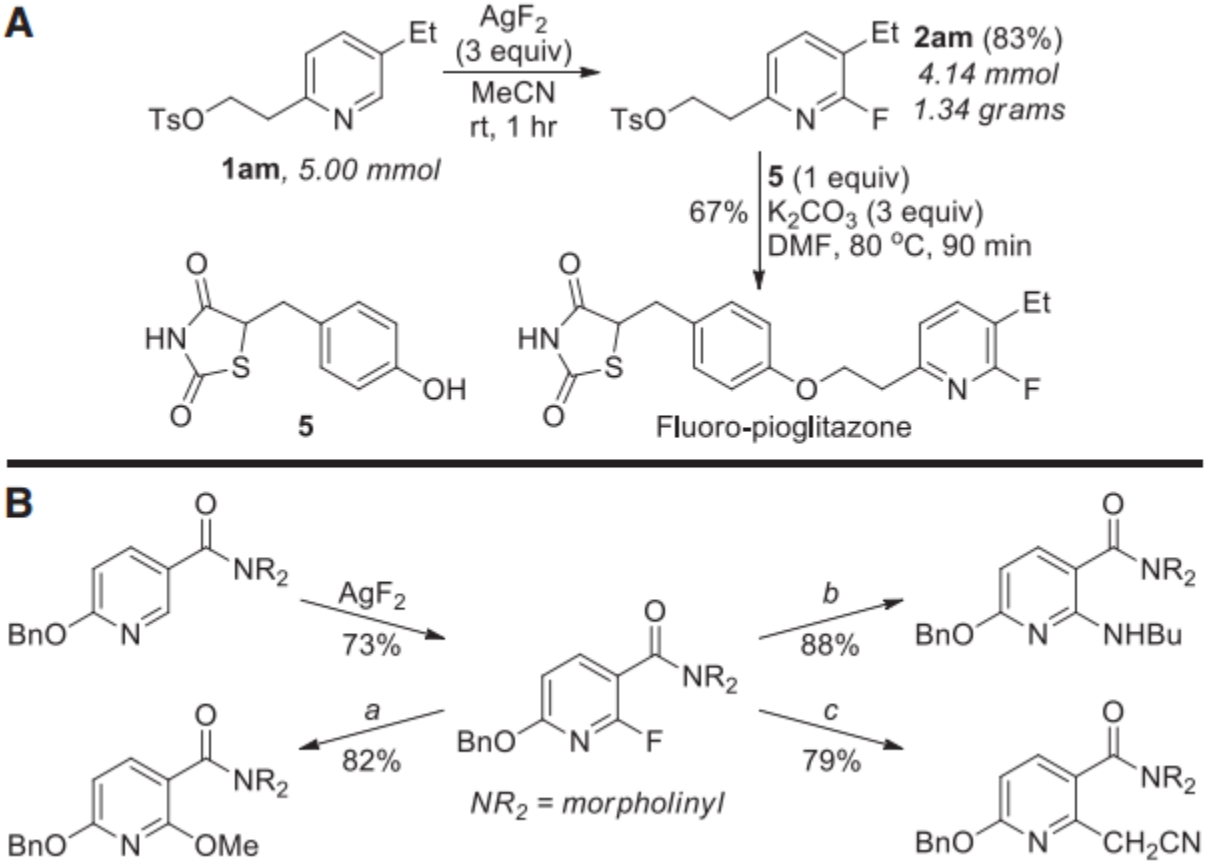
4. Multigram reactions and functionalisation



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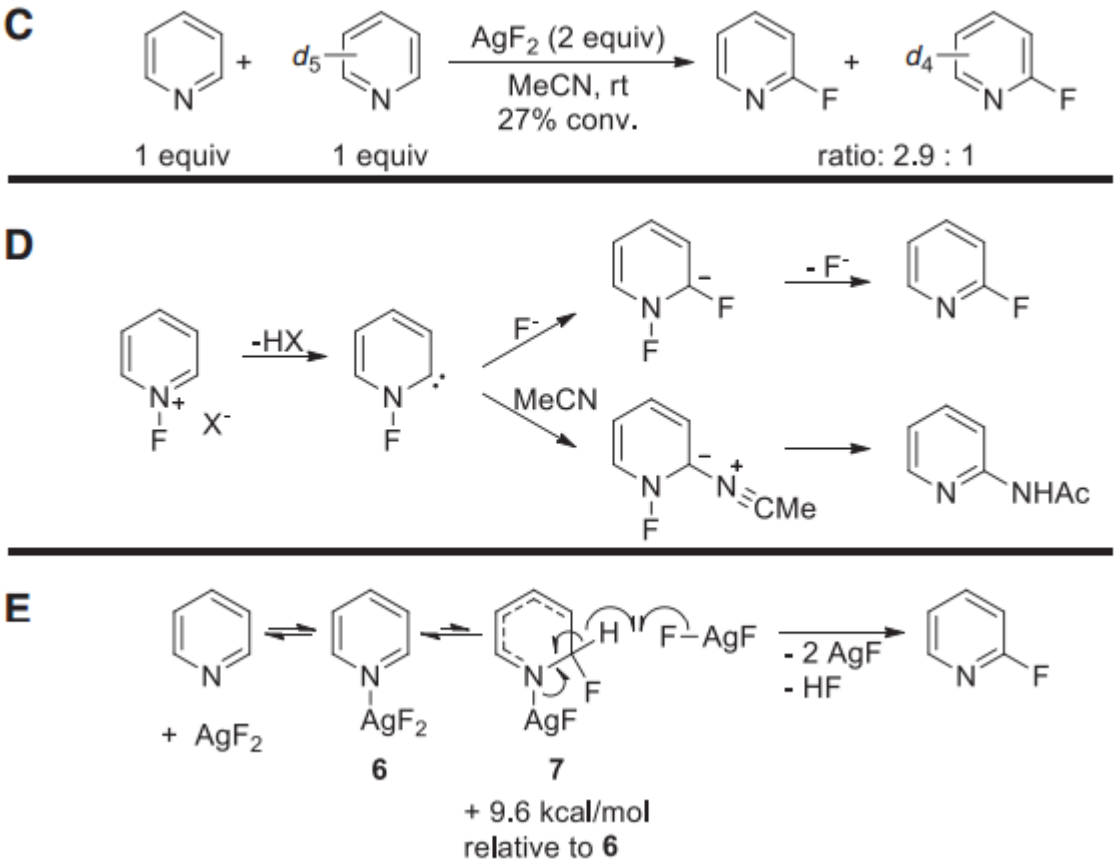
5. Note on mechanism



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6. Summary

- Mild conditions
- Short reaction times
- Broad substrate scope
- High regioselectivity
- Commercially available reagent
- High synthetic utility