GAS CHROMATOGRAPHY - TANDEM MASS SPECTROMETRY WITH ATMOSPHERIC PRESSURE CHEMICAL IONIZATION FOR FLUOROTELOMER ALCOHOLS AND PERFLUORINATED SULFONAMIDES DETERMINATION

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ABSTRACT

Ionization and in source-fragmentation behavior of four fluorotelomer alcohols (FTOH) (4:2 FTOH, 6:2 FTOH, 8:2 FTOH and 10:2 FTOH) and four N-alkyl fluorooctane sulfonamides/-ethanols (N-MeFOSA, N-EtFOSA, N-MeFOSE and N-EtFOSE) by APCI has been studied and compared with the traditionally used EI and CI. Protonated molecule was the base peak of the APCI spectrum in all cases giving the possibility of selecting it as a precursor ion for MS/MS experiments. Following, CID fragmentation showed common product ions for all FOSAs/FOSEs (C_4F_7 and C_3F_5). Nevertheless, the different functionality gave characteristic pattern fragmentations. For instance, FTOHs mainly loss H_2O+HF, FOSAs showed the losses of SO_2 and HF while FOSEs showed the losses of H_2O and SO_2. Linearity, repeatability and LODs have been studied obtaining instrumental LODs between 1 and 5 fg. Finally, application to river water and influent and effluent waste water samples has been carried out in order to investigate the improvements in detection capabilities of this new source in comparison with the traditionally used EI/CI sources. Matrix effects in APCI have been evaluated in terms of signal enhancement/suppression when comparing standards in solvent and matrix. No matrix effects were observed and concentrations found in samples were in the range of 1-100 pg L^{-1} far below the LODs achieved with methods previously reported. Unknown related perfluoroalkyl substances, as methyl-sulfone and methyl-sulfoxide analogues for FTOHs, were also discovered and tentatively identified.

1. INTRODUCTION

Perfluorinated alkyl substances (PFAS) are a class of chemicals used in a range of applications due to their water and stain-resistant properties. They have been produced in high volumes for several decades and combine bioaccumulative potential, toxic effect and extreme persistence [1]. As a consequence of their use for more than 60 years, residues of PFAS are widely spread in the environment [2,3]. Some of these compounds can bioaccumulate and biomagnify in the food chain [4–6], and have been detected in humans [7,8]. The ubiquitous presence of these PFAS in the general population, their long half-lives, and increasing evidence of potential adverse health effects, is of concern. Among these ubiquitously found anthropogenic chemicals are perfluoroalkane sulfonates and perfluorocarboxylates with 4-15 carbon atoms in chain length. The most widely investigated compounds of these groups are the C_8-chemicals perfluorooctanoate (PFOA) and perfluorooctane sulfonate (PFOS) [9]. They have been used for over 50 years in the production of consumer products including carpet and upholstery stain-protectants, food-contact paper coating, nonstick cookware, waterproofing sprays, and windshield wash [10].

Due to their non-volatile and lower water-soluble properties of PFOA/PFOS, two different theories are their concerning transportations pathways. Either the moderately water-soluble compounds including shorter-chain perfluorocarboxylates could be transported directly by sea currents or by means of sea-spray. Alternatively, a suite of volatile, neutral precursors could undergo long-range atmospheric transport and be degraded in situ to form persistent PFOA and PFOS [11]. Possible atmospheric precursors include a number of fluorotelomer alcohols (FTOHs) as well as N-alkylated fluorooctane sulfonamides and sulfonamidoethanols (FOSAs/FOSEs). The second hypothesis is

strongly supported by the number of smog chamber degradation experiments, and by the determination of neutral PFAS at ground level at the North American troposphere [9].

Analytical methods for neutral PFAS (volatile FTOHs and FOSAs/FOSEs) in environmental and indoor air include mainly gas chromatography coupled to mass spectrometry with chemical ionization (GC/CI–MS) usually in positive mode (PCI) because it produced the molecular ion $[M+H]^+$, and one or two characteristic fragment ions for all FTOHs and FOSEs with the exception of FOSAs for which only one ion could be detected in PCI [9]. Therefore, confirmation of FOSAs in samples is always performed in negative ion chemical ionization (NICI) mode, wherein three fragments can be monitored [12]. In contrast, electronic ionization (EI) is not frequently used because of the low intensity of the molecular ions and the lack of specific fragments. As an alternative to GC/MS methods, the analysis of neutral PFAS by LC/MS was also reported [13,14]. However, in LC/MS methods the co-analysis of nonionic and ionic PFAS is impeded by ionization suppression of FTOHs caused by the buffered mobile phases needed for the chromatographic separation of ionic PFAS [14].

The recently revived atmospheric pressure chemical ionization (APCI) source has been satisfactorily applied for GC-amenable compounds such as pesticides, PAHs, PCBs and, very recently, PBDEs, dioxins and dioxin-like PCBs [15–18]. The soft ionization generated by this source promotes the formation of the molecular ion and/or the protonated/deprotonated molecule (quasi-molecular ions) as the base peak of the spectrum in most cases, with low fragmentation degree, if we compare against the high fragmentation generally observed by EI. This allows the selection of ($[M+H]^+$ or $M^{+\cdot}$) as a precursor ion for the SRM transitions which turns into a sensitive and specific analyte detection and identification. Moreover, this source has also been revealed more universal than the traditional CI source, which is not as universal as EI and requires various

injections of the sample to cover a wider range of analytes being rarely used in multiresidue methods [19].

In the present work the potential of atmospheric pressure chemical ionization (APCI) combined with GC-MS/MS with triple quadrupole analyzer has been investigated for the sensitive determination of FTOHs and FOSAs/FOSEs in surface water. GC-(APCI)QTOF MS has been also explored for the investigation of new related PFAS. Up to our knowledge this is the first study of this APCI source applied to FTOHs and FOSAs/FOSEs analysis.

2. EXPERIMENTAL

2.1 Reagents and Standards

The fluorotelomer alcohols (FTOHs): 4:2 FTOH) was purchased from Fluorochem Ltd. (Derbyshire, UK), while 6:2 FTOH, 8:2 FTOH and 10:2 FTOH were supplied from Alfa Aesar GmbH & Co KG (Karlsruhe, Germany) with purity higher than 96%. Individual standard solutions of the perfluoroalkyl sulfonamides at a concentration of 50 mg L^{-1} in methanol of N-MeFOSE, N-EtFOSE and N-MeFOSA were supplied by Wellington Laboratories Inc. (Guelph, Ontario, Canada), while N-EtFOSA was purchased from Dr. Ehrenstorfer Gmbh (Augsburg, Germany) (**Table 1S)**. Individual stock standard solutions of each pure standards and the internal standard of 1000 mg L^{-1} were prepared in ethyl acetate from their respective pure standards. An intermediate standard mixture of all compounds (1 ng mL^{-1}) were obtained by dilution of the stock standard solutions in ethyl acetate and stored at 0°C.

Ethyl acetate and methanol of residue analysis grade were obtained from Sigma-Aldrich (Steinheim, Germany). In addition, ultra-pure water was obtained from a Milli-Q system coupled to an Elix 3 (Millipore, Bedford, MA, USA). Helium of high purity (≥99.98%)

was purchased from Abelló Linde, S.A. (The Linde Group, Spain). All glassware was treated with chromosulphuric acid, rinsed consecutively with Milli-Q water and acetone, and heated to 400 ºC before use.

2.2 Samples

Three water samples were collected in the Llobregat River (Barcelona, NE Spain) at the lower section. This river run through very densely populated and industrialized areas, receiving extensive urban and industrial waste water discharges from more than 3 million inhabitants. Sampling sites in the Llobregat River were located downstream of the towns of Sant Feliu de Llobregat, Sant Boi de Llobregat and el Prat de Llobregat (a total of 3 water samples). Additionally, 6 samples were also taken, 3 influent (at three different sampling times) and 3 effluent (at three different sampling times) wastewater samples of the San Feliu de Llobregat wastewater treatment plant (WWTP). Glass bottles (1000 mL) fitted with black Viton septa were filled with water without headspace and stored in the dark at 4 ºC before being analysed. Field blanks consisting of 1000 mL of natural mineral water were prepared at the same sampling points and they were analysed along with the water samples.

2.3 Sample treatment

The target compounds were extracted from water samples using solid-phase extraction (SPE) technique. The SPE procedure was carried out as follows: a volume of 1000 mL of centrifuged (if needed) water samples were passed through an Oasis HLB® cartridge (500 mg, 6 mL) (Waters, Milford, MA, USA) at a flow-rate of 10 mL min^{-1} using a Visiprep System (Supelco, Bellefonte, PA, US). Before use, SPE cartridges were conditioned with 20 mL methanol and 20 mL Milli-Q water and dried under a gentle

nitrogen stream during 15 min. After sample extraction, the cartridges were washed with 10 mL of a 5:95 mixture of MeOH/Milli-Q water and dried for 30 min. The analytes were eluted with 4 mL ethyl acetate. The extract was then evaporated under a gentle nitrogen stream at 25ºC down to 500 µL and it was transferred to a 1 mL-conic vial. Then, the extract was evaporated until 20 µL and the extract volume was adjusted to 50 µL with ethyl acetate. Finally, 2 µL of the extract was injected into the GC-MS(/MS) systems. The suitability of the method was further evaluated with a blank river water sample spiked with all the compounds at two concentration levels (1 ng L^{-1} and 10 ng L^{-1}) using Oasis HLB. Recoveries of all the compounds ranged from 80% to 97% with a relative standard deviation (RSD %) lower than 10%.

2.4 Instrumentation

2.4.1 GC-(APCI) MS/MS

Data were acquired using a GC system (Agilent 7890A, Palo Alto, CA, USA) equipped with an autosampler (Agilent 7693) and coupled to a triple quadrupole (QqQ) mass spectrometer (Xevo TQ-S, Waters Corporation, Manchester, UK), operating in APCI mode. A TraceGold™ TG-WaxMS fused-silica capillary column (100% polyethylene glycol) of 30 m x 0.25 mm I.D. and a film thickness of 0.25 µm (Thermo Scientific, USA), was used for GC separation of target compounds. The injector was operated in pulsed splitless mode (30 psi), injecting 2 µL at 250 ºC. The oven temperature was programmed as follows: 60ºC (2 min); 10ºC min^{-1} to 200ºC; 25ºC min^{-1} to 240ºC (2 min). Helium was used as carrier gas at a constant flow mode (1.4 mL min^{-1}). In the SRM method, automatic dwell time (values ranging from 9 to 46 ms) was applied in order to obtain 15 points per peak. The interface temperature was set to 240 ºC using N_2 as auxiliary gas at 250 L hr^{-1}, a make-up gas at 300 mL min^{-1} and cone gas at 170 L hr^{-1}. The APCI corona discharge

pin was operated at 1.6 µA. The ionization process occurred within an enclosed ion volume, which enabled control over the protonation/charge transfer processes. Targetlynx (a module of MassLynx) was used to handle and process the acquired data.

2.4.2 GC-(APCI)QTOF MS analysis

An Agilent 7890N gas chromatograph (Palo Alto, CA, USA) equipped with an Agilent 7683 autosampler was coupled to a quadrupole time-of-flight mass spectrometer, Xevo G2 QTOF (Waters Corporation, Manchester, UK), operating in APCI mode. The GC separation was performed as explained in the previous section. The interface temperature was set to 240 ºC and of the source to 150 ºC using N_2 as an auxiliary gas at 150 L hr^{-1}, a make-up gas at 300 mL min^{-1} and a cone gas at 16 L hr^{-1}. The APCI corona pin was operated at 1.6 µA with a cone voltage of 20 V. The Xevo G2 QTOF MS was operated at a scan time of 0.4 s acquiring the mass range *m/z* 50-650. The TOF MS resolution was approximately 18,000 (FWHM) at *m/z* 614. For MS^E measurements, two alternating acquisition functions were used applying different collision energies: a low energy function (LE), selecting 4 eV, and a high energy function (HE). In the latter case a collision energy ramp (10-40 eV) rather than a fixed higher collision energy was used. Heptacosa (Sigma Aldrich, Madrid, Spain), was used for the daily mass calibration. Internal calibration was performed using a background ion coming from the GC-column bleed as lock mass (*m/z* 257.2473).

2.4.3 GC-(EI) MS and GC-(CI) MS analysis

GC-MS determination of the target compounds using both electron ionization (EI) and chemical ionization (CI) modes were performed on a Thermo Trace GC 2000 Series gas chromatograph (ThermoFisher Scientific, Milan, Italy) coupled to a DSQ II mass

spectrometer (ThermoFisher Scientific). Chromatographic separation was carried out using the same GC conditions than those previously described. The QMS operating conditions were as follow: ion source and transfer line temperatures were set to 180°C and 240°C, respectively; electron energy was 70 eV and 120 eV for EI and CI (positive and negative modes), respectively; and an emission current of 50 µA. Methane was used as reagent for CI experiments at an optimum flow rate of 2 mL min^{-1} for PCI and 2.5 mL min^{-1} for NICI. For the optimization of the MS operating parameters full-scan data acquisition was performed over the range *m/z* 45–650 at a scan rate of 0.75 s $scan^{-1}$. After optimization, GC-MS in positive CI and working at selected ion monitoring (SIM) mode was chosen as optimum configuration for quantification purposes. Xcalibur *v* 1.4 software was used to control the instrument setup and data acquisition.

3. RESULTS AND DISCUSSION

3.1 Ionization and fragmentation behaviour under EI and CI.

In general, the electron ionization (EI) full-scan spectra of FTOHs showed a high fragmentation pattern, wherein $[CF_3]^+$ and $[CF_2\text{-}CH_2\text{-}CH_2\text{-}OH]^+$ were the most intense ions produced with a minor presence of the molecular ions (<10%) as can be seen in **Figure 1** for 8:2 FTOH. In contrast, positive CI mode showed MS spectra with an intense $[M+H]^+$ protonate molecule and a base peak corresponding to the loss of H_2O+HF. Regarding FOSAs and FOSEs, similar EI fragmentation behaviour than that found for FTOH was observed with low relative abundance for ions at high *m/z* and intense fragment ions corresponding to $[SO_2NH(CH_3)]^+$ for N-MeFOSA, $[SO_2NH(C_2H_5)]^+$ for N-EtFOSA (**Figure 1**), $[SO_2N(CH_3)(CH_2CH_2OH)]^+$ for N-MeFOSE and $[SO_2N(CH3)(CH_2CH_2OH)]^+$ for N-EtFOSE, as the base peak. For positive chemical ionization (PCI) mode, FOSAs yielded exclusively the protonated molecule $[M+H]^+$

(**Figure 1)**, while for FOSEs the base peak corresponded to $[M+H-H_2O]^+$. In negative ion chemical ionization (NICI) mode, FOSAs were the only compounds that yielded the deprotonated molecule $[M-H]^-$ with a significant abundance. The mass spectra for FTOHs were very complex involving the formation of adducts (e.g. $[M+F_2]^+$) and fragments that may arise from interaction with HF in the source. The NICI mass spectra of FOSEs showed as major characteristic fragments corresponding to $[CF_3(CF_2)_7SO_2]^-$ and $[C_8F_{16}]^-$ ions. Comparing the three ionization modes, EI yielded highly fragmented mass spectra with the absence of the molecular ion. Although PCI gave the best signal intensity for FTOHs and NICI showed the best performance for FOSAs and FOSEs, the signal intensity were lower than those frequently observed when using these ionization techniques. The instrumental limits of detection estimated for this family of compounds using GC-(PCI) MS and GC-(NICI) MS ranged from 0.8 to 1.8 pg injected, which are relatively high for environmental analysis.

3.2 Ionization and fragmentation behaviour under APCI.

The "soft" ionization behaviour of the new interface was tested using volatile FTOHs and FOSAs/FOSEs standards in solvent. Two mechanisms of ionization are commonly observed under this APCI source: i) charge transfer in which the nitrogen plasma created by the corona discharge needle promotes the formation of $M^{+\bullet}$ and ii) proton transfer, where the presence of water vapour traces in the source favours the formation of the $[M+H]^+$ ion [20]. In the case of these compounds, observed ionization mechanism was the proton transfer ionization. In this work, proton transfer mechanism was observed in the ionization of FTOHs and FOSAs/FOSEs being $[M+H]^+$ the base peak of the spectrum in all cases. It is worth to mention that negative mode was also tested, and no response was observed.

As an example, **Figure 1 (bottom)** shows the APCI spectrum of 8:2 FTOH and N-EtFOSA where the $[M+H]^+$ can be observed as base peak of the spectrum with very low in-source CID (collision induced dissociation) fragmentation degree. Cone voltage values between 5 and 50 V were tested in order to select the optimum value for each compound. No significant differences on in-source CID fragmentation pattern were observed, although voltages higher than 40 V generally led to a loss of abundance of the molecular ion and/or protonated molecule. For each compound, the optimized cone voltage that gave the highest intensity for the quasi-molecular ion (10-40 V) was selected for further experiments.

Finally, the fragmentation of the FTOHs and FOSAs/FOSEs in the collision cell was studied. The molecular ion $[M+H]^+$ was selected as precursor ions for all the compounds studied. Fragmentation was performed at collision energies in the range 5-60 eV. The main loss showed by FTOHs in the collision cell was (H_2O+HF), which was selected as the quantification transition. They also showed losses involving (H_2O+2HF+C_2H_2) or (H_2O+2HF+CF_2) groups. Other product ions obtained were C_4F_7, $C_4H_2F_5$, C_3F_5, C_3HF_4 and $C_3H_2F_3$. In all cases, the confirmation transitions (q) were quite less intense than the quantification (Q) one with q/Q ratios among 0.01-0.2. N-EtFOSA showed losses involving the groups C_2H_4 (quantification transition), SO_2 and HF while M-MeFOSA showed losses of SO_2 (quantification transition), HF and CF_2. The main loss showed by N-MeFOSE and N-EtFOSE in the collision cell was H_2O, which was selected as quantification transition. N-MeFOSE also showed the loss of (H_2O+SO_2) while N-EtFOSE showed the loss of (H_2O+SO_2+C_2H_4). Fragment ions corresponding to C_4F_7 and C_3F_5 were common to all FOSAs/FOSEs. q/Q ratios for FOSAs were found to be within 0.03-1 while for FOSEs were found to be within 0.005-0.09. Considering the observed q/Q ratios, limits of confirmation (LOC) would be around 5-15 times higher than the

limits of detection (LOD), as the most favourable confirmation transitions ratios are among 0.06-0.2 for all the studied analytes, except for N-MeFOSE for which confirmation is more favourable (q/Q=1). The selected reaction monitoring (SRM) transitions optimized for each compound are shown in **Table 1.** In some cases where the accurate mass measurements was necessary for fragmentation study, GC-(APCI)QTOF MS data was also used (see **Table 1**).

3.3 GC-(APCI) MS/MS method performance

As explained above, FTOHs, FOSAs and FOSEs showed already the presence of $[M+H]^+$ on APCI spectra even under "dry" conditions. Some "modifiers" were added in the gas phase to favour this protonation and improve sensitivity and reproducibility of the absolute response. Thus, the addition of only water or acidified water with HCOOH (0.5% v/v) as modifiers was studied and compared with the results obtained without them. The modifier was placed in an uncapped vial, which was located within a specially designed holder placed in the source door and transferred to the gas phase due to the source heat. Absolute response for $[M+H]^+$ increased around 3 times for FTOHs and around 5 times for FOSAs/FOSEs, except for N-MeFOSA (only twice) when adding simply water as modifier. Thus, the addition of HCOOH 0.5% to improve protonation was evaluated, however, a slight decrease was observed for all compounds in comparison to "dry" conditions (see **Figure 1S**). The repeatability of response (n=10 at 0.1 and 1 ng mL^{-1}) was also studied under different conditions and was found to be similar in all cases, with RSDs among 3-12%. Finally, the addition of non-acidified water as modifier was selected for further experiments.

Linearity of absolute response of analytes was established by analyzing standards solutions, in triplicate, in the range of 0.01 – 100 ng mL^{-1}. The correlation coefficients (r) were higher than 0.99, with residuals lower than 20% for all the compounds. Instrumental LODs obtained were among 1-2 fg for all the compounds (5 fg for N-MeFOSA) being always lower than those previously reported in the literature using other ionizations sources. **Figure 2** shows the excellent sensitivity that can be reached by GC-(APCI)MS/MS. At 0.01 ng mL^{-1} (10 fg injected) S/N was still around 50 for all compounds. As can be observed in **Figure 3**, the LODs (fg injected) obtained with GC-(APCI) MS/MS are even 100 times lower than those found in the literature as EI with high resolution MS (EI-HRMS), NICI-QMS (SIM) and NICI-MS/MS (SRM) [21] and also experimentally as ion trap detector (ITD) with EI-SIM (EI-ITD (SIM), EI-QMS (SIM), PCI-ITD (SIM) and PCI-QMS (SIM) [22], all of them based on the use of combinations of GC with EI, NICI and PCI with quadrupole, ion traps and high resolution mass spectrometry.

3.4 Study of matrix effects

Matrix effects were checked comparing responses of standards prepared in hexane (10 µg L^{-1}) (R1) with those of standards added into the final ethyl acetate extract obtained after applying the overall SPE procedure (10 µg L^{-1} in the extract) (R2) for three different blank water samples. Then, matrix effects were quantified by determining the R2/R1 ratio (%). As can be seen in **Figure 2S**, most of studied compounds exhibited a relative response factor between 80 and 120 %, which means that no severe matrix effects affected the response of the analytes after application of the overall analytical procedure in any of the three samples selected, so calibration could be prepared with standards in solvent

independently of the water samples analyzed. This was in contrast to other applications in food matrices, where a signal suppression was observed [15].

3.5 Analysis of water samples

The developed methodology was applied to the determination of volatiles FTOHs, FOSAs and FOSEs in nine different water samples. Also, a system blank was included in the sequence to prove the absence of laboratory contamination. Samples that had been previously analyzed by GC-(PCI) MS and reported as negative samples (< 0.1-1 ng L^{-1}) were run again by GC-(APCI)MS/MS. **Table 2** shows that concentrations found were all below 100 pg L^{-1}. Among the positive findings, those found at higher concentrations were 6:2 FTOH and 8:2 FTOH (up to 60 and 100 pg L^{-1}) while the FOSAs/FOSEs were found at lower concentrations (up to 20 pg L^{-1}). As an example **Figure 4** shows positive finding 6:2 and 10:2 FTOH and N-MeFOSA detected in water that had been previously reported as a negative sample (< 0.3 ng L^{-1}) under GC-(EI) or (PCI) MS conditions. Re-analysis by GC-(APCI) MS/MS allowed detection at concentrations as low as 3.5 pg L^{-1} clearly illustrating the improved method sensitivity for water samples. Despite de unfavorable q/Q ratios observed, all the positive findings could be confirmed with at least the presence of one confirmation transitions and the q/Q ratios within stablished tolerances (< 30% relative error).

3.6 GC-(APCI)QTOF MS analysis

During the GC-(APCI)MS/MS analysis, one additional peak was observed in the three influent wastewater samples that shared four out of the six transitions studied for the N-EtFOSA and which appeared at a slightly higher retention time (relative retention time, *r*

= 1.012 with respect to N-EtFOSA) (see **Figure 5A**). The common SRM transitions were the following: 528>416, 528>231, 528>181, 528>131. In order to try to identify this unknown compound, and due to the availability of GC coupled to (Q)TOF analyzer by APCI, full spectrum data was studied at r = 1.012 with respect to N-EtFOSA. The accurate mass of the protonated molecule of this unknown compound was determined to be *m/z* 526.9966 from the APCI spectrum, which revealed that 527.9987 would correspond to the ^{13}C isotopic ion. Isotopic pattern gave us also the information of the presence of an S atom in the structure. Elemental composition resulted on $C_{11}H_8O_2F_{17}S$. Looking at the HE spectrum (**Figure 5B**), a fragment ion with *m/z* 506.9919 corresponds to the loss of HF (1.5 mDa error). Then, product ions with *m/z* 426.9991 and 380.9780 would correspond to subsequent losses of CH_3-SO_2H (0.4 mDa error) and HF+C_2H_2 (0.8 mDa error). It is also observed the loss of 70.0056 *m/z* units that could correspond to the loss of CHF_3 (2.6 mDa error). In the low *m/z* region, product ions at *m/z* 81.0012 and 145.0078 could correspond to CH_5O_2S and $C_4H_2F_5$. With this information, we could propose for this unknown compound the structure shown in **Figure 5B** that could be explained as an analogue of 8:2 FTOH but with a methyl-sulfone moiety instead of the alcohol group. This compound was also observed in the three effluent water samples and also in the three river samples but with a signal intensity around 3% (effluent) and 1% (river) of that observed in the three influent water samples. Up to our knowledge this compound family has not been reported until now in environmental waters. In order to investigate the presence in the samples of other perfluorinated compounds belonging to this new family, and taking profit of the MS^E acquired data, low *m/z* product ions were investigated in the HE function. Extracted ion chromatograms at *m/z* 81.0010 and 145.0077 revealed the presence of another related compound at t_R = 10.71 (see **Figure 5C**). The accurate mass of the protonated molecule of this unknown compound was

determined to be *m/z* 427.0034 from the APCI spectrum at low energy. Isotopic pattern gave us also the information of the presence of an S atom in the structure. Elemental composition resulted $C_9H_8O_2F_{13}S$. Looking at the HE spectrum, losses HF, CH-SO_2H, HF-C_2H_2 and CHF_3 were also observed. This compound would be the analogue to 6:2 FTOH with the methyl-sulfone moiety instead of the alcohol group. This compound was again observed in the effluent water samples as well as in the river samples but with a signal intensity around 8% (effluent) or 4% (river) of that observed in the three influent water samples.

The presence of these methyl-sulfone analogues of 6:2 FTOH and 8:2 FTOH, encouraged us to investigate also the presence of their respective 4:2 FTOH and 10:2 FTOH methyl-sulfone analogues. Results showed that only methyl-sulfone analogue of 10:2 FTOH was also present in the three influent water samples. This fact is in accordance with the concentration levels of FTOHs in the samples, as the higher concentration levels were found for 6:2 and 8:2 FTOH (5-57 pg L^{-1} for 6:2 FTOH and 4-68 pg L^{-1} for 8:2 FTOH) (see **Table 2**).

These methyl-sulfone compounds and its relation with FTOHs structure could be explained as an oxidative process of FTOHs. For this reason, other more reductive states (methyl-sulfoxide, methyl-thio and thiol analogues) were investigated in the samples. Among them only methyl-sulfoxide analogues for 6:2 and 8:2 FTOH were present in the influent water samples. As illustrative examples of this fact, **Figure 6** shows positive findings of 6:2 and 8:2 FTOH in influent wastewater together with their respective methyl-sulfoxide (around 5 times higher than FTOHs) and methyl-sulfone analogues (among 150-250 times higher than FTOHs) using GC-(APCI)QTOF MS.

The low concentrations of fluorotelomer alcohols found as well as N-alkylated fluorooctane sulfonamides and sulfonamidoethanols would not support the hypothesis to consider them as possible atmospheric precursors of PFOA and PFOS. On the other hand, the presence of these unknown sulfone analogues of FTOHs in influent wastewater samples at 150-250 times higher than the FTOHs would deserve to consider the possibility that these new contaminants could undergo long-range atmospheric transport and be degraded in situ to form persistent PFOA and PFOS.

4. CONCLUSIONS

Ionization behavior of fluorotelomer alcohols as well as N-alkylated fluorooctane sulfonamides and sulfonamidoethanols by APCI has been studied. $[M+H]^+$ was the base peak of the spectrum in all cases giving the possibility of selecting it as a precursor ion for MS/MS experiments. The CID fragmentation showed common product ions for all FOSAs/FOSEs (C_4F_7 and C_3F_5). Nevertheless, the different functionality gave characteristic pattern fragmentations. For instance, FTOHs mainly loss (H_2O+HF), FOSAs showed the loss of SO_2 and HF, FOSEs showed the losses of H_2O and SO_2.

Linearity, repeatability and LODs have been studied obtaining instrumental LODs between 1-5 fg. Concentrations found in water samples were in the range of 1-100 pg L^{-1} showing the improvements in detection capabilities of this new technique in comparison with the traditionally used methodologies but do not support the hypothesis as possible atmospheric precursors of PFOA and PFOS. Alternatively, the new perfluoroalkyl substances related to FTOHs, might be studied as a potential source for PFOS/PFOA in the environment.

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6. FIGURE CAPTIONS

Figure 1. Spectra of 8:2 FTOH (left) and N-EtFOSA (right) under EI (up), PCI (middle) and APCI (bottom) conditions.

Figure 2. GC-(APCI) MS/MS (QqQ) chromatograms of all compounds at 0.01 µg L^{-1} (0.05 µg L^{-1} for N-MeFOSA) under proton transfer conditions (water as modifier). S/N:PtP: peak-to-peak signal-to-noise ratio

Figure 3 Instrumental limit of detections (fg) for different instrument under different ionization conditions (log scale). Box plots are defined as follows: center line, median; circle symbol, mean; boxplot edges, 25th and 75th percentiles; whiskers, range of data values.

Figure 4. Positive findings of 6:2 FTOH, 8:2 FTOH and N-MeFOSA (3.5 – 57 pg L^{-1}) in influent waste water (A,B) and river water (C), respectively, detected by applying GC-(APCI) MS/MS.

Figure 5. (A) GC-(APCI) MS/MS chromatograms for a positive finding of N-EtFOSA in an influent wastewater sample. (B) APCI accurate mass spectrum in the HE function for the unknown compound at r = 1.012 with respect to N-EtFOSA. (C) GC-(APCI)QTOF MS narrow-window-XIC of protonated molecule (*m/z* 526.9966) and fragments of the unknown compound at r = 1.012.

Figure 6. GC-(APCI)QTOF MS extracted ion chromatograms for 6:2 and 8:2 FTOHs (bottom); sulfoxide analogues (middle); sulfone analogues (top).

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Table 1. Experimental conditions of the optimized GC-(APCI)MS/MS method for FTOHs and FOSAs/FOSEs. Accurate mass measurements for their precursor and product ions measured by GC-(APCI)QTOF MS

		GC-(APCI)MS/MS					GC-(APCI)QTOF MS		
Compound	t_R (min)	Cone voltage (V)	Precursor ion *(m/z)*	Collision energy (eV)	Product ion *(m/z)*	q/Q ratio	Precursor ion *(m/z)*	Product ion *(m/z)*	Product ion assigment
4:2 FTOH	4.31	20	265	10	227	Q	265.0272	227.0098	$[M+H-H_2O-HF]^+$
				20	207	0.12		207.0038	$[M+H-H_2O-2HF]^+$
				20	181	0.20		180.9881	$[M+H-H_2O-2HF-C_2H_2]^+$
				30	157	0.06		157.0071	$[M+H-H_2O-2HF-CF_2]^+$
				30	145	0.06		145.0074	$[C_4H_2F_5]^+$
				40	131	0.05		130.9916	$[C_3F_5]^+$
				40	113	0.08		113.0012	$[C_3HF4]^+$
				20	95	0.14		95.0105	$[C_3H_2F_3]^+$
6:2 FTOH	5.25	30	365	10	327	Q	365.0205	327.0024	$[M+H-H_2O-HF]^+$
				10	281	0.02		280.9807	$[M+H-H_2O-2HF-C_2H_2]^+$
				10	257	0.01		256.9999	$[M+H-H_2O-2HF-CF_2]^+$
				40	181	0.06		180.9880	$[C_4F_7]^+$
				20	145	0.10		145.0070	$[C_4H_2F_5]^+$
				50	131	0.04		130.9914	$[C_3F_5]^+$
				40	113	0.05		113.0009	$[C_3HF4]^+$
				40	95	0.04		95.0104	$[C_3H_2F_3]^+$
8:2 FTOH	6.39	30	465	10	427	Q	465.0150	426.9980	$[M+H-H_2O-HF]^+$
				10	381	0.02		380.9754	$[M+H-H_2O-2HF-C_2H_2]^+$
				10	357	0.01		356.9945	$[M+H-H_2O-2HF-CF_2]^+$
				30	181	0.08		180.9889	$[C_4F_7]^+$
				20	145	0.12		145.0075	$[C_4H_2F_5]^+$
				30	131	0.08		130.9919	$[C_3F_5]^+$
				40	113	0.06		113.0004	$[C_3HF4]^+$
				40	95	0.05		95.0119	$[C_3H_2F_3]^+$
10:2 FTOH	7.61	30	565	10	527	Q	565.0084	526.9906	$[M+H-H_2O-HF]^+$
				20	481	0.14		480.9691	$[M+H-H_2O-2HF-C_2H_2]^+$
				20	457	0.08		456.9878	$[M+H-H_2O-2HF-CF_2]^+$
				30	181	0.09		180.9885	$[C_4F_7]^+$
				20	145	0.19		145.0074	$[C_4H_2F_5]^+$
				40	131	0.15		130.9917	$[C_3F_5]^+$
				40	113	0.07		113.0012	$[C_3HF4]^+$
				30	95	0.05		95.0117	$[C_3H_2F_3]^+$
N-EtFOSA	12.04	10	528	20	500	Q	527.9925	499.9603	$[M+H-C_2H_4]^+$
				20	436	0.13		435.9990	$[M+H-C_2H_4-SO_2]^+$
				20	416	0.13		415.9923	$[M+H-C_2H_4-SO_2-HF]^+$
				20	231	0.03		230.9853	$[C_5F_9]^+$
				30	181	0.04		180.9885	$[C_4F_7]^+$
				30	131	0.20		130.9919	$[C_3F_5]^+$
N-MeFOSA	12.6	10	514	20	450	Q	513.9758	450.0138	$[M+H-SO_2]^+$
				30	430	0.80		430.0076	$[M+H-SO_2- HF]^+$
				30	380	0.15		380.0110	$[M+H-SO_2- HF-CF_2]^+$
				30	181	0.19		180.9883	$[C_4F_7]^+$
				30	131	0.80		130.9917	$[C_3F_5]^+$
				40	111	1.00		111.0297	$[C_3H_4NF_3]^{+\bullet}$
				40	91	0.19		91.0238	$[C_3H_3NF_2]^{+\bullet}$
N-MeFOSE	13.8	40	558	20	540	Q	558.0018	539.9914	$[M+H-H_2O]^+$
				30	476	0.09		476.0302	$[M+H-H_2O-SO_2]^+$
				30	181	0.02		180.9885	$[C_4F_7]^+$
				40	131	0.07		130.9919	$[C_3F_5]^+$
N-EtFOSE	13.85	30	572	10	554	Q	572.0193	554.0074	$[M+H-H_2O]^+$
				30	462	0.06		462.0143	$[M+H-H_2O-SO_2-C_2H_4]^+$
				40	442	0.01		442.0089	$[M+H-H_2O-SO_2-C_2H_4-HF]^+$
				40	181	0.005		180.9883	$[C_4F_7]^+$
				40	131	0.03		130.9917	$[C_3F_5]^+$

Table 2. Concentrations (pg L^{-1}) of FTOHs and FOSAs/FOSEs found in the analysed water samples

Sample	4:2 FTOH	6:2 FTOH	8:2 FTOH	10:2 FTOH	N-MeFOSA	N-EtFOSA	N-MeFOSE	N-EtFOSE
River water 1	d	17.0	59.5	15.0	3.5	2.5	20.5	19.5
River water 2	d	12.5	42.0	10.0	1.0	1.5	5.0	7.0
River water 3	d	14.0	67.5	6.0	d	1.0	1.5	1.5
Influent ww 1	19.5	57.0	56.5	9.0	d	d	1.5	3.5
Influent ww 2	d	8.0	97.5	d	nd	d	d	d
Influent ww 3	d	6.0	15.5	d	nd	d	d	d
Effluent ww 1	3.0	13.5	21.5	d	nd	d	d	1.5
Effluent ww 2	d	5.0	16.5	d	nd	d	d	2.0
Effluent ww 3	d	4.5	4.0	d	nd	d	d	d

d: detected, below lowest calibration level
nd: not detected

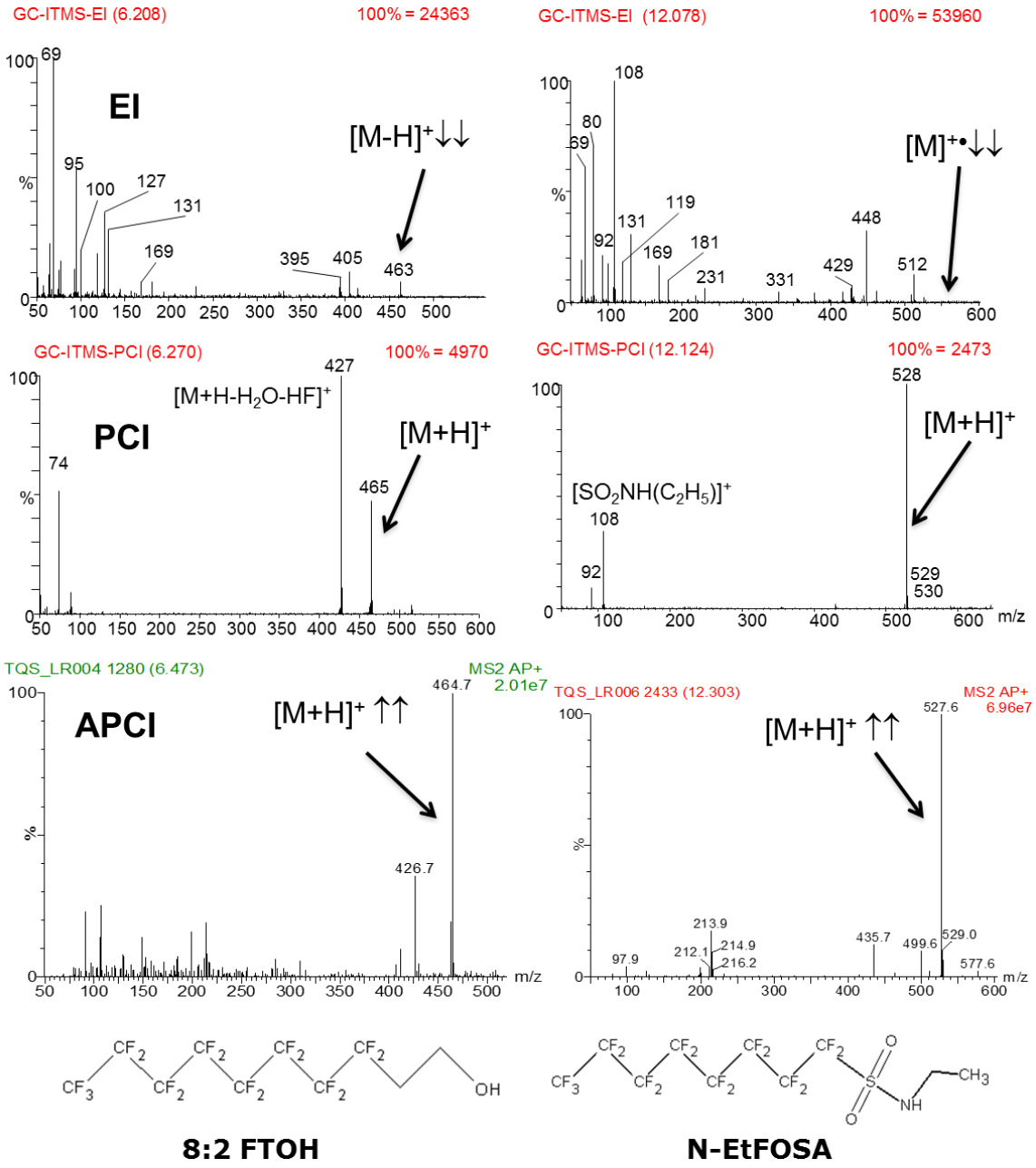

GC-ITMS-EI (6.208)
100% = 24363
EI
[M-H]+↓↓
GC-ITMS-EI (12.078)
100% = 53960
[M]+•↓↓
GC-ITMS-PCI (6.270)
100% = 4970
PCI
[M+H-H2O-HF]+
[M+H]+
GC-ITMS-PCI (12.124)
100% = 2473
[SO2NH(C2H5)]+
[M+H]+
TQS_LR004 1280 (6.473)
MS2 AP+
2.01e7
APCI
[M+H]+ ↑↑
TQS_LR006 2433 (12.303)
MS2 AP+
6.96e7
[M+H]+ ↑↑
m/z
8:2 FTOH
N-EtFOSA

Figure 1

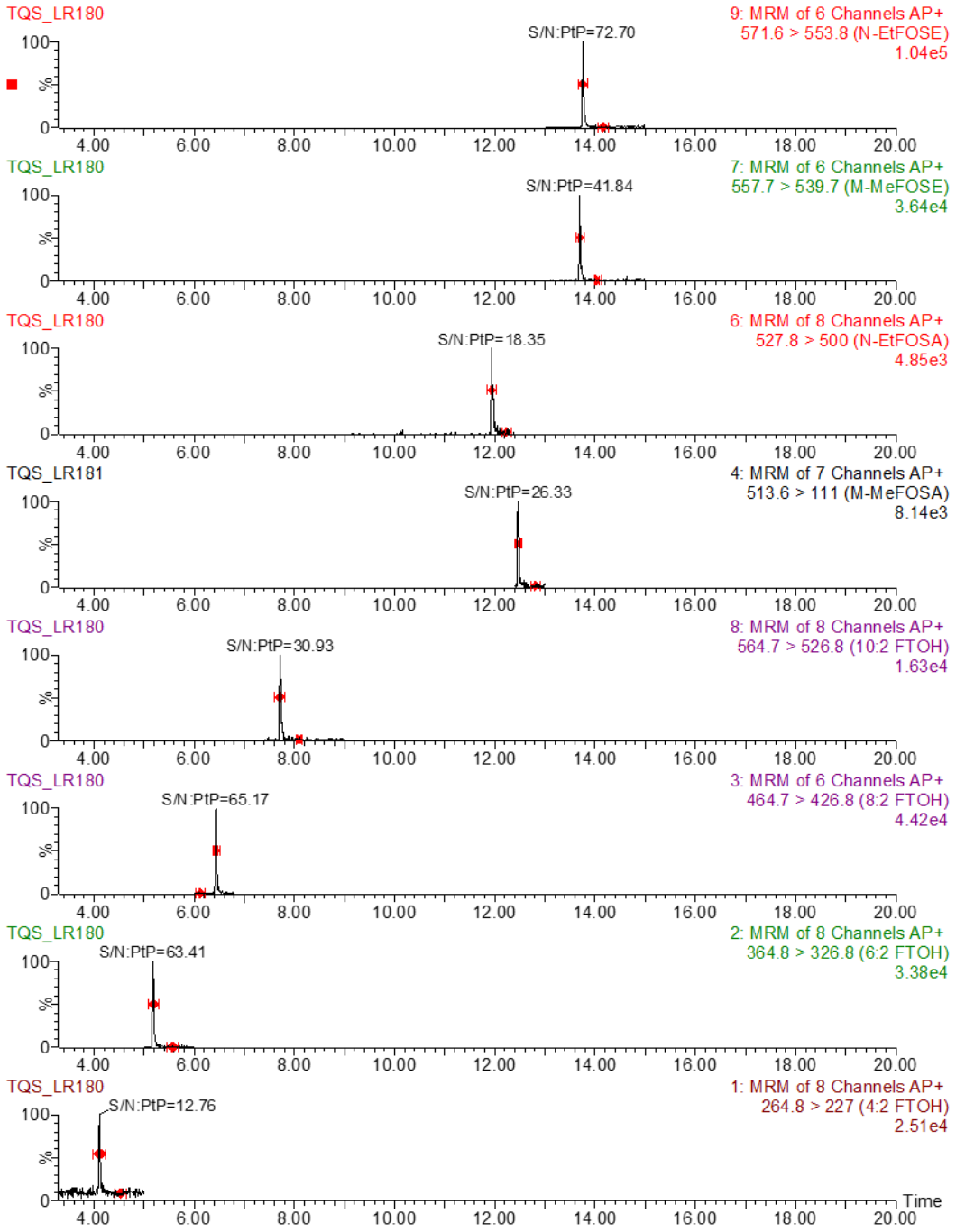

TQS_LR180
9: MRM of 6 Channels AP+
571.6 > 553.8 (N-EtFOSE)
1.04e5
S/N:PtP=72.70
TQS_LR180
7: MRM of 6 Channels AP+
557.7 > 539.7 (M-MeFOSE)
3.64e4
S/N:PtP=41.84
TQS_LR180
6: MRM of 8 Channels AP+
527.8 > 500 (N-EtFOSA)
4.85e3
S/N:PtP=18.35
TQS_LR181
4: MRM of 7 Channels AP+
513.6 > 111 (M-MeFOSA)
8.14e3
S/N:PtP=26.33
TQS_LR180
8: MRM of 8 Channels AP+
564.7 > 526.8 (10:2 FTOH)
1.63e4
S/N:PtP=30.93
TQS_LR180
3: MRM of 6 Channels AP+
464.7 > 426.8 (8:2 FTOH)
4.42e4
S/N:PtP=65.17
TQS_LR180
2: MRM of 8 Channels AP+
364.8 > 326.8 (6:2 FTOH)
3.38e4
S/N:PtP=63.41
TQS_LR180
1: MRM of 8 Channels AP+
264.8 > 227 (4:2 FTOH)
2.51e4
S/N:PtP=12.76
100
%
0
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00
20.00
Time

Figure 2

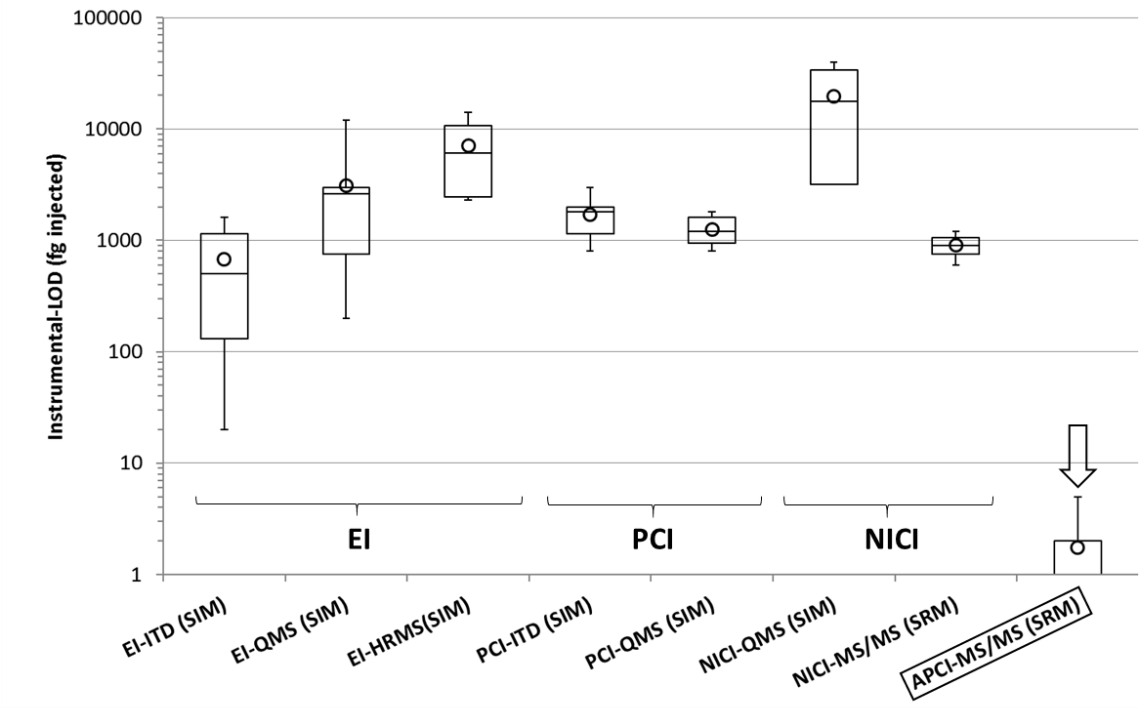
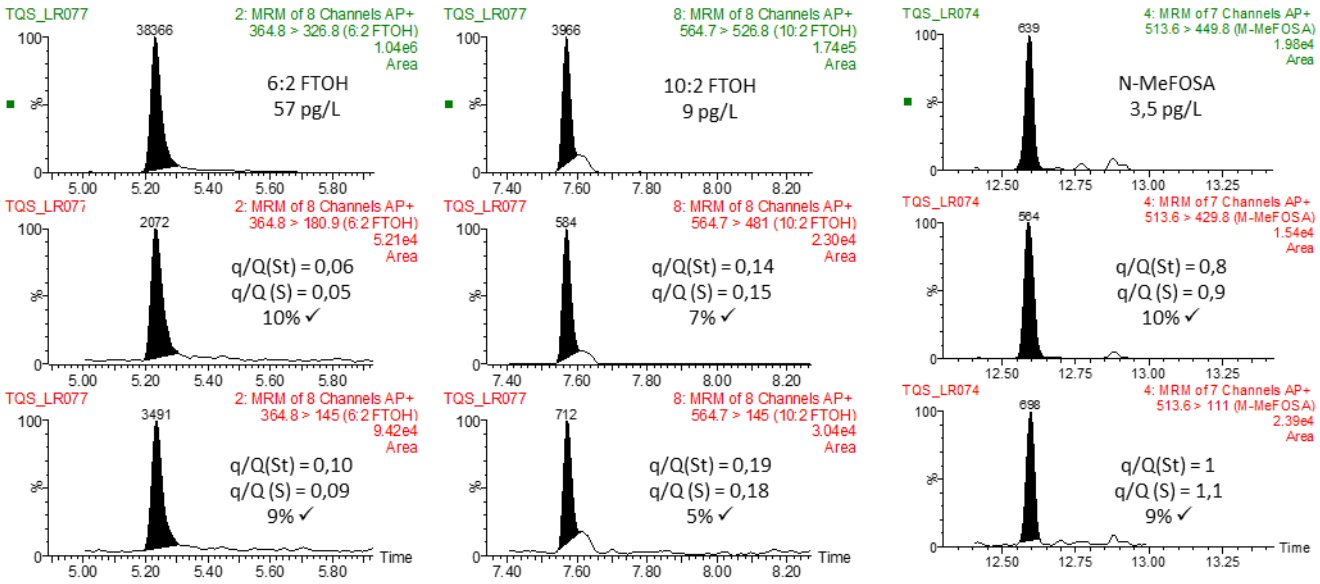

Instrumental-LOD (fg injected)
100000
10000
1000
100
10
1
EI
PCI
NICI
EI-ITD (SIM)
EI-QMS (SIM)
EI-HRMS(SIM)
PCI-ITD (SIM)
PCI-QMS (SIM)
NICI-QMS (SIM)
NICI-MS/MS (SRM)
APCI-MS/MS (SRM)

Figure 3



(A) (B) (C)

Figure 4

16

17

18

19

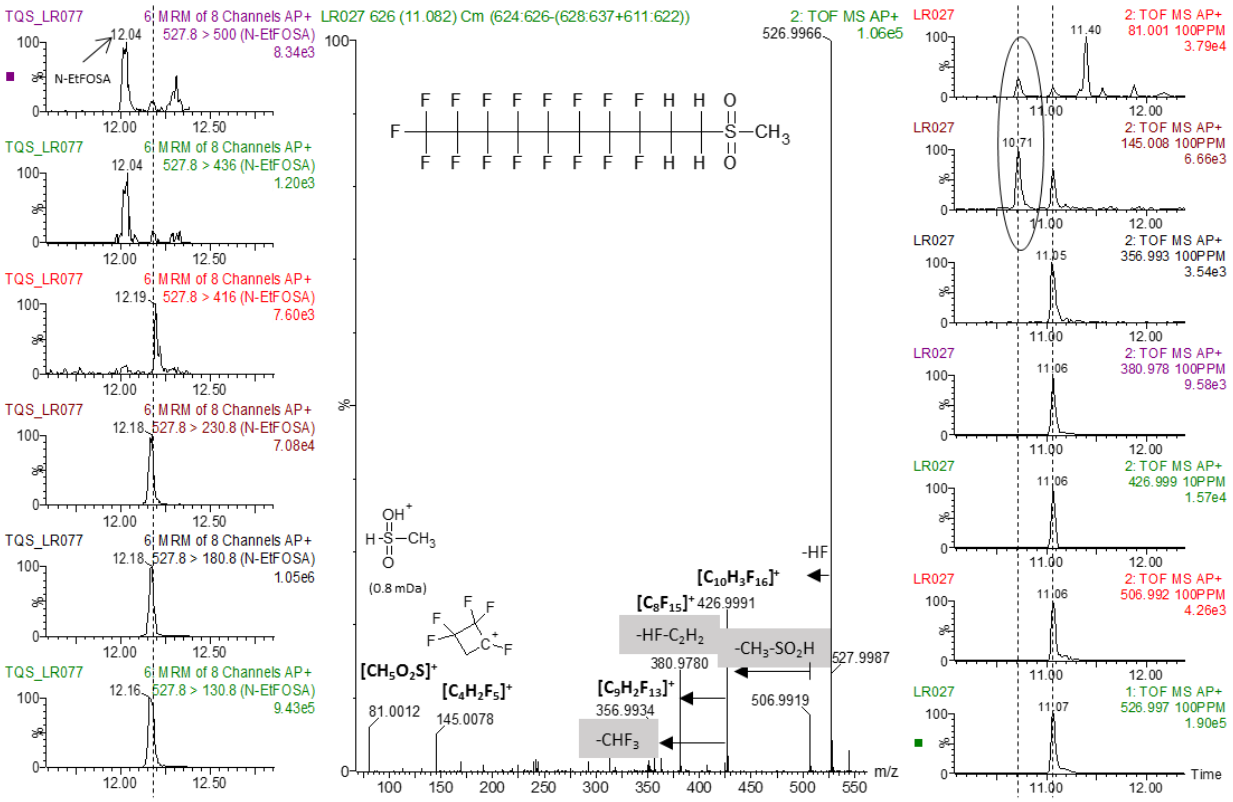


Figure 5

20

21

22

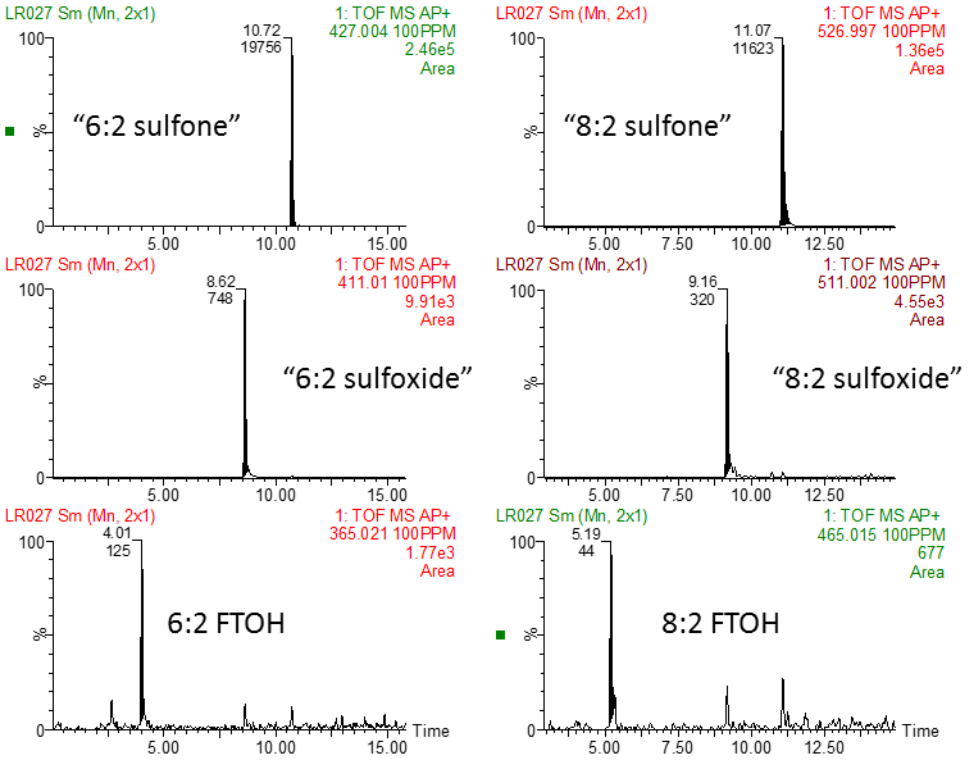

LR027 Sm (Mn, 2x1)
1: TOF MS AP+
427.004 100PPM
2.46e5
Area
10.72
19756
"6:2 sulfone"
LR027 Sm (Mn, 2x1)
1: TOF MS AP+
526.997 100PPM
1.36e5
Area
11.07
11623
"8:2 sulfone"
LR027 Sm (Mn, 2x1)
1: TOF MS AP+
411.01 100PPM
9.91e3
Area
8.62
748
"6:2 sulfoxide"
LR027 Sm (Mn, 2x1)
1: TOF MS AP+
511.002 100PPM
4.55e3
Area
9.16
320
"8:2 sulfoxide"
LR027 Sm (Mn, 2x1)
1: TOF MS AP+
365.021 100PPM
1.77e3
Area
4.01
125
6:2 FTOH
LR027 Sm (Mn, 2x1)
1: TOF MS AP+
465.015 100PPM
677
Area
5.19
44
8:2 FTOH
Time

Figure 6