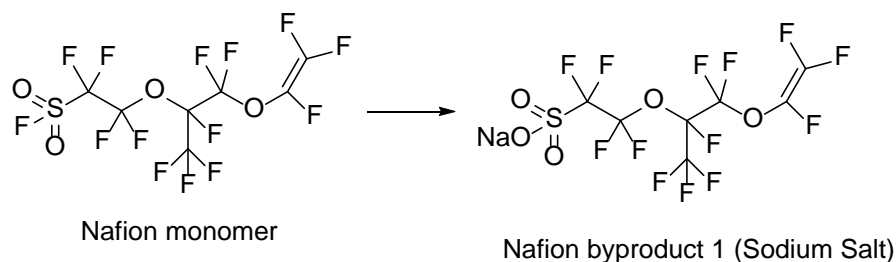


## PFAS Standard Synthesis

All PFASs with carbon chain lengths greater than 2 are anthropogenic and are produced almost exclusively by one of the two major manufacturing processes. Electrochemical fluorination (ECF) used since the 1970s produced mixtures of linear and branched isomers of approx. 70% and 30%, respectively; and telomerization in use since the 1950s, yielding exclusively linear compounds. Report on the synthesis of PFAS in academic literature are disproportionately rare probably due to proprietary protection and investigation on the synthesis are mainly limited to internal business of major manufactures. PFAS has unique chemical physical property compared to most other organic compounds that are familiar to most organic chemist and the synthesis of PFAS standards is a very specialized area. All those facts contribute to the limited accessibility of many PFAS standards, especially those that are newly discovered in environment. Laboratory synthesis becomes an important tool for the availability of those standards. We have managed to develop the protocol for the synthesis of Nafion by product 1, Nafion by product 2 and Hydro-EVE.

### 1, Synthesis of Nafion byproduct 1:



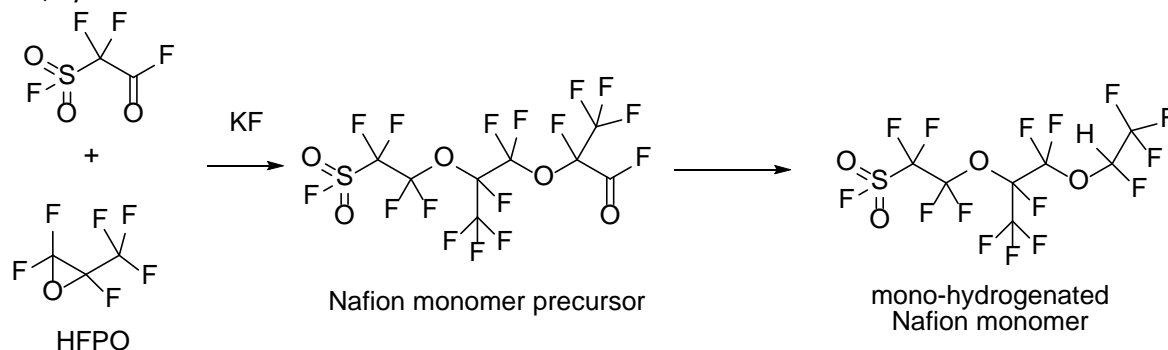
Synthesis of Nafion byproduct was achieved through the hydrolysis of Nafion monomer. There were contradictory report for this transformation. A patent in 1966 reported that ‘alkaline acetone water mixture’ as the hydrolysis medium without much detail process. Later this process was attempted by another researcher but failed to reproduce the same result, and basic hydrolysis was then reported to ‘led to extensive vinyl attack and difficulty in obtaining pure’ product, the author eventually went around to develop a fluoride catalyzed process for such transformation. However, while this hydrolysis was reported to be quantitative in 5 days without attack on the vinyl group, the same condition was reported to completely convert the vinyl group as well when the reaction time is doubled to 12 days. Without original spectroscopy to support such claim, there is highly uncertainty that merely double up the reaction time would clearly differentiate those two transformations. It is tempting to think that the attack on the vinyl group may very well have happened in the first half the time during which only the hydrolysis was claimed to have happened. There is other recent reports states that the hydrolysis with aqueous NaOH and acetone was successful without event, and the base and solvent seemed to play a role. Based on the literature, we reason that basic hydrolysis still worth a try. Initial test was attempted with sodium carbonate in acetone with residue water, the reaction was monitored with <sup>19</sup>F Nuclear Magnetic Resonance (NMR). After overnight stirring, such condition failed to facilitate the transformation. Excess water was then added, and the hydrolysis was extended at room temperature for half a day, complete transformation was observed. The disappearance of the signal around 45 ppm for SO<sub>2</sub>F whereas that of CF<sub>2</sub>SO<sub>2</sub>F shift from -112 to -117 is the indication of such transformation. The absence of any significant chemical shifts of the NMR signal of the vinyl-F is also another evidence for the survival of the vinyl group

to any further transformations. The product was isolated as sodium salt, around 1 gram for the successful try, and characterized with NMR. The process can be easily scaled up.

## 2, Synthesis of Nafion byproduct 2.

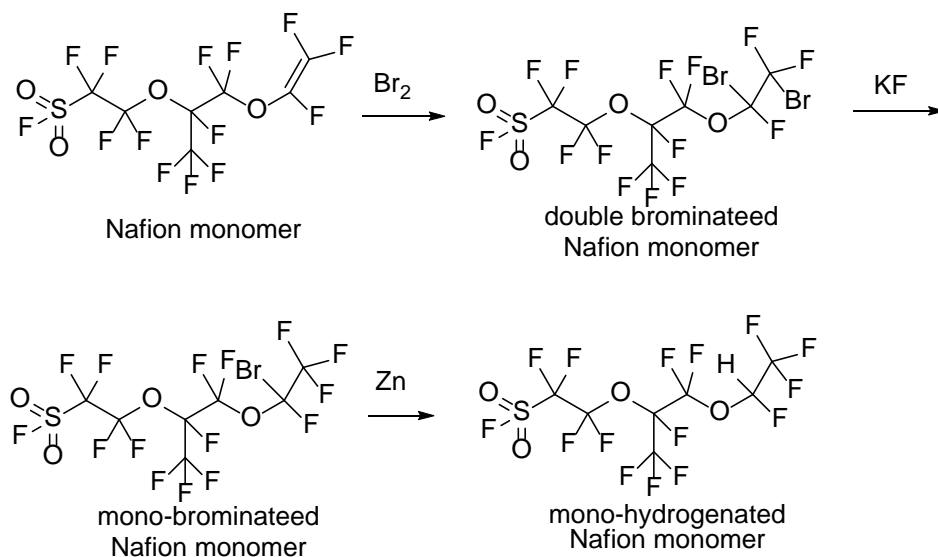
To speed up the whole process, we designed two routes for the synthesis of the mono-hydrogenated Nafion monomer, which is the crucial intermediated for the synthesis of Nafion byproduct 2.

### 2.1, Synthesis of the crucial intermediate: route 1



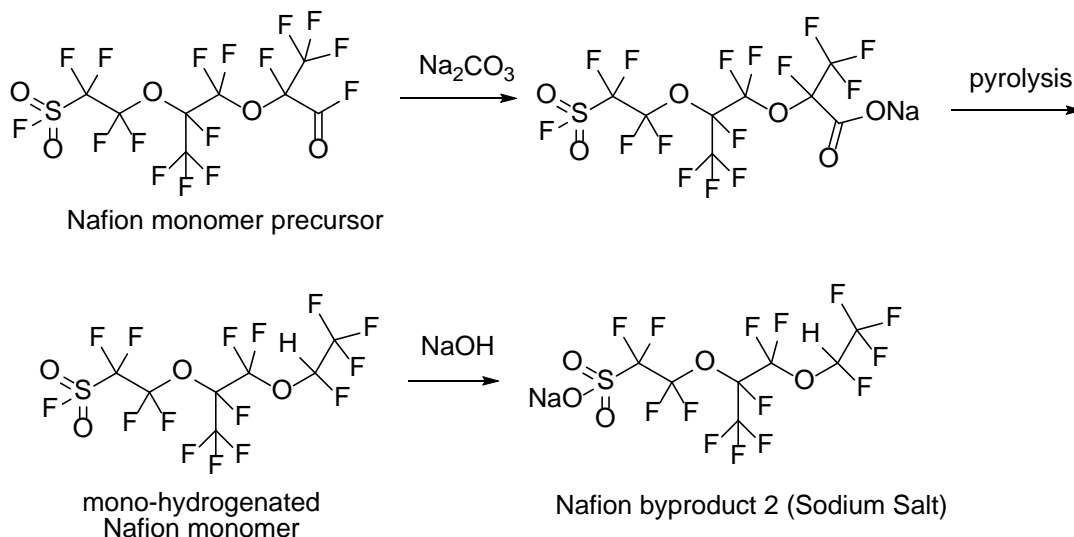
Ideally, the synthesis of Nafion byproduct 2 would start with Nafion monomer precursor. The availability of the precursor is inconsistent and likely due the production cycle of the manufacturer. We started out with the preparation of the precursor itself from more basic starting material, HFPO and 2-(Fluorosulfonyl)-difluoroacetyl fluoride, which are more readily available from commercial sources. First, this transformation usually is not a clean and robust reaction and the products would vary widely based on reaction conditions due to their reactive nature of both starting material. The major concern was the degree of polymerization and the formation of products with different degree of polymerization is highly variable. Many factors would affect the outcome, such as reaction time, temperature, addition sequence and reactants ratio. Industrial manufacture resorts to rectification for the product purification. To reproduce the process in common lab environment, we devised an in-house setup with available equipment and minimum parts procurement to incorporate gaseous agents as the unusual starting material. With this set up, we managed to get the desired Nafion monomer precursor after a few times of trial.

### 2.2, Synthesis of the crucial intermediate: route 2



In the meantime, since we have Nafion monomer from the preparation of Nafion byproduct 1, we designed another route for the synthesis of the mono-hydrogenated Nafion monomer. First, bromination of Nafion monomer would produce double-brominated Nafion-monomer, this step is a conventional strategy for the protection of perfluorovinyl ether group, and in our hands it proceeded without event. The resulting intermediate was then followed by fluoro-bromo-exchange to afford mono-brominated Nafion monomer, which would provide the crucial intermediate: mono-hydrogenated Nafion monomer upon reduction. The reduction step was not tested further after route one succeeded.

### 2.3, Synthesis of the final product Nafion byproduct 2.



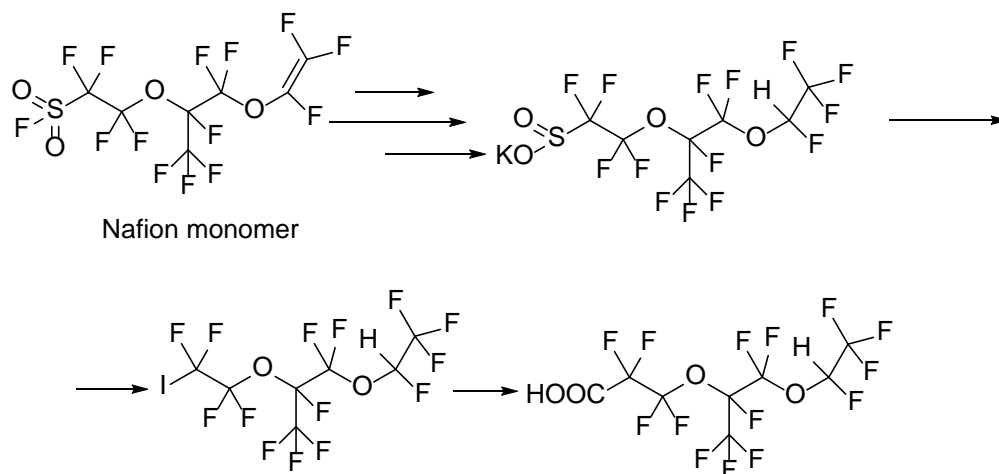
After Nafion monomer precursor is obtained, that second step was investigated for the synthesis of the mono-hydrogenated Nafion monomer, and then Nafion byproduct 2 itself. The acyl fluoride was transformed into sodium salt and then subjected to pyrolysis in the presence of proton source to afford the crucial intermediate, which was then hydrolyzed to afford Nafion byproduct 2. All the intermediates

and final product were characterized with NMR. Again, the product was isolated as sodium salt, around 2 gram for the successful try, and characterized with NMR. The process can be easily scaled up.

### 3. Synthesis of Hydro-EVE

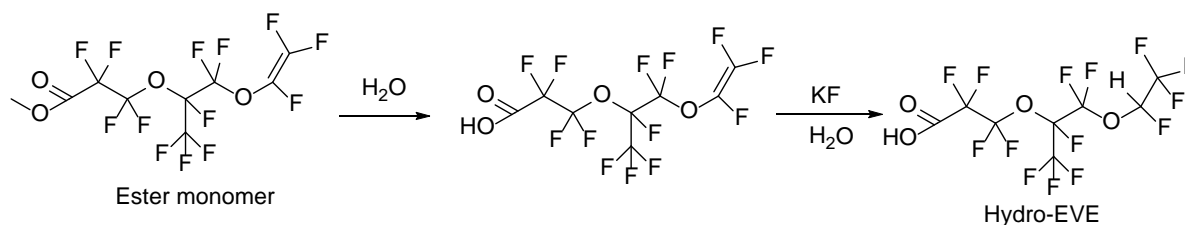
The synthesis of Hydro-EVE has never been reported before. Initial effort to synthesis Hydro-EVE was attempted to start with Nafion monomer as we had this material from previous synthesis of Nafion byproduct 1 and 2, and this common intermediate was considered for the synthesis of hydro-EVE.

#### Route 1



However, after some initial test of steps this route was abandoned due to lengthy steps and a new route was devised as the following. Even though we have to start with a new starting material, an ester monomer, this route was envisioned to be more efficient and the new starting material was not prohibitively expensive:

#### Route 2

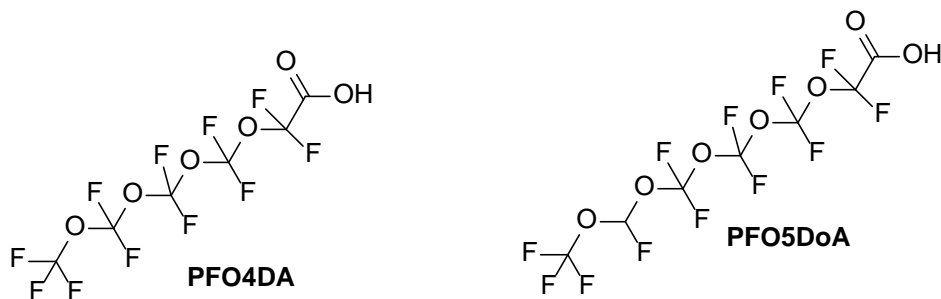


Thus the ester monomer was hydrolyzed to afford the free acid. This transformation could be readily achieved with water under basic condition. The addition of HF to the double bond was more difficult. After some test, it was noticed that temperature played an important role. The reaction is driven by increased temperature. The other problem of this reaction is the solubility of fluoride in the reaction mixture. Quaternary ammonium fluoride has the best solubility in organic solvents; however it is hard to be cleaned from the reaction mixture afterwards. Most of the inorganic fluoride has very low solubility in organic solvent, we chose potassium fluoride as the fluorine source and acetonitrile as the solvent to

largely alleviate the problem. Hydro-EVE was successfully isolated as potassium salt. The current scale is close to one gram, but it can be scaled up if needed.

### Future directions

The next conceived targets of synthesis are PFO4DA and PFO5DoA, we are still looking for the sources of some possible starting material.



Overall, we gain first-hand experience about the synthesis and analysis of this group of highly specialized compounds that have unique chemical-physical property, which necessitates different technique and knowledge. In the future we are looking to utilize this capability and knowledge to understand health effect of PFAS and to develop method of PFAS remediation.

Zhenfa Zhang, Ph.D.

NC PFAST Network Synthetic Organic Chemist

Associate Professor, Department of Environmental Sciences and Engineering

University of North Carolina at Chapel Hill