2,2-Difluorocyclopropanamine: Tentative Structure or Useful Building Block?

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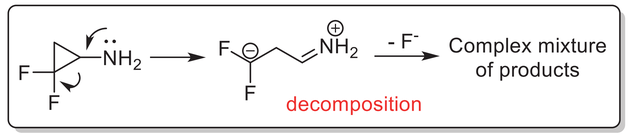
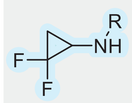
Background of the project

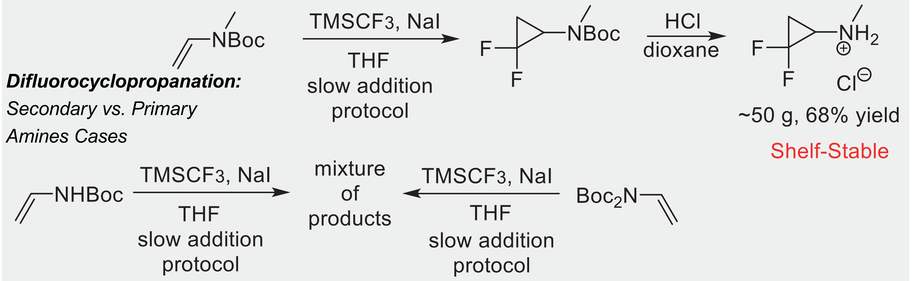
- Amines directly attached to the 2,2-difluorocyclopropane core are attractive but often unstable.
- Their instability is driven by a Grob-type fragmentation, initiated by the lone pair on the nitrogen atom.
- EW protection, like N-Boc, can stabilize these intermediates and enable successful cyclopropanation.



Gassen, K. R.; Baasner, B., *J. Fluor. Chem.* **1990**, 49 (1), 127



Sec. Amines:
Direct Synthesis;
Stable without Basic Impurities

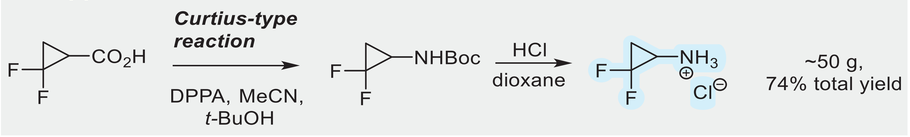


Difluorocyclopropanation:
Secondary vs. Primary Amines Cases

The solution for primary amines

- Deprotected amines can be stored as stable salts, given there are no basic impurities.
- Primary amines often decompose under reaction conditions and are not isolable in pure form.
- A Curtius rearrangement of the corresponding carboxylic acids offers a viable and scalable rout.

Our approach:



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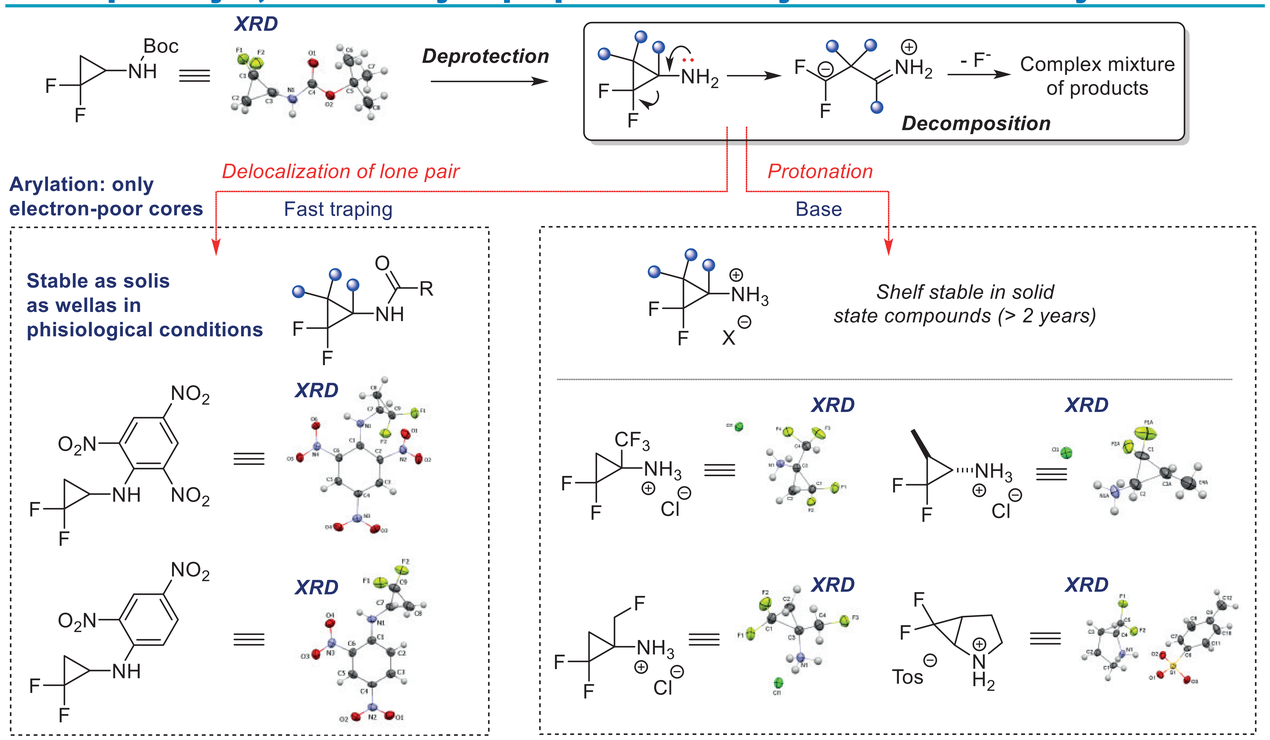
N-Boc primary 2,2-difluorocyclopropanamines: arylation and stability evaluation



The synthesized 2,2-difluorocyclopropanamines: scope, scale and yields