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SYNOPSIS

This work describes the kinetics of performic acid autodecomposition and oxidation of organic compounds, and the most reactive functional groups leading to oxidation byproducts.

ABSTRACT

Performic acid (PFA) has gained interest as an alternative chemical disinfectant for wastewater (WW) treatment, but its reactivity with WW constituents remains poorly understood. This study evaluated PFA's ability to oxidize 45 inorganic and organic compounds commonly found in WW (amino acids, simple organic compounds with specific functional groups, e.g., amines and phenolic compounds, and pharmaceutical micropollutants). PFA does not react with most major ions, except for iodide ion, and reacts with iron(II) in the absence of phosphate buffer. While many organic molecules do not react with PFA, compounds containing reduced-sulfur moieties (e.g., thioether or thiol) are the most reactive (i.e., ranitidine, benzenethiol and 3-mercaptophenol), followed by compounds with tertiary amine groups (e.g., lidocaine). The reactions follow second-order kinetics with respect to both organic compounds and PFA concentrations. Similar trends were observed in real WW effluents, although removals of pharmaceuticals were lower than expected due to the probable consumption of PFA by WW constituents (dissolved organic carbon, other micropollutants, or transition metals). The results highlight PFA's selective reactivity with specific functional groups, and a low transformation of compounds mostly through oxygen addition (e.g., S-oxide or sulfonyl compounds formed from thiol and thioether moieties and N-oxides from amine groups) with similar mechanisms to peracetic acid.

1. INTRODUCTION

Among organic peracids, performic and peracetic acids (PFA and PAA, respectively) have recently emerged in wastewater (WW) treatment as alternative disinfectants because of their efficiency against a wide range of microorganisms[1–3] and because they are easy to implement technically.[4] The effectiveness of PFA has been demonstrated for disinfecting primary,[2] secondary,[5,6] and tertiary[7] WW, as well as combined sewer overflow (CSO) reservoirs,[8,9] with faster disinfection kinetics than PAA and/or chlorine.[5,10] Furthermore, peracids form very few disinfection byproducts (DBPs) compared to traditional disinfectants such as chlorine or ozone.[3,7,11] Under typical water treatment conditions (oxidant < 10 mg/L), the formation of halogenated DBPs and N-nitrosamines by PFA and/or PAA is negligible.[6,12] In addition, the use of PFA has been associated with the absence of toxicological effects in disinfected secondary WW.[13,14]

Due to its instability, PFA is not commercially available as a ready-to-use chemical solution and must be produced on-site through the reaction ((1) between hydrogen peroxide (H_2O_2) and formic acid (FA), which can be acid-catalyzed by a strong acid, typically sulfuric acid.[15] As the reaction is reversible, the resulting solution is a quaternary equilibrium mixture always containing FA, water, and two oxidants, PFA and H_2O_2. At the industrial scale, Kemira Oyj has developed a PFA production system that has already been implemented in Italy, Germany, and France.[5,16]

$$HCOOH + H_2O_2 \overset{H^+}{\leftrightarrow} HCOOOH + H_2O \quad (1)$$

In addition to its disinfectant properties, the oxidation potential of PFA (1.537 V/Standard Hydrogen Electrode, SHE) is higher than those of H_2O_2 (1.349 V/SHE), PAA (1.361 V/SHE), and chlorine (1.288 V/SHE), but lower than that of ozone (1.720 V/SHE).[17] Despite the growing use of PFA, little attention has been paid to its ability to react with the organic and inorganic

65 compounds commonly present in WW. A poor removal (<8%) of 8 pharmaceutical
66 micropollutants was previously reported from primary-treated WW (dissolved organic carbon
67 = 90−110 mg/L) with a PFA dose of 6 mg/L.[18] Bisphenol-A was not degraded by PFA in
68 deionized water and within 1 hour of reaction.[7] Ragazzo et al. [5] also found that PFA had poor
69 oxidation power toward phenols (at PFA doses of 0.7−1.4 mg/L for 14−30 min) or hormones
70 such as estrone (at doses of 2−20 mg/L for 30 min). As PAA and PFA have been identified as
71 weak oxidants for the removal of organic micropollutants, they require activation in order to
72 become effective oxidizers. The activation of PAA has already been tested using transition
73 metals (Cu^{2+}, Co^{2+}, Fe^{2+}, and Mn^{2+}) or UV irradiation,[19,20] which has been proven to enhance
74 the degradation of organic compounds.

75 This study aimed to acquire a deeper understanding of the reactivity of PFA and its oxidation
76 potential toward substances containing various chemical functional groups. Specifically, the
77 study aimed to: 1) investigate the reactivity of PFA in pure solutions by examining its
78 consumption by various organic and inorganic compounds potentially present in WW; 2)
79 determine the kinetic rate constants of decomposition of some simple organic compounds and
80 pharmaceutical compounds by PFA; 3) evaluate some factors that influence the reaction
81 kinetics (e.g., WW matrix, pH); and 4) identify some transformation products and elucidate the
82 reaction pathways. To the best of our knowledge, this is the first study to address these
83 objectives.

84 ## 2. MATERIALS AND METHODS
85

86 ### 2.1. Chemical Reagents

87 All the solvents and chemicals were used as received without further purification. Details
88 regarding chemicals (purity and suppliers) are provided in Text S1 (Supporting Information,

89 SI). The solutions of organic compounds were prepared in methanol, and working solutions
90 were obtained by dilution in deionized (DI) water (Milli-Q, 18 MΩ·cm).

91 2.2. PFA Preparation and Measurement

92 PFA was prepared using a method developed by Kemira (KemConnect DEX) and adapted by
93 Nihemaiti et al.,[21] consisting of two steps (31.20 mL of 99% formic acid mixed with 0.15 mL
94 of cold water and 2.65 mL of 98% sulfuric acid and 5.43 mL of this mixture reacted with 6.89
95 mL of 50% H_2O_2 for 90 min in an ice bath). The resulting PFA stock solution contained
96 approximately 19.5 ± 1.4% (233.9 ± 16.6 g/L) and 19.2 ± 1.2% (230.4 ± 13.8 mg/L) by weight
97 of H_2O_2 and PFA, respectively.

98 The quantification of high concentrations (>10 mg/L) of PFA and H_2O_2 was performed using
99 the iodometric method, as reported by Rocher & Azimi (Text S2, SI).[6] For PFA concentrations
100 <10 mg/L, the measurement was performed with the DPD colorimetric method developed by
101 Dominguez et al.[22] for PAA and adapted here for PFA (Text S2, Figure S1, SI).

102 2.3. Autodecomposition Kinetics of Peracids

103 The autodecomposition rates of PFA and PAA were determined either in DI water or in 10 mM
104 phosphate buffer solution (PBS) at different pHs (from 2.3 to 11.0). After PFA titration by the
105 iodometric method, the required volume of peracid was injected into 200 mL of PBS or DI
106 water in a beaker to achieve a peracid initial concentration of 1.8 ± 0.3 mg/L for PFA and 0.4
107 or 0.8 mg/L for PAA (respectively for pH 5.9 and 7.7). Samples were periodically taken to
108 measure the residual peracid concentration by the DPD colorimetric method. All experiments
109 were conducted at least in duplicate. Kinetic modeling was performed using COPASI.[23]

110 The autodecomposition of peracids followed first-order kinetics (eq 2).

$$\frac{\mathrm{d\,[peracid]}}{\mathrm{dt}} = -\,k_{\mathrm{peracid}} \times [\mathrm{peracid}] \qquad (2)$$

111 Where k_{peracid} is the observed first-order rate constant for PFA or PAA and [peracid] is the
112 concentration of PFA or PAA (mg/L).

113 The linearization of eq 2 (eq 3) showed a good fit with experimental values, confirming the
114 first-order kinetics, and kinetic rate constants were derived from the slope of 3 and are expressed
115 in min^{-1}.

$$\ln\left(\frac{[\text{peracid}]}{[\text{peracid}]_0}\right) = -\,k_{\text{peracid}} \times \text{t} \qquad (3)$$

116 Where $[\text{peracid}]_0$ is the initial concentration of PFA or PAA (mg/L).

117 2.4. Reactivity of PFA with Inorganic and Organic Compounds

118 The reactivity of PFA was studied by examining its consumption by 45 compounds: 7 inorganic
119 compounds (ammonia nitrogen, nitrite, bromide, iodide, chloride, iron(II), and hydrogen
120 phosphate ions), 8 amino acids (glycine, methionine, cysteine, histidine, glutamine, tyrosine,
121 tryptophan, and asparagine), 1 derived amino acid (taurine), 14 simple model organic
122 compounds [morpholine, aniline, dimethylamine (DMA), trimethylamine (TMA), urea, furan,
123 thiophene, resorcinol, phenol, hydroquinone, catechol, benzenethiol, 3-mercaptophenol and 4-
124 aminophenol], and 15 pharmaceutical compounds (diclofenac, acetaminophen, lidocaine,
125 naproxen, 17α-ethinylestradiol, carbamazepine, sulfadiazine, sulfamethoxazole, ciprofloxacin,
126 bisphenol A, tramadol, trimethoprim, ranitidine, furosemide and amoxicillin).

127 The 7 inorganic compounds were selected because they are typically present in WW, and some
128 are known to interact with various oxidants, such as ozone,[24] chlorine,[25,26] and PAA.[27]
129 Regarding organic compounds, it was important to first understand the degradation mechanisms
130 of simple functional groups (using model organic compounds) before studying the reactivity of
131 pharmaceuticals that typically contain multiple functional groups. The selection of
132 pharmaceuticals was based on their frequent detection in Parisian WW,[28] while amino acids

were studied due to their common occurrence in WW as constituents of organic matter. Two sets of experiments were conducted: one in PBS (10 mM, pH 7.0) for all compounds and another in DI water (with the initial pH adjusted at 7.1 with NaOH before PFA addition) for iron(II) only. In all experiments, the solutions of the investigated compounds were prepared at 8 μM, and 16 μM of PFA was added under stirring to initiate the reaction. After 10 min of reaction, aliquots of the solution were collected to measure the PFA consumption by each compound. All experiments were performed at least in triplicates and at 20.0 ± 1.0 °C. The PFA consumption was normalized by dividing the residual concentrations of PFA in the solution containing the compound by the concentration in the solution of PFA alone (PFA control obtained by autodecomposition), resulting in the residual concentration ratio (RCR).

2.5. Decomposition Kinetics of Model and Pharmaceutical Compounds

All decomposition kinetic rate constants were determined in 100 mL of PBS (10 mM, pH 7.0) containing 1 μM of each molecule of interest. The working solution was placed under stirring in a thermostatic chamber at 20.0 ± 1.0 °C (in an amber bottle and protected from light), and PFA was added to initiate the reaction ($[PFA]_0$ = 500 μM). In order to be in pseudo-first-order and facilitate the calculation of kinetic rate constants, the initial concentration of the oxidant was 500 (PFA) or ~900 times (H_2O_2) that of the molecule. Under these conditions, ~30% of the initial PFA concentration remained at the end of the reaction (~150 μM), which indicates that PFA was still in excess compared to the organic compound. At fixed time intervals, 1.5 mL of the sample was transferred to an amber vial containing 50 μL of 0.1 M $Na_2S_2O_3$ ($[Na_2S_2O_3]_0/[PFA]_0$ = 7) to stop the reaction before analysis (Section 2.7). Since H_2O_2 (892 μM, 30.34 ± 0.75 mg/L) is always present in the PFA working solution (500 μM, 31 mg/L), control experiments were conducted using pure H_2O_2 at the same concentration as that present in the PFA solution in order to evaluate its contribution to decomposition kinetics. All kinetic

experiments were performed in triplicates with a maximum reaction time of 30 min. Sample vials were kept at 4 °C prior to analysis.

For all model and pharmaceutical compounds, the plots of ln([organic compound]/[organic compound]$_0$) versus time showed good linearity, suggesting that the reaction was pseudo-first-order with respect to the organic compound, and the observed rate constant, k_{obs} (min^{-1}), was derived from the slope. The decomposition of the model and pharmaceutical compounds by PFA can thus be described as second-order kinetics (eq 4), and the kinetic rate constants, k_{app} ($M^{-1}\,s^{-1}$), were calculated by dividing k_{obs} by the initial concentration of PFA.

$$\begin{aligned} &\frac{\mathrm{d}\,[\text{organic compound}]}{\mathrm{dt}} \\ &= -\,k_{obs} \times [\text{organic compound}] \\ &= -\,k_{app} \times [\text{PFA}] \times [\text{organic compound}] \end{aligned} \tag{4}$$

where k_{obs} (min^{-1}) is the observed kinetic rate constant for the pseudo-first-order and k_{app} ($M^{-1}\,s^{-1}$) is the second-order rate constant for the organic compound; [PFA] and [organic compound] are the concentrations of PFA and the organic compound, respectively.

2.6. Reactions in Wastewater Effluent

Treated WW effluent was collected from the Seine Amont WWTP located in Valenton, France, as previously described.[21] Samples were collected directly before the discharge channel and were filtered upon arrival in the laboratory through a 0.7 μm glass fiber filter (Whatman). The WW quality parameters were as follows (mean ± standard deviation (SD) over three samples): pH 7.9 ± 0.1, total suspended solids 5.5 ± 2.8 mg/L, UV254 1.1 ± 0.6, nitrite 0.55 ± 0.12 mg/L as N, ammonium 1.56 ± 1.00 mg/L as N, phosphate 3.08 ± 0.93 mg/L as P, dissolved organic carbon 8.06 ± 0.73 mg/L, and temperature 22.9 ± 0.6 °C.

Batch oxidation experiments were conducted on the actual WW effluent without pH adjustment. The effluent was spiked with 7 pharmaceutical compounds at 1 μg/L (~4×10^{-3} μM)

each: ranitidine (RAN), lidocaine (LID), furosemide (FUR), diclofenac (DCF), acetaminophen (ACT), sulfamethoxazole (SMX), and carbamazepine (CBZ). The analysis of the non-spiked WW sample revealed the presence of these pharmaceuticals at various concentrations (C_0, ranging from 0.25 μg/L for SMX to 1.25 μg/L for DCF, except RAN which was never detected, and FUR and ACT reached, respectively, ~3 and 15 μg/L in one sample). The 7 pharmaceuticals were spiked in WW in order to detect them after oxidation and to calculate their removals. PFA was added to the sample at 5 different concentrations (1, 2, 5, 10, and 100 mg/L equivalent to 16, 32, 81, 161, and 1613 μM) under constant stirring. $Na_2S_2O_3$ was added in excess after 1 h to stop the reaction before extraction and analysis (see Section 2.7). All experiments were conducted at least in duplicate.

2.7. Analytical Methods

Organic compounds used in kinetics experiments were quantified using high-performance liquid chromatography coupled to a diode array detection (HPLC-DAD, PD-M20A, Shimadzu). Analytical details (stationary and mobile phases elution gradient) are described in Text S3 (SI), and the operating wavelengths with maximum UV absorbance for all compounds are reported in Table S1 (SI).

The 7 pharmaceutical compounds spiked in WW effluent samples were analyzed by ultrahigh-performance liquid chromatography (UPLC) coupled with tandem mass spectrometry (MS/MS) with triple quadrupole detection (Acquity-TQD, Waters) after extraction using an automated solid-phase extraction (SPE) system (Dionex Autotrace 280, Thermo Scientific) with multilayer SPE cartridges as described previously.[21,29] Analytical details (stationary and mobile phases, internal standards, elution gradient, and ionization mode) and the MS/MS acquisition parameters are provided in SI (Text S3, Table S2).

The transformation products (TPs) were characterized by high-resolution mass spectrometry (HRMS) using UPLC coupled with ion mobility time-of-flight mass spectrometry (Vion IMS-QTof, Waters) and equipped with an ESI source. The analysis was performed in both negative and positive ionization modes, and mass spectra were acquired in $HDMS^E$ (data independent analysis) mode to obtain low and high collision energy fragments. All information regarding the instrument parameters and the method was published previously.[21]

3. RESULTS AND DISCUSSION

3.1. Autodecomposition Kinetics of Peracids

Since PFA solutions are unstable, the autodecomposition rates of PFA and PAA were determined at different pH levels (ranging from 2.3 to 11.0) in PBS (prior experiments showed no influence of phosphate ion, Text S4) to understand their behavior in the absence of other compounds. All autodecomposition experiments followed first-order kinetics for both PFA (Figure 1) and PAA (Figure S2).

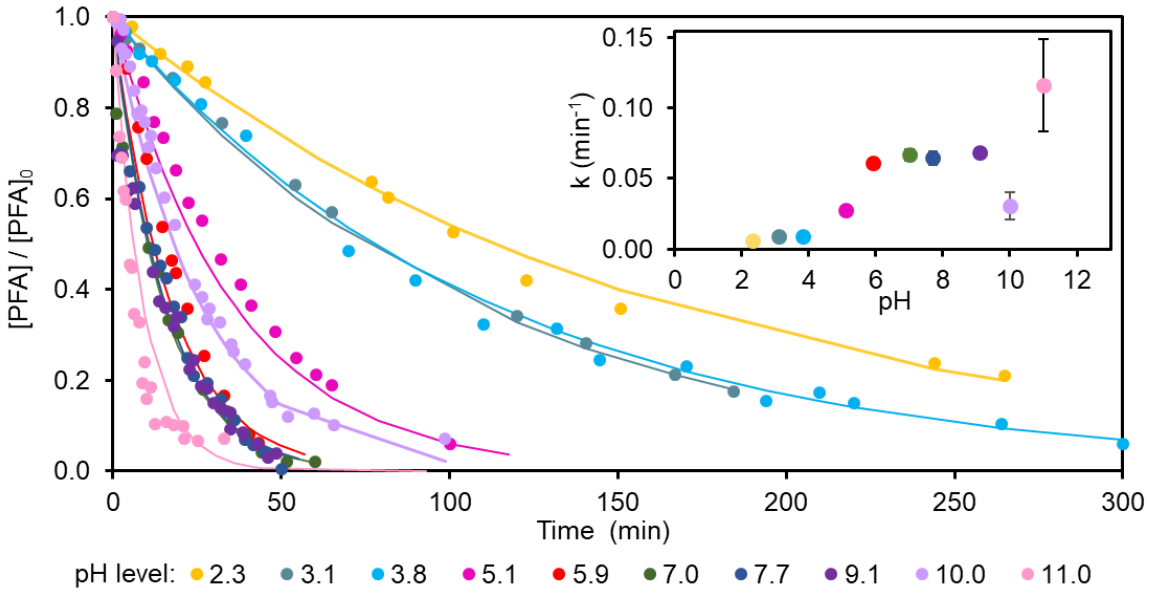


Figure 1. Autodecomposition of PFA in 10 mM phosphate buffer solution (PBS) at various initial pH levels, except for pH 3.8 representing the autodecomposition of PFA in DI water

without controlling pH (see Text S4). $[PFA]_0$ = 1.8 ± 0.3 mg/L (29 μM). Errors bars on the rate constant values represent standard deviation from triplicate experiments.

The autodecomposition of PFA generally increased with increasing pH as reported for PAA,[30,31] showing similar decomposition rates between pH 5.9 and 9.1 and a decrease at pH 10.0 (Figure 1). The autodecomposition of PFA was much slower at acidic pH (k_{PFA} = 6.1×10^{-3}, 9.3×10^{-3}, and 2.8×10^{-2} min^{-1} at pH 2.3, 3.1, and 5.1, respectively). Such a low degradation of PFA in acidic conditions and a higher degradation above pH 7.0 were reported in simulated combined sewer overflow waters.[8] This is in accordance with previous research showing that high acidity has a stabilizing effect on PFA.[15] In addition to its hydrolysis (reverse reaction in eq 1), PFA is generally considered to follow a decomposition reaction as described in eq 5.[15,32,33]

$$HCOOOH \rightarrow CO_2 + H_2O \quad (5)$$

Kinetic modeling using eqs 1 and 5 could not explain the higher decomposition rates obtained near neutral pH and the restabilization at pH 10 because the kinetic constants proposed in the literature were obtained in acidic conditions (either with formic acid only or in the presence of sulfuric or phosphoric acid). The high decomposition rate observed in our study around the pK_a value of PFA (7.1[7,34]) was consistent with a spontaneous decomposition of PFA by reaction between its acidic form (PFAH) and its basic form (PFA^-) (eq 6), as reported for PAA in several studies.[31,35,36]

$$HCOOOH + HCOOO^- \rightarrow 2\,HCOO^- + O_2 + H^+ \quad (6)$$

The decrease in PFA decomposition at pH 10 can thus be explained by a lower presence of PFAH, limiting the occurrence of this reaction. Base-catalyzed reactions with hydroxide ions (OH^-) or the presence of carbonate ions (from the dissolution of carbon dioxide in the solution)

however probably played a role in the higher decomposition rate observed at pH 11. Kinetic modeling was attempted by introducing such reactions and the speciation of carbonate and phosphate ions (Figure S3D and E), but some discrepancies remained between the model and the experimental data (Table S3, Figure S4). Further research would be needed to fully elucidate the role of all present species and to provide a comprehensive kinetic model. In contrast to PFA, PAA was stable in both acidic and neutral pH conditions, and its lower autodecomposition was confirmed at pH 7.7 (k_{PAA} = 3.1 × 10^{-3} min^{-1} and k_{PFA} = 6.5 × 10^{-2} min^{-1}) and at pH 5.9 (k_{PAA} = 3.6 × 10^{-3} min^{-1} and k_{PFA} = 6.5 × 10^{-2} min^{-1}) (Figure S2). This result agrees with previous findings that demonstrate the low decomposition of PAA in the pH range of 5.5 to 8.2.[30] In these experiments performed in DI water, the high stability of PAA compared to PFA can be attributed to its longer carbon chain, as aliphatic peracids tend to become more stable with longer chain lengths.[37]

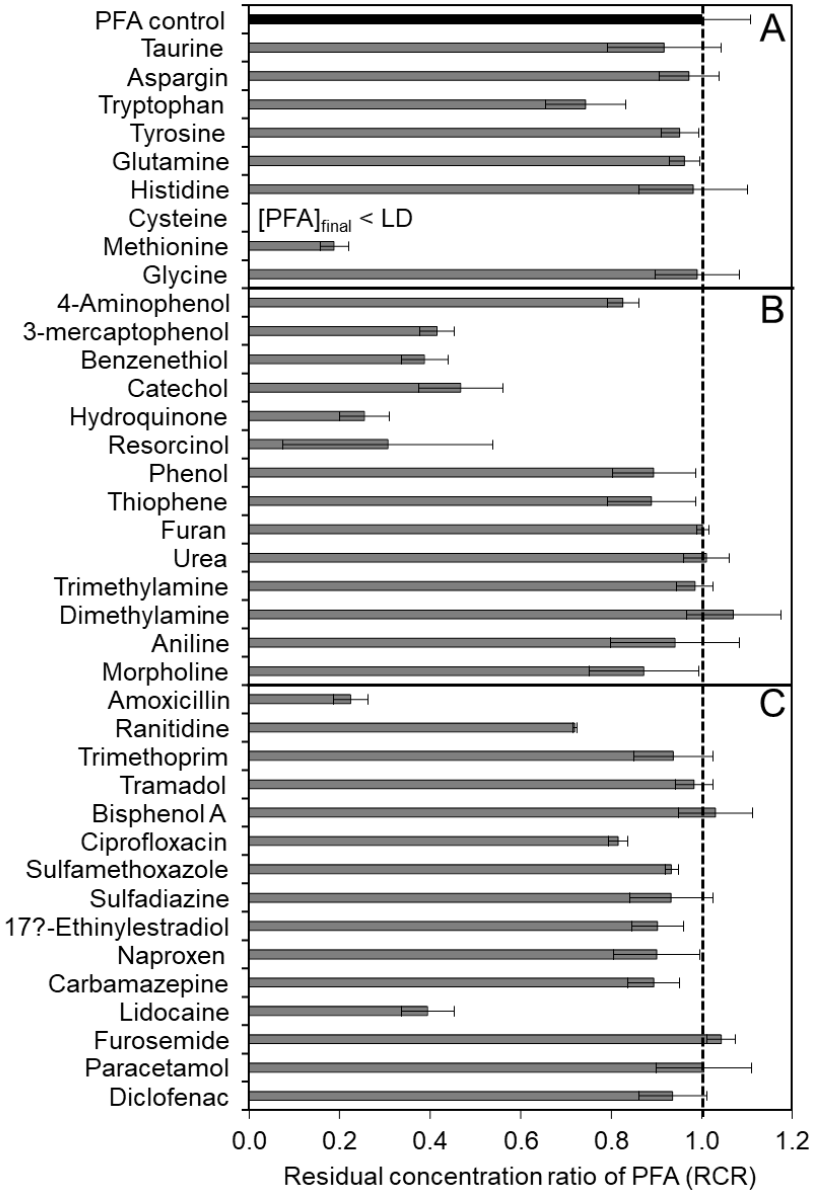
3.2. Reactivity of PFA with Inorganic and Organic Compounds

The reactivity of PFA with inorganic and organic compounds was first assessed by measuring the consumption of PFA by various compounds after 10 min of reaction to quickly identify the most reactive chemical structures. The PFA consumption results were expressed as residual concentration ratio (RCR, i.e., PFA residual normalized with the PFA autodecomposition).

Among the 7 inorganic ions studied (i.e., ammonia nitrogen, nitrite, bromide, iodide, chloride, iron(II) and hydrogen phosphate ions), only iodide ion consumed PFA in PBS (Figure S5). In DI water, reduced iron (Fe^{2+}) exhibited a different reactivity, consuming around 20% of PFA (Figure S5). The difference in PFA consumption in PBS (pH 7.0) and DI water (pH 7.1) for Fe^{2+} suggests that hydrogen phosphate ion can act as a chelating compound and decrease the consumption of PFA by Fe^{2+}. This effect has also been observed for PAA (DI water, pH 7.5),

where the presence of hydrogen phosphate ions decreased the impact of Fe^{2+} on PAA decomposition.[27]

Among the 9 amino acids, cysteine, methionine, and, to a lesser extent, tryptophan were the most reactive with PFA (Figure 2A). PFA was completely consumed by cysteine (RCR = 0), which is consistent with the high reactivity of cysteine with PAA[38] and the recent findings by Wang et al.,[39] showing the higher reactivity of cysteine and methionine with PFA. The reactivity of tryptophan with PFA is also in agreement with the reactivity of protein-like compounds (such as tryptophan and tyrosine) measured by fluorescence spectroscopy during the disinfection of WW.[6] In addition, the lack of PFA consumption by tyrosine, glutamine, histidine, and glycine, indicating their lower reactivity, is consistent with the results of Wang et al.,[39] who reported rate constants lower than 0.1 $M^{-1} s^{-1}$ for these amino acids at neutral pH (7.1).



273

274 Figure 2. Relative consumption of 16 μM of PFA by 8 μM amino acids (A), model organic
275 compounds (B), and pharmaceutical compounds (C) at pH 7.0, 20.0 ± 1.0 °C, and 10 min of
276 reaction time. Results expressed as residual concentration ratio (RCR). The black bar
277 corresponds to the RCR of PFA self-decomposition (RCR = 1), and gray bars correspond to the
278 RCR of PFA in the presence of an organic compound. Values close to zero (as for cysteine)
279 indicate significant consumption of PFA. $[PFA]_{final}$ < LD means that the residual concentration
280 of PFA is lower than the detection limit after 10 min of reaction.

281

PFA reacted with 9 of the 14 model organic compounds: resorcinol, hydroquinone, benzenethiol, 3-mercaptophenol, 4-aminophenol, thiophene, morpholine, aniline and phenol (Figure 2B). The reactivity of metalloles (derivatives of cyclopentadiene in which a carbon atom is replaced by a heteroatom) increased when they contained a sulfur heteroatom instead of an oxygen heteroatom (i.e., thiophene compared to furan). The strong reactivity of thiophene with PAA has been previously demonstrated during the oxidation of subbituminous carbons, resulting in the formation of sulfate ions or sulphone compounds.[40] PFA was slightly consumed by phenol and very slightly by aniline (considering the standard deviation of RCR results). The reactivity of substituted benzenic compounds largely increased with the addition of a second electron-donating group such as hydroxyl (−OH) (resorcinol, hydroquinone, and catechol compared to phenol, and 4-aminophenol compared to aniline). The presence of a thiol group (−SH) instead of hydroxyl (−OH) also dramatically increased the reactivity of the molecule (benzenethiol compared to phenol) but the addition of another −OH group to benzenethiol (3-mercaptophenol) did not increase its reactivity.

Out of the 15 pharmaceutical compounds investigated, 8 were found to react with PFA: amoxicillin, ranitidine, ciprofloxacin, sulfamethoxazole, sulfadiazine, 17α-ethinylestradiol, carbamazepine, and lidocaine (Figure 2C). For naproxen and trimethoprim, no significant PFA consumption was observed given the variability of the results. PFA weakly reacted with some aromatic and amide compounds (e.g., 17α-ethinylestradiol and carbamazepine) as well as compounds containing aromatic amine groups (e.g., sulfamethoxazole and sulfadiazine), in accordance with the results obtained with aniline. This reactivity of aromatic amine compounds was also demonstrated for PAA, with an oxygen attack occurring on the aromatic ring.[41] PFA was highly reactive with other organic compounds containing reduced-sulfur or nitrogen moieties (e.g., amoxicillin, ranitidine, and lidocaine). The high consumption of PFA by lidocaine is in accordance with a previous study and can be attributed to the reactivity of the

307 deprotonated tertiary amine group to form lidocaine N-oxide.[21] In contrast, the very low
308 reactivity of tramadol, which also has a tertiary amine group, can be attributed to the absence
309 of its deprotonated form at pH 7.0 (pK_a = 9.23).[21] Carbamazepine, another compound with a
310 tertiary amine moiety in a non-protonated form, also showed low consumption of PFA. This
311 can be attributed to the higher stability of the nitrogen atom in the tertiary amine group due to
312 steric hindrance and/or the electron-withdrawing effect of the aromatic rings and the carbonyl
313 group.[42] The moderate consumption of PFA by ciprofloxacin can be explained by its secondary
314 amine heteroatom group similar to morpholine that showed comparable consumption of PFA.
315 Ciprofloxacin also has tertiary amine groups but similar to carbamazepine, they were probably
316 not reactive due to their high stability and inability to be protonated (no pK_a on these nitrogen
317 atoms) or attacked by oxygen. Compounds containing secondary amine groups (e.g.,
318 diclofenac, acetaminophen, sulfadiazine, furosemide, or trimethoprim) did not consume or were
319 very weakly reactive with PFA, which can be explained by similar stabilization effects.
320 Dimethylamine and trimethylamine also did not consume any significant amount of PFA,
321 indicating that N-oxide formation requires the presence of groups that destabilize the molecule
322 (e.g., electron-donating groups). Given the low reactivity of PFA with phenol and
323 primary/secondary amines, the high reactivity of amoxicillin should be attributed to other
324 functional groups such as the thioether sulfur heteroatom. The reactivity of this thioether group
325 of *β*–lactams has been demonstrated with PAA, generating sulfoxide products.[43] Taking into
326 account all these results, the moderate consumption of PFA by ranitidine could be explained by
327 the reactivity of both its thioether and deprotonated tertiary amine groups. Taurine, sulfadiazine
328 and sulfamethoxazole, while sulfur-containing, have a fully oxidized sulfur atom (i.e., sulfonyl
329 moiety, O=S=O), which results in their very low PFA consumption, as previously reported for
330 their reactivity with PAA.[41]

These results especially demonstrate the high reactivity of compounds containing reduced-sulfur moieties such as thiol and thioether groups (cysteine, methionine, benzenethiol, 3-mercaptophenol, amoxicillin, and ranitidine), as well as deprotonated tertiary amine groups destabilized by electron-donating groups. This reactivity follows similar trends as that of ozone since it has been demonstrated that tertiary amines have a higher reactivity with ozone than secondary amines due to the inductive effects of alkyl groups and also that the deprotonated form of amines is generally more reactive than the protonated form.[42,44]

3.3. Kinetics of Organic Compound Oxidation by PFA

Since PFA consumption could be biased by the presence of transformation products (TPs) with potential PFA reactivity, further experiments were carried out to study the oxidation kinetics of 13 organic compounds (chosen among model and pharmaceutical compounds) by monitoring their degradation. A control experiment revealed that there was no significant difference in PFA consumption in the presence or absence of the organic compound (Figure S6). This supports the assumption of pseudo-first-order kinetics with respect to the organic compound and shows that in these conditions, PFA remained in excess and its degradation was mainly due to its autodecomposition (i.e., negligible consumption by organic compounds). Other control experiments also showed no contribution of background H_2O_2 concentration to the degradation of organic compounds (Text S5).

3.3.1. Kinetic Constants of Model Compounds

The kinetic constants of 6 model organic compounds, containing only one aromatic ring, were determined (Table 1). The compounds included 2 sulfur molecules containing thiol groups (benzenethiol and 3-mercaptophenol) and 4 phenolic molecules (phenol, resorcinol, hydroquinone, and catechol). The kinetic reactivities followed similar trends to PFA consumptions (Section 3.2), with sulfur molecules and benzenediols showing higher reactivity

355 compared to simple phenol. PFA completely oxidized benzenethiol and 3-mercaptophenol in
356 less than 1 min (Table S4) so their rate constants (k_{PFA}) were estimated to be greater than 2×10^2
357 $M^{-1} s^{-1}$. The reactions of the 4 phenolic compounds followed second-order kinetics with respect
358 to both the organic compound and PFA concentrations. Their apparent rate constants (k_{app})
359 ranged from 0.04 ± 0.01 to 3.04 ± 0.06 $M^{-1} s^{-1}$ at pH 7.0, with phenol being the least reactive
360 and catechol the most reactive molecule. The kinetic rate constants of the various types of
361 benzenediols showed clear differences depending on the position of −OH substituents despite
362 similar PFA consumption observed for them (Table 1 and Figure 2B). This confirms that adding
363 a second −OH substituent to phenol plays a crucial role in the reactivity of phenolic compounds
364 with PFA but also reveals that its relative position influences the oxidation rate. The ortho
365 position of the –OH group in catechol enhanced its reactivity compared to hydroquinone (para
366 position) and resorcinol (meta position). The enhanced reactivity of phenolic compounds
367 containing multiple –OH substituents can be attributed to an increase in electron density from
368 electron-donating groups, as previously observed for PAA.[41] The reported k_{PAA} values for
369 phenol and catechol (0.08 ± 0.04 and 33.00 ± 0.40 $M^{-1} s^{-1}$ at pH 5, respectively [41]) were in the
370 same range as k_{PFA} (0.04 ± 0.01 and 3.04 ± 0.06 at pH 7.0, respectively) (Table 1).

371 3.3.2. Kinetic Constants of Pharmaceutical Compounds

372 The kinetics of 7 pharmaceutical compounds were studied (Table 1): ranitidine (RAN),
373 lidocaine (LID), furosemide (FUR), diclofenac (DCF), acetaminophen (ACT),
374 sulfamethoxazole (SMX), and carbamazepine (CBZ). Similar to PFA consumption, the highest
375 reactivities were observed for compounds containing reduced-sulfur and deprotonated amine
376 moieties. RAN (containing a thiother and a tertiary amine group) was fully degraded by PFA
377 in less than 30 seconds, so its k_{PFA} was estimated to be greater than 2×10^3 $M^{-1} s^{-1}$. LID and
378 FUR (two secondary amines with no reduced-sulfur group) were moderately degraded with
379 k_{PFA} values of 2.24 ± 0.14 and 0.41 ± 0.18 $M^{-1} s^{-1}$, respectively. A similar kinetic rate constant

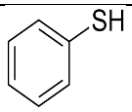
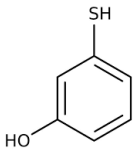
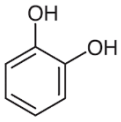
was obtained for LID in a previous study (k_{PFA} = 2.76 ± 0.37 M^{-1} s^{-1} at pH 7.0).[21] Additional experiments performed with FUR confirmed the increase of its k_{obs} with increasing PFA concentrations, in accordance with second-order oxidation kinetics (Text S6, Figure S7). Three other pharmaceutical compounds (SMX, DCF, ACT) exhibited weaker reactivity with PFA (kinetic rate constants in the range from 0.11 to 0.14 ± 0.02 M^{-1} s^{-1}), in the same range as those observed for simple phenolic molecules (Table 1). CBZ was the least reactive compound, with a rate constant of 7.15 ± 0.97 × 10^{-3} $M^{-1}.s^{-1}$. Different trends between oxidation rate constants were observed compared to the PFA consumption of the same molecules (i.e., a lower PFA consumption of RAN than that of LID and a similar or even higher PFA consumption for CBZ than those of SMX, DCF, ACT, and FUR). As mentioned earlier, PFA consumption of some molecules could be increased by the formation of more reactive TPs, while some highly reactive molecules (e.g., RAN) could form less-reactive TPs resulting in decreased PFA consumption.

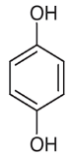
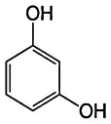
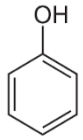
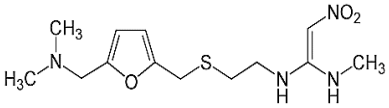
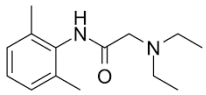
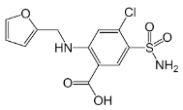
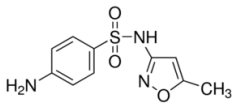
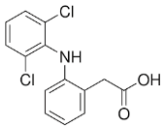
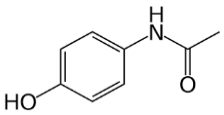
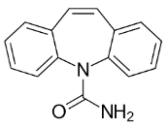
Similar to these results obtained with PFA, the high reactivity of reduced-sulfur compounds (e.g., cysteine and methionine) with PAA has been described, with k_{PAA} values ranging from ~5 to > 6 × 10^2 M^{-1} s^{-1}.[38] The kinetic rate constants of cysteine and methionine have recently been evaluated for both PFA and PAA, with values reaching >1 × 10^5 M^{-1} s^{-1}.[39] This was attributed to the strong susceptibility of the reduced sulfur atom to electrophilic attack, corresponding to an electron transfer mechanism.[38,39] The k_{PFA} values of CBZ, SMX, DCF, ACT, FUR, and LID were in the same range as the k_{PAA} values reported for similar nitrogen-containing compounds (from 2.5 × 10^{-3} to 1.6 × 10^1 M^{-1} s^{-1}).[41] The k_{PFA} of some investigated pharmaceutical compounds (SMX and DCF) were about 100 times higher than their reported k_{PAA} values (Table 1).[41] Some other molecules exhibited lower reactivity with PFA than with PAA (i.e., 5 times lower k_{PFA} for CBZ, 10 times lower k_{PFA} for catechol, and a slightly lower k_{PFA} for phenol). This suggests that PFA and PAA globally share similar reaction pathways for certain types of molecular groups, but the oxidation power of PFA can vary greatly depending

405 on the targeted molecule, being either lower or higher than that of PAA. This reactivity
406 difference could also be due to the pH values, as the k_{PAA} values were reported at pH 5.0,[41]
407 while the pH level in the present study was 7.0. Other differences in experimental conditions
408 (e.g., different buffer species, different ratios between reactive species, or the presence of
409 unknown reactive species formed during the degradation of peracids) could also play a role in
410 these different behaviors. Kinetics of LID and DCF decomposition at different pH showed a
411 much stronger reactivity at neutral or alkaline pH, suggesting a major role of the PFA
412 deprotonated form (PFA^-) (Text S7, Figures S3, S8). An even more diverse set of molecular
413 structures should be investigated to fully understand the reactivity of PFA and potentially
414 predict the kinetic rates of organic molecules (e.g., with quantitative structure–activity
415 relationship models). Overall, PFA was found to be less oxidative than ozone toward the studied
416 pharmaceuticals, as indicated by the significantly higher kinetic rate constants reported in the
417 literature for ozone (from 10^4 to $>10^6$ M^{-1} s^{-1}).[45,46]

418 Table 1. Second-Order Rate Constants (k_{app}, M^{-1} s^{-1}) of Model Organic and Pharmaceutical
419 Compounds Oxidation by PFA. Experimental conditions: $[compound]_0$ = 1 μM, $[PFA]_0$ =
420 500 μM. k_{PAA} from Kim &Huang[41] at pH 5.0 and 22.0 °C.

421

compounds	**structure**	k_{PFA} **(M^{-1} s^{-1})**	k_{PAA} **(M^{-1} s^{-1})**
benzenethiol		$> 2 \times 10^2$	
3-mercaptophenol		$> 2 \times 10^2$	
catechol		3.04 ± 0.06	3.33 ± 0.40 x10^1

hydroquinone		0.80 ± 0.21	
resorcinol		0.10 ± 0.02	
phenol		0.04 ± 0.01	$8.00 \pm 0.40 \times 10^{-2}$
ranitidine		$> 2 \times 10^{3}$	
lidocaine		2.24 ± 0.14	
furosemide		0.41 ± 0.18	
sulfamethoxazole		0.14 ± 0.02	$3.7 \pm 0.10 \times 10^{-3}$
diclofenac		0.13 ± 0.03	$3.1 \pm 0.80 \times 10^{-3}$
acetaminophen		0.11 ± 0.02	
carbamazepine		$7.15 \pm 0.97 \times 10^{-3}$	$3.4 \pm 0.40 \times 10^{-2}$

3.4. Influence of the PFA Dose in Environmental Water Matrices

The reactivity of the 7 pharmaceuticals for which oxidation kinetics are determined in Section 3.3 (RAN, LID, FUR, SMX, DCF, ACT, and CBZ) was investigated in real WW effluent to

assess the effect of the WW matrix. The water quality parameters of the WW sample were described in Section 2.6.

The removal of the chosen micropollutants in real WW was low and very selective. RAN was the best-eliminated compound, and its removal increased from 10 to 99% when the PFA concentration varied between 1 and 100 mg/L (16 to 1613 μM) (Figure 3). CBZ, ACT, and DCF were recalcitrant to PFA oxidation, showing low removals (<10%) at all concentrations. SMX also exhibited low removals, but some increase was observed at 100 mg/L (1613 μM), reaching ~18%. FUR and LID were slightly removed at PFA concentrations <5 mg/L (81 μM) and their removal significantly increased at higher concentrations. Contrary to RAN, their removal did not exceed 35% even at the highest concentrations. In addition, a slightly negative removal (−5%) was obtained for FUR at a 1 mg/L PFA concentration, which can be considered as not significant due to analytical uncertainties (e.g., discrepancies in the extraction of internal standards and matrix effects), especially at low concentrations of micropollutants.

Overall, even though most pharmaceuticals exhibited lower removals than expected after 1 h based on their oxidation rate constants in PBS, their reactivities in WW followed the same trends (Section 3.3), with RAN being the most reactive compound followed by LID and FUR. In PBS and at pH 7.0, 1 μM of LID and FUR resulted in 91 ± 1 and 38 ± 10% removal, respectively, with 31 mg/L (500 μM) of PFA (Figure S9). At 100 mg/L (1613 μM) of PFA and at the pH of the WW effluent (7.9), it was expected that their removal rates would be even higher especially since LID has been found to be more reactive at pH 8.0 than at pH 7.0 (k_{app} of 2.24 ± 0.14 and 7.54 ± 0.90 M^{-1} s^{-1} at pH 7.0 and 8.0, respectively).[21] The decrease of organic micropollutants (OMP) removal in real WW can be related to the presence of total suspended solids (TSS), organic matter (OM), and other species that could consume PFA (e.g., transition metals such as Fe^{2+}, Cu^{2+}, and Mn^{2+}) and thus compete with the OMP removal. More

systematic experiments (e.g., with synthetic OM) are needed to understand such competition effects during PFA oxidation.

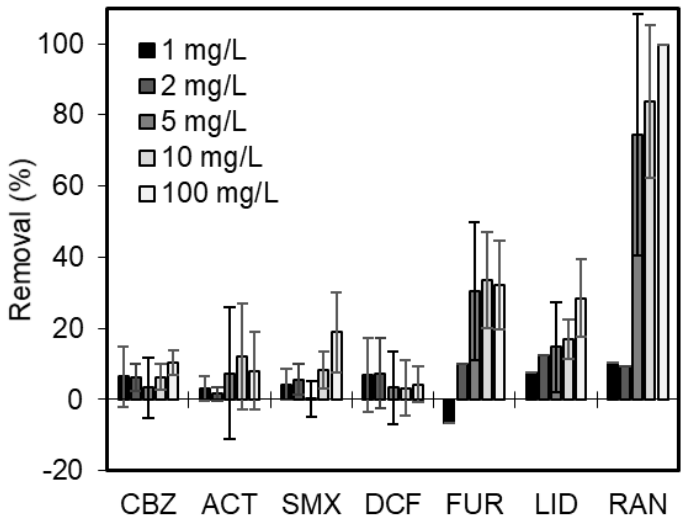


Figure 3. Removal of pharmaceuticals in wastewater by PFA. Experimental conditions: [Pharmaceutical compound]$_0$ = C_0 + 1 μg/L (~4×10^{-3} μM) spiked in WW, with C_0, the initial concentration of the compound in the WW effluent, reaction time = 60 min, pH = 7.88 ± 0.10, 20.0 °C, [PFA]$_0$ = 1, 2, 5, 10, and 100 mg/L (16, 32, 81, 161, 1613 μM). Error bars represent the standard deviation from triplicate samples.

3.5. Identification of Oxidation Byproducts

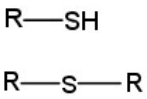
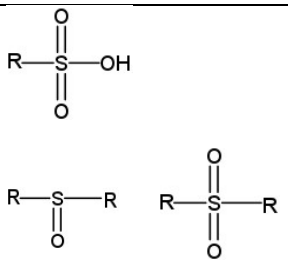
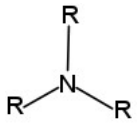
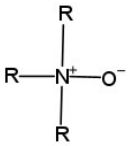
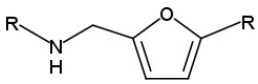
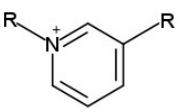
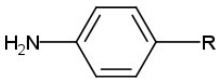
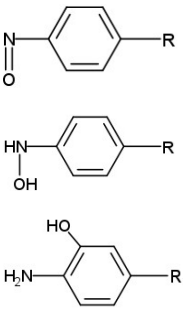
To better understand the oxidation mechanisms of organic compounds by PFA, TPs produced by the reaction between PFA and individual solutions of organic compounds in 10 mM PBS (pH 7.0) were characterized by HRMS. Among the model organic compounds (Sections 3.2 and 3.3), only benzenethiol (BZT), 3-mercaptophenol (3MP), and catechol (CTL) were studied, as the other compounds or their TPs were not adequately detected. The exact masses of the parent compounds and their TPs, as well as their detection parameters and main fragments, are

467 described in Tables S5 and S6, and the detailed identifications for each parent compound are
468 described in Text S8 (SI).

469 For both model organic and pharmaceutical compounds, the addition of oxygen atoms on
470 specific functional groups (such as thioether, thiol, and tertiary amine) was the major
471 mechanism observed, with N-oxides, S-oxides, or hydroxylated compounds being the main
472 observed types of TPs (Table 2). The oxidation of thiol compounds (BZT and 3MP) resulted in
473 the addition of three oxygen atoms (i.e., sulfonic acid compounds), and the oxidation of the
474 thioether group in RAN formed the S-oxide (1 additional oxygen atom) and sulfonyl (2 oxygen
475 atoms) analogues. Compounds containing tertiary amine groups (RAN and LID) formed N-
476 oxides (as previously reported for LID[21]), and SMX (aniline moiety) formed hydroxylated TPs.
477 Similar mechanisms were reported for PAA oxidation[38,41,43,47] and ozonation,[48,49] suggesting
478 similar sites of attack by these three oxidants. This is also in accordance with the higher
479 reactivity of compounds containing reduced-sulfur or amine molecular groups (Sections 3.2
480 and 3.3). The TPs of SMX confirmed that aniline is a reactive site, even if its reactivity is very
481 weak (considering the low consumption of PFA by SMX, sulfadiazine and aniline itself). Other
482 TPs with no addition of oxygen but a rearrangement of aromatic rings (pyridiniums) were also
483 detected from FUR and RAN. The formation of pyridinium of FUR was previously reported
484 during anodic oxidation or with electro-Fenton process.[50,51] The TPs identified in this study
485 were chemically similar to their parent compounds, and almost no TPs of lower mass could be
486 detected. This indicates a low transformation effect of PFA even for the most reactive
487 compounds (i.e., sulfur-containing compounds such as RAN, BZT or 3MP), leading to their
488 low mineralization. This should however be confirmed with other analytical techniques to target
489 smaller, more polar or more volatile TPs (e.g., gas chromatography coupled to mass
490 spectrometry).

491

Table 2. Reactive Sites of the Studied Organic Compounds with the Possible Pathways and Produced Byproducts for PFA Oxidation, from the Most Reactive (1) to the Least Reactive (4) Site (Based on Kinetic Constants Shown in Table 1).

reactive site of studied organic compounds	reactive site structure	reaction mechanism	possible oxidation byproducts (OBPs)
(1) reduced-sulfur moiety (thiol and thioether) (e.g., 3MP, BZT, RAN)		O addition	
(2) tertiary amine (e.g., LID, RAN)		O addition	
(3) furan ring with secondary amine at the benzylic position (e.g., FUR, demethylated RAN)		ring rearrangement	
(4) aniline (e.g., SMX)		O addition, hydroxylation	

N-oxides are known to be persistent and not biodegradable,[44,52] and some aromatic N-oxides have been shown to induce genotoxicity or to be potential carcinogens.[53,54] The stability and persistence of other main TPs produced from PFA (S-oxide, sulfonyl compounds) should thus

499 be evaluated to assess their potential impact in comparison to their parent molecules as well as
500 their respective toxicity.

501 ## 4. ENVIRONMENTAL IMPLICATIONS

502 The increasing implementation of PFA disinfection units in WWTPs highlights the need to
503 understand the effect of PFA on inorganic and organic compounds as well as its behavior under
504 various conditions (e.g., pH, presence of OM). Autodecomposition experiments revealed that
505 PFA was more stable in acidic conditions compared to neutral or alkaline conditions.
506 Conversely, the oxidation of DCF and LID was more effective in alkaline conditions. The
507 influence of the deprotonated form of PFA (PFA^{-}) and its enhanced oxidation power while
508 experiencing higher autodecomposition requires further investigation. Systematic PFA
509 decomposition studies are still lacking to provide a comprehensive kinetic model that accurately
510 reflects the behavior of PFA at various pH levels.

511 Major inorganic ions (such as ammonium, nitrite, bromide, chloride, and orthophosphate ions)
512 did not consume PFA, indicating a low impact on the optimal dose of PFA to be used in
513 WWTPs. PFA demonstrated a high selectivity towards specific organic moieties (e.g., reduced
514 sulfur and tertiary amines), with apparent low transformation and mineralization of organic
515 compounds, even for highly reactive ones (i.e., sulfur-containing compounds such as ranitidine,
516 benzenethiol, or 3-mercaptophenol). This suggests a low concern for the formation of numerous
517 and toxic TPs during PFA disinfection as compared to other oxidation processes. However, it
518 is crucial to evaluate the stability, persistence, and potential toxicity of S-oxides, sulfonyl, or
519 N-oxides compounds in the environment to assess their impact compared to their parent
520 molecules. The high selectivity of PFA toward reduced sulfur is also consistent with recent
521 findings showing its high reactivity with cysteine and methionine, responsible for its specific
522 disinfection properties (i.e., bacterial inactivation through accumulation in cells and
523 intracellular oxidation).[39]

Due to the presence of TSS, OM and/or transition metals, pharmaceutical compounds were less effectively eliminated in real WW compared to PBS. The impact of TSS has been observed on PFA disinfection,[6] but it would require further investigation regarding oxidation reactions as well as the competition between OM and micropollutants.

Overall, PFA does not appear to be an efficient oxidant for the advanced treatment of micropollutants. Therefore, future research could focus on its activation (e.g., through irradiation or metals) to enhance the removal of organic compounds while still utilizing its advantages in disinfection.

SUPPORTING INFORMATION

The Supporting Information is available free of charge e at

https://pubs.acs.org/doi/10.1021/acsestwater.3c00279.

Additional analytical details, effect of several parameters (phosphate ion, background H_2O_2 concentration, PFA initial concentration, pH) on PFA autodecomposition and oxidation kinetics, additional kinetics results, species distribution diagrams of PFA and selected micropollutants or inorganic ions, HRMS detailed identifications and the corresponding reaction pathways, and HRMS spectra of micropollutants and their transformation products.

NOTES

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

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QTOF and HPLC-DAD analysis, Michael Rivard for synthesizing and providing pyridinium of furosemide, Maysar Bouslah, Melissia Ben-Iken, and Ilyess Taibi for their contributions to the experiments, and Lila Boudahmane for her assistance with laboratory experiments.

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