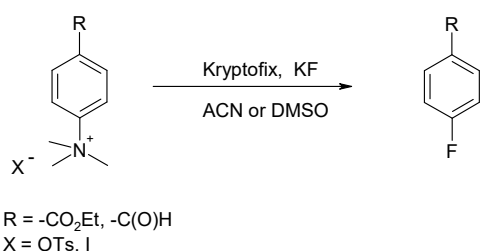


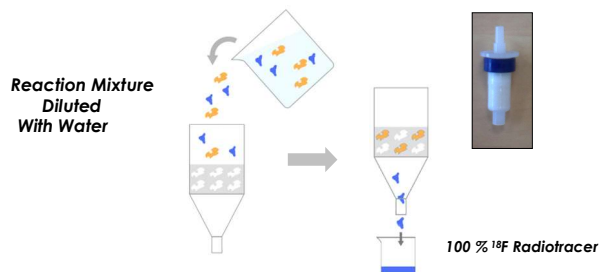
## Selective Solid Phase Extraction for Purification of Fluorous Radiotracer issued from an Aromatic Nucleophilic Substitution using Molecularly Imprinted Polymers

### Easy Removal of Ammonium Precursors and By-Products using a Single SPE Cartridge

Aromatic nucleophilic substitution is widely used to synthesize fluorous radiotracers. Due to the short lifetime of <sup>18</sup>F radiotracers, the purification is a key step of the synthesis. It must be fast and effective to ensure a high radiochemical purity. This application note shows the effectiveness of the purification method for two different radiotracers using a **AFFINIMIP® SPE <sup>18</sup>F Aromatic Nucleophilic Substitution** cartridge.



At 95°C were mixed 5 mg of ammonium salt, 6.7 mg of Kryptofix 2.2.2 and 1 mg of potassium fluoride in 400 µL of ACN or DMSO. After 15 minutes and the cooling of the reaction mixture, 2 mL of water were added to obtain the loading solution (L).



#### Solid phase extraction (SPE) protocol

The SPE procedure used first an **AFFINIMIP® SPE <sup>18</sup>F Aromatic Nucleophilic Substitution** cartridge. The details of each step are as follows:

- Condition the SPE Cartridge with 5mL of Acetonitrile (ACN)
- Load the loading solution (L)
- Wash the cartridge with 5mL of 80-20 Water-ACN
- Dry the cartridge. **Force the water down into the cartridge and out the bottom or apply vacuum 30 seconds**
- Elute the fluorous radiotracer with 1-2mL of ACN until dryness (E1). Ethanol can be used as the elution solvent in some cases depending on the nature of the radiotracer/impurity.

The flow has to be as slow as possible so as to favour the interactions between the phase and the different compounds.

For some applications, a second SPE procedure has been developed to change the solvent of the pure radiotracer solution from Acetonitrile to Ethanol by using a **AttractSPE™ W/O - HLB** cartridge. The details of each step are as follows:

- Condition the SPE Cartridge with 2mL of Ethanol and 2 mL of Water
- Load the loading solution constituted of E1 (1mL) diluted with 15 mL of Water
- Dry the cartridge. **Force the water down into the cartridge and out the bottom or apply vacuum 30 seconds**
- Elute the fluorous radiotracer with 1-2mL of Ethanol until dryness (E2)

#### Analytical conditions

HPLC was performed on a ThermoFinnigan Spectra System with an Hypersil Gold column 50mm x 2.1mm, 1.9 µm (Thermo). The separation was carried out using a gradient (see Table 1) at a flow rate of 0.2mL/min.

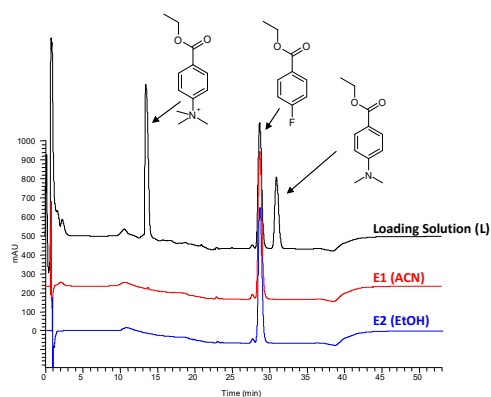
**Table 1.** Gradient used for the analysis.

Time (min)	% (0.1 % HCOOH Water)	% ACN
0	100	0
3	100	0
15	70	30
32	70	30
33	100	0
53	100	0

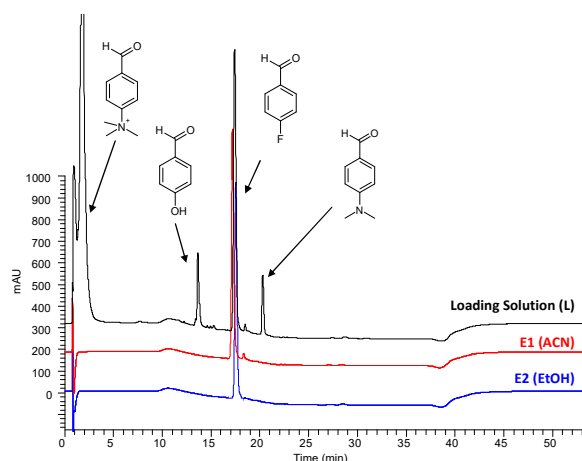
The detection system was a ThermoFinnigan Spectra System Model UV6000LP set to 235nm. The injection volume was 10µL.

#### Results

**Recovery of more than 95 % of the fluorous radiotracer was obtained without any contamination of other identified compounds (phenolic and dimethylaminobenzyl compounds, precursor and fluoride). More than 95 % of Kryptofix 2.2.2 was also eliminated. (MS control)**



**Figure 1.** Fluorination of Ethyl 4-trimethylammoniumbenzoate iodide in DMSO. Chromatograms obtained before (black) and after AFFINIMIP® SPE <sup>18</sup>F Aromatic Nucleophilic Substitution Clean-up (E1 : red) and after AttractSPE™ W/O- HLB Clean-up (E2 : blue)



**Figure 2.** Fluorination of 4-Trimethylammoniumbenzaldehyde Tosylate in DMSO. Chromatograms obtained before (black) and after AFFINIMIP® SPE <sup>18</sup>F Aromatic Nucleophilic Substitution Clean-up (E1 : red) and after AttractSPE™ W/O - HLB Clean-up (E2 : blue)

### Conclusion

The use of an AFFINIMIP® SPE <sup>18</sup>F Aromatic Nucleophilic Substitution cartridge is a simple, fast, and selective tool for the purification of a reaction mixture issued from aromatic nucleophilic substitution. The fluororous radiotracer is obtained in ACN without any identified impurities such as Kryptofix, dimethylammonium/phenolic derivatives or precursor. In addition, the use of AttractSPE™ W/O - HLB allows to get the radiotracer in a minimum of Ethanol.