Trimethylsilyltrifluoromethane – Effective Difluorocarbene-Surrogate for Scalable Organic Synthesis

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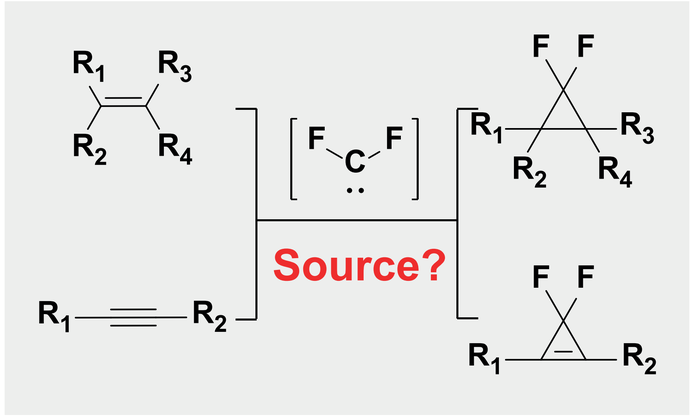
Background of the project



Me_3SiCF_2X Based Reagents!

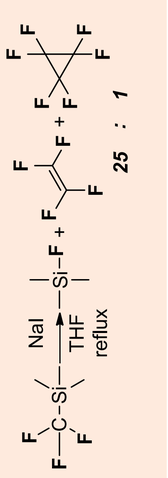
- Available and safe reagents
- Promising yields
- Reasonable reaction temperature
- Only FG-less substrates

X	reactivity	availibility
F	*	*****
Cl	***	**
Br	***	**
I	****	*

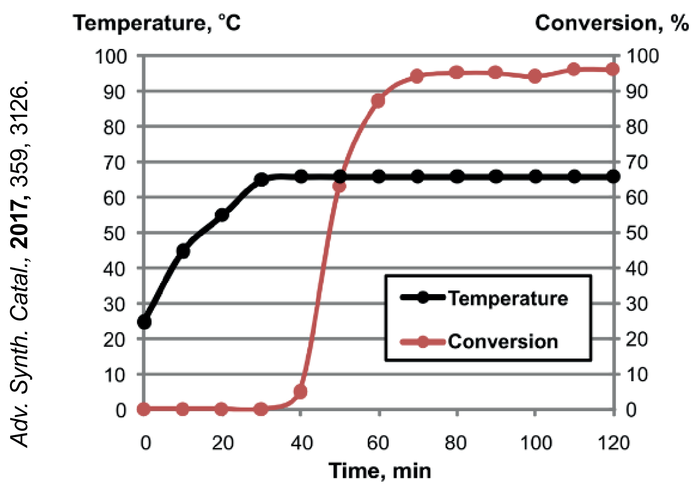
Me_3SiCF_3 – Ruppert-Prakash Reagent!

- 2009 — First 1 kilo was purchased
- 2013 — 5 kilos were purchased the price decreased ~3 times
- 2015 — 20 kilos were purchased the price decreased ~7 times
- Nowdays — We have ~150 kilos in stock the average price decreased more than 25 times

$TMSCF_3$/NaI synthetic protocol (:CF_2 generation) optimization: *Blank experiment*



Adv. Synth. Catal., **2017,** 359, 3126.



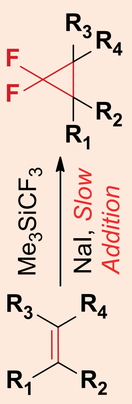
Org. Lett., **2016,** *18,* pp 1988–1991

Batch Prakash protocol to Flow Charette protocol (10 min residence time) leads to increasing of the yield. **9-77% Yields**

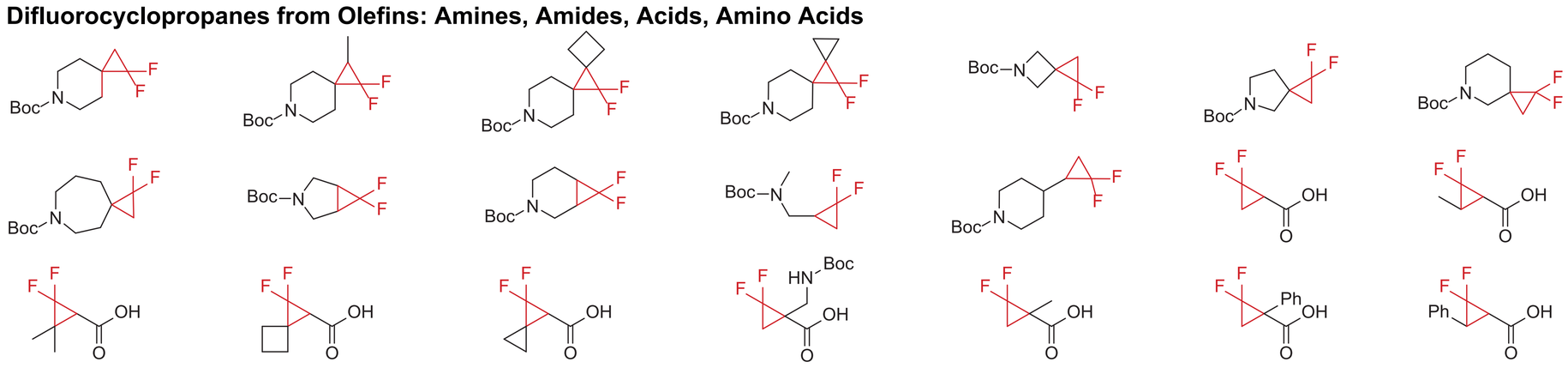
35-97% Yields

"SLOW ADDITION PROTOCOL"
Modified batch: Slow (up to 24h) addition of the excess of Me_3SiCF_3 (up to 10 eq) to the reaction mixture according to the difluorocyclopropanation kinetics.

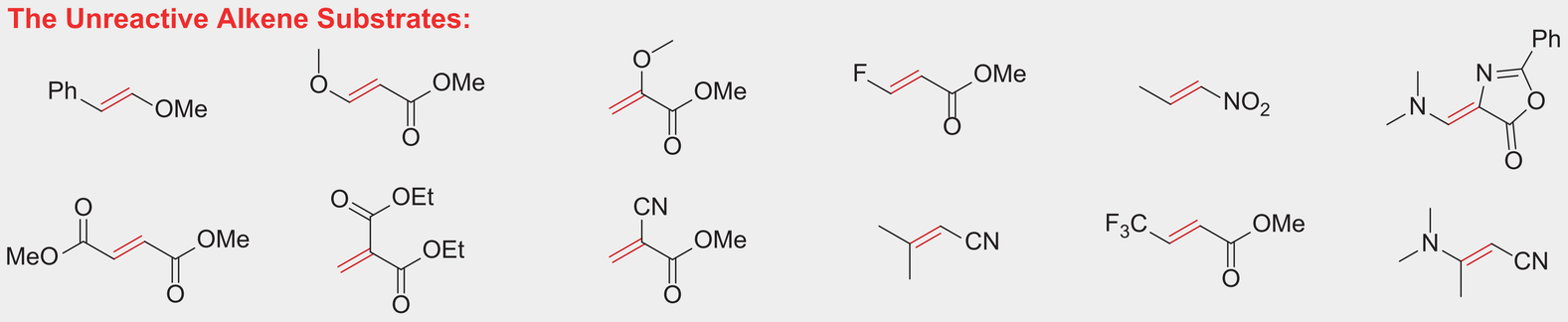
Applying the "Slow Addition Protocol" for Cyclopropanation: Scope and Limitations



Difluorocyclopropanes from Olefins: Amines, Amides, Acids, Amino Acids

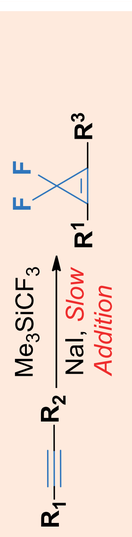


The Unreactive Alkene Substrates:

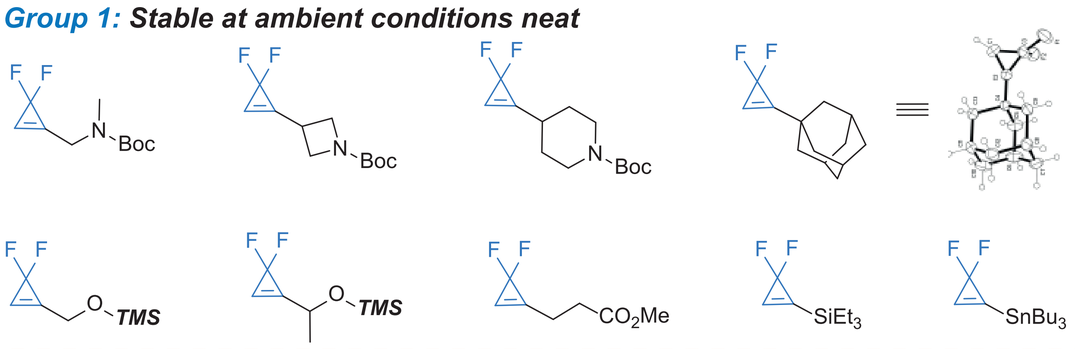


Examples > 100;
Scale = 10-200 g;
Hields = 37–97%

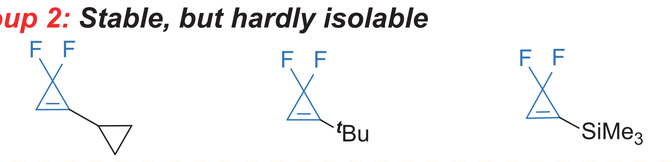
Applying the "Slow Addition Protocol" for Cyclopropenation: Scope and Limitations



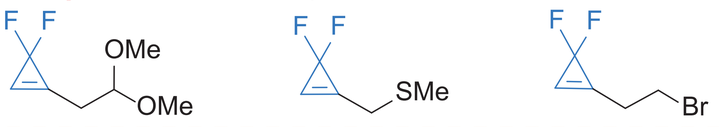
***Group 1:* Stable at ambient conditions neat**



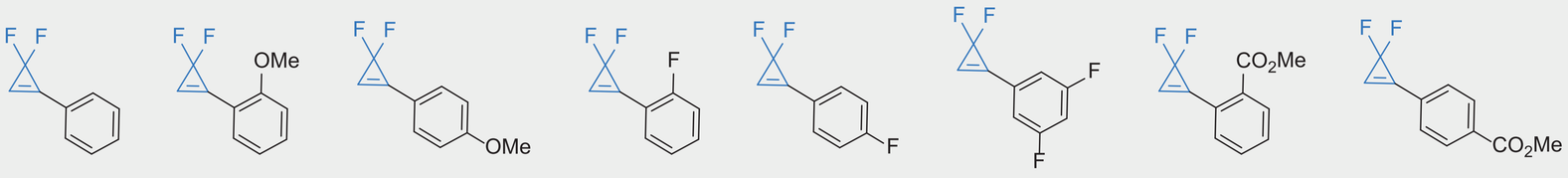
***Group 2:* Stable, but hardly isolable**



***Group 3:* Unstable neat, usable in solution**



***Group 4:* Relatively stable neat, readily hydrolyze on air at rt**



Examples > 100;
Scale = 10-200 g;
Yields = 35–96%

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