Creating cocktails for ^{19}F NMR-assisted FBDD approach based on Enamine's in-stock collection

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Status quo of ^{19}F NMR-assisted FBDD

- **2003** — Fluorine-NMR Experiments for HTS: Theoretical Aspects, Practical Considerations, and Range of Applicability
- **2009** — Design and NMR-Based Screening of LEF, a Library of Chemical Fragments with Different Local Environment of Fluorine
- **2009** — Fluorine local environment: from screening to drug design
- **2013** — Design and generation of highly diverse fluorinated fragment libraries and their efficient screening with improved ^{19}F NMR methodology
- **2019** — Ligand-Based Fluorine NMR Screening: Principles and Applications in Drug Discovery Projects
- **2019** — Ligand-Based Fluorine NMR Screening: Principles and Applications in Drug Discovery Projects
- **2022** — Efficient Screening of Target-Specific Selected Compounds in Mixtures by 19F NMR Binding Assay with Predicted ^{19}F NMR Chemical Shifts

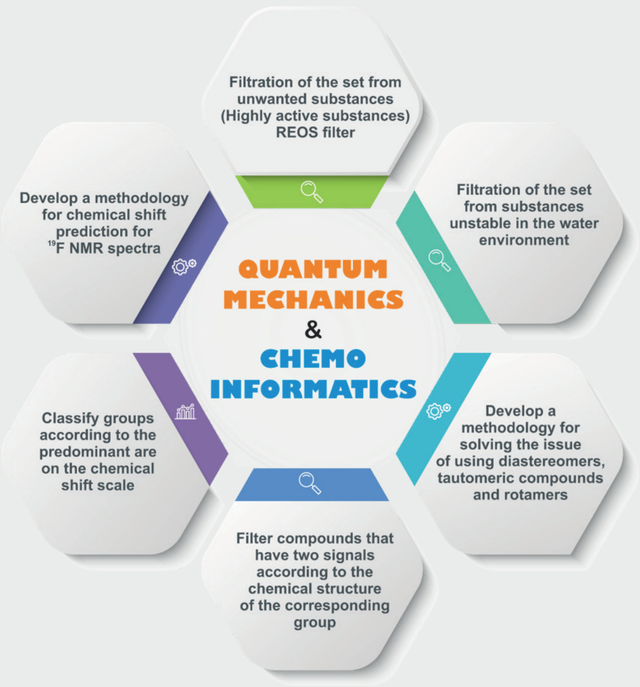
⊕ FAXS (FLUORINE CHEMICAL SHIFT ANISOTROPY AND EXCHANGE FOR SCREENING) ⊖

- One of the biophysically available and **highly effective tools** for analyzing the presence of ligand-protein
- **Fast and requires only a limited amount of protein**, and therefore compares favorably with other established non-NMR methods used in high throughput screening
- Although ^{1}H detection was used in the original competition-based approaches, there are significant advantages of using ^{19}F detection
- **The absence of spectrum overlap** allows you to check large chemical mixtures and automatically analyze spectra even in the presence of protonated buffers, solvents, and detergents.

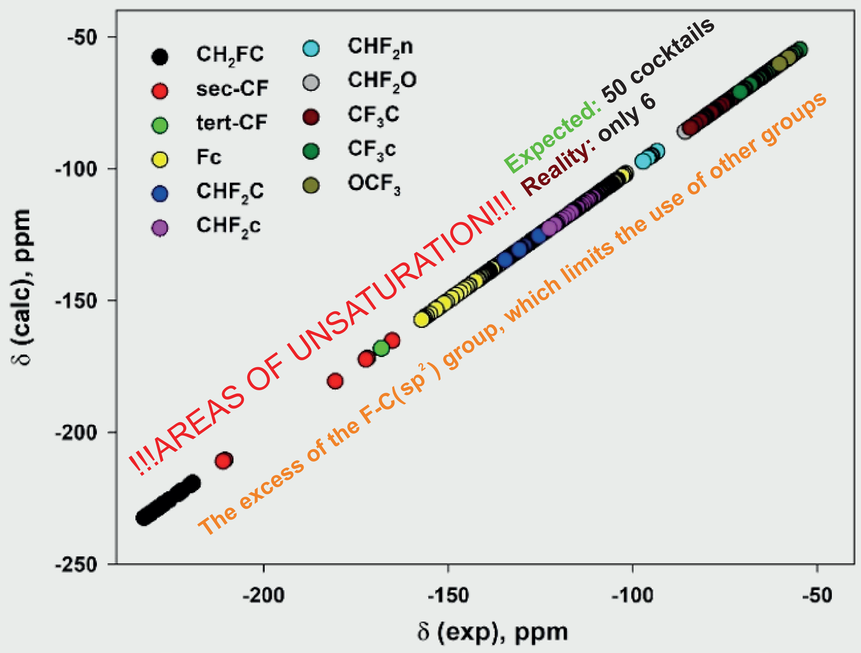
- The problems with human/semiautomated data mining (especially for diastereomeric "CF_2" cpd)
- Doubling of signals in amide spectra (hindered rotation) and NH-pyrazoles (slow tautomeric exchange)
- Doubling of signals due to their instability in the aquatic environment (oxadiazoles)
- Solubility problems for some compounds
- The presence of a mixture of diastereomers and compounds with two non-equivalent fluorines
- Not everyone passed the filters for unwanted compounds

Cocktails for ^{19}F NMR Fragment Screening: From Theory to Application

METHODOLOGY

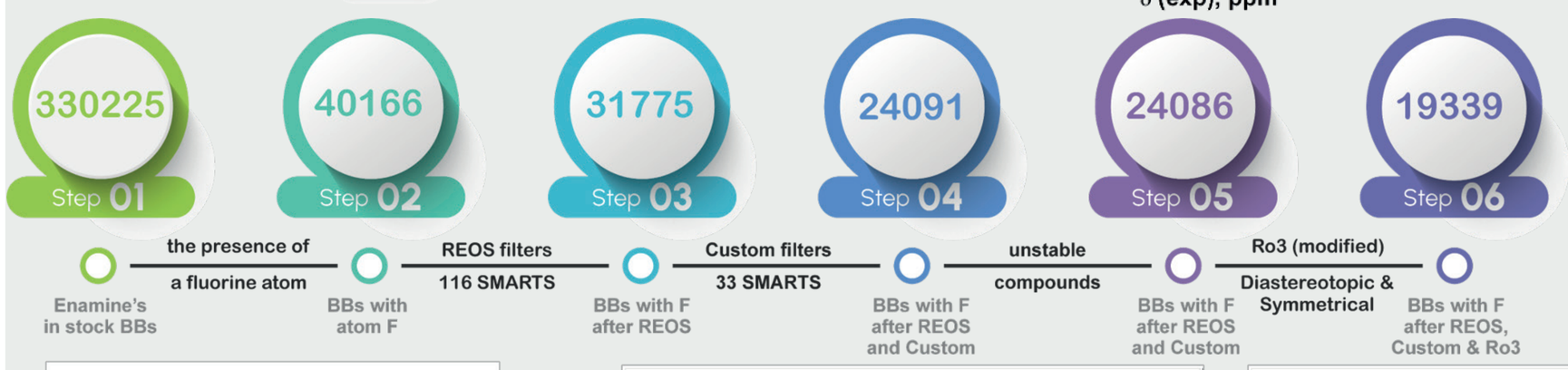


ANALYZING ENAMINE'S LIBRARY (1280 compounds)

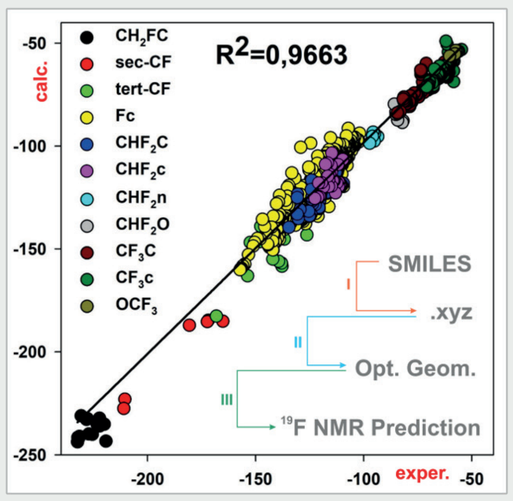


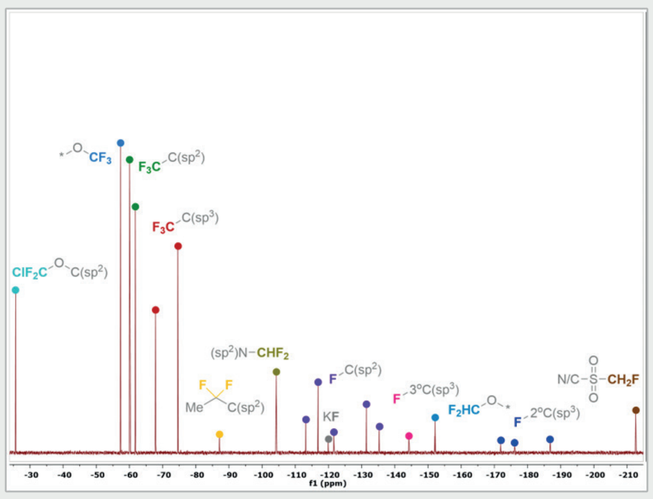
CF_3O → 5
F_2CH-O → 18
F_2CH-N(sp^2) → 6
CF_3-C(sp^3) → 133
F_2CH-C(sp^3) → 43
FCH_2-C(sp^3) → 20
CF_3-C(sp^2) → 117
F_2CH-C(sp^2) → 31
F-C(sp^2) → 886
F-2°C(sp^2) → 6
F-3°C(sp^2) → 15

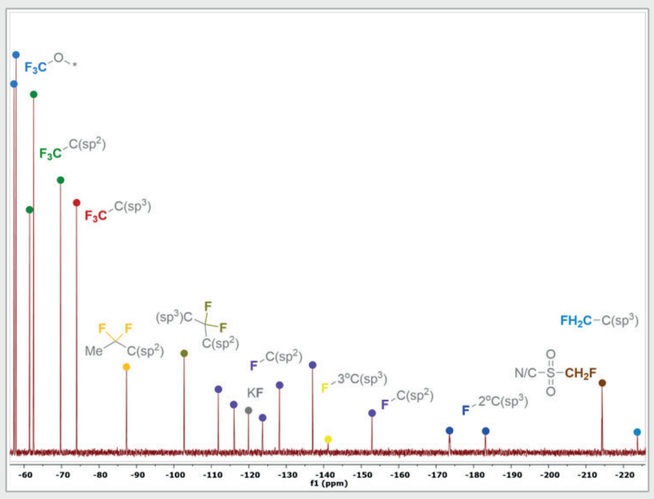
- 52 SMARTS
- 19 339 cmpds
- 57 groups



Enamine in-stock BB's collection







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