High purity and n-isomer specific PFAS reference standards

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Introduction: Since 1950, PFASs and surfactants and polymers made with the aid of PFASs have been widely used in numerous industrial and commercial applications. In the over half-century of global manufacturing, two principal processes have been used to produce compounds containing perfluoroalkyl chains, and the two techniques used have produced PFASs with very different isomeric purities. Electrochemical fluorination (ECF, major use from 1950s-2002) results in a product containing both linear and branched isomers, while telomerization (major use from 2002 - now) typically yields an isometrically pure (or enriched), linear product. Despite the fact that both branched and linear isomers exist in the environment, quantitative analysis of PFASs is normally conducted by eluting all isomers together and integrating them as a single peak. It is well documented that many environmental samples contain both branched and linear isomers of PFASs, and the mixture of linear and branched isomers presents challenges in providing an accurate quantification of many PFAS in environmental matrices. Isomer-specific analysis of PFAS is difficult due to development of analytical instrument and methods, lack of analytical reference standards of high quality and fully characterized for isomer-specific identification and purity is another issue for the accurate and adequate analysis of PFASs. The goal of this project is to synthesize, purify and characterize isometrically pure PFAS reference materials, the focus has been on the synthesis of n-isomers of different PFASs.

Materials and Methods: Various n-isomer of PFASs were prepared by chemical synthesis, and /or purification of commercially available tech mixtures. The focus has been on the preparation of high quality reference materials of perfluoroalkane carboxylic acids (PFCAs), Fluorinated telomer acids (FTAs)**,** Unsaturated fluorinated Telomer Acids (FTUAs), Perfluoroalkane sulfonamide derivatives and Perfluoroalkane sulfonates. The synthesis routes were designed for the individual PFAS group with commercially available starting materials, the synthesized products have been purified by conventional purification techniques to remove chemical impurities and isomers. Flash column chromatographic method using flurorinated silica gel has also been developed. Perfluroalkylcarboxylic acids (**PFCAs**, $C_nF_{2n+1}COOH$) for examples, the synthesis have been effects on the long chain PFCAs ($n \geq 14$), which are not commercially available as tech. mixtures. The optimized synthesis methods were applied for the synthesis of mass-labelled PFASs as well. Chemical purity is analysed by one or several of the following chromatographic-methods: GC-FID/MS, high resolution GC-MS, HPLC-MS and UHPLC-MS. 19F-NMR and qNMR techniques are also developed for the determination of chemical and isomeric purity.

Results: Numbers of individual n-isomer of native PFASs have been synthesized in gram quantities. The synthesis of perfluoroalkanesulfonates is challenging due to the low product yeild and difficulty in purification. Deuterated FTAs, FTUAs and Perfluoroalkane sulfonamide derivatives with the deutrium-labelling on the un-fluorinated carbons have also been synthesized and purified for the n-isomers. Synthesis of ^{13}C-labelled those PFASs are onging. Isomer-profile of the PFASs synthesized is variable and depending on the carbon-chain length, the longer the chain (>C8), the more isomers are in the products. Purification of all synthesized compounds have been performed in order to remove isomers and any other impurities. Most of the compounds reached a purity of >98% for the n-isomer, based on both chromatographic analysis and NMR characterizations. Purification of commercial technical PFASs have also been tried, while the impurities such as inorganic salts, water are easy to be removed, isolation of n-isomers from the technical mixtures are not always possible, especially for the longer carbon-chain (>C8) PFASs, due to the high content of branched-chain isomers.

Conclusions: Both individual PFASs, and deuterium-labelled PFASs are prepared as n-isomers. which can be used as reference materials and internal standards for the PFASs analysis. Chemical synthesis gave high quality (purity >98%) PFAS compounds and these reference standards will give more accurate measurements and are more suitable reference materials compared to the technical mixtures which are used as reference materials today.

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