Predicting the Congener-Specific Environmental Behaviour of Perfluorinated Acid Contaminants Using Semi-Empirical Computational Methods

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Introduction

- Perfluorinated acids (PFAs) are contaminants detected worldwide in a range of abiotic and biotic environmental matrices
- Two major classes of PFAs include the perfluorinated sulfonic acids (PFSAs) and perfluorinated carboxylic acids (PFCAs)

- Both classes are considered persistent, bioaccumulative, and subject to long-range transport
- Both generally have low rates of hydrolysis, direct photolysis, and biodegradation/metabolism in environmental systems (*1,2*)
- Current research and regulatory efforts focussed on the straight-chain members of each PFA class and homologue group, primarily because these congeners are the major components of technical mixtures and are also available as pure standards
- Numerous potential branched congeners in each PFA class are a poorly understood family of contaminants whose environmental and toxicological properties may be more important than the straight-chain members
- Current work applied established quantitative structure and reactivity (QSAR) models for other multi-class emerging and legacy contaminants to estimate key parameters related to the congener-specific environmental fates of PFSAs and PFCAs

Methods

- Number of PFA congeners increases exponentially with perfluorinated chain length
- Practical to compute properties for all congeners only up to ~C_8 (there are 161 C_1 through C_8 congeners)
- Then look for statistical relations between chain length and C_1 through C_8 properties to extend our understanding to ≥C_9
- Semiempirical molecular descriptors were calculated for all C_1 through C_8 PFSA and PFCA and the straight-chain C_9, C_{10}, and C_{11} PFCA congeners
- Initial geometry optimization using MM2 followed by energy minimization and computations using AM1 and PM3 basis sets

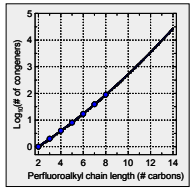


Figure 1. Relationship between number of congeners in each homologue group and the perfluoroalkyl chain length (PCL). The actual number of congeners in each homologue group was determined for C_1 through C_8 and extrapolated for C_9 though C_{12}. A second-order polynomial regression equation of the form $\log_{10}$(# of congeners) = -0.5 + 0.248 × PCL + 0.00758 × PCL² (r^2=0.9999) is shown.

Results

1. Bioconcentration Factors (BCFs)

- Model developed with regressions between computed molecular areas and volumes and BCFs reported for straight-chain C_6 to C_8 PFSAs and C_7 to C_{11} PFCAs (*3*)
- Used to estimate BCFs for all C_4 through C_8 PFSA and PFCA congeners ⇨ PFSAs ~10-fold higher BCFs than PFCAs

Area-based approaches result in a more continuous C_4 to C_8 BCF distribution and significant homologue mixing versus volume-based approach = homologue isolation

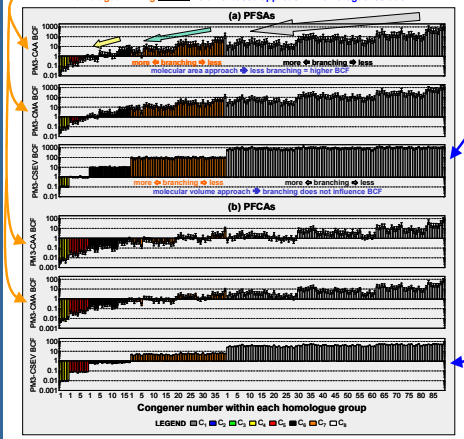


Figure 2. Estimated BCFs of all C_4 through C_8 (a) PFSA and (b) PFCA congeners based on correlations with the calculated Connelly accessible area (CAA), Connelly molecular area (CMA), and Connelly solvent excluded volume (CSEV) using the PM3 semiempirical basis set (AM1 data not shown for brevity). Values represent the mean BCF value from the correlations. Error bars signify lower and upper error limits based on the regression relationships.

Summary statistics for the PFSA and PFCA C_4 through C_8 BCF training sets can be reliably predicted ➔ allows reliable estimation of homologue-specific BCF distributions for ≥C_9

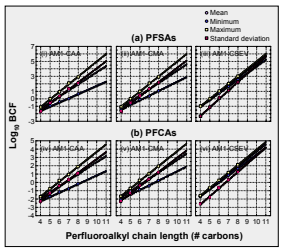


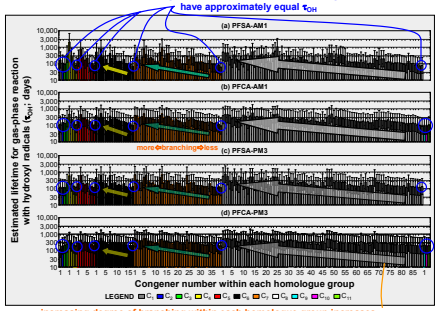
Figure 3. Predicted mean, minimum, maximum, and standard deviation of estimated BCFs for C_4 through C_{11} (a) PFSA and (b) PFCA congeners using the calculated Connelly accessible areas (CAA; (i) and (iv)), Connelly molecular areas (CMA; (ii) and (v)), and Connelly solvent excluded volumes (CSEV; (iii) and (vi)) with the AM1 and PM3 semiempirical basis sets. Regression lines were developed based on calculated BCFs for all C_4 through C_8 PFSA congeners.

Results

2. Atmospheric Reaction with Hydroxyl Radicals (k_{OH})

- Model developed with well-established regressions between ionization potentials (IPs) and k_{OH} values for a wide range of aliphatic compounds (*4-6*)
- Calibrated for PFAs using published experimental k_{OH} data for the C_1-C_4 straight chain PFCAs (*7*), C_1-C_8 fluorotelomer alcohols/aldehydes (*8-10*), and C_4 perfluoroalkyl sulfonamide derivatives (*11,12*)
- Used to estimate atmospheric lifetimes (τ_{OH}) for all C_1 through C_8 PFSA and PFCA and the straight-chain C_9, C_{10}, and C_{11} PFCA congeners ⇨ PFSAs and PFCAs have ≅ τ_{OH}

straight-chain members of each homologue have approximately equal τ_{OH}

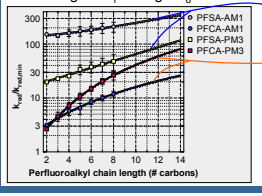


increasing degree of branching within each homologue group increases τ_{OH}
branching effect more important than chain length for τ_{OH}

Figure 4. Estimated atmospheric lifetimes of the C_1 through C_8 PFSA and PFCA and C_9, C_{10}, and C_{11} straight-chain PFCA congeners using the AM1 ((a) and (b)) and PM3 ((c) and (d)) basis sets.

3. Abiotic Reductive Defluorination Rates (k_{red})

- Recent work shows qualitative proof-of-principle that C_2-C_8 PFSAs can be reductively defluorinated (*13,14*)
- Model developed with established relationships between the energy of the lowest unoccupied molecular orbital (e_{LUMO}) and surface-area normalized reduction rate constants (k_{red}) using zero-valent metal reductants (*e.g.*, Fe, Mg) across a range of halogenated aliphatic and aromatic contaminants (*15-17*)
- In absence of quantitative PFA k_{red} "benchmarks", values were normalized to the minimum estimated k_{red} within each basis set among all C_1 through C_8 PFSA and PFCA congeners ($k_{red}/k_{red,min}$)



PFSAs about 0.5-2 orders of magnitude more amenable to reduction than PFCAs

Figure 5. Estimated average relative rates of abiotic reductive defluorination within each C_1 through C_{14} homologue group for PFSAs and PFCAs. Regression lines were developed based on calculated BCFs for all C_4 through C_8 PFSA congeners. Error bars show standard deviations in $k_{red/red,min}$ within each homologue group.

Results

Both AM1 and PM3 basis sets predict higher reductive defluorination rates for the more branched PFSA congeners in each homologue group

➔ no similar trends expected for PFCAs (chain-length effect dominates)

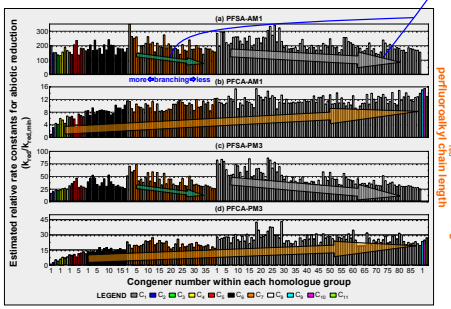


Figure 6. Estimated relative rate constants for the abiotic reductive defluorination ($k_{red}/k_{red,min}$) of the C_1 through C_8 PFSA and PFCA and C_9, C_{10}, and C_{11} straight-chain PFCA congeners using the AM1 ((a) and (b)) and PM3 ((c) and (d)) basis sets.

Conclusions and Recommendations

- Findings provide guidance for:
  - developing new analytical methods for separating and identifying PFAs in environmental and technical mixtures
  - prioritizing efforts on synthesizing authentic standards
  - focussing toxicological studies on the congeners most likely to be of concern
- Molecular area approach to estimating BCFs suggests wide variability within homologue groups ⇨ while volume approach indicates low variability:
  - **need to determine which model best applies** via targeted synthesis of selected congeners and BCF testing
  - *e.g.*, (C_8 PFSA-23) perfluoro-1,1',2,2'-tetramethylbutylsulfonic acid predicted to have **BCF >120-fold higher using volume versus area**
  - *also*, (C_8 PFCA-28) perfluoro-2,2,3,3'-tetramethylbutylcarboxylic acid predicted to have **BCF >100-fold higher using volume versus area**

Acknowledgements

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