Molecular design of new derivatizing agents for ultra-sensitive ESI(-) LC-MS-MS determination of non-ionic environmental pollutants of emerging concern

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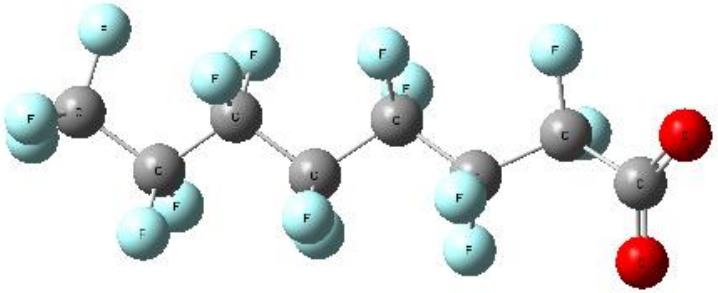
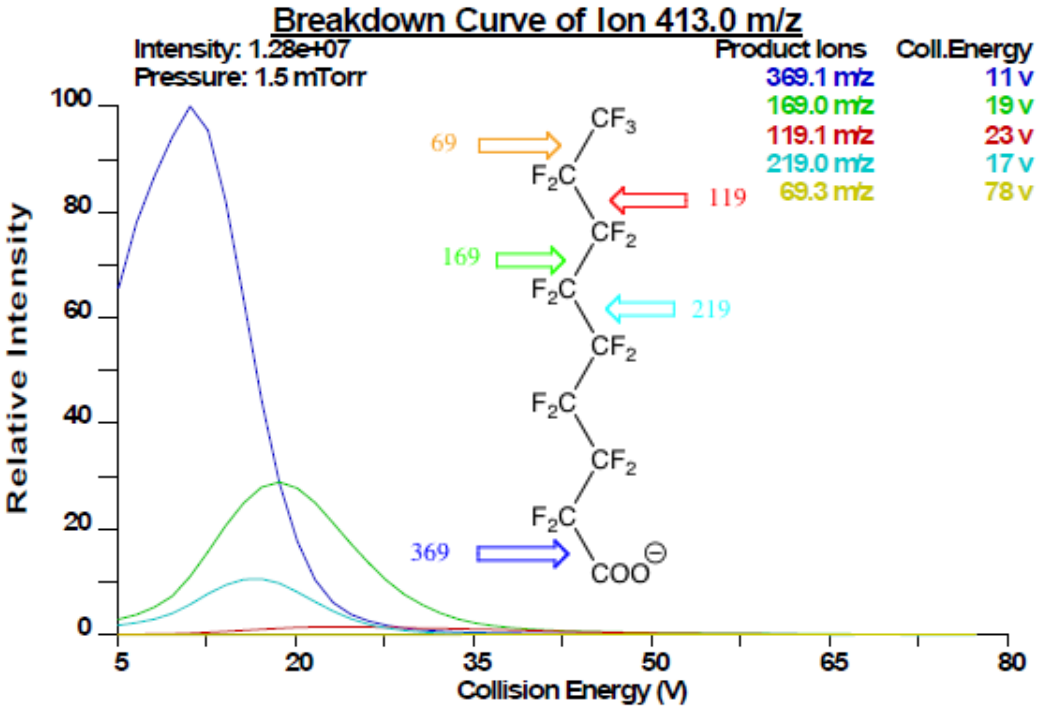
Starting point: PFOA and other PFCAs– bad or good?



Structure optimized
Gaussian-09
RB3LYP/6-31+G(d,p)

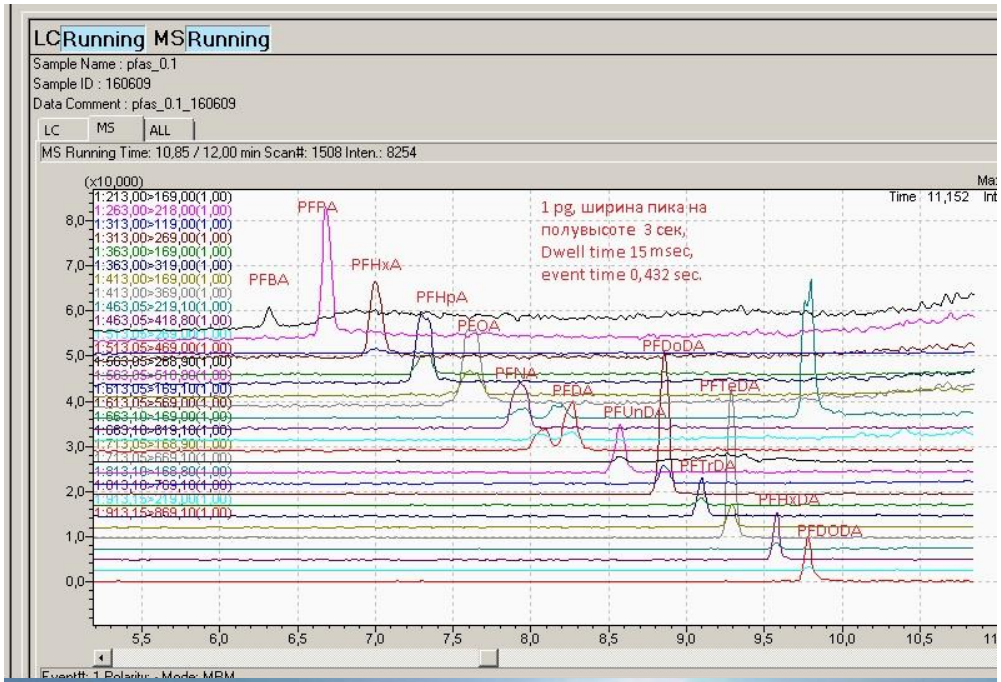


Useful chemicals, stable!
Environmental contaminants
Anions are good surfactants
Acids are strong acids
PFOA by LC-MS-MS :

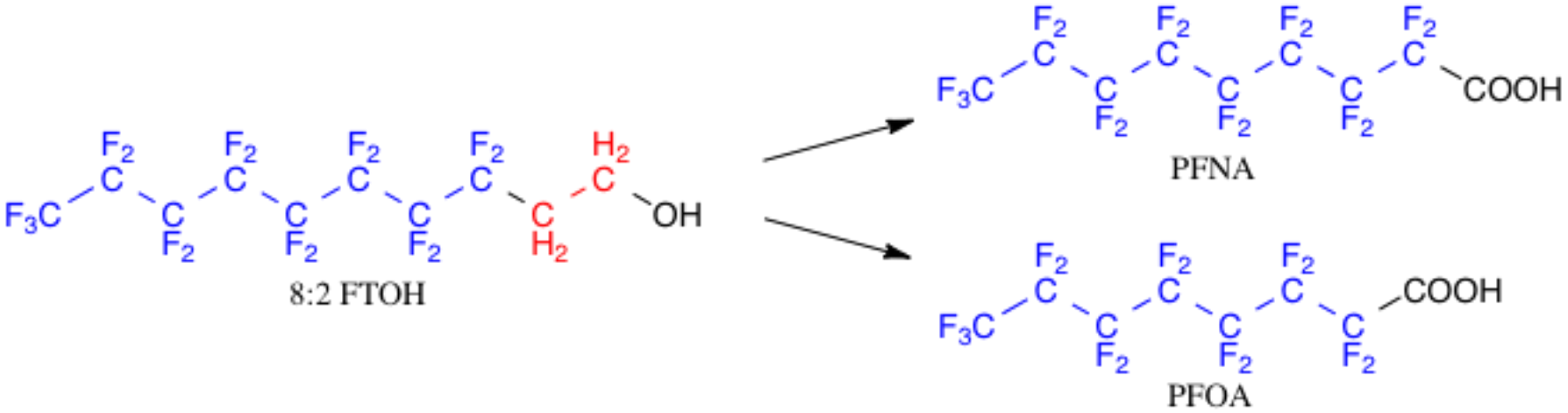
Good ionization in ESI
Good fragmentation in MS

< 1pg/injection

From Barentsburg, with love: Northernmost LC-MS-MS (courtesy of Mr. Valery Smutin)



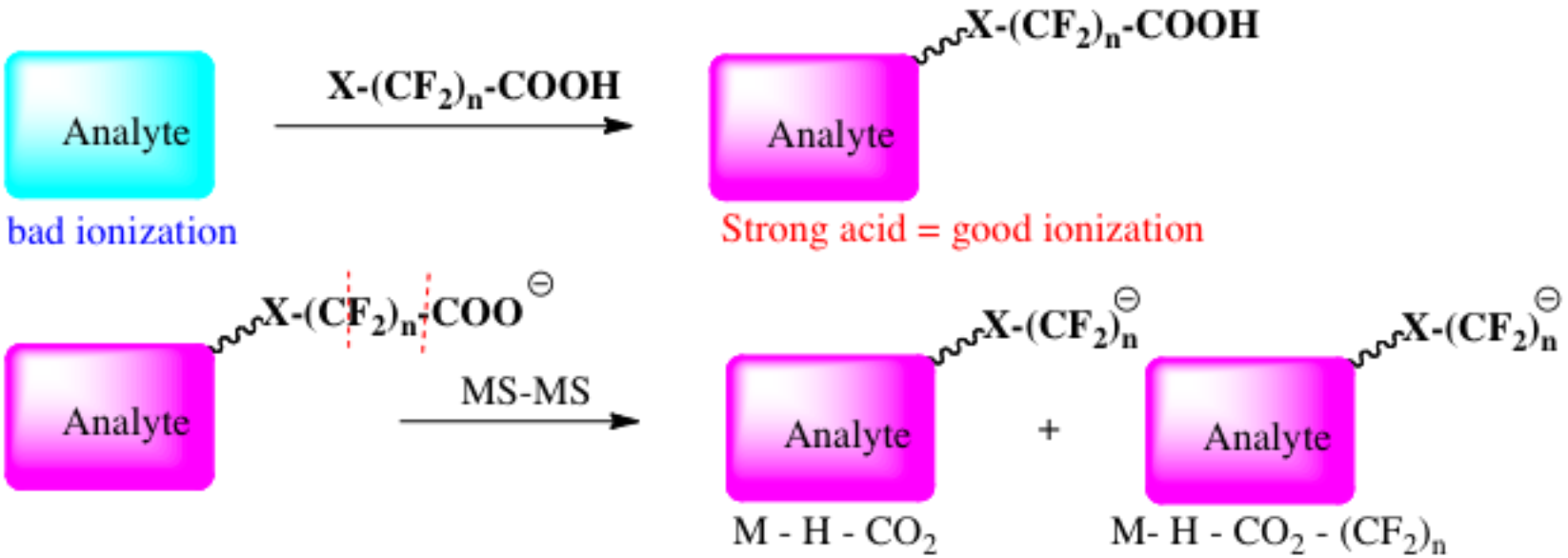
Fluorotelomer alcohols (FTOH) – bad or good?



FTOHs are not as hazardous as PFCAs (?)
FTOHs may yield PFCAs in the environment
FTOHs are weak acids, not ionized well in ESI
Good for the purpose, bad for the environment, bad in the lab…
How to make them **good again**?

How can we make FTOHs and all other contaminants **as good as PFOA for us**?

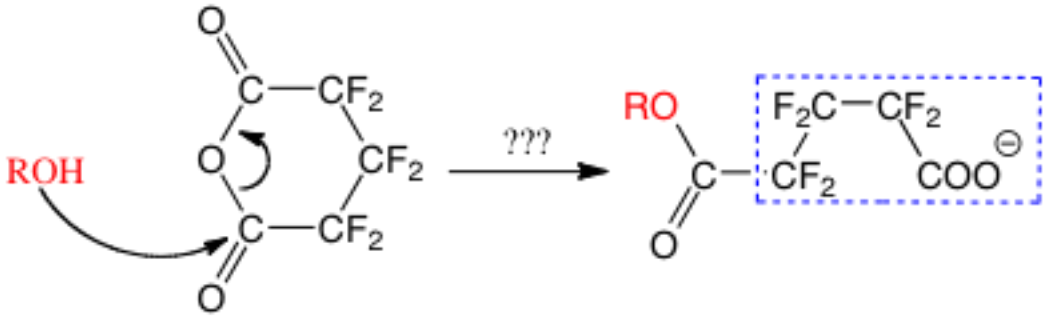
Derivatization = conversion to ”substituted PFOA”

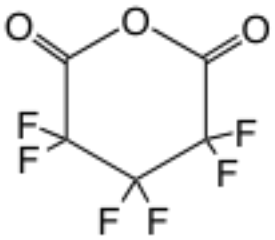


A derivative should have ionization and fragmentation properties of common PFCAs, like PFOA

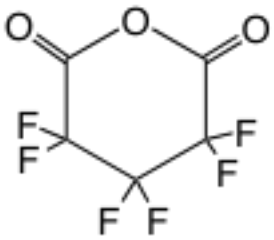
Test 1: GluF

Perfluoroglutaric anhydride





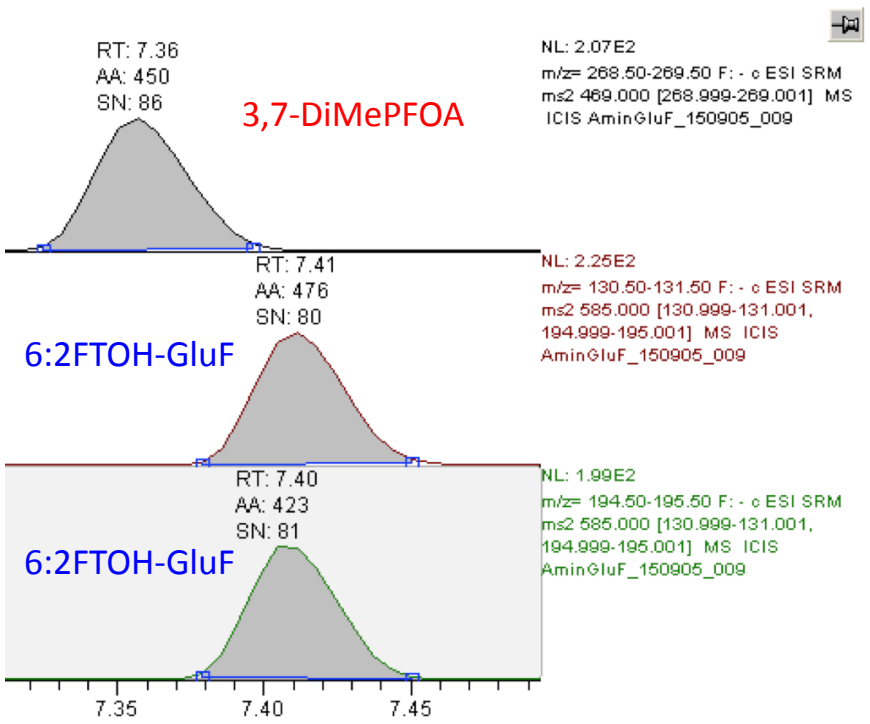
Testing the idea: GluF = PerfluoroGlutaric Anhydride

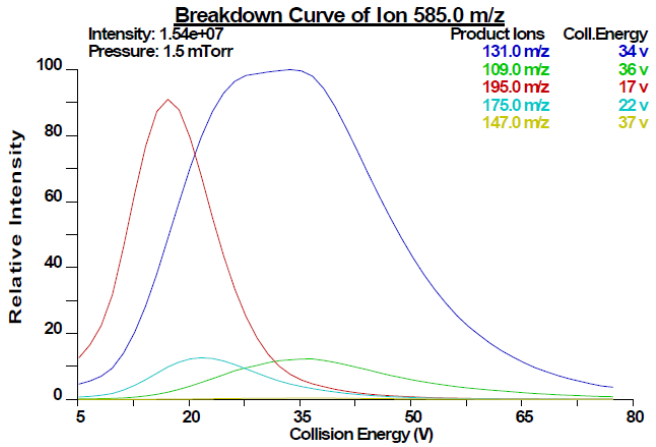


6:2 FTOH

$CF_3CF_2CF_2CF_2CF_2CF_2CH_2CH_2OH$ + GluF

$CF_3CF_2CF_2CF_2CF_2CF_2CH_2CH_2OCOCF_2CF_2CF_2COOH$





C_3F_5 m/z = 131

HC_3F_6COO m/z = 195

The idea was great indeed…

But:

Reagent volatile,

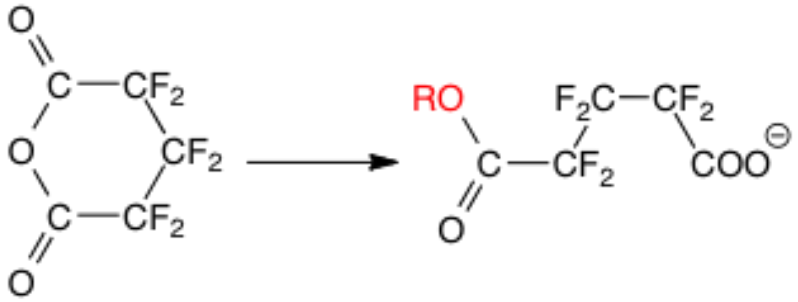
Aggressive (hazard),

Moisture-sensitive

Derivative not very stable (several hours)

Optimization of GluF

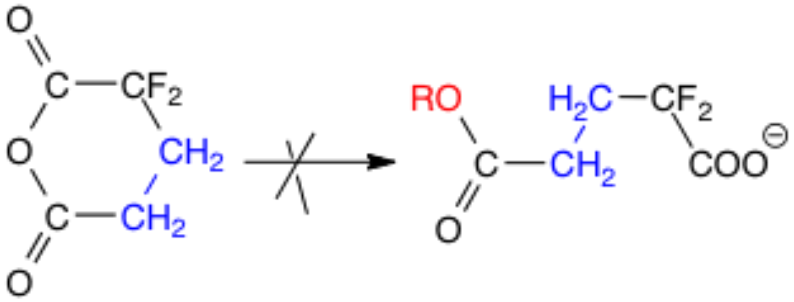
GluF



Unstable to hydrolysis/alcoholysis

NOT good for LC

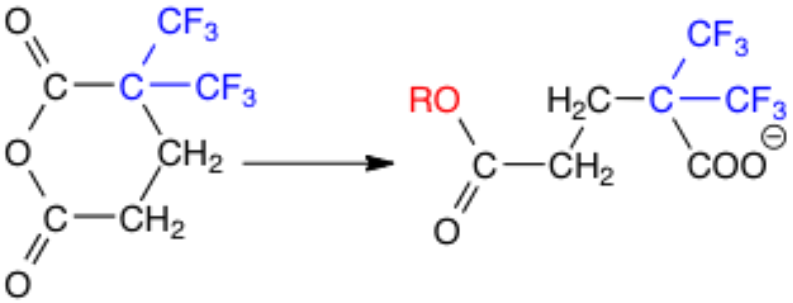
GluF +



DFT computations:

Another isomer will be formed

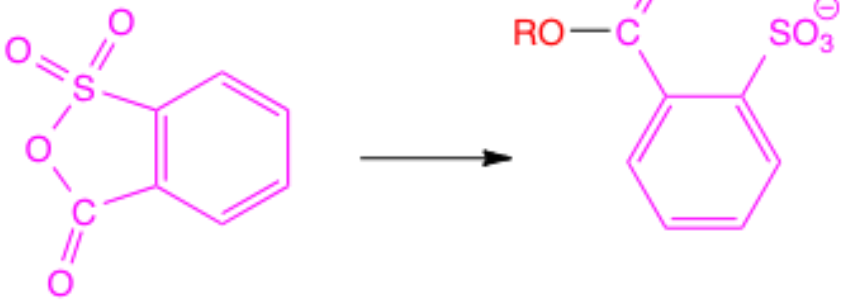
GluF Pro



DFT computations:
Good!

Reagent not available...

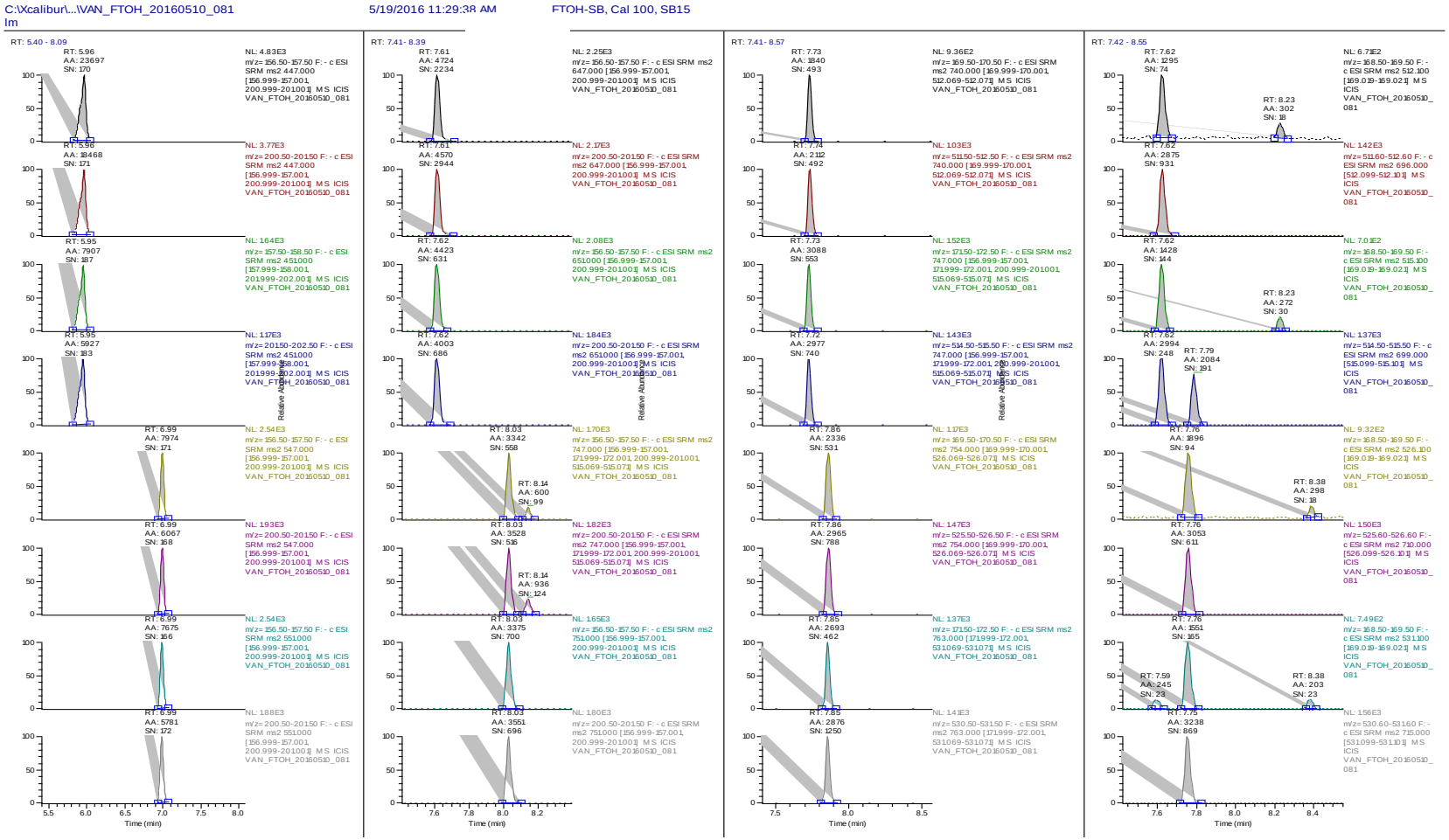
SB or SBA
SulfoBenzoic Anhydride



Literature and DFT:
Derivative stable
Ionization even better
Reagent stable and cheap

Wednesday, 17.00: Linda Hanssen et al,

Sulfobenzoic anhydride – new derivatizing reagent for high sensitivity LC-MSMS analysis of Fluorotelomer alcohols



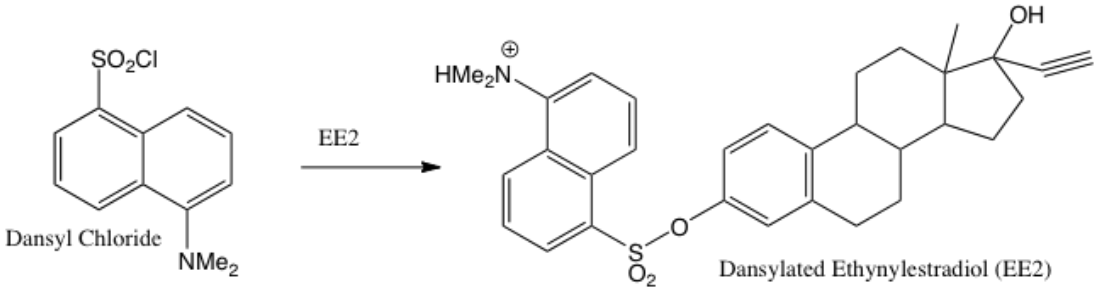
4:2 FTOH
6:2 FTOH

8:2 FTOH
10:2 FTOH

N-MeFOSE
N-MeFOSA

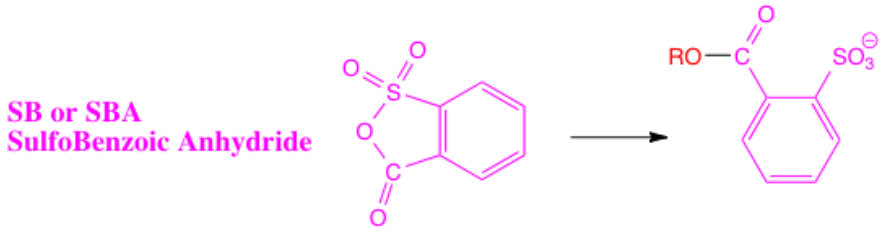
N-MeFOSE
N-MeFOSA

Dansyl Chloride for derivatization of steroid estrogens:



LOQ for EE2 < 0.035ng/L surface water

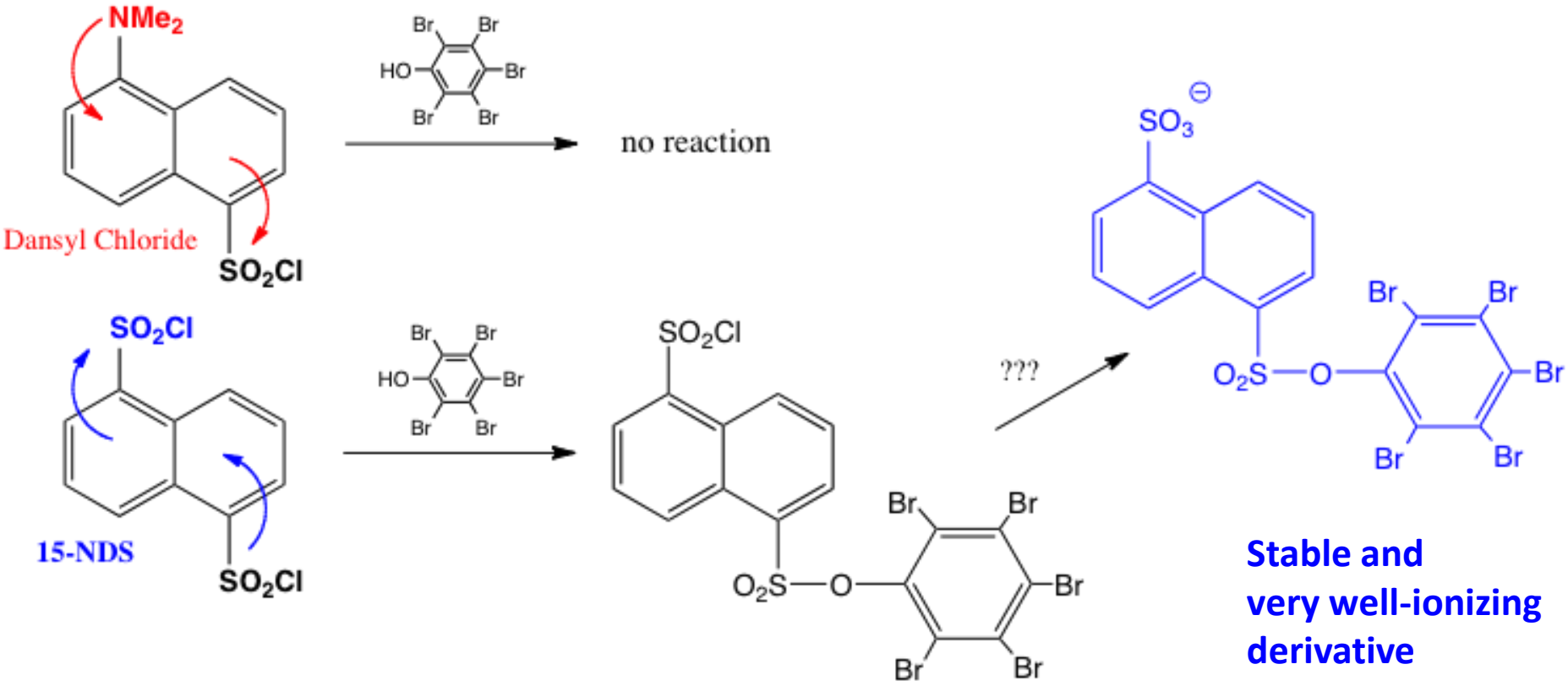
Thomas, K.V., Langford, K., Reid, M., Vogelsang, C., Øxnevad, S., Bæk, K., Fjeld, E., Brooks, S., Pampanin, D.M., Nikiforov, V., Schlabach, M. (2016). *Screening programme 2015. Pharmaceuticals and hormones* (Miljødirektoratet rapport, M-597/2016) (NIVA report, 7076-2016). Oslo: NIVA.



SB vs Dansyl Chloride, FTOH vs Phenolic analytes

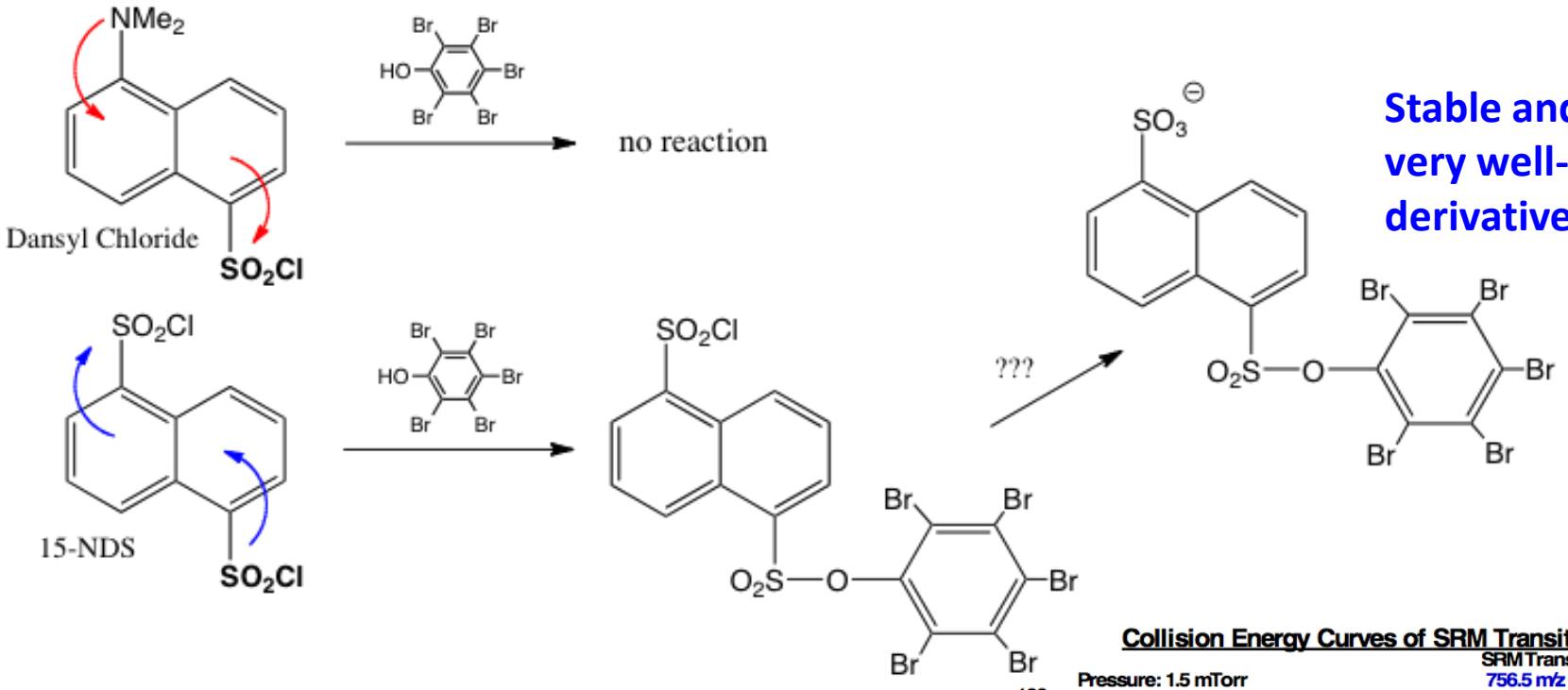
- SB more reactive in general (DsCl – no reaction with FTOH)
- SB derivatives are less stable in general (not good for phenolics)
- SB reactive centre is Carbon (S_N1 type), in DsCl – Sulfur (S_N2 type)
- Increase of reactivity of DsCl would allow derivatization of **"tough phenols"**, while derivatives could still be stable
- DFT computations suggest increase of electrophilicity of SO_2Cl would help

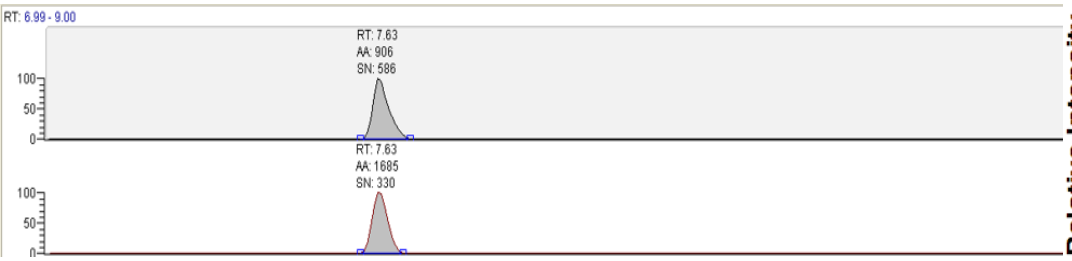
1,5-Naphthalene Disulfonyl Chloride (15-NDS) – "up side down" Dansyl Chloride



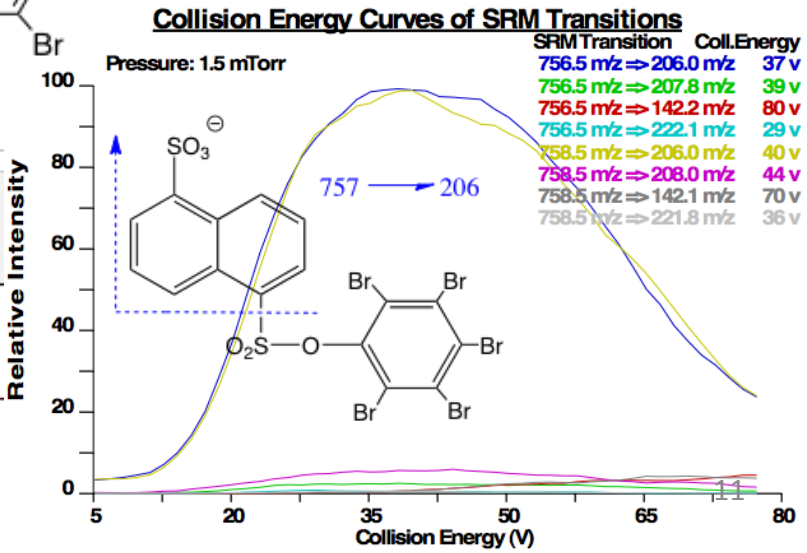
- Electron-withdrawing substituent instead of e-donating
- Anionic derivative instead of cationic one
- Stronger acid instead of weaker base
- 2 steps instead of 1

1,5-NDS derivatives of PBP (Pentabromophenol) and PCP (Pentachlorophenol)





15NDS-PCP, 5 pg derivatized



Highlights

- A series of derivatization reagents/reactions developed for emerging pollutants
- Dansylation allowed Ethynylestradiol (EE2) in water below 0.035ng/L (< EQS)
- Sulfobenzoic anhydride (SB) allowed sensitive LC analysis of FTOH (tomorrow, Linda Hansen, 17.00)
- Naphthalenedisulfonylchloride (15-NDS) is superior to Dansylchloride and is promising for “tougher phenols”
- Perfluoroglutaric anhydride (Glu-F) was not only a model compound: can be used for derivatization of amines, for example
- All mentioned anionic derivatives are formed merely upon mixing

To be continued…

Thank you for your attention!