Theoretical Studies on Perfluorinated Acids of Environmental Significance

by

Abdel Hidalgo Puertas

B.Sc., University of Havana, Cuba, 2001

A Thesis Submitted in Partial Fulfillment of the
Requirements for the Degree of

MASTER OF SCIENCE

in the Department of Chemistry

University of Victoria

Theoretical Studies on Perfluorinated Acids of Environmental Significance

by

Abdel Hidalgo Puertas

B.Sc., University of Havana, Cuba, 2001

Supervisory Committee

Dr. Nelaine Mora-Diez, (Department of Chemistry, Thompson Rivers University, Kamloops, BC)
Supervisor

Dr. Alexander G. Brolo, (Department of Chemistry)
Departmental Member

Dr. Irina Paci, (Department of Chemistry)
Departmental Member

Supervisory Committee

Dr. Nelaine Mora-Diez, (Department of Chemistry, Thompson Rivers University, Kamloops, BC)
Supervisor

Dr. Alexander G. Brolo, (Department of Chemistry)
Departmental Member

Dr. Irina Paci, (Department of Chemistry)
Departmental Member

Abstract

A new approach for predicting octanol-water partition coefficients (Log P) of linear perfluorinated compounds, making use of the limited experimental data available, previous observations and the consistent similarities observed between the experimental and calculated (with electronic structure methods and using EPI suite) slopes of the linear plots of Log P values with the number of carbon atoms (N = 2 to 11) is described here. Eight families of linear organic compounds were investigated: carboxylic acids, perfluorinated carboxylic acids, sulfonic acids and perfluorinated sulfonic acids, together with their corresponding conjugate bases. To the best of our knowledge, this work reports the first application of density functional theory methods to the calculation of Log P values of perfluorinated compounds. A second part of the thesis, describes the study of the thermodynamic stability of the PFOA family of 39 structural isomers with the M06-2X, LC-ωPBE, B97D and B3LYP functionals and with the PM6 method. The PM6 results closely resemble the M06-2X results for neutral PFOAs, but greatly disagree regarding anions. The four functionals applied behave similarly from a qualitative point of view, but quantitatively speaking, the LC-ωPBE and B97D results are between the M06-2X and B3LYP stability results. M06-2X ranks highly substituted isomers as more stable than did B3LYP, and ranks less-branched isomers quite low in relative stability compared to B3LYP. Various similarities with a former PFOSs study applying the M06-2X and B3LYP functionals have been identified. The degree of branching within structural isomers cannot always be precisely determined, and is not the only aspect that determines thermodynamic stability; the pattern of substitution seems to also play a significant role.

Table of contents

List of Figures

List of Tables

List of Acronyms

BO	Born-Oppenheimer
HF	Hartree-Fock
MO	Molecular orbital
STO	Slater-type orbital
AO	Atomic orbital
DZ	Double-zeta
TZ	Triple-zeta
DFT	Density functional theory
KS	Kohn-Sham
LDA	Local density approximation
LSDA	Local spin-density approximation
GGA	Generalized gradient approximation
SCRF	Self-consistent reaction field
PCM, D-PCM	Polarizable continuum model
IPCM	Isodensity polarizable continuum method
SMD	Continuum solvation model where the D stands for density
UAHF	Radii; United-atom HF (PCM method)
UFF	Radii; it places a sphere around each solute atom, with the radii scaled by a factor of 1.1
IEF-PCM	Integral equation formalism-PCM
PFAs	Perfluorinated acids
PFAAs	Perfluoroalkyl acids

PFCAs	Perfluorocarboxylic acids
PFSAs	Perfluorosulfonic acids
PFCs	Perfluorocarboxylates
PFSs	Perfluorosulfonates
TCG_{gas}	Gas-phase thermal correction to the Gibbs free energy
EPI	Estimation program interphase
SMILES	Simplified molecular input line entry system
SI	Supporting information
PFOSs	89 structural isomers of perfluorooctane sulfonic acid
PFOAs	39 structural isomers of perfluorooctane carboxylic acid
AD	Absolute differences
ECF	Electrochemical fluorination
MAD	Mean of absolute differences

List of Symbols

$\widehat{H}$	Hamiltonian operator
Ψ	Wave function
χ_i	Spin orbital
H_{ii}^{core}	One-electron Hamiltonian
J_{ij}	Coulomb integrals
K_{ij}	Exchange integrals
V_{NN}	Energy of inter-nuclear repulsion
ϕ_i	Molecular orbitals
θ_i	Basis function
α_{i}	Expansion coefficient
$\mathrm{E}_{\mathrm{corr}}$	Correlation energy
$\mathrm{E}_{\mathrm{limiting\ HF}}$	Limiting Hartree-Fock energy
$\mathrm{E}_{\mathrm{Exact}}$	Non-relativistic exact Schrödinger energy
$\rho(\mathrm{r})$	Electron density
E_0	Ground-state molecular energy
$\rho_0(x, y, z)$	Ground-state probability density
∇_i^2	Laplacian operator
$v(r_i)$	Potential energy due to the interaction of electrons and nuclei
Z_α	Atomic number. For 1 electron system Z = 1
r	Distance from electron to nucleus
$\hbar$	Dirac constant or reduced Planck constant

m_e	Mass of the electron
V_{Ne}	Potential energy due to electron nuclei atraction
V_{ee}	Electron-electron repulsion energy
E^{avg}	Average ground-state enegry
T^{avg}	Average on kinetic energy
χ_i^{KS}	Kohn-Sham spin orbitals
ϕ_i^{KS}	Spatial component of Kohn-Sham spin orbitals
σ_i	Spin function
E_{xc}	Exchange-correlation energy
ε_x	Exchange energy
ε_c	Correlation energy
$\nabla\rho$	Gradient of the electron density
B88	Becke's functional
PWx91	Exchange component of Perdew-Wang functional from 1991
LYP	Lee-Yang-Parr functional
PWc86	Correlation component of Perdew and Wang's 1986 functional
PWx86	Exchange component of Perdew and Wang's 1986 functional
PBE	Perdew-Burke-Ernzerhof's functional
B3LYP	Hybrid DFT functional B3 + LYP
M05, M06, M05-2X, M06-2X, M06-L, M06-HF, M08-SO, M08-HX, M11	Minnesota functionals. M06-2X is a global hybrid functional with 54% HF exchange
P95	Becke's τ-dependent gradient-corrected correlation functional

TPSS	Exchange functional of Tao, Perdew, Staroverov, and Scuseria
LYP	Lee-Yang-Parr functional
B3PW91	Becke's 1991 functional
α_0, α_x, α_c	Non-local parameter of B3LYP functional
B97, B97-1, B97-2, B98	Family of functionals proposed by Becke in 1997, 1998
B97D	Becke's functional including dispersion
E_{disp}	Dispersion energy
MP2	Second-order Møller-Plesset perturbation theory
B2PLYP, mPW2PLYP	Double-hybrid density functionals
E_R	Electric field
μ	Dipole moment
$\hat{V}_{int}$	Potential energy of electrostatic interaction
N	Number of carbon atoms
X	Solute
X_{water}	Solute dissolved in water
$X_{octanol}$	Solute dissolved in octanol
$\Delta G°$	Standard Gibbs free energy
P	Equilibrium constant of the equilibrium between octanol and water
$\Delta G°_{ow}$	Standard Gibbs free energy change of the equilibrium between octanol and water
$\Delta_f G°$	Standard Gibbs free energy of formation
R	Ideal gas constant
T	Temperature in K

E_o	SCF energy in octanol
E_w	SCF energy in water
K_a	Acid dissociation constant
Log P	Octanol-water partition coefficient
Log D	Octanol-water distribution constant
K_{oc}	Soil organic carbon-water partition coefficient
Log K_{ow}	Octanol-water partition coefficient
R^2	Square of the correlation coefficient R
KOWWIN	Module of the EPI Suite software dedicated to the estimation of octanol-water partition coefficients
LC-ωPBE	Corrected functional that optimizes the PBE functional
PM6	Semiempirical method
H	Enthalpy
S	Entropy

Acknowledgments

I would like to thank, in the first place, my supervisor Dr. Nelaine Mora-Diez. Without her unconditional support since 2009, I would not have been able to accomplish what I have accomplished today. Her guidance was beyond that of a supervisor-student relationship to become a friend and model to follow. My sincere and eternal gratitude to her. I hope she accomplishes much success in her future scientific research.

I also would like to give my thanks to the members of the Department of Chemistry at the University of Victoria for always being so helpful and committed to the success of every student in this department. Especially, I would like to say thanks to Dr. Alexander Brolo and Dr. Irina Paci, for being part of my Master's committee, for reviewing my work and for their feedback and support.

Thank you to all my friends and my family, who have always been there all along this journey.

Chapter 1. Introduction

1.1 Computational chemistry and its applicability in physico-chemical determinations

Knowledge has evolved to the point that much information is available prior to running an experiment. Computational chemistry is one of many branches of theoretical chemistry where mathematical and physical tools, converted into computer codes, describe chemical systems that make use of simulations through approximations. Since each computational method uses approximations to simplify the system, the choice of a method, usually known as level of theory, must be carefully studied.

There are a huge number of developed computational methods that researchers can use,[1] none of which is suitable for every calculation; thus, the current focus on the development of methods with broad applicability. Consequently, the search for a convenient and effective method very often includes the screening of several that may be available, in order to find the one that best fits the experimental data in the literature. Some examples include *ab-initio* (Hartree-Fock, HF, post-HF, multi-reference methods), density functional theory, DFT and semiempirical methods.

Computational chemistry has been used, for example, for conformational predictions through geometry optimizations, frequency calculations, electronic and charge distributions and thermodynamic determinations, such as enthalpies and Gibbs free energies. These determinations enable the calculation of other physico-chemical properties of the molecules and materials that are either too difficult to determine or too expensive to acquire.

Partition coefficients, acid constants, and standard entropies are only some of the physico-chemical properties that may easily be estimated making use of theoretical determinations and the general physico-chemistry equations that govern the physical world. The common procedure includes the testing of a particular method with previously known experimental data. Upon demonstration of the feasibility of such a prediction system to reproduce recognized experimental values for a given group of molecules, it is very common to use the same method

as a basis for calculation of an unknown group. Sometimes, there are un-reported values for the molecules investigated and a more flexible approach making use of similar systems, or even indirect estimations based on other properties, must be followed.

1.2 Perfluorinated acids: Current environmental and health concerns

Perfluoroalkyl acids (PFAAs) belong to a group of anthropogenic compounds that were initially produced in the late 1940s and have been since used, for example, as surfactants,[2] in the production of synthetic materials, such as the widely recognized Teflon, and as coating agents for waterproof fabrics.[3] Only recently have they been included in the list of chemicals with potential to damage environmental and human health.[4] Among many others,[5] perfluoroalkyl carboxylic acids (PFCAs) and perfluoroalkyl sulfonic acids (PFSAs), have gained much interest since they are highly persistent and have been detected globally.[6] Long-chain PFAAs (more than seven carbon atoms) bioaccumulate along the food chain[6] which raises special concerns about the way they interact with the environment and the biota, especially the human body.

Contrary to traditional accumulation in lipidic compartments characteristic of many other similar compounds, these PFAAs attach to proteins. Liver and blood seem to be the preferred organs, but PFAAs have been detected in other tissues.[7] Even though linear isomers predominate in environmental samples, many researchers consider the inclusion of branched isomers in the analysis of either environmental fate or the interaction with biota necessary as well.[8] Many of the possible branched isomers of the most common perfluorocompounds, such as perfluorooctanoic acid and perfluorosulfonic acid, have not been detected in many environmental samples. However, the possibility that many of them could be present has not been completely ruled out, and a possible explanation for why they remain undetected has been the limits of the techniques used.[8] In fact, the question of whether branching patterns influence the physical, chemical and/or biological properties of PFAAs (and other perfluorinated compounds) has recently gained more scientific interest. Some researchers believe that branching determines the relative differences regarding environmental fate, bioaccumulation and even toxicity. Such differences may provoke errors when it comes to total PFAA quantification, which casts doubt on previous human and environmental exposure studies.[8]

1.3 Theoretical calculations of physico-chemical properties of perfluorinated acids

The mechanisms of local and global transport, as well as those controlling the bioaccumulation of PFAAs in live organisms are yet to be completely understood. Some models have been created in order to describe distribution around the globe and many of these mathematical predictors need a minimum of input data in order to generate possible scenarios. Acidic constants and partition coefficients are traditionally used as the input methods for many of these models and there is currently debate about what data should or should not be used.[9] In addition, many experimental and theoretical methods have been developed to determine the physico-chemical properties of chemical substances, but the determination of these properties for PFAAs has proved a very hard task, with many contradictory results, thus generating much controversy.[9]

Several software packages that act as predictors have been very popular, but output values vary (sometimes by several orders of magnitude) between them. The scarce experimental data for these families of compounds makes it very difficult to validate or even calibrate the internal parameters of such software packages, since these molecules cannot be used in their training sets.[9]

DFT, one of the most commonly used methods, has gained in importance in the past 20 years. It overcomes the main disadvantage of HF (consideration of electron correlation) without the need for the highly demanding post-HF methods. The use of DFT has been a very popular choice for theoretical analysis of PFAAs, however, notably different results may be obtained depending on the particular method used.[10]

1.4 References

[1] Gaussian 09, Revision A.1, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A. Jr; Peralta J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, **2009**.

[2] Renner, R. Concerns over common perfluorinated surfactant. *Environ. Sci. Technol.* **2003**, *37*, 201A–202A.

[3] *Petition for expedited CIC consideration of perfluorooctanic Acid (PFOA).* Office of Environmental Health Hazard and Assessment, California, United States, 2007; http://www.oehha.ca.gov/Prop65/public_meetings/pdf/PFOACIC%20Slides121206.pdf

[4] *Environment Program Secretariat of the Stockholm Convention on Persistent Organic Pollutants. Conference: The Nine New POPs; An Introduction to the Nine Chemicals Added to the Stockholm Convention by the Conference of the Parties at Its Fourth Meeting Date.* United Nations, 2010; http://chm.pops.int/programmes/newpops/publications/tabid/695/language/en-us/default.aspx.

[5] Schultz, M. M.; Barofsky, D. F.; Field, J. A. Fluorinated alkyl surfactants. *Environ. Eng. Sci.* **2003**, *20*, 487-501.

[6] Houde, M.; De Silva, A. O.; Muir, D. C. G.; Letcher, R. J. Monitoring of perfluorinated compounds in aquatic biota: An updated review: PFCs in aquatic biota. *Environ. Sci. Technol.* **2011**, *45*, 7962−7973.

[7] Lau, C; Anitole, K; Hodes, C; Lai, D; Pfahles-Hutchens, A; Seed, J. Perfluoroalkyl Acids: A Review of Monitoring andToxicological Findings. *Toxicol. Sci.* **2007**, *99*, 366-394.

[8] Benskin, J. P; De Silva, A. O.; Martin, J.W. Isomer Profiling of Perfluorinated Substances as a Tool for Source Tracking: A Review of Early Findings and Future Applications. *Rev. Environ. Contam. T.* **2010**, *208*, 111-160.

[9] Rayne, S.; Forest, K. Perfluoroalkyl sulfonic and carboxylic acids: A critical review of physicochemical properties, levels and patterns in waters and wastewaters, and treatment methods. *J. Environ. Sci. Health A* **2009**, *44*, 1145-1199.

[10] Rayne, S.; Forest, K. Comparative semiempirical, ab initio, and density functional theory study on the thermodynamic properties of linear and branched perfluoroalkyl sulfonic acids/sulfonyl fluorides, perfluoroalkyl carboxylic acid/acyl fluorides, and perhydroalkyl sulfonic acids, alkanes, and alcohols. J. Mol. Struct.: Theochem 2010, 941, 107-118.

Chapter 2. Theoretical Background

2.1 Time-independent Schrödinger equation and the Born–Oppenheimer approximation

In classical physics, the movement of an object in time is described by its momentum and exact position. However, the equations applied to the "Newtonian universe" do not apply to the atomic level of matter. Quantum theory assumed this role, but it is accepted that it can only describe a probability of the different values a quantum particle can take in terms of velocity and position. The wave-particle duality of quantum systems was described at the beginning of the 20th century and its consideration would be determinant for the development of the quantum mechanics postulates.

In 1926, Erwin Schrödinger published his work[1] describing the evolution of a physical system in time, which plays a central role as the foundation of modern quantum physics. The time-independent Schrödinger equation, eq. 2.1, for a system of *n* interacting particles takes several forms depending on the Hamiltonian operator, $\widehat{H}$, which represents the sum of kinetic and potential energies of the system, and it acts on the multi-electronic wave function Ψ.

$$\widehat{H}\Psi = E\Psi \tag{2.1}$$

In 1927, Max Born in collaboration with J. Robert Oppenheimer proposed a separation of both electronic and nuclear degrees of freedom.[2] This joint work is known as the Born-Oppenheimer (BO) approximation. In a system containing electrons and nuclei, there would be very little momentum transfer between these particles; since the mass of electrons is significantly lower than the mass of nuclei (mass ratio is on the order of 10^4). Because the speed of electrons is much greater than that of nuclei, electrons can be assumed to move in the field created by "fixed" nuclei. The BO approximation significantly simplifies $\widehat{H}$ and it is applied in most electronic-structure calculations. The Schrödinger equation shown in eq. 2.1 can only be solved exactly for systems with one electron. Approximate methods have to be applied for more complex systems.

2.2 Molecular orbital theory and the multi-electronic wave function

Molecular Orbital Theory assigns electrons to spin-orbitals, which are a combination of a spatial function (also known as the molecular orbital, which can accommodate up to two electrons of opposite spin) and a spin function (alpha or beta). Electrons are assigned to individual spin orbitals following the Aufbau Principle (the lowest-energy orbitals are filled before the higher-energy ones) and Pauli Exclusion Principle (no two electrons can have the same four quantum numbers).

A well-behaved wave function in quantum mechanics must be single-valued, continuous (as well as its partial derivatives) and quadratically integrable. Furthermore, because electrons are fermions, it must be antisymmetric with respect to the exchange of electrons, *i.e.*, if two electrons are exchanged, Ψ must change sign as per eq. 2.2. The Pauli Exclusion Principle is a consequence of the antisymmetric nature of Ψ.[3] A correct representation of the wave function of a system of N indistinguishable electrons must satisfy the above mentioned properties.

$$\Psi(1,2,\dots,i,\dots,j,\dots,N) = -\Psi(1,2,\dots,j,\dots,i,\dots,N) \tag{2.2}$$

The simplest representation of a multi-electronic wave function within the framework of Molecular Orbital Theory is the Slater determinant, see eq. 2.3. The factor $1/\sqrt{N!}$ guarantees that Ψ is normalized if the individual spin-orbitals χ_i are also normalized. Rows correspond to electrons and columns to spin-orbitals.

$$\Psi(1,..,N) = \frac{1}{\sqrt{N!}}\begin{vmatrix} \chi_1(1) & \chi_2(1) & \dots & \chi_N(1) \\ \chi_1(2) & \chi_2(2) & \dots & \chi_N(2) \\ \vdots & \vdots & & \vdots \\ \chi_1(\mathrm{N}) & \chi_2(\mathrm{N}) & \dots & \chi_N(\mathrm{N}) \end{vmatrix} \tag{2.3}$$

The best way to represent a multi-electronic wave function is by linearly combining the Slater determinants of the ground electronic state with all possible electronic configurations resulting from distributing the electrons in the system among the total number of spin-orbitals (occupied and virtual).

2.3 The Hartree-Fock method

Hartree and Fock developed an *ab initio* theory, later adapted to molecules by making use of Molecular Orbital Theory, in which the multi-electronic wave function is represented by a single Slater determinant.[3,4,5] This is an independent-particle model based on the variational theorem. The Hartree-Fock (HF) method is said to be variational because the energy it gives (see eq. 2.4) is always an upper bound to the exact energy. In this method, the many-electron problem that cannot be solved exactly is replaced by a one-electron problem in which the electronic repulsions are treated in an average way. The instantaneous interactions between pairs of electrons are replaced with the interaction of each electron with the average electronic cloud formed by all the other electrons present.

$$E_{HF} = 2\sum_{i=1}^{n/2} H_{ii}^{core} + \sum_{i=1}^{n/2}\sum_{j=1}^{n/2}(2J_{ij} - K_{ij}) + V_{NN} \qquad (2.4)$$

In eq. 2.4, which applies to a closed-shell system, H_{ii}^{core} are the matrix elements of the core or one-electron Hamiltonian. This term represents the energy of a single electron in the field of bare nuclei. J_{ij} and K_{ij} are the Coulomb and Exchange integrals, respectively. The second term in eq. 2.4, represents the average potential experienced by one electron due to the presence of the other (N -1) electrons. V_{NN} represents the inter-nuclear repulsion energy for a given molecular geometry.

The limited applicability of the HF equations to atoms prompted the need for an extension of this theory to be used in molecules. In 1951, Roothaan proposed an expansion of molecular orbitals (MOs, ϕ_i) as a linear combination of basis functions, θ_i, as shown in eq. 2.5.[6]

$$\phi_i = \alpha_{i1}\theta_1 + \alpha_{i2}\theta_2 + \cdots \alpha_{in}\theta_n = \sum_{p=1}^{b} \alpha_{ip}\theta_p, \qquad \alpha'_s \text{ are expansion coefficients} \qquad (2.5)$$

An infinite number of basis functions (complete basis set) would be required for a proper mathematical representation of molecular orbitals, but given that this is impractical, the MO

expansion is to be truncated which is another source of error in quantum-mechanical calculations.[3] The larger and more flexible the basis set used, the longer and more accurate the calculations.

When transforming the HF equations into the Roothaan-Hall equations, the matrix elements of the one-electron Hamiltonian, and the Coulomb and Exchange operators become integrals over basis functions that can be centred on up to four atoms. An iterative procedure called the self-consistent field procedure must be followed to solve them.

2.4 Basis functions and basis sets

As previously mentioned, a basis set is a set of basis functions which are used to mathematically calculate molecular orbitals by linearly combining the basis functions. Several types of basis functions have been proposed but the two most popular ones, both with advantages and disadvantages, are Slater-type orbitals (STOs) and Gaussian-type orbitals (GTOs).

If when dealing with molecules one STO function is used per atomic orbital (AO), we are in the presence of what is called a minimal basis set. A double-zeta (DZ) basis set is used when two STOs are used to describe each AO, in a same way a triple-zeta (TZ) basis set uses three STOs. Intermediate solutions have been used in which only one STO is used to describe core AOs, but the valence AOs are described with two or more basis functions. These are the split-valence basis sets.[3] Nowadays, the use of GTOs is much more extended. However, GTOs are not as good as STOs when describing the electronic density at the nucleus or far away from it. The normal practice is to approximate a single STO by a linear combination of GTOs called primitives.

When atoms bind to form molecules, AOs become distorted and have their centers of charge shifted depending on the electronegativity of the atoms bonded. A simple way to deal with this in calculations is by increasing the size of the basis set by adding basis functions with higher angular momentum than needed by the atoms in a given molecule, *e.g.*, *p*-basis functions for hydrogen or *d*-basis functions for carbon. These additional basis functions are called polarization

functions. They confer more flexibility to the basis set to better represent electron density in bonding regions.[3]

Diffuse basis functions are basis functions with very small orbital exponents (usually of s-type or p-type) that are added to the basis set. They are especially important to properly describe the electron density far from the nucleus when calculating anions, excited states or intermolecular complexes. [3]

Pople basis sets are a popular group of split-valence basis sets of GTOs with the general notation N-M1G (for a DZ split-valence basis set) or N-M11G (for a TZ split-valence basis set).[7] The letters N and M are integers representing the number of Gaussian primitives used to represent the core and valence AO, respectively. For example, the notation 6-31G indicates that one basis function made of 6 (linearly combined) Gaussian primitives is used to represent each of the core AOs and two basis functions of 3 and 1 Gaussian primitives are used to describe each valence AO. The notation 6-311+G(d,p) indicates a TZ split-valence basis set in which three basis functions of 6, 1 and 1 Gaussian primitives are used to represent each of the valence AOs. The (d,p) part indicates that *d*-type polarization functions are added when describing non-hydrogen atoms and *p*-type functions are added on hydrogen atoms. The + identifies that a set of *sp*-type diffuse basis functions are added when describing non-hydrogen atoms.

HF calculations that employ an infinite number of basis functions (complete basis set) are labelled as limiting HF calculations. In practice, these are calculations with very large and flexible basis sets. Because the HF method is variational, limiting HF calculations produced the lowest-possible HF energy.

2.5 Electron correlation and post-Hartree-Fock methods

The most significant weakness of HF methods is the insufficient treatment of the electron correlation. Because electron-electron interactions are treated indirectly by considering the interaction between each electron and the average field produced by all the others, the Hartree-Fock theory neglects the instantaneous interaction (dynamic correlation) that actually occurs

between electrons in a multi-electronic system. Electrons repel each other and it is said that around each electron there is a zone, known as the Coulomb hole, where the probability of finding another electron is almost null. This correlation between the position and motion of electrons is called electron correlation. It is easy to realize that some correlation is already present in the Hartree-Fock methods since the anti-symmetric nature of the wave function is accounted for. The difference between the limiting HF energy, $E_{\text{limiting HF}}$, and the non-relativistic exact Schrödinger energy, E_{Exact}, is by definition the correlation energy, E_{corr}.

$$E_{\text{corr}} \equiv E_{\text{limiting HF}} - E_{\text{Exact}} \tag{2.6}$$

Finding the correct terms accounting for dynamic or instantaneous electron correlation is accomplished in many ways, some with more success than others. Some of the main methods that deal with electron correlation are Configuration Interaction, Møller-Plesset perturbation theory, the Coupled Cluster approach (all three out of the scope of this thesis) and the most popular density functional theory (DFT). The first three methods are capable of very high accuracy but are computationally more expensive than DFT, thus only practical for small systems.

To more efficiently account for electron correlation, which affects much more energy values than geometries, it is common practice to initially perform a geometry optimization and a frequency calculation (to characterize the stationary point calculated as either a minimum or a transition state) at a particular level of theory (e.g., $\text{Method}_1/\text{Basis set}_1$) and later on, use that geometry to perform a single-point energy calculation at a higher level of theory (e.g., $\text{Method}_2/\text{Basis set}_2$). This combination of calculations is represented by means of the following notation: $\text{Method}_2/\text{Basis set}_2$ //$\text{Method}_1/\text{Basis set}_1$.

There are a number of desirable properties for the methods used in quantum-chemistry when dealing with electron correlation. It is very convenient that the methods applied be variational, size-consistent and size-extensive. A method is said to be variational when the energy it calculates is always an upper-bound to the exact energy of the system; DFT methods are not variational. Size-consistency and size-extensivity are more widely recognized properties that

influence the way electron correlation is treated. Size extensivity means that the energy scales in direct proportion to the number of particles in the system. A method is size extensive if the energy of n non-interacting identical systems equals n times the energy of one subsystem obtained by the same method, and the computed energy of a uniform system is proportional to the number of particles in it. A method is size consistent if the energy of a system that undergoes dissociation into two or more infinitely separated fragments equals the sum of the energies of each fragment.

2.6. Density functional theory

> *"DFT is a convenient and universal language for electronic structure theory, which substantially helps unify organic chemistry, inorganic chemistry, surface chemistry, and materials science. It helps unify chemistry and physics."* [8]

A function is a set of mathematical operations performed on one or more inputs (variables) that results in an output.[3] For example, in the quadratic function $f(x) = x^2$, the value 10 of x associates with the value 100 for $f(x)$. Every value of x will be related to a value of $f(x)$. Similarly, a functional relates a number to every function $f(x)$ and can be denoted as $F[f(x)]$, where the square brackets mean that there is a functional relationship.

In 1927, Thomas[9] and Fermi[10] proposed to calculate the energy of a many-electron system by considering the atom as a uniformly distributed cloud of electrons under the influence of a known potential which would depend only on the distance from the nucleus. They expressed the kinetic energy of atoms as a functional of the electron density, $\rho(\mathrm{r})$, and added two classical terms for the nuclear-electron and electron-electron interactions, which can be represented in terms of the electron density, to compute the energy of the atom. This approximation neglected the exchange energy of an atom which was later on added by Dirac.[11] Even though the Fermi-Thomas-Dirac attempt is regarded as the first important step towards the use of the electron density to calculate molecular properties, it was highly criticized as it was unable to self-consistently reproduce the atomic shell[12] structure or even account for the binding of atoms in molecules.[13]

In 1964, which is mostly accepted as the "true" beginning of DFT,[12] Pierre Hohenberg and Walter Kohn demonstrated that for a multi-electron system with a non-degenerate ground-state, the ground-state molecular energy E_0, the wave function, and any other molecular properties are exactly determined by the ground-state electron probability density $\rho_0(x, y, z)$, a function of only three variables, as seen in eq. 2.7.[14]

$$E_0 = E_0[\rho_0] \tag{2.7}$$

A wave function for the ground-state of a many-electron system, ψ_0, is an eigenfunction of the Hamiltonian from eq. 2.1, which in atomic units is

$$\hat{H} = -\frac{1}{2}\sum_{i=1}^{n} \nabla_i^2 + \sum_{i=1}^{n} v(r_i) + \sum_{j}\sum_{i>j} \frac{1}{r_{ij}} \tag{2.8}$$

In eq. 2.8, the potential energy due to the interaction of electrons and nuclei, $v(r)$, is calculated using eq. 2.9.

$$v(r_i) = -\sum_{\alpha} \frac{Z_\alpha}{r_{i\alpha}} \tag{2.9}$$

$v(r)$ is regarded as the external potential acting on electron i and it is only a function of the Cartesian coordinates.[3] Consequently, Hohenberg and Kohn demonstrated that for any n-electron system with a non-degenerate ground-state, the ground-state electron probability density $\rho_0(r)$ determines the external potential and the number of electrons, n (i.e., $\int \rho(\mathrm{r})\, d\mathrm{r} = n$).[14]

Equation 2.7 can be re-written as shown by eq. 2.10, which better depicts the dependence of E_0 on the external potential, $v(r)$.

$$E_0 = E_v\ ,\ E_0 = E_v[\rho_0] \tag{2.10}$$

The pure electronic Hamiltonian[3] can be written as

$$\hat{H}_{el} = -\frac{\hbar^2}{2m_e}\sum_i \nabla_i^2 - \sum_\alpha \sum_i \frac{Z_\alpha e^2}{4\pi\varepsilon_0 r_{i\alpha}} + \sum_j \sum_{i>j} \frac{e^2}{4\pi\varepsilon_0 r_{ij}} \quad (2.11)$$

The first term in eq. 2.11 represents the kinetic energy, T, the second term is the potential energy due to nuclei-electron attractions, V_{Ne} and the last term is the electron-electron repulsion energy, V_{ee}. The average calculated ground-state energy (denoted by the superscript *avg*) can be written as

$$E^{avg} = T^{avg} + V_{Ne}^{avg} + V_{ee}^{avg} \quad (2.12)$$

Each energy value in eq. 2.12 is a molecular property and as such they can be calculated from ρ_0, thus eq. 2.12 can be transformed into

$$E_v^{avg}[\rho_0] = T^{avg}[\rho_0] + V_{Ne}^{avg}[\rho_0] + V_{ee}^{avg}[\rho_0] \quad (2.13)$$

From eq. 2.13, the operator $\hat{V}_{Ne} = \sum_{i=1}^{n} v(r_i)$, where $v(r_i)$, in atomic units, represents the nuclear attraction potential-energy function, defined in eq. 2.9, for an electron at spatial coordinate r. The parameter $v(r_i)$ is a function of the spatial coordinates x_i, y_i, z_i for each i electron, thus it can be said that $V_{Ne}^{avg} = \int \rho_0(r)\, v(r)\mathrm{d}r$.[3]

If the remaining two terms in the Hamiltonian, which are not influenced by the external potential, are grouped into the functional $F^{HK}(\rho)$, i.e., $F^{HK}(\rho) = T^{avg}[\rho] + V_{ee}^{avg}[\rho]$, then[14]

$$E_0 = E_v[\rho_0] = \int \rho_0\,(r) v(r)\mathrm{d}r + F^{HK}(\rho_0) \quad (2.14)$$

Following their first approach, Hohenberg and Kohn demonstrated a second theorem known as the Variational Theorem of Hohenberg and Kohn[3,15], showing that the energy obtained using the true ground-state electron density, ρ_0, is never higher than that obtained with another electron density, ρ_1, ($E_0 = E_v[\rho_0] \leq \int \rho'\,(r) v(r)\mathrm{d}r + F^{HK}(\rho')$). In other words, the energy will reach

its minimum possible value only when ρ is the ground-state electron density. The very clever demonstration of this theorem goes through the demonstration of the no possibility of the contrary.

In practice, calculating E_0 is not possible, since the functional $F^{HK}(\rho_0)$ is unknown.[3] Finding ρ_0 without first calculating the molecular wave function is not supported by Hohenberg and Kohn ideas. However, two remarkable results derive from this work. Firstly, it draws a one to one map between the external potential and ρ, and secondly, it shows that the variational principle can be used to determine the ground-state density.

In 1965, Kohn teamed up with Lu Jeu Sham to find a method to determine ρ_0 and consequently E_0.[15] Kohn and Sham suggested that the lack of success of the Thomas-Fermi theory resulted, in principle, from the insufficient description of the kinetic energy. They considered a hypothetical n-electron system (or reference system) where the electrons do not interact with each other but are under the influence of an external potential, $v'(r_i)$, such that $\rho'(r) = \rho_0(r)$, where ρ_0 is the exact ground-state density of a real molecule and ρ' is the ground-state density of the reference system. Eq. 2.13 then becomes eq. 2.15.

$$\widehat{H} = \sum_{i=1}^{n} -\frac{1}{2}\nabla_i^2 + \sum_{i=1}^{n} v'(r_i) \tag{2.15}$$

Additionally, spin orbitals derived from the non-interacting i particles system are called Kohn-Sham spin orbitals, $\chi_i^{\mathrm{KS}} = \phi_i^{KS}\,\sigma_i$, where $\phi^{KS}$is the spatial part and σ is either one of the spin functions α or β. Kohn-Sham (KS) orbital energies, ε^{KS}, can be obtained by solving eq. 2.16.

$$\left(-\frac{1}{2}\nabla_i^2 + v'(r_i)\right)\phi_i^{KS} = \varepsilon^{KS}\phi_i^{KS} \tag{2.16}$$

In principle, Kohn and Sham conveniently defined two new terms $\Delta T^{avg}[\rho]$ and $\Delta V_{ee}^{avg}[\rho]$ as

$$\Delta T^{avg}[\rho] = T^{avg}[\rho_0] - T'^{avg}[\rho'] = T^{avg}[\rho] - T'^{avg}[\rho], \quad \rho_0 = \rho' \tag{2.17}$$

$$\Delta V_{ee}^{avg}[\rho] = V_{ee}^{avg}[\rho] - \frac{1}{2}\int\int \frac{\rho(r_1)\rho(r_2)}{r_{12}} dr_1 dr_2 \qquad (2.18)$$

Now, eq 2.14 transforms into eq. 2.19.

$$\mathrm{E}_v[\rho] = \int \rho\,(r) v(r) \mathrm{d}r \; + \; T'^{avg}[\rho] + \frac{1}{2}\int\int \frac{\rho(r_1)\rho(r_2)}{r_{12}} dr_1 dr_2 + E_{xc}[\rho] \qquad (2.19)$$

where $E_{xc}[\rho]$ is the exchange-correlation energy functional, $E_{xc}[\rho] = \Delta T^{avg}[\rho] + \Delta V_{ee}^{avg}[\rho]$.

The ρ of the KS system (ρ'), *i.e.*, that of the real system, is readily obtained by the eq. 2.20.

$$\rho = \rho' = \sum_{i=1}^{n} \left|\phi_i^{KS}\right|^2 \qquad (2.20)$$

Not much work is needed to arrive to the central equation in KS-DFT, which is the one-electron eq. 2.21.[3,15]

$$\left(-\frac{1}{2}\nabla_1^2 + v(r_1) + \int \frac{\rho(r_2)}{r_{12}} dr_2 + v_{1xc}\right)\phi_{1i}^{KS} = \varepsilon_i^{KS}\phi_{1i}^{KS} \qquad (2.21)$$

where the four terms on the left side represent the kinetic energy of the non-interacting reference system, the external potential, the Hartree potential, and the exchange-correlation potential (which corresponds to the functional derivative $\delta E_{xc}[\rho(r)]/\delta\rho(r)$ of the exchange correlation from eq. 2.18), respectively.

The central drawback of the KS methodology is that the exact functional $E_{xc}[\rho]$ is unknown, hence the values for E_{xc} and v_{xc}. Since E_{xc} is not exactly known, it has to be approximated.[3] Various approximate functionals $E_{xc}[\rho]$ are used in DFT (some of which are discussed below). However, there is not a systematic procedure for improving $E_{xc}[\rho]$ and the calculated molecular properties. This constitutes a serious weakness in DFT.

Ab-initio correlation methods (also called wave-function correlation methods[12]) depend heavily on the size of the basis set. Calculations with small basis sets are usually unreliable and extrapolation to a complete basis set limit is required in order to obtain the desired accuracy. However, for DFT methods the size of the basis set plays a minor role in many types of calculations and it has been shown that the use of DZ or ultimately TZ basis sets is enough to obtain good results.[3]

2.6.1 Exchange-correlation functionals

For a system where the value of $\rho(r)$ remains practically unchanged when the position, $r(x, y, z)$, changes such that each small element of the electronic system can be considered uniform, the Kohn-Sham local-density approximation[3,14,15] (LDA) says that $E_{xc}[\rho]$ can be obtained by eq. 2.22.

$$E_{xc}^{LDA}[\rho] = \int_{-\infty}^{\infty} \rho(r)\varepsilon_{xc}\big(\rho(r)\big)dr \tag{2.22}$$

where $\varepsilon_{xc}(\rho) = \varepsilon_x(\rho) + \varepsilon_c(\rho)$ [16] for each electron of an homogeneous or uniform electron gas with electron density ρ. The procedure requires finding the functional derivative of eq. 2.22, shown by eq. 2.23.

$$v_{xc}^{LDA} = \frac{\delta E_{xc}^{LDA}}{\delta\rho} = \varepsilon_{xc}\big(\rho(r)\big) + \rho(r)\frac{\partial\varepsilon_{xc}(\rho)}{\partial\rho} \tag{2.23}$$

Equations 2.22 and 2.23 give approximations to find the values of E_{xc} and v_{xc} for the Kohn-Sham equations,[3,15] *i.e.*, eq. 2.19 and eq. 2.21.

The functional $E_x(\rho)$ is calculated similarly to the exchange energy in eq. 2.4, K_{ij}. The HF orbitals are simply substituted by the KS orbitals and for a closed-shell system it is approximated by

$$E_x \equiv -\frac{1}{4}\sum_{i=1}^{n}\sum_{i=1}^{n}\langle\phi_{1i}^{KS}\phi_{2j}^{KS}\left|\frac{1}{r_{12}}\right|\phi_{1j}^{KS}\phi_{2i}^{KS}\rangle \tag{2.24}$$

From eq. 2.24, $\varepsilon_x(\rho)$ is evaluated through $E_x^{LDA} \equiv \int \rho\varepsilon_x\, dr$. Then, E_c^{LDA} is found as a function of ρ which allows one to find $\varepsilon_c(\rho)$.[16,17]

The original LDA formulation assigns the same spatial orbital to paired electrons with different spins. A latter approach called the local spin density approximation, LSDA, initially proposed by J. C. Slater,[18] allows these electrons to occupy different KS spatial orbitals.[3,15] This idea gives much better results when open-shell systems and systems near dissociation are being studied. Based on this, the $E_{xc}^{LDA}[\rho]$ now becomes $E_{xc}^{LSDA}\left[\rho^{\alpha},\rho^{\beta}\right]$, which shows how the exchange-correlation functional becomes a function of both ρ^{α} and ρ^{β} showing a spin dependence of the functionals. Within this approximation the exchange functional is obtained as shown in eq. 2.25.[19]

$$E_x^{LSDA}[\rho] = -2^{1/3}C_x\int(\rho^{\alpha\,4/3}+\rho^{\beta\,4/3})dr \tag{2.25}$$

where

$$C_x = -\frac{3}{4}\left(\frac{3}{\pi}\right)^{1/3} \tag{2.26}$$

LDA and LSDA are based on a system where the ρ change slowly with position. A more realistic system must deal with the presence of non-homogenous ρ and a way to do this is by using the gradient of a function which represents the tri-dimensional rate of change of that function. The generalized gradient approximation, GGA, assumes that at infinitesimal changes of r, the ρ changes. In other words, rather than just making E_{xc} dependent on ρ, GGA makes the exchange and correlation energies also dependent on the gradient of the density, $\nabla\rho(r)$.[3]

The sound popularity gained by DFT acquired real momentum with the advent of GGAs.[20,21] A way to define the electron-correlation energy is by constructing a new functional according to eq. 2.27.[3]

$$E_{xc}^{GGA}[\rho^{\alpha},\rho^{\beta}] = \int f\left(\rho^{\alpha}(r),\rho^{\beta}(r),\nabla\rho^{\alpha}(r),\nabla\rho^{\beta}(r)\right)dr \qquad (2.27)$$

Commonly regarded as a semilocal method,[3] GGA approximations usually calculate E_{xc}^{GGA} as the sum of E_{x}^{GGA} and E_{c}^{GGA} and this has been developed in several ways. One popular approach relies on the use of fitting data from a very large set of molecules. Some commonly used exchange functionals based on this idea are Becke's functional (B88 or B)[22] and the exchange component of Perdew-Wang functional from 1991 (PWx91).[23] Also, some GGA correlation functionals implemented are the Lee-Yang-Parr functional (LYP) and the correlation component of Perdew and Wang's 1986 functional PWc86. A second group of GGA functionals contains no empirical parameters and includes the exchange part of Perdew and Wang's 1986 functional PWx86[24] and Perdew-Burke-Ernzerhof (PBE)[21] which has shown good results for calculations on solids.

The apparent success of GGA methods in terms of energy and structural determinations[20,22,25,26] was overshadowed by a deficient description of some chemical properties of molecules, in fact, failing in describing essential van der Waals interactions proved to be a major drawback for these methods.[27,28]

A more recently developed group of functionals depend not only on ρ and the first derivative of ρ (such as in GGAs), but also depend on the second derivative of ρ and the kinetic energy density. The so-called meta-GGA functionals, deemed as third generation functionals according to the rung of Jacob's ladder,[29] have demonstrated much better results when compared to the GGAs[3,19] and have the form shown in eq. 2.28.

$$E_{xc}^{meta-GGA}[\rho^{\alpha},\rho^{\beta}] = \int f\left(\rho^{\alpha}(r),\rho^{\beta}(r),\nabla\rho^{\alpha}(r),\nabla\rho^{\beta}(r),\nabla^{2}\rho^{\alpha}(r),\nabla^{2}\rho^{\beta}(r),\tau_{\alpha},\tau_{\beta}\right)dr \qquad (2.28)$$

where τ is the kinetic energy which involves derivatives of the occupied Kohn-Sham orbitals and represents an additional degree of freedom.

Some examples of meta-GGA functionals are Becke's τ-dependent gradient-corrected correlation functional P95,[30] which uses two empirically fitted parameters, and the exchange functional of Tao, Perdew, Staroverov, and Scuseria (TPSS).[31] A much better known meta-GGA correlation functional is Lee-Yang-Parr (LYP) functional,[32] which is a consequence of the further development of a previous idea from Colle and Salvetti published in 1975.[33]

Since its development,[34] hybrid exchange correlation functionals have been extensively used.[3] This type of functionals combines the exchange-correlation of GGA methods with a certain percentage of exact HF exchange. This exact exchange was previously defined here in the form of K_{ij} in section 2.3 which takes the form of eq. 2.24 when Kohn-Sham orbitals are used. The overwhelmingly popular hybrid GGA functional B3LYP takes the format suggested for the B3PW91 functional by Becke in 1993,[34] which includes three non-local parameters for the exchange functional ($\alpha_0 = 0.20$, $\alpha_x = 0.72$, $\alpha_c = 0.81$; determined by a linear least-squares fitting to 56 atomization energies, 42 ionization potentials, 8 proton affinities, and 10 total atomic energies for the first-row from Gill, et. al.[35]) and the correlation functional of Lee-Yang-Parr. This hybrid functional was first implemented in Gaussian 92/DFT.[36] The parameter α_0 modifies the amount of exact exchange a functional of this type has. For example, for B3LYP the equations used are

$$E_{xc}^{B3LYP} = (1 - \alpha_0 - \alpha_x)E_x^{LSDA} + \alpha_0 E_x^{exact} + \alpha_x E_x^{B88} + (1 - \alpha_c)E_c^{VWN} + \alpha_c E_c^{LYP} \quad (2.29)$$

$$E_{xc}^{B3LYP} = 0.08E_x^{LSDA} + 0.20E_x^{exact} + 0.72E_x^{B88} + 0.19E_c^{VWN} + 0.81E_c^{LYP} \quad (2.30)$$

According to eq. 2.30, the B3LYP functional contains 20% of exact HF exchange. E_c^{VWN} denotes the Vosko-Wilk-Nusair LSDA correlation fuctional.[17]

In 1997, working on improving the functionality of their previous hybrid functionals, Becke proposed the functional B97, which became the precedent to a family of functionals such as B97-1, B97-2[37] and the revision B98, which implements equation 2c from the work of Schmider and Becke.[38] The poor description of the long-range electron correlation that is responsible for van der Waals dispersive forces,[39,40] motivated further development in the implementation of

dispersion forces for this type of functionals. A GGA functional for general chemistry applications labelled B97-D,[41] which is based on Becke's B97 series of functionals, was proposed and was explicitly parameterized by including damped atom-pairwise dispersion corrections with the form $C6/r^6$. The general approach followed in this case was to add an energy-correction term for dispersion after performing the KS-DFT calculation.

$$E_{DFT-D} = E_{DFT} + E_{disp} \tag{2.31}$$

Despite the apparent need for considering dispersion forces to account for non-bonding interactions, some functionals with a very high number of parameters and no explicit consideration of these forces are able to describe fairly well systems with such interactions.[3] The functional M06-2X (see Section 2.6.2), which belongs to a group of meta-GGA functionals called Minnesota functionals, is a very good example of this type of functionals.

Another group of functionals are called double-hybrid density functionals[42] and require a significant larger amount of time to compute, as well as a larger basis sets than the previous groups described. Double-hybrid density functionals are based on a mixing of standard GGA for exchange and correlation with HF exchange and some correlation obtained at the MP2 (second-order Møller-Plesset perturbation theory) level of theory. In general,

$$E_{xc} = E_{xc}^{hybrid-GGA} + (1 - \alpha_2)E_c^{KS-MP2} \tag{2.32}$$

where

$$E_{xc}^{hybrid-GGA} = \alpha_1 E_x^{GGA} + (1 - \alpha_1)E_x^{exact} + \alpha_2 E_c^{GGA} \tag{2.33}$$

Similarly to what is has been shown for hybrid functionals, the two parameters α_1 and α_2 are obtained by fitting this equation to a set of data. Two functionals obtained by this methodology are B2PLYP[42] and mPW2PLYP.[43] Even though this approach is considered by Grimme as the one that produces "the most accurate DFT methods",[44] its applicability is limited because they have the same very high computational cost as the MP2 method.

2.6.2 The Minnesota group of density functionals

A very popular group of meta-GGA-functionals named M*yz(-suffix)* are known as Minnesota functionals, where the *yz* denotes the year 20*yz* and M stands for Minnesota or meta. According to Perverati and Truhlar, one cannot expect the highest possible accuracy if the dependence on kinetic energy density is not considered when proposing a functional.[45]

The first Minnesota functional was the M05[46,37] functional, which demonstrated a very good performance when the molecules contained transition metals. However, for other systems the results were poor and no improvement over other methods was observed. M05-2X[37] followed and this functional was designed to contain double the amount of exchange than the original M05 (from there the 2X). This new approach showed a significant improvement in the determination of energies for almost every system where M05 performed poorly.

A second group of Minnesota functionals were the M06 family. This set of meta-GGA exchange-correlation functionals were designed to have different percent of exact exchange. M06-L[47] (with L meaning "local") has no exchange and as such is considered a local functional. This lack of exchange allows for a very rapid calculation, thus larger systems can be considered. M06[48] contains 27% of exact exchange and has shown an overall good performance. The M06-2X[48] has 54% exchange which makes it extremely suitable for very good performances in a broad spectrum of areas in chemistry, from thermochemistry to kinetic of reactions and much more. However, it has been shown that it does not perform well for systems containing transition metals. The last of this family is the M06-HF,[49] which contains 100% exact exchange and has shown to be better than B3LYP when determining many chemistry properties.[45] All these functionals have about 35 parameters.

Following the success of M05 and M06 family of functionals, Truhlar's group continued with the improvement of their functionals, following a similar approach but using what they call a cleaner functional form for both the exchange and correlation.[45] Functionals M08-HX[50], with 52.23% exact exchange and M08-SO[45] with a higher exchange of 56.79%, were created and served as a base to the most recent M11 family of functionals. Here, the authors introduced a

new strategy called dual range exchange, claimed to have brought the search for a universal functional much more closer than ever before, as M11 is in theory able to substitute M06-2X, M08-HX, M08-SO and M06-HF, whereas M06-L is replaced by either M11 or M11-L.[45] A negative characteristic present to some extent in all the Minnesota functionals is related to SCF convergence problems, which represents a common problem for most DFT methods.[45]

2.7 Modelling solvent effects

Most processes in nature occur in solution, and the solvent often plays a decisive role in the path a chemical or biochemical process takes. The effect a molecule induces on the solvent mediated by the non-homogeneous distribution of charge densities on the molecule is known as bulk polarization, and the electric field generated by the solvent is called reaction field.[3] The molecular geometry in solution is distorted from that in the gas phase and a dynamic dipole moment is generated, which adds to the permanent gas-phase dipole of the molecule. As a consequence of the solute-solvent interaction, molecular properties in solution differ in many cases from those in the gas-phase, especially in the presence of strong solute-solvent interactions.[3]

There are two main ways to perform electronic quantum chemical calculations considering solvent effects. One group of calculations involves a discrete high-number of solvent molecules surrounding the solute. These methods are called explicit-solvent calculations and due to the high number of particles in the system, calculations usually converge very slowly. Because these methods are so computationally demanding, other more practical approaches are followed.

The most common way to account for solvent effects represents the solvent as a continuous dielectric that extends infinitely. The molecular structure of the solvent, which surrounds a cavity containing the solute, is not considered. The so called continuum solvation methods include the dielectric constant of the solvent, ε_r, in addition to other parameters.

To account for self-consistency between the solute and the reaction field when going from the gas phase to the solvent phase, the $\rho(r)$ and the electronic wave function of the solute are in

principle supposed to change. The self-consistent reaction field (SCRF) model accounts for this effect and the difference between methods relies mainly on the way the size and shape of the cavity and the solute-solvent interactions are modeled.

The classical SCRF method developed by Born[51], Kirkwood[52] and Onsager[53] considers the molecular cavity as a sphere with a definite radius α. The molecular charge distribution is seen as an electric dipole, with electric dipole moment μ located at the center of the cavity. The electric field E_R in the cavity would depend on the polarization of the solvent by μ,[53] such that

$$E_R = \frac{2(\varepsilon_r - 1)}{(2\varepsilon_r + 1)\alpha^3}\mu \tag{2.34}$$

This method must be solved self-consistently. First, ρ is calculated by a method of choice (*e.g.*, a DFT method) The μ of the isolated molecule ($\mu^{(0)}$) is found using eq. 2.35.[3]

$$\mu^{(0)} = -\int \rho^{(0)}(r) r dr + \sum_{\alpha} Z_\alpha r_\alpha \tag{2.35}$$

After the reaction field of the isolated molecule is found using eq. 2.34, the potential energy of electrostatic interaction, $\hat{V}_{int}$ is determined by $\hat{V}_{int} = -\hat{\mu}E_R$. The operator $\hat{\mu} = -\sum_i r_i + \sum_\alpha Z_\alpha r_\alpha$, where r_i is a vector from the origen to electron i and r_α is the vector to the nucleus with atomic number Z_α. The potential energy found is used in the initial method and a new ρ' is found. This procedure is repeated until no change in potential energy is found.

The extremely simple approximations of the Onsager SCRF method, which considers a dipole to describe the distribution of charges in the molecule and a sphere (sometimes an ellipse) to describe the cavity shape, have given limited good results probably due to cancelation of errors.[54] The multipole expansion addresses this problem by considering an infinite series in which several terms include not only the dipole moment, but the quadrupole, octupole, etc.

Another type of reaction field is the polarizable continuum model (PCM) initially proposed by Tomasi,[55],[56] and Miertus,[57] *et. al.* also known as D-PCM (for dielectric). According to the PCM method, the cavity is defined by a set of overlapping spheres having 1.2 times the van der Waals radius of the atom. A smooth surface is drawn on the points where the spheres interact. The surface potential is calculated by numerical differentiation,[3] and its interaction with the solvent can then be computed self-consistently. This is equivalent to carrying out the dipole expansion to infinite order.

Some modifications of the original PCM method have been proposed. The isodensity polarizable continuum method, IPCM,[54] considers the surface of the cavity as having a constant electron probability density. Another approach is the united-atom HF (UAHF) PCM method.[58] In this method, atomic radii are used to define the cavity and no spheres are assigned to hydrogen atoms because they are placed inside the sphere belonging to the atom at which they are attached. This method contains specific parameters to study aqueous solutions. If other media is to be used, these parameters need to be found. The integral equation formalism (IEF) version of the PCM method, IEF-PCM[59] is a generalization of PCM and opens the spectrum of analysis to both isotropic and anisotropic solvents.

A different set of solvent methods are grouped as SMx,[60,61,62] where $x = 1 - 8$. The most recent proposal on this series is the SMD method.[63] The D stands for "density" and indicates that the non-linear Poisson equation is solved self-consistently for the continuous quantum mechanical charge density. SMD is considered a universal solvation model because it is applicable to any solute, independently of its charge, in any solvent or liquid medium for which a few descriptors must be known. The observable solvation free energy is calculated by computation of two separate components. The first component is known as the bulk electrostatic contribution obtained from a self-consistent reaction field calculation where the cavities are represented by the superposition of nuclear-centered spheres. The other component represents the sum of terms that are proportional to the solvent-accessible surface areas of the individual atoms of the solute. A very representative training set was used in order to parameterize the SMD method. It is the result of using 2821 solvation data, including 112 aqueous ionic solvation free energies, 220 solvation free energies for 166 ions in acetonitrile, methanol, and dimethyl sulfoxide, 2346

solvation free energies for 318 neutral solutes in 91 solvents (90 non-aqueous organic solvents and water), and 143 transfer free energies for 93 neutral solutes between water and 15 organic solvents.

2.8 References

[1] Schrödinger, E. An undulatory theory of the mechanics of atoms and molecules. *Phys. Rev.* **1926**, *28*, 1049-1070.

[2] Born, M.; Oppenheimer, J. R. Zur quantemtheorie der molekeln. *Annalen der Physik* **1927**, *389*, 457-484.

[3] Levine, I. N. *Quantum Chemistry*. 7th ed., New York: Pearson, 2014.

[4] Hartree, D. R. The wave mechanics of an atom with a non-Coulomb central field. Part I. Theory and methods. *Proc. Cambridge Phil. Soc.* **1928**, *24*, 89-110.

[5] Fock, V. Näherungsmethode zur Lösing des quantenmechanischen Mehrkörperproblems. *Z. Physik* **1930**, *61*, 126-148.

[6] Roothaan, C. C. J. New Developments in Molecular Orbital Theory. *Rev. Mod. Phys.* **1951**, *23*, 69-89.

[7] Ditchfield, R.; Hehre, W. J.; Pople, J. A. Self-Consistent Molecular-Orbital Methods. IX. An Extended Gaussian-Type Basis for Molecular-Orbital Studies of Organic Molecules. *J. Chem. Phys.* **1971**, *54*, 724-728.

[8] Kohn, W.; Becke, A. D.; Parr, R. G. Density Functional Theory of Electronic Structure. *J. Phys. Chem.* **1996**, *100*, 12974-12980.

[9] Thomas, L. H. The calculation of atomic fields. *Proc. Cambridge Phil. Soc.* **1927**, *23*, 542-548.

[10] Fermi, E. Un Metodo Statistico per la Determinazione di alcune Prioprietà dell'Atomo. *Rend. Accad. Naz. Lincei* **1927**, *6*, 602-607.

[11] Dirac, P. A. M. Note on Exchange Phenomena in the Thomas Atom. *Proc. Cambridge Phil. Soc.* **1930**, *26*, 376385.

[12] Becke, A. D. *J. Chem. Phys.* **2014**, *18A301*.

[13] Teller, E. On the stability of molecules in the Thomas-Fermi theory. *Rev. Mod. Phys.* **1962**, *34*, 627-631.

[14] Hohenberg, P.; Kohn, W. Inhomogeneous electron gas. *Phys. Rev*. **1964**, *136*, B864-B871.

[15] Kohn, W.; Sham, L. J. Self-Consistent Equations Including Exchange and Correlation Effects. *Phys. Rev*. **1965**, *140*, A1133-A1138.

[16] Parr, R. G; Yang, W. *Density-Functional Theory of Atoms and Molecules*. Oxford: Oxford University Press, 1994.

[17] Vosko, S. H.; Wilk, L.; Nusair, M. Accurate spin-dependent electron liquid correlation energies for local spin density calculations: a critical analysis. *Can. J. Phys.* **1980**, *58*, 1200-1211.

[18] Slater, J. C. A Simplification of the Hartree-Fock Method. *Phys. Rev.* **1951**, *81*, 385-390.

[19] Sousa, S. F.; Fernandes, P. A.; Ramos M. J. General Performance of Density Functionals. *J. Phys. Chem. A* **2007,** *111,* 10439-10452.

[20] Langreth, D. C.; Mehl, M. Beyond the local-density approximation in calculations of ground-state electronic properties. *J. Phys Rev B* **1983**, *28*, 1809-1834.

[21] Perdew, J. P.; Burke, K.; Ernzerhof, M. Generalized Gradient Approximation Made Simple. *Phys. Rev. Lett.* **1996**, *77*, 3865-3868.

[22] Becke, A. D. Density-fnnctional exchange-energy approximation with correct asymptotic behavior. *Phys. Re*v. *A* **1988**, *38*, 3098-3100.

[23] Perdew, J. P.; Chevary, J. A.; Vosko, S. H.; Jackson, K. A.; Pederson, M. R.; Singh, D. J.; Fiolhais, C. Atoms, molecules, solids, and surfaces: Applications of the generalized gradient approximation for exchange and correlation. *Phys. Rev. B* **1992,** *46,* 6671-6687.

[24] Perdew, J. P.; Wang, Y. Accurate and simple density functional for the electronic exchange energy: Generalized gradient approximation. *Phys. Re*v. *B* **1986**, *33*, 8800-8802.

[25] Proynov, E. I.; Ruiz, E.; Vela, A.; Salahub, D. R. Determining and extending the domain of exchange and correlation functionals. *Int. J. Quantum Chem.* **1995**, *29*, 61-78

[26] Becke, A. D. Density functional thermochemistry. I. The effect of the exchange only gradient correction. *J. Chem. Phys.* **1992**, *96*, 2155-2160.

[27] Patton, D. C.; Pederson, M. R. Application of the generalized-gradient approximation to rare-gas dimers. *Phys. Re*v. *A* **1997**, *56*, 2495-2498.

[28] Tao, J. M.; Perdew, J. P. Test of a nonempirical density functional: Short-range part of the van der Waals interaction in rare-gas dimers. *J. Chem. Phys.* **2005**, *122,* Art. No. 114102.

[29] Perdew, J. P.; Schmidt, K. Density Functional Theory and Its Application to Materials, ed. VanDoren, V., AIP Press, Melville, New York, 2001.

[30] Becke, A. D. Density-functional thermochemistry. IV. A new dynamical correlation functional and implications for exact-exchange mixing. *J. Chem. Phys.* **1996**, *104*, 1040-1046.

[31] Tao, J. M.; Perdew, J. P.; Staroverov, V. N.; Scuseria, G. E. Climbing the density functional ladder: nonempirical meta–generalized gradient approximation designed for molecules and solids. *Phys. Rev. Lett.* **2003**, *91*, 146401.

[32] Lee, C.; Yang, W.; Parr, R. G. Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. *Phys. Re*v. *B* **1988**, *37*, 785-789.

[33] Colle, R.; Salvetti, O. Approximate calculation of the correlation energy for the closed shells. *Theor. Chim. Acta* **1975**, *37*, 329-334.

[34] Becke, A. D. A new mixing of Hartree–Fock and local density functional theories. *J. Chem. Phys.* **1993**, *98*, 1372-1377.

[35] Gill, P. M. W.; Johnson, B. G.; Pople, J. A.; Frisch, M. J. An Investigation of the Performance of a Hybrid of Hartree-Fock and Density Functional Theory. *Int. J. Quantum Chem.* **1992**, *26*, 319-331.

[36] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Wong, M. W.; Foresman, J. B.; Robb, M. A,; Head-Gordon, M.; Replogle, E. S.; Gomperts, R.; Andres. J. L.; Raghavachari, K.; Binkley, J. S; Gonzalez, C.; Martin, R. L.; Fox, D. J.; DeFrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. Gaussian 92/DFT. Rev. G.3; Gaussian, Inc., Pittsburgh, PA, **1993**.

[37] Zhao, Y.; Schultz, N. E.; Truhlar D. G. Design of density functionals by combining the method of constraint satisfaction with parametrization for thermochemistry, thermochemical kinetics, and noncovalent interactions. *J. Chem. Theory Comput.* **2006**, *2*, 364-382.

[38] Schmider, H. L.; Becke, A. D. Optimized density functionals from the extended G2 test set. *J. Chem. Phys.* **1998**, *108*, 9624-9631.

[39] Grimme, S. Density functional theory with London dispersion corrections. *WIREs Comput. Mol. Sci.* **2011**, *1*, 211-228.

[40] Grimme, S.; Steinmetz, M. Effects of London dispersion correction in density functional theory on the structures of organic molecules in the gas phase. *Phys.Chem.Chem.Phys.* **2013**, *15*, 16031-16042.

[41] Grimme, S. Semiempirical GGA-type density functional constructed with a long-range dispersion correction. *J. Comp. Chem.* **2006**, *27*, 1787-1799.

[42] Grimme, S. Semiempirical hybrid density functional with perturbative second-order correlation. *J. Chem. Phys.* **2006**, *124*, 034108.

[43] Schwabe, T.; Grimme, S. Towards chemical accuracy for the thermodynamics of large molecules: new hybrid density functionals including non-local correlation effects. *Phys. Chem. Chem. Phys.* **2006**, *8*, 4398-4401.

[44] Grimme, S.; Goerigk, L.; Fink, R. F. Spin-component-scaled electron correlation methods. WIREs Comput. Mol. Sci. **2012**, *2*, 886-906.

[45] Peverati, R.; Truhlar, D. G. Quest for a universal density functional: the accuracy of density functionals across a broad spectrum of databases in chemistry and physics. *Phil. Trans. R. Soc. A* **2014**, *372*, 20120476.

[46] Zhao, Y.; Schultz, N. E.; Truhlar, D. G. Exchange-correlation functional with broad accuracy for metallic and nonmetallic compounds, kinetics, and noncovalent interactions. *J. Chem. Phys.* **2005**, *123*, 161103.

[47] Zhao, Y.; Truhlar, D. G. A new local density functional for main-group thermochemistry, transition metal bonding, thermochemical kinetics, and noncovalent interactions. *J. Chem. Phys.* **2006**, *125*, 194101.

[48] Zhao, Y.; Truhlar, D. G. The M06 suite of density functionals for main group thermochemistry, thermochemical kinetics, noncovalent interactions, excited states, and transition elements: two new functionals and systematic testing of four M06-class functionals and 12 other functionals. *Theor. Chem. Acc.* **2008**, *120*, 215-241.

[49] Zhao, Y.; Truhlar, D. G. Density functional for spectroscopy: No long-range self-interaction error, good performance for Rydberg and charge-transfer states, and better performance on average than B3LYP for ground states. *J. Phys. Chem. A* **2006**, *110*, 13126.

[50] Zhao, Y.; Truhlar, D. G. Exploring the Limit of Accuracy of the Global Hybrid Meta Density Functional for Main-Group Thermochemistry, Kinetics, and Noncovalent Interactions. *J. Chem. Theory Comput.* **2008**, *4*, 1849-1868.

[51] Born, M. Volumen und hydratationswärme der ionen. *Z. Phys.* **1920**, *1*, 45-48.

[52] Kirkwood, J. G. Theory of solutions of molecules containing widely separated charges with special application to zwitterions. *J. Chem. Phys.* **1934**, *2*, 351-361.

[53] Onsager, L. Electric moments of molecules in liquids. *J. Am. Chem. Soc.* **1936**, *58*, 1486-1493.

[54] Foresman, J. B.; Keith, T. A.; Wiberg, K. B.; Snoonian, J; Frisch, M. J. Solvent effects .5. Influence of cavity shape, truncation of electrostatics, and electron correlation *ab initio* reaction field calculations. *J. Phys. Chem.* **1996**, *100*, 16098-16104.

[55] Tomasi, J.; Bonaccorsi, R.; Cammi, R.; delValle, F. J. O. Theoretical chemistry in solution-some results and perspectives of the continuum methods and in particular of the polarizable continuum model. *J. Mol. Struct.: THEOCHEM* **1991**, *80*, 401-424.

[56] Tomasi, J.; Bonaccorsi, R. Methodological aspects of the solvation models based on continuum solvent distributions. *Croat. Chem. Acta* **1992**, *65*, 29-54.

[57] Miertus, S.; Scrocco, E.; Tomasi, J. Electrostatic interaction of a solute with a continuum- A direct utilization of *ab-initio* molecular potentials for the prevision of solvent effects. *Chem. Phys*. **1981**, *55*, 117-129.

[58] Barone, V.; Cossi, M.; Tomasi, J. A new definition of cavities for the computation of solvation free energies by the polarizable continuum model. *J. Chem. Phys.* **1997**, *107*, 3210-3221.

[59] Cances, E; Mennuci, B. Tomasi, J. A new integral equation formalism for the polarizable continuum model: Theoretical background and applications to isotropic and anisotropic dielectrics. *J. Chem. Phys.* **1997**, *107*, 3032-3041.

[60] Cramer, C. J.; Truhlar, D. G. General parameterized SCF model for free energies of solvation in aqueous solution. *J. Am. Chem. Soc.* **1991**, *113*, 8305-8311.

[61] Cramer, C. J.; Truhlar, D. G. In *Trends and Perspectives in Modern Computational Science*; Maroulis, G., Simos, T. E., Eds; Brill Academic: Amsterdam. 2006

[62] Cramer, C. J.; Truhlar, D. G. A universal approach to solvation modeling. *Acc. Chem. Res.* **2008**, *41*, 760–768.

[63] Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Universal solvation model based on solute electron density and on a continuum model of the solvent defined by the bulk dielectric constant and atomic surface tensions. *J. Phys. Chem. B* **2009,** *113*, 6378-6396.

Chapter 3. Predicting Partition Coefficients of Linear Perfluorinated Compounds

3.1. Introduction

Long-chain linear perfluorinated acids (PFAs) such as perfluorocarboxylic acids ($CF_3(CF_2)_{N-2}COOH$, PFCAs), perfluorosulfonic acids ($CF_3(CF_2)_{N-1}SO_2OH$, PFSAs), and their conjugate bases, perfluorocarboxylates ($CF_3(CF_2)_{N-2}COO^-$, PFCs), and perfluorosulfonates ($CF_3(CF_2)_{N-1}SO_2O^-$, PFSs), where N is the number of carbon atoms in the molecule, have received significant attention in the past few years. Substitution of hydrogen by fluorine confers new physicochemical and biological properties to these molecules.[1,2] They show resistance to both chemical and biological degradation, which allows those with more than seven carbon atoms in their structure to bio-accumulate in living organisms, increasing the potential risk associated with their concentrated action.[3,4] Measurable quantities of branched perfluorinated acids have been found in mixtures analyzed by several groups.[5] However, the linear isomers predominate. These compounds have even been found in the arctic and the troposphere.[6,7] Furthermore, they have been detected in animals and in human blood,[8-10] which raises awareness about the need for a deeper understanding of their possible degradation pathways and routes of environmental distribution.[11]

PFAs have been postulated to exist almost completely dissociated; hence, some papers ignore the non-dissociated species in calculations of the environmental fate of these compounds.[12,13] However, several studies have tried to demonstrate the potential mistake of this approach by showing the need for taking both species into account.[14-16] The importance of considering both species arises when studying the chemical exchange between different environments (*e.g.*, aqueous or non-polar solutions) involved in the global fate of these compounds. The way these chemicals reach the atmosphere and their atmospheric transport have been widely discussed and are still an issue of discussion. However, many agree that the formation of aerosols could be the mechanism to explain the exchange of these families of compounds between aqueous media and the atmosphere. The pH of aerosol-related samples of these compounds ranges from 0 to 5.4.[17-19] In the lower limit of this pH range, or in less polar environments at higher pH values, both the acid and its conjugate base should coexist. Much remains to be done to better understand how PFAs bio-accumulate and how they get to reach waters, soil, air and humans. To that end, the determination of physicochemical properties such as acid dissociation constants (K_a, pK_a

= -log K_a) and partition (or distribution) coefficients are key factors to understand how these molecules behave in the environment or interact with the biota.

Zhao and Abraham[20] studied a large group of linear ionic organic salts. To their surprise, they found a strong linear correlation between the number of carbon atoms in these species and the logarithm of their octanol-water partition coefficient (Log P). They were initially expecting that the decrease of the effect of the positive charge as the carbon chain increases would produce a slope change. They also found that the slopes of the graphs for the neutral and the charged species were different and that the difference between the LogP of cations and their neutral counterparts becomes less as the length of the linear carbon chain increases.

The experimental determination of Log P (or Log D) values of PFCAs and PFSAs is a challenging task.[21] Hence, most values have not been determined and estimated data are mainly used.[15,16,22-25] Jing *et al.*[26] recently reported octanol-water partition coefficients for a homologous series of carboxylates and perfluorocarboxylates and for one sulfonate and perfluorosulfonate, determined by a voltammetry method. They observed that the lipophilicity of perfluorinated anionic compounds was two orders higher than that of their non-fluorinated counterparts. Furthermore, applying a fragment method, they demonstrated that perfluoroalkyl and alkyl chains of the same length have similar contributions to molecular lipophilicity. This result led them to hypothesize that the lipophilicity difference is determined by the charged head group ($–CO_2^-$ or $–SO_3^-$) and the electron-withdrawing effect upon it by the fluorine substitution on the alkyl chain. Like Zhao and Abraham,[20] they found a strong linear correlation between the number of carbons in the linear chain and Log P of the ionic species analyzed.

More recently, Rayne and Forest[27] analysed the apparently constant CF_2 fragment contribution to the somehow limited set of K_{oc} (soil organic carbon-water partition coefficient) values reported by Higgins and Luthy[28] for linear PFCAs. They found differences between the slope of the graph of average Log K_{oc} values with the length of the perfluoroalkyl chain originally reported by Higgins and Luthy, and the average slope obtained when using each individual data set, instead of working with the correlations separately. Additionally, Rayne and Forest suggested that the previously observed linear CF_2 contribution is debatable, as they observed an apparent change of CF_2 contribution with the increase in chain length. When discussing the results obtained by Jing *et al*, Rayne and Forest claimed that lack of consideration of the chemical interface could be a factor for the constant slope observed

with the increase in the number of CF_2 group. As a consequence, more studies must be done in order to determine whether the formation of micelles (due to the surfactant nature of these compounds) could influence the Log P values observed.

Software packages and online calculators used for predicting Log P (and/or Log D) values include EPI Suite, CLog P, COSMOtherm and SPARC.[22] All of them base their calculations on molecular structure and atomic or fragment contributions. The Log P values obtained for PFAs using several versions of these software packages have been compared with some limited experimental results, and the inaccuracies found are in the order of one unit or more, which shows the need for more research in this field.[22,24] The analysis of recent improvements in the predictions of some of these packages suggests that better parameterizations have been performed. However, doubts still remain as to whether these new results are a product of a specific parametrization to fit some particular groups of perfluorinated compounds or if there have been major changes to the software that could improve the calculation of Log P values for any group of molecules.[24] Table 3.S1, in the Supporting Information (SI) section, shows some of the previously calculated/reported values for PFCAs, which are also displayed in Figure 3.S1.

This work deals with the calculation of octanol-water partition coefficients for the linear PFAs with 2 to 11 carbon atoms (PFCAs and PFSAs, as well as their conjugate bases). The non-fluorinated analogues of these compounds are also studied. A new approach which makes use of electronic structure calculations, empirical observations and the limited experimental data available to predict the octanol-water partition coefficients of PFAs is described. To the best of our knowledge, no previous electronic structure calculations (using DFT methods) of log P values of these compounds have been previously reported.

3.2. Methodology

3.2.1. Calculation of Partition coefficients

A solute X partitions between n-octanol and water according to Scheme 3.1. The octanol-water partition equilibrium constant or coefficient, P, describes this process according to eq. 3.1.

$$X_{water} \leftrightarrows X_{n\text{-}octanol} \qquad \text{Scheme 3.1}$$

$$P = [X_{n\text{-}octanol}]/[X_{water}] \qquad (3.1)$$

The standard Gibbs free energy change of this equilibrium, $\Delta G°_{ow}$, can be determined from the difference between the calculated standard Gibbs free energies of formation ($\Delta_f G°$) of the solute in the two partitioning media as shown in eq. 3.2. Log P values can then be determined using eq. 3.3, where R is the ideal gas constant and T is the temperature in Kelvin.

$$\Delta G°_{ow} = \Delta_f G°_o (X) - \Delta_f G°_w (X) \qquad \text{eq. 3.2}$$

$$\text{Log P} = -\Delta G°_{ow}/(RT\ln 10) \qquad \text{eq. 3.3}$$

Two approaches were followed to calculate the $\Delta_f G°$ values in octanol and water, $\Delta_f G°_o$ and $\Delta_f G°_w$, respectively. The simplest approach, which led to the best results reported in this chapter, involved the application of solvent effects through a single-point energy calculation using gas-phase optimized geometry and frequency corrections. The $\Delta_f G°$ values in either octanol or water were obtained by combining the uncorrected energy in solution, E_o or E_w (for octanol and water, respectively), with the gas-phase thermal correction to the Gibbs free energy, TCG_{gas}; eq 3.3 then becomes eq. 3.4

$$\text{Log P} = (E_w - E_o)/(RT\ln 10) \qquad \text{eq. 3.4}$$

Another approach considers solvent effects in both geometry optimizations and frequency calculations. The $\Delta_f G°$ values in solution are calculated by combining the energy in solution with the corresponding TCG value. Since experimental data has been obtained between 295.15 and 298.15 K, this second approach was applied to verify that using a temperature of 298.15 K in our calculations had no significant effect on the calculated Log P values. We were unable to obtain a global minimum during the optimization of several carboxylic acids and carboxylates which prevented us from using this procedure; however, the overall results for the neutral acids were not better than when using solvent effects only on the energies.

Log P (also used as Log K_{ow}) is the value most frequently reported when referring to neutral solutes. The partitioning behaviour of ionizable molecules is usually described through the distribution coefficient, Log D, which depicts how the dissociated/undissociated pair distributes between these two phases. At high enough pH values, PFAs can be assumed to be completely dissociated, since the reported pK_a values are close to zero (a range of values from -0.5 to 3.8 has been reported and debate is still on-going).[29] Thus, the Log D values of the anionic species can be considered equal to the Log P under these conditions. This approach was used by Jing *et al*.[26] for reporting the first experimental Log P values for PFCs and perfluorooctane sulfonate (the PFS with N = 8). In this study, Log P will be the reported values for anions.

3.2.2. Computational Details

The bulk of the Log P calculations reported in this work are based on electronic structure calculations performed with the Gaussian 09 software package.[30] The B3LYP functional[31,32] was applied with the 6-31++G(d,p) basis set. Solvent effects were accounted for by means of the SMD method.[33] A previous study by our group[34a] on the thermodynamic stability of the perfluorooctanosulfonic acid isomers, led to B3LYP/6-311++G(d,p) results in close agreement with previous B3LYP/6-31++(d,p) calculations for the mono-methylated isomers.[34b] Based on this, the smaller basis set was chosen for the current study. Stationary points were verified as legitimate minima by a harmonic frequency calculation at the same level of theory. Since there is experimental evidence (confirmed by computations) of the helical conformation of perfluorinated compounds,[35] to avoid optimizing other conformers of higher energy, the geometries of the species studied were built starting from the helical optimized structure of the acid with eight carbon atoms, as done in our previous studies.[34a,c] Calculations were also performed using the M06-2X functional[36] and the results obtained were not significantly different from the B3LYP results discussed in the following sections.

The estimation of Log P was also performed using EPI Suite,[37] one of the most widely used tools for predicting physico-chemical properties of molecules, especially for environmental purposes. This freeware software bases its calculations on quantitative structure-activity relationships.[38,39] It requires a SMILES (Simplified Molecular Input Line Entry System: line notation for describing the structure of molecules) string as the input structure. EPI Suite calculates Log P values of neutral and ionic species; however, it seems that, if ionizable compounds are calculated, only one pH is considered. It corrects calculations at pH 7.4, which is the physiological pH. Hence, assuming that pK_a values of the PFAs are close to zero, at physiological pH the acids are fully ionized and the calculated Log P values of the anions ignore the existence of any undissociated species.

3.3. Results and Discussion

3.3.1. *Ab initio* calculation of Log P values of carboxylic acids, perfluorocarboxylic acids and their conjugate bases

Figure 3.1 shows the linear correlation between experimental and calculated (using eq. 3.4) Log P values with the number of carbon atoms (N) for the two families of carboxylic acids and their

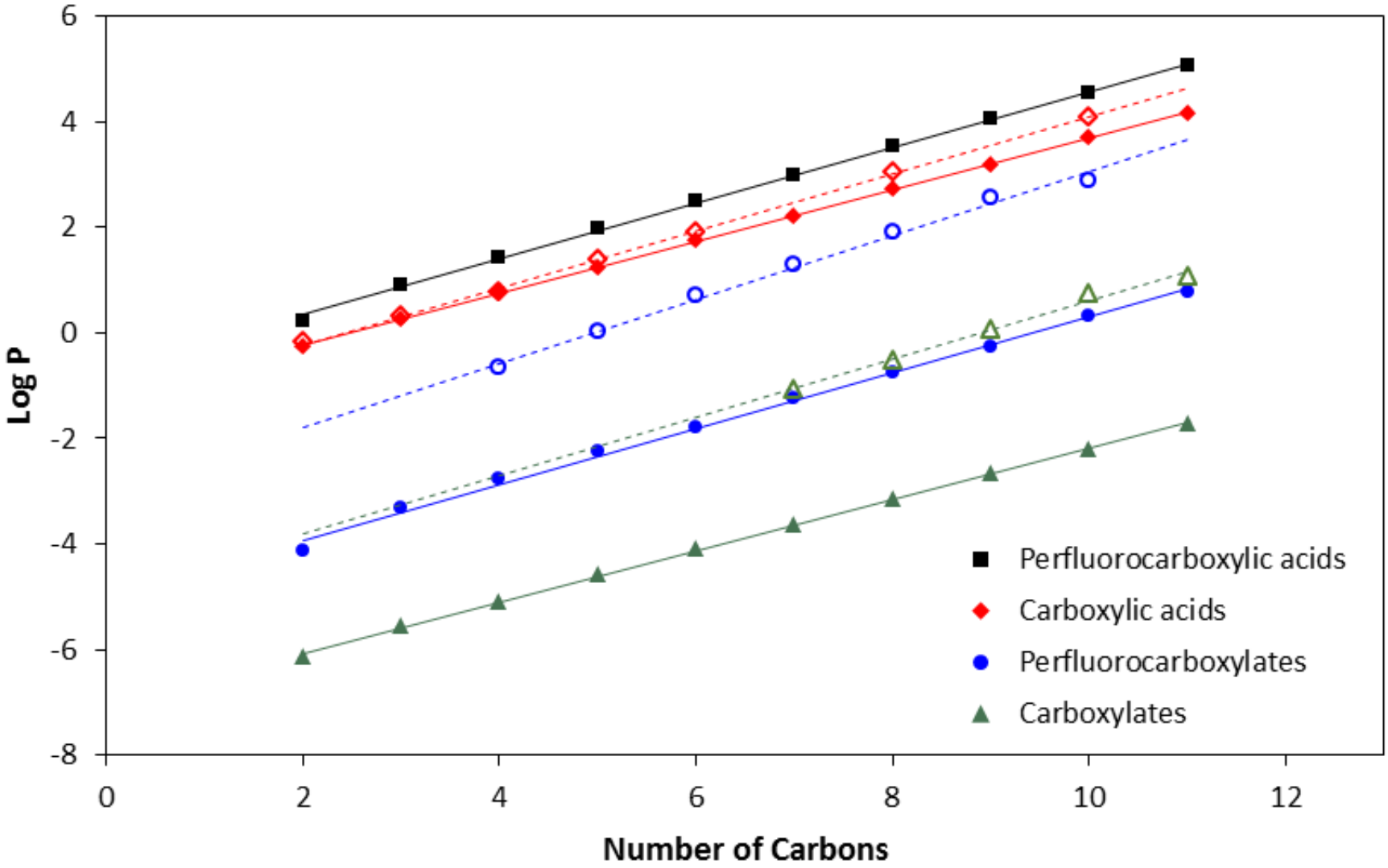


Figure 3.1. Plot of the experimental (broken lines and unfilled markers) and calculated (using eq. 3.4, solid lines and filled markers) Log P values (reported in Table 3.1) with the number of carbon atoms for carboxylic acids, perfluorocarboxylic acids, and their conjugate bases.

conjugate bases studied. Figure 3.S2 of the SI section contains the independent graphs for the experimental and calculated data. Remarkably high linear correlations ($R^2 > 0.997$) are obtained for the four curves shown. Similar R^2 values are obtained when correlating the experimental and calculated sets of data with each other. Table 3.1 displays the experimental[26,40-45] and calculated Log P values for the four groups of species. Experimental values for the PFCs were determined using the data provided by Jing *et al.*,[26] as described in the SI section (see Section 3.S1 and Table 3.SS1). The calculated (uncorrected) energies in solution, E_w and E_o, for the four families of linear compounds are reported in Tables 3.S2a and 3.S2b of the SI section.

A higher value of P corresponds to a higher log P value, which means that the molecule dissolves better in octanol than water, thus it is more lipophilic. If P values are smaller than 1, the Log P values will be smaller than zero, which means that the concentration of the solute in octanol is lower than its concentration in water. The calculated Log P values are slightly underestimated for the carboxylic acids with an average error of -0.18 units, which is an excellent result. Larger underestimated values are obtained for the anions, with average errors of -2.74 for the carboxylates and -2.50 for the PFCs. The calculated error tends to increase with the size of the species considered. Calculations predict these compounds, especially the anions, to be less lipophilic than they have been found to be experimentally. However, the general trends are well reproduced. Calculated and experimental values correlate linearly with N. Log P values for PFCs determined by Jing *et al.*[26] are almost two orders of magnitude higher than the values of the carboxylates with the same number of carbon atoms; our results also reproduce this. Furthermore, the calculated lipophilic order (carboxylates < PFC < carboxylic acids) corresponds with experiment.[26,44]

Our calculations indicate that, as expected,[26] the perfluorinated species have greater Log P values than the non-fluorinated ones. The increase in Log P is much greater for the anions than for the neutral acids, which is to be expected based on polarity arguments and the charge of these species. The electron-withdrawing effect of the fluorine atoms in the alkyl chain reduces the negative charge of the head group, making the anions more thermodynamically stable and increasing the acidity of the corresponding PFCAs. Calculated Mulliken atomic charges (see Table 3.S3a) clearly indicate this effect which increases when going from the gas phase to octanol and water. Larger negative charges on the oxygen atoms bonded to the acidic hydrogen atom also explain the higher acidity of the PFCAs

relative to their non-fluorinated analogues (the same situation applies to PFSAs and PFSs, see Table 3.S3b).

Table 3.1 also displays the slopes and intercepts of the linear correlations between the experimental and calculated Log P values with N for the four groups of species. A very interesting observation is the fact that the curves for the carboxylic acids and the carboxylates, using both experimental and calculated data, are almost parallel, with slopes of 0.538-0.561 (experimental) and 0.491 (calculated). The same situation arises between the calculated curves for the PFCAs and the PFCs with slopes of 0.529 (calculated), which are just slightly greater (by 0.04 units) than the calculated slopes of the non-fluorinated species. From this it is not difficult to imagine that the corresponding slope for the linear correlation using the experimental Log P values of the PFCAs may be very close to 0.606, the value obtained for the slope using the experimental Log P values of the PFCs. The calculated slopes for the carboxylic acids, the carboxylates and the PFCs are only 0.05-0.08 units smaller than the corresponding experimental curves.

Log P values were also obtained from calculations including solvent effects by means of the IEF-PCM solvation method,[46] using both the UFF and UAHF radii to define the solvent cavities. Even though the Log P *vs* N curves obtained showed strong linear correlations, the slopes were negative in contradiction to the experimental data. Previous computational studies have also indicated that SMD is the continuum solvation method used to predict an increase in lipophilicity with an increase of chain length for acids with more than two carbon atoms.[29c]

To the best of our knowledge, there are no experimental Log P values reported for PFCAs with more than two carbon atoms in their structure. The calculation for trifluoroacetic acid (N = 2) seems to be overestimated (by 0.44 or 2.34 units; see follow up discussion in section 3.3.2.1), and at this point not much more can be said about the calculated Log P values of other PFCAs. The parallel relationships previously identified between experimental and calculated (based on electronic structure calculations) Log P values for the two groups of acids with their corresponding conjugate bases, are investigated in the following section using online calculators based on molecular structure.

Table 3.1. Experimental [or predicted] and calculated (using EPI Suite and from electronic structure calculations) Log P values of carboxylic acids, perfluorocarboxylic acids (PFCAs) and their conjugate bases.

N[a]	Carboxylic acids $CH_3(CH_2)_{N-2}COOH$			Carboxylates $CH_3(CH_2)_{N-2}COO^-$			PFCAs $CF_3(CF_2)_{N-2}COOH$			PFCs $CF_3(CF_2)_{N-2}COO^-$		
	Exp[b]	**EPI Suite**	**Calc**	**Exp**[c]	**EPI Suite**	**Calc**	**Exp**[f]	**EPI Suite**	**Calc**	**Exp**[c]	**EPI Suite**	**Calc**
2	-0.17	0.09	-0.26	[-3.87]	-3.72	-6.15	-2.1[d]; [-0.2][e]	0.50	0.24	[-1.78]	-3.31	-4.12
3	0.33	0.58	0.25	[-3.31]	-3.23	-5.57	[0.41]	1.47	0.91	[-1.17]	-2.34	-3.32
4	0.79	1.07	0.78	[-2.75]	-2.74	-5.10	[1.01]	2.14	1.43	-0.66	-1.67	-2.78
5	1.39	1.56	1.24	[-2.19]	-2.25	-4.59	[1.62]	2.81	1.98	0.03	-1.00	-2.25
6	1.92	2.05	1.74	[-1.63]	-1.76	-4.11	[2.22]	3.48	2.49	0.7	-0.34	-1.78
7	[2.48]	2.54	2.22	-1.1	-1.27	-3.63	[2.83]	4.15	3.00	1.30	0.33	-1.23
8	3.05	3.03	2.72	-0.51	-0.78	-3.15	[3.44]	4.81	3.53	1.9	1.00	-0.76
9	[3.56]	3.52	3.19	0.07	-0.29	-2.67	[4.04]	5.48	4.06	2.57	1.67	-0.25
10	4.09	4.02	3.69	0.74	0.20	-2.20	[4.65]	6.15	4.55	2.9	2.34	0.31
11	[4.63]	4.51	4.17	1.08	0.70	-1.71	[5.25]	6.82	5.08	[3.68]	3.01	0.79
Slope[g]	0.539	0.491	0.490	0.561	0.491	0.488	[0.606]	0.685	0.529	0.606	0.685	0.529
Intercept[g]	-1.295	-0.895	-1.214	-4.993	-4.703	-7.059	[-1.412]	-0.671	-0.714	-2.991	-4.483	-4.977

[a] Number of carbon atoms; [b] From Ref. 40 [values in square brackets have been predicted using the experimental slope and intercept]; [c] From Ref. 26 (see Section 3.S1) [values in square brackets have been predicted using the experimental slope and intercept]; [d] From Refs. 41-43; [e] From Refs. 43-45; [f] Values in square brackets have been predicted using one experimental value (-0.2, N=2) and the experimental slope of PFCs (0.606); [g] From a linear regression analysis: Log P = Slope x N + Intercept (excluding predicted values, unless the slope and intercept are shown in square brackets).

3.3.1.1. Calculation of Log P values using EPI Suite

Log P values used in the vast majority of publications dealing with global fate predictions and partitioning behaviour of PFAs, have been obtained using available software packages which provide very fast results and have demonstrated their applicability for predicting other properties. Even though no software package is able to accurately predict Log P values for all PFAs,[24] they continue to be used.[15,16,22-25]

EPI Suite is the online calculator used in this work because, since its creation, PFAs have been included in its training set for the calculation of octanol-water partition coefficients. The values obtained for the carboxylic and perfluorocarboxylic acids and their conjugate bases are displayed in Table 3.1 (and plotted in Figure 3.S3). Once again, the calculated Log P values linearly correlate with N for each of the four groups of compounds. Interesting similarities between the slopes of these graphs when using both EPI Suite Log P values and those derived from electronic structure calculations can be observed. The EPI Suite slopes for the carboxylic acids and the carboxylates are identical to each other (parallel graphs with 0.491 slope) and to the slopes of the graphs that use the calculated Log P values previously presented. These slopes are only 0.05-0.06 units smaller than the slopes of the quasi-parallel experimental graphs. Parallel lines (with slopes of 0.685) are also obtained for the PFCAs and PFCs; the slopes of the previous calculated graphs of these compounds were 0.529. In addition, the experimental lipophilic order (carboxylates < PFC < carboxylic acids) and the slightly greater slope obtained for the perfluocarboxylates (PFC) relative to the non-fluorinated compounds using experimental data are well matched by the Log P predictions made with EPI Suite.

Values calculated with this software depend on the version used (See Table 3.S1 in the SI section). When EPI suite 2009 is used, the slope of the Log P *vs.* N graph for PFCAs (0.966) is much larger than when using the 2015 version (0.685) or when using the experimental Log P values of PFCs (0.606). The 2009 EPI Suite values from Rayne and Forest[24] seem to be identical to a set of values reported in 2006.[22] Both EPI Suite versions (2006 and 2009) made use of the KOWWIN module v1.67; however, the results reported in this thesis use version v1.68.

3.3.2. Predicting Log P values for perfluorinated acids

3.3.2.1. Assessing the available Log P values for trifluoroacetic acid

To the best of our knowledge, the only PFCA for which experimental Log P values have been reported is trifluoroacetic acid (TFAA, N = 2; see Table 3.1): -2.1[41-43] and -0.2.[43-45] The reported value of -2.1 is much smaller than the -1.78 value derived by Jing *et al.*[26] for trifluoroacetate (TFA, N = 2) by extrapolation from the Log P *vs.* N curve using their experimental values for PFCs. As can be seen from our previous discussion using the data reported in Table 3.1, the Log P values of the acids are always larger than those of their corresponding conjugate bases. Hence, the -2.1 value might need to be revised.

Using a fragment method, Jing *et al.*[26] demonstrated that a perfluoroalkyl chain is as lipophilic as a non-fluorinated alkyl chain with the same number of carbons (*i.e.*, CH_2 and CF_2 groups contribute similarly to the lipophilicity of these compounds). In addition, they explained the differences between the Log P values of the anions (PFC *versus* carboxylates) due to the strong electron-withdrawing effect of the fluorine atoms that quenches the negative charge of the head group of PFCs. According to this explanation, the affinity of PFCs for water is less than that of carboxylates and the overall effect is that PFCs have greater P (and Log P) values than their analogue carboxylates. If these ideas are applied to neutral compounds (the PFCAs and the carboxylic acids with similar carbon chain lengths), then given that the head group is not charged, much smaller differences between their Log P values would be expected (as can be seen from the calculated curves displayed in Figure 3.1). Their lipophilicity would be very similar, and the absence of a charged head group would also make their interaction with water similar between fluorinated and non-fluorinated carboxylic acids.[47]

The -0.2 value,[43-45] which follows the expected trend for this compound given the estimated value for its conjugate base (-1.78), was obtained by the Rekker's fragment additivity scheme.[48] Furthermore, this value is not too different from the -0.17 Log P value reported for acetic acid (N = 2), in agreement with the ideas previously shared. Hence, we have taken this Log P value as the most probable one for TFAA.

3.3.2.2. Predicting Log P values for PFCAs and related compounds

From the observation of the various pairs of similar slopes (using experimental, EPI Suite or electronic structure calculation Log P values) for the Log P *vs.* N graphs of carboxylic acids and carboxylates, and separately for PFCAs and PFCs (see Table 3.1), better predictions of Log P values for the PFCA group with three to eleven carbons in the linear chain can be attempted. Given that the slope of the experimental Log P values of PFCs is 0.606,[26] we could anticipate the same slope for the graph of the experimental Log P values of PFCAs. With the slope of the line that these points would form, and knowing one of these points (the Log P value for TFAA (N=2) is -0.20), the Y-intercept can be calculated (-1.412). Eq. 3.5 can then be used to calculate the desired Log P values for each value of N.

$$\text{Log P} = \text{Slope} \cdot \text{N} + \text{Intercept} = 0.606 \cdot \text{N} - 1.412 \qquad \text{eq. 3.5}$$

The predicted Log P values for PFCAs are shown in square brackets in Table 3.1. As expected from our previous discussion, these values are very similar to the experimental Log P values of the carboxylic acid analogues.[40] Because the slope of the carboxylic acids is smaller (0.538) than the slope of the PFCAs (0.606), the Log P values of the latter become slightly greater as the length of the linear carbon chain increases. The differences in Log P values between these two families go from -0.03 (for N = 2) to 0.62 (for N = 11). Using the slope and intercept of the curve that best fits the experimental points for the carboxylic acids, carboxylates and PFCs (see Table 3.1), the unavailable experimental data has been predicted and these values are shown in square brackets in Table 3.1. Experimental and predicted values for the four groups of compounds are displayed in Figure 3.2.

3.3.2.3. Predicting Log P values for sulfonic acids, sulfonates, PFSAs and PFSs

Electronic structure calculations of Log P values for the linear sulfonic acids, PFSAs and their conjugate bases were also performed, together with EPI Suite calculations. The calculated (uncorrected) energies in solution, E_w and E_o, are reported in Tables 3.S2c and 3.S2d of the SI section. The values obtained and details of the linear correlations (slopes and intercepts) of the different sets of Log P values with the number of carbon atoms in the linear chain (N) are reported in Table 3.2. Strong linear correlations were found in all cases (see Figures 3.3 and 3.S4).

Experimental Log P values have only been reported for octanesulfonate (0.6) and

Table 3.2. Predicted and calculated (using EPI-Suite and from electronic structure calculations) Log P values of sulfonic and perfluorosulfonic (PFSAs) acids and their conjugate bases.

N[a]	Sulfonic acids $CH_3(CH_2)_{N-1}SO_2OH$			Sulfonates $CH_3(CH_2)_{N-1}SO_2O^-$			PFSAs $CF_3(CF_2)_{N-1}SO_2OH$			PFSs $CF_3(CF_2)_N-SO_2O^-$		
	Pred[b]	**EPI Suite**	**Calc**	**Pred**[c]	**EPI Suite**	**Calc**	**Pred**[d]	**EPI Suite**	**Calc**	**Pred**[e]	**EPI Suite**	**Calc**
2	0.41	-1.89	-1.71	-2.77	-4.04	-6.90	0.41	0.48	-0.60	-1.19	-1.67	-4.63
3	0.95	-1.40	-1.23	-2.21	-3.55	-6.38	1.01	1.15	-0.09	-0.58	-1.00	-4.12
4	1.49	-0.91	-0.72	-1.64	-3.06	-5.92	1.62	1.82	0.42	0.03	-0.33	-3.55
5	2.03	-0.42	-0.23	-1.08	-2.56	-5.41	2.22	2.49	0.99	0.63	0.34	-3.03
6	2.57	0.07	0.25	-0.52	-2.07	-4.95	2.83	3.16	1.49	1.24	1.01	-2.5
7	3.11	0.56	0.74	0.04	-1.58	-4.46	3.44	3.82	1.99	1.84	1.68	-2.03
8	3.64	1.06	1.22	0.6[g]	-1.09	-3.98	4.04	4.49	2.51	2.45[g]	2.35	-1.49
9	4.18	1.55	1.71	1.16	-0.60	-3.50	4.65	5.16	3.07	3.06	3.02	-0.98
10	4.72	2.04	2.20	1.72	-0.11	-3.01	5.25	5.83	3.55	3.66	3.68	-0.46
11	5.26	2.53	2.68	2.28	0.38	-2.52	5.86	6.50	4.08	4.27	4.35	0.03
Slope[f]	0.539	0.492	0.488	0.561	0.491	0.484	0.606	0.669	0.521	0.606	0.669	0.518
Intercept[f]	-0.668	-2.876	-2.681	-3.888	-5.021	-7.850	-0.804	-0.855	-1.643	-2.398	-3.006	-5.644

[a] Number of carbon atoms; [b] Predicted values using the experimental slope of the carboxylic acids (0.539, see Table 3.1) and the predicted value for N = 2 (Log P = 0.41, see Section 3.3.2.3); [c] Predicted values using the experimental slope of the carboxylates (0.561, see Table 3.1) and one experimental value (Log P = 0.6, N = 8); [d] Predicted values using the experimental slope of PFCAs (0.606, see Table 3.1) and the predicted value for N = 2 (Log P = 0.41, see Section 3.3.2.3), are the values of the PFCAs with the same perfluorinated chain length (*i.e.*, N + 1); [e] Predicted values using the experimental slope of the PFCs (0.606, see Table 3.1) and one experimental value (Log P = 2.45, N = 8); [f] From a linear regression analysis: Log P = Slope x N + Intercept; [g] Experimental values from Ref. 26 (see Section 3.S1).

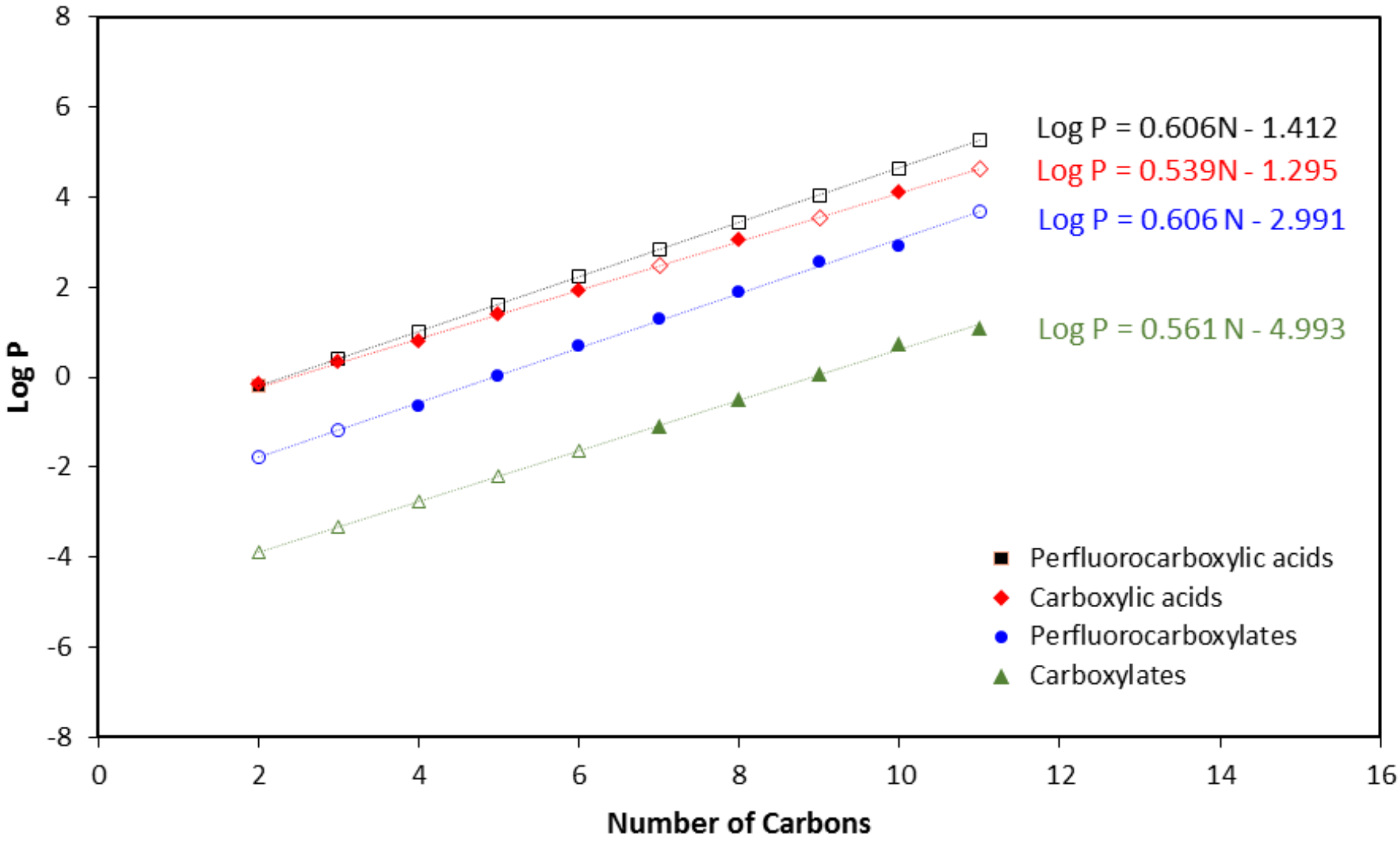


Figure 3.2. Plot of the experimental (filled coloured marker) and predicted (unfilled marker) Log P values (reported in Table 3.1) with the number of carbon atoms for carboxylic and perfluorocarboxylic acids, and their conjugate bases.

perfluorooctanesulfonate (2.45), N = 8.[26] The calculated values are -1.09 (-3.98) and 2.35 (-1.49) for octanesulfonate and perfluorooctanesulfonate, respectively, using EPI Suite (electronic structure calculations). Jing *et al.*[26] concluded that the 1.85 difference between the Log P values of these compounds (which is similar to the Log P difference of 2.16-2.50 units they obtained between PFCs and carboxylates) was due to the sulfonate group ($-SO_2O^-$), which is affected by the electron-withdrawing effect of the fluorine atoms that stabilizes the negative charge of the head group. The calculated Log P difference for these compounds is 3.44 (with EPI Suite) and 2.49 (with electronic structure calculations).

As previously observed for PFCAs/PFCs and carboxylic acids/carboxylates, the calculated curves of PFSAs and PFSs have greater slopes than those of their corresponding non-fluorinated analogues. A surprisingly interesting result is that the calculated slopes (using both EPI Suite and electronic structure calculations) for the carboxylic acids (0.491, 0.490), carboxylates (0.491, 0.488), PFCAs (0.685, 0.529) and PFCs (0.685, 0.529) are almost identical to the slopes of the corresponding sulfur-compounds: sulfonic acids (0.492, 0.488), sulfonates (0.491, 0.484), PFSAs (0.669, 0.521) and PFSs (0.669, 0.518). Acids and their corresponding conjugate bases show the same Log P *vs.* N slope in all cases as well.

From these results we could infer that the slopes of these curves are mainly determined by the presence of the alkyl or perfluoroalkyl chains in these compounds and not by the head group ($–COOH/–COO^-$ versus $–SO_2OH/–SO_2O^-$). More importantly, this observation backs up the idea that the same equality in slopes would also be observed when comparing the slopes of experimental Log P values of these eight families of compounds. Given the almost-complete absence of experimental data for the four families of sulfur-containing compounds under study, these ideas provide an interesting route for predicting their Log P values. That is, if the experimental slope for PFCAs and PFCs is 0.606, we should expect a similar slope when plotting the experimental Log P values of PFSAs and PFSs. Similarly, the experimental slopes of 0.539 and 0.561, for carboxylic acids and carboxylates, respectively, should also be the experimental slopes for sulfonic acids and sulfonates, respectively. Given that experimental values are only available for the sulfonate and PFS with N = 8, with a point and the slope, the intercept of what would be the experimental correlation line can be calculated and the remaining Log P values can be predicted. Predicted values for sulfonates and PFSs are shown in

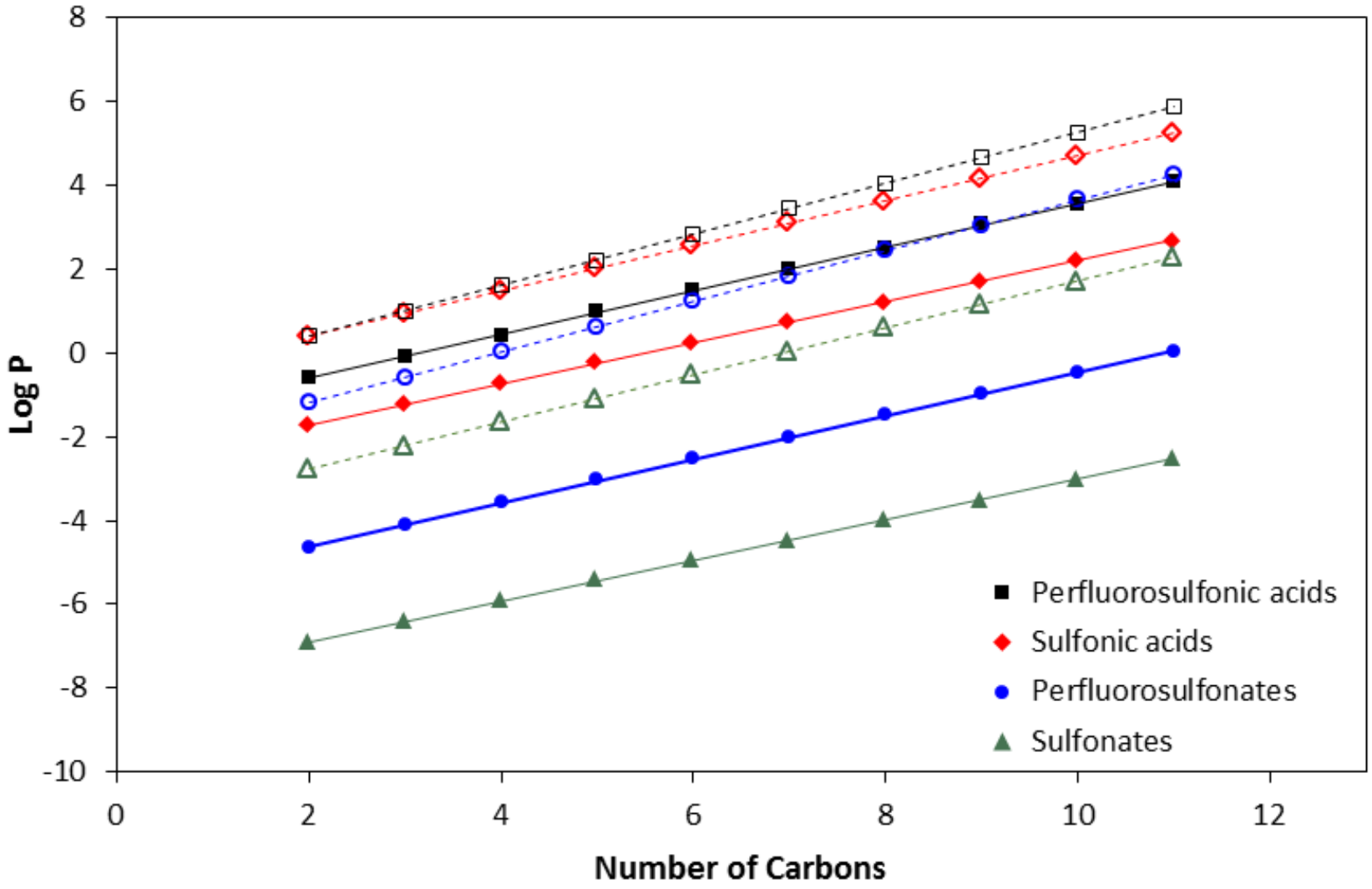


Figure 3.3. Plot of the predicted (unfilled marker) and calculated (using eq. 3.4, colour filled marker) Log P values (reported in Table 3.2) with the number of carbon atoms for sulfonic, perfluorosulfonic acids and their conjugate bases.

Table 3.2. Figure 3.3 displays the combined plots of the predicted and calculated (using eq. 3.4) Log P values; separate plots appear in Figure 3.S4. Graphs that combine predicted and EPI Suite calculated Log P values are shown in Figure 3.S3 of the SI section. To undertake the prediction of Log P values for PFSAs and sulfonic acids, we make use of observations from previous studies.

Rayne and Forest[24] gave evidence of a strong relationship between linear PFSs and PFCs. They suggested, based on the results obtained by Jing *et al.*,[26] Kelly *et al.*,[23] and Higgins and Luthy,[28,49] that the Log D values obtained for the perfluorinated anions (sulfonic and carboxylic) should be the same as long as these molecules have the same perfluorinated chain length. The previous comparison could be made because the determinations upon which Rayne and Forest based their findings favoured the almost complete ionization of the corresponding acids that have pK_a values very close to zero. Apparently, as also observed from our calculations, the structural differences of the head group (sulfonate or carboxylate) do not produce Log P differences between PFSs and PFCs, as long as they have the same number of carbon atoms in the perfluorinated alkyl chain. That is, the Log P of the PFS with N carbon atoms should be very similar to the Log P value of the PFC with N+1 carbon atoms. The experimental and predicted data we have gathered (see Tables 3.1 and 3.2) fully support this idea. The average difference between the previously described pairs of Log P values for PFCs and PFSs is 0.01, and the mean absolute difference is 0.06.

The same correspondence should also be expected between the Log P values of a PFSA with N carbon atoms and a PFCA with N+1 carbon atoms. Hence, we can assume that for the PFSA of N=2, Log P = 0.41, the predicted value for the PFCA of N=3. With this point and the predicted slope of 0.606, the remaining Log P values for PFSAs are predicted (see Table 3.2 and Figures 3.3 and 3.S2).

As previously discussed in Section 3.3.2.1, fluorinated and non-fluorinated carboxylic acids with the same carbon chain length should have similar Log P values, and this similarity is the greatest for the smallest family member (N=2). Figure 3.2 shows this for the experimental and predicted Log P values of the PFCAs. If we extend this idea to the sulfonic acids and the PFSAs, we can estimate with some small error the Log P value of the sulfonic acid of N=2 to be 0.41, and with the previously estimated slope of 0.539, the remaining Log P values can be estimated (see Table 3.2 and Figures 3.3 and 3.S2).

The predicted Log P values for the four sulphur-containing families of compounds are plotted in Figure 3.S4. The strong similarities to the experimental plot of the fluorinated and non-fluorinated carboxylic acids (see Figure 3.2) can be clearly appreciated. The perfluorinated anions (PFCs and PFSs) have greater Log P values than the non-fluorinated ones. The perfluorinated acids (PFCAs and PFSAs) have similar Log P values, just slightly higher as the length of the carbon chain increases, relative to the non-fluorinated acids. From a qualitative point of view, the relative order of the experimental or predicted curves is well reproduced by the calculated curves using Log P values derived from electronic structure calculations (see Figures 3.1 and 3.3). This consistency is not observed when comparing with the calculated curves using EPI Suite, in particular when considering the sulfur-containing compounds (see Figure 3.S3). In general, even though both electronic structure calculations and EPI Suite predictions of Log P values introduce consistent systematic errors when calculating Log P values that are different for fluorinated- and non-fluorinated-compounds, the calculated curves of Log P values using electronic structure methods reproduce experiments better than the curves using EPI Suite predictions.

Given the lack of experimental Log P values to verify the predictions made, further investigation is needed. However, given that most environmental studies so far make use of Log P values which have been estimated by various software of similar nature to EPI Suite or using empirical results,[15] the Log P values predicted in this study could provide a much better alternative for comparison when analyzing the environmental fate of these kinds of compounds.

3.3.3. Potential applicability of the Log P predictions made in this study

Because of their persistence and inertness to most degrading agents, concerns have been raised about the bioaccumulation of PFAs in the environment. It has been previously indicated that knowledge of their Log P values does not allow the correct prediction of their bioaccumulation because the potential association of PFAs with proteins instead of lipids changes their behaviour relative to other bio-accumulative lipophilic compounds.[4] Nonetheless, estimated Log P values of PFAs are widely used in a variety of environmental studies, some of which have been compiled below.

Attempts have been made to relate Log P values to the trophic magnification factor at different trophic levels. Kelly *et al*.[23] took into account linear PFCAs ranging from seven to thirteen carbon atoms, as

well as perfluorooctane sulfonic acid (PFSA with N = 8). These authors followed a methodology guided by empirical considerations as recommended by Dr. David Ellis, published five years later.[7] We found excellent agreement (with differences smaller than 0.5 units) between the Log P values they used and the ones predicted here for the PFSA with N = 8 (a value also in close agreement with our reported value for PFCA with N = 9) and the PFCAs with N = 7, 8, 9 (see Table 3.S1 in the SI section).

A long-term environmental fate simulation of PFCAs and PFCs with eight to thirteen carbon atoms was reported by Armitage *et al.*[16] The Log P values used in their work were taken from the COSMOtherm and SPARC calculations published by Arp *et al.*,[22] also shown in Table 3.S1 and plotted in Figure 3.S1. The COSMOtherm values are greater than the Log P values we predict in this work, but the differences become smaller and less significant as N increases. Similarly, the SPARC values are also greater than our predictions, but the differences increase as N increases. In our opinion, these simulations were performed using overestimated Log P values. In addition, Webster *et al.*[15] used a multispecies environmental fate model to predict the overall partitioning of the PFCA/PFC pair with N = 8 in different media. The Log P value predicted for the PFCA with N = 8, using previously published data by Higgins and Luthy,[28] was 3.73, remarkably close to the 3.44 value predicted in this study.

3.4. Conclusions

Partition coefficients (as well as acid dissociation constants) are key physico-chemical properties when determining the environmental fate of chemical species. The lack of experimental determinations of Log P values, especially for fluorinated compounds, have led researchers to use limited predictive tools available when attempting to explain the observed environmental distribution and transport between different media of these compounds. However, the use of inaccurate values when performing environmental simulations could lead to incorrect long-term predictions, with important consequences.

To the best of our knowledge, this thesis reports the first application of DFT methods to the calculation of Log P values of perfluorinated compounds. Eight families of linear organic compounds were investigated: carboxylic acids, perfluorinated carboxylic acids (PFCAs), sulfonic acids and perfluorinated sulfonic acids (PFSAs), together with their corresponding conjugate bases. It has been

shown that the consistent similarities observed between experimental and calculated (with electronic structure methods and using EPI suite) slopes of the linear plots of Log P values with the number of carbon atoms (N = 2 to 11), together with the available experimental Log P data and previously published observations, provide a much better predictive alternative of Log P values to be used for comparison when modeling the environmental fate and transport of these compounds. The most relevant Log P predictions made in the present work refer to PFCAs, PFSAs, and PFSs, but predictions were also made for the other families of linear organic compounds studied.

3.5. References

[1] Krafft, M. P.; Riess, J. G. Highly fluorinated amphiphiles and colloidal systems, and their applications in the biomedical field. A contribution. *Biochimie.* **1998**, *80*, 489-514.

[2] Lopez-Fontan, J. L.; Sarmiento, F.; Schulz, P. C. The aggregation of sodium perfluorooctanoate in water. *Colloid Polym Sci.* **2005**, *283*, 862-871.

[3] Rosen, M. B.; Lau, C.; Corton, J. C. Does Exposure to Perfluoroalkyl Acids Present a Risk to Human Health? *Toxicol. Sci.* **2009**, *111*, 1-3.

[4] Conder, J. M.; Hoke, R. A.; de Wolf, W.; Russel M. H.; Buck, R. C. Are PFCAs bioaccumulative? A critical review and comparison with regulatory lipophilic compounds. *Environ. Sci. Technol.* **2008**, *42*, 995–1003.

[5] See, for example: (a) Arsenault, G.; Chittim, B.; Gu, J.; McAlees, A.; McCrindle, R.; Robertson, V. Separation and fluorine nuclear magnetic resonance spectroscopic (F-19 NMR) analysis of individual branched isomers present in technical perfluorooctanesulfonic acid (PFOS). *Chemosphere **2008**, 73*, S53-S59. (b) Seacat, A. M.; Thomford, P. J.; Hansen, K. J.; Clemen, L. A.; Eldridge, S. R.; Elcombe, C. R.; Butenhoff, J. L. Sub-chronic dietary toxicity of potassium perfluorooctanesulfonate in rats. *Toxicology* **2003**, *183*, 117–131. (c) Olsen, G. W.; Church, T. R.; Miller, J. P.; Burris, J. M.; Hansen, K. J.; Lundberg, J. K.; Armitage, J. B.; Herron, R. M.; Medhdizadehkashi, Z.; Nobiletti, J. B.; O'Neill, E. M.; Mandel, J. H.; Zobel, L. R. Perfluorooctanesulfonate and other fluorochemicals in the serum of American Red Cross adult blood donors. *Environ. Health Perspect.* **2003**, *111*, 1892–1901.

[6] Martin, J. W.; Smithwick, M. M.; Braune, B. M.; Hoekstra, P. F.; Muir, D. C. G.; Mabury, S. A. Identification of long-chain perfluorinated acids in biota from the Canadian Arctic. *Environ. Sci. Technol.* **2004**, *38*, 373–380.

[7] Ellis, D. A.; Martin, J. W.; De Silva, A. O.; Mabury, S. A.; Hurley, M. D.; Andersen, M. P. S.; Wallington, T. J. Degradation of fluorotelomer alcohols: A likely atmospheric source of perfluorinated carboxylic acids. *Environ. Sci. Technol.* **2004**, *38*, 3316–3321.

[8] Riddell, N.; Arsenault, G.; Benskin, J. P.; Chittim, B.; Martin, J. W.; McAlees, A.; McCrindle, R. Branched Perfluorooctane Sulfonate Isomer Qantification and Characterization in Blood Serum Samples by HPLC/ESI-MS(/MS). *Environ. Sci. Technol.* **2009**, *43*, 7902-7908.

[9] De Silva, A. O.; Mabury S. A. Isolating isomers of perfluorocarboxylates in polar bears (Ursus maritimus) from two geographical locations. *Environ. Sci. Technol.* **2004**, *38*, 6538-6545.

[10] De Silva, A. O.; Mabury, S. A. Isomer distribution of perfluorocarboxylates in human blood: Potential correlation to source. *Environ. Sci. Technol.* **2006**, *40*, 2903-2909.

[11] Wallington, T. J.; Hurley, M. D.; Xia, J.; Wuebbles, D. J.; Sillman, S.; Ito, A.; Penner, J. E.; Ellis, D. A.; Martin, J.; Mabury, S. A.; Nielsen, O. J.; Sulbaek Andersen, M. P. Formation of C7F15COOH (PFOA) and other perfluorocarboxylic acids during the atmospheric oxidation of 8 : 2 fluorotelomer alcohol. *Environ. Sci. Technol.* **2006**, *40*, 924-930.

[12] Prevedouros, K.; Cousins, I. T.; Buck, R. C.; Korzeniowski, S. H. Sources, fate and transport of perfluorocarboxylates. *Environ. Sci. Technol.* **2006**, *40*, 32–44.

[13] Armitage, J.; Cousins, I. T.; Buck, R. C.; Prevedouros, K.; Russell, M. H.; MacLeod, M.; Korzeniowski, S. H. Modeling global-scale fate and transport of perfluorooctanoate emitted from direct sources. *Environ. Sci. Technol.* **2006**, *40*, 6969–6975.

[14] Burns, D. C.; Ellis, D. A.; Li, H.; Mcmurdo, C. J.; Webster, E. Experimental pK(a) Determination for Perfluorooctanoic Acid (PFOA) and the Potential Impact of pK(a) Concentration Dependence on Laboratory-Measured Partitioning Phenomena and Environmental Modeling. *Environ. Sci. Technol.* **2008**, *42*, 9283-9288.

[15] Webster, E; Ellis, D. A.; Reid, L. K. Modeling the environmental fate of perfluorooctanoic acid and perfluorooctanoate: an investigation of the role of individual species partitioning. *Environ. Toxicol. Chem.* **2010**, *29*, 1466-1475.

[16] Armitage, J. M.; MacLeod, M.; Cousins, I. T. Comparative Assessment of the Global Fate and Transport Pathways of Long-Chain Perfluorocarboxylic Acids (PFCAs) and Perfluorocarboxylates (PFCs) Emitted from Direct Sources. *Environ. Sci. Technol.* **2009**, *43*, 5830-5836.

[17] Zhang, Q.; Jimenez, J. L.; Worsnop, D. R.; Canagaratna, M. A case study of urban particle acidity and its influence on secondary organic aerosol. *Environ. Sci. Technol*. **2007**, *41*, 3213-3219.

[18] Keene, W. C.; Pszenny, A. A. P.; Maben, J. R.; Stevenson, E; Wall, A. *J. Geophys. Res.* **2004**, *109*, D23307.

[19] Pszenny, A. A. P.; Moldanová, J.; Keene, W. C.; Sander R.; Maben J. R.; Martinez, M.; Crutzen, P. J.; Perner, D.; Prinn, R. G. Halogen cycling and aerosol pH in the Hawaiian marine boundary layer. *Atmos. Chem. Phys*. **2004**, *4*, 147-168.

[20] Zhao, Y. H.; Abraham, M. H. Octanol/water partition of ionic species, including 544 cations. *J. Org. Chem.* **2005**, *70*, 2633-2640.

[21] *Hazard assessment of perfluorooctane sulfonate (pfos) and its salts*; ENV/JM/RD(2002)17; Organisation for Economic Co-operation and Development, Paris, France, 2002; http://www.oecd.org/env/ehs/risk-assessment/2382880.pdf

[22] Arp, H. P. H.; Niederer, C.; Goss, K. U. Predicting the partitioning behavior of various highly fluorinated compounds. *Environ. Sci. Technol*. **2006**, *40*, 7298-7304.

[23] Kelly, B. C.; Ikonomou, M. G.; Blair, J. D.; Blair, S.; Hoover, D.; Grace, R.; Gobas, F. A. P. C. Perfluoroalkyl Contaminants in an Arctic Marine Food Web: Trophic Magnification and Wildlife Exposure. *Environ. Sci. Technol.* **2009**, *43*, 4037-4043.

[24] Rayne, S.; Forest, K. Perfluoroalkyl sulfonic and carboxylic acids: A critical review of physicochemical properties, levels and patterns in waters and wastewaters, and treatment methods. *J Environ. Sci. Health A.* **2009**, *44*, 1145-1199.

[25] Armitage, J. M.; MacLeod, M.; Cousins, I. T. Modeling the Global Fate and Transport of Perfluorooctanoic Acid (PFOA) and Perfluorooctanoate (PFO) Emitted from Direct Sources Using a Multispecies Mass Balance Model. *Environm. Sci. Technol.* **2009**, *43*, 1134-1140.

[26] Jing, P.; Rodgers, P. J.; Amemiya S. High Lipophilicity of Perfluoroalkyl Carboxylate and Sulfonate: Implications for Their Membrane Permeability. *J. Am. Chem. Soc.* **2009**, *131*, 2290–2296.

[27] Rayne, S.; Forest, K. Congener-specific organic carbon-normalized soil and sediment-water partitioning coefficients for the C-1 through C-8 perfluoroalkyl carboxylic and sulfonic acids. *J Environ. Sci. Health A.* **2009**, *44*, 1374-1387.

[28] Higgins, C. P.; Luthy, R. G. Sorption of perfluorinated surfactants on sediments. *Environ. Sci. Technol.* **2006**, *40*, 7251–7256.

[29] See, for example: (a) Moroi, Y.; Yano, H.; Shibata, O.; Yonemitsu, T. Determination of acidity constants of perfluoroalkanoic acids. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 667–672. (b) Goss, K. U. The pK(a) values of PFOA and other highly fluorinated carboxylic acids. *Environ. Sci. Technol.* **2008**, *42*, 456–458. (c) Rayne, S.; Forest, K. Theoretical studies on the pK(a) values of perfluoroalkyl carboxylic acids. *J. Mol. Struct. (Theochem)* **2010**, *949*, 60-69. (d) Kutsuna, S.; Hori, H. Experimental determination of Henry's law constant of perfluorooctanoic acid (PFOA) at 298 K by means of an inert-gas stripping method with a helical plate. *Atmos. Environ.* **2008**, *42*, 8883–8892.

[30] Gaussian 09, Revision **A.1**, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A. Jr; Peralta J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2009.

[31] Becke, A. D. Density functional thermochemistry. 3. The role of exact exchange . *J. Chem.. Phys*. **1993**, *98*, 5648-5652.

[32] Lee, C.; Yang, W. T.; Parr, R. G. Development of the Colle-Salvetti correlation-energy formula into a functional of the electron-density. *Phys. Rev*. B. **1988**, *37*, 785-789.

[33] Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Universal Solvation Model Based on Solute Electron Density and on a Continuum Model of the Solvent Defined by the Bulk Dielectric Constant and Atomic Surface Tensions. *J. Phys. Chem. B* **2009**, *13*, 6378-6396.

[34] (a) Montero-Campillo, M. M.; Mora-Diez, N.; Lamsabhi, A. M. Thermodynamic Stability of Neutral and Anionic PFOS: A Gas-Phase, n-Octanol, and Water Theoretical Study. *J. Phys. Chem. A*, **2010**, *114*, 10148-10155. (b) Torres, F. J.; Ochoa-Herrera, V.; Blowers, P.; Sierra-Alvarez, P. Ab initio study of the structural, electronic, and thermodynamic properties of linear perfluorooctane sulfonate (PFOS) and its branched isomers. *Chemosphere* **2009**, *76*, 1143-1149. (c) Giroday, T.; Montero-Campillo, M. M.; Mora-Diez, N. Thermodynamic stability of PFOS: M06-2X and B3LYP comparison. *Comput. Theor. Chem.* **2014**, *1046*, 81-92.

[35] (a) Bunn, C. W.; Howells, E. R. Structures of molecules and crystals of fluorocarbons. *Nature* **1954**, *174* (4429), 549–551. (b) Monde, K.; Miura, N.; Hashimoto, M.; Taniguchi, T.; Inabe, T. Conformational analysis of chiral helical perfluoroalkyl chains by VCD. *J. Am. Chem. Soc.* **2006**, *128*, 6000–6001. (c) Zhang, X.; Lerner, M. M. Structural refinement of the perfluorooctanesulfonate anion and its graphite intercalation compounds. *Phys. Chem. Chem. Phys.* **1999**, *1*), 5065–5069. (d) Jang, S. S.; Blanco, M.; Goddard, W. A.; Caldwell, G.; Ross, R. B. The source of helicity in perfluorinated N-alkanes. *Macromolecules* **2003**, *36*, 5331–5341. (e) Lehmler, H. J.; Rama, R. V. V. V. N. S.; Nauduri, D.; Vargo, J. D.; Parkin, S. Synthesis and structure of environmentally relevant perfluorinated sulfonamides. *J. Fluorine Chem.* **2007**, *128*, 595–607.

[36] (a) Zhao, Y.; Truhlar, D. G. Density functionals with broad applicability in chemistry. *Acc. Chem. Res.* **2008**, *41*, 157–167. (b) Zhao, Y.; Truhlar, D. G. The M06 suite of density functionals for main group thermochemistry, thermochemical kinetics, noncovalent interactions, excited states, and

transition elements: two new functionals and systematic testing of four M06-class functionals and 12 other functionals. *Theor. Chem. Acc.* **2008,** *120*, 215-241.

[37] US EPA. 2015. Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.11. United States Environmental Protection Agency, Washington, DC, USA.

[38] Meylan, W. M.; Howard, P. H. Bond contribution method for estimating Henry's law contants. *Environ. Toxicol. Chem.* **1991**, *10*, 1283-1293.

[39] Meylan, W. M.; Howard, P. H. Atom fragment contribution method for estimating octanol-water partition coefficients. *J. Pharm. Sci.* **1995**, *84* 83-92.

[40] CRC Press Online: CRC Handbook of Chemistry and Physics, 91st Edition: http://www.hbcpnetbase.com/toc/default.asp?exp=*toc*

[41] Feenstra-Bieders, G. C.; Olthof, J. A. Determination of the solubility of trifluoroacetic acid and sodium trifluoroacetate in various aqueous media. *Solvay Duphar Report*: 56630/182/91, 1992.

[42] Thus, J. L. G. Addendum report: determination of the partition coefficient of trifluoroacetic acid. *Solvay Duphar Report:* 56834/45/97, 1997.

[43] Boutonnet, J. C.; Bingham, P.; Calamari, D.; de Rooij, C.; Franklin, J.; Kawano, T.; Libre, J. M.; McCulloch, A.; Malinverno, G.; Odom, J. M.; Rusch, G. M.; Smythe, K.; Sobolev, I.; Thompson, R.; Tiedje, J. M. Environmental risk assessment of trifluoroacetic acid. *Hum. Ecol. Risk Assess.* **1999**, *5*, 59-124.

[44] *Environmental effects of ozone depletion: 1998 assessment*. United Nations Environment Programme: Nairobi, Kenya, 1998; http://ozone.unep.org/pdfs/Environmental-Effects-Assess98.pdf

[45] *Safeguarding the Ozone Layer and the Global Climate System: Issues related to Hydrofluorocarbons*; Intergovernmental Panel on Climate Change*:* New York, USA, 2005; https://www.ipcc.ch/publications_and_data/_safeguarding_the_ozone_layer.htm.

[46] (a) Cancès, E; Mennucci, B.; Tomasi, J. A new integral equation formalism for the polarizable continuum model: Theoretical background and applications to isotropic and anisotropic dielectrics. *J. Chem. Phys.* **1997**, *107*, 3032-3041. (b) Cossi, M.; Barone, V.; Mennucci, B.; Tomasi, J. Ab initio study of ionic solutions by a polarizable continuum dielectric model. *Chem. Phys. Lett.* **1998**, *286*, 253-260. (c) Mennucci, B.; Tomasi, J. Continuum solvation models: A new approach to the problem of solute's charge distribution and cavity boundaries. *J. Chem. Phys.* **1997**, *106*, 5151-5158.

[47] Ideas shared with Dr. Shigeru Amemiya, corresponding author of Ref. 26, through a personal communication.

[48] Rekker, R. F.; Mannhold, R. *Calculation of Drug Lipophilicity: The Hydrophobic Fragmental Constant;* 1st ed., VCH: Michigan, United States, 1992.

[49] Higgins, C. P.; Luthy, R. G. Modeling sorption of anionic surfactants onto sediment materials: An a priori approach for perfluoroalkyl surfactants and linear alkylbenzene sulfonates. *Environ. Sci. Technol.* **2007**, *41*, 3254–3261.

3.6. Supporting Information

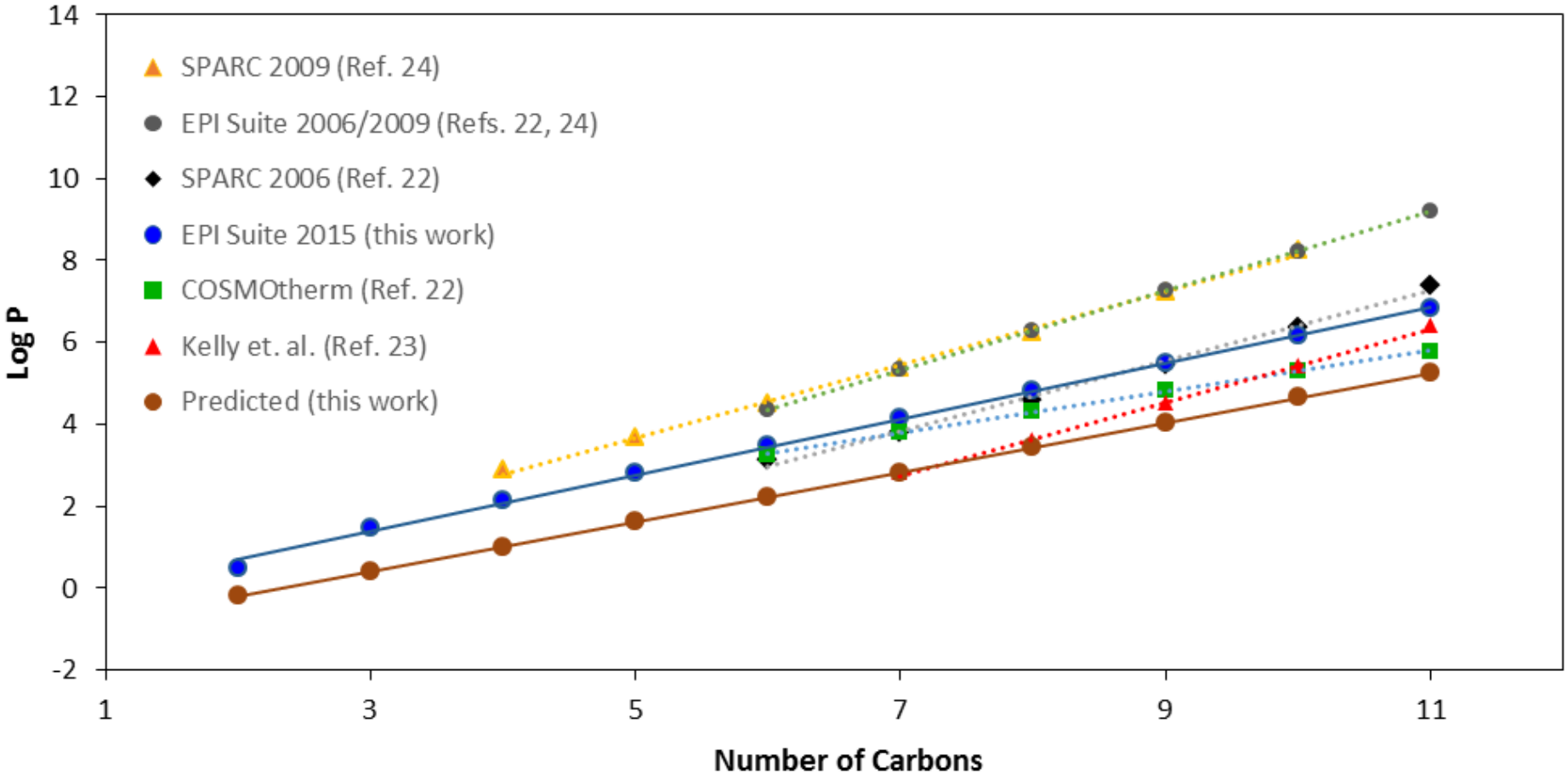


Figure 3.S1. Comparative plots of calculated and predicted (this work) Log P values (shown in Table 3.S1) with the number of carbon atoms of PFCAs).

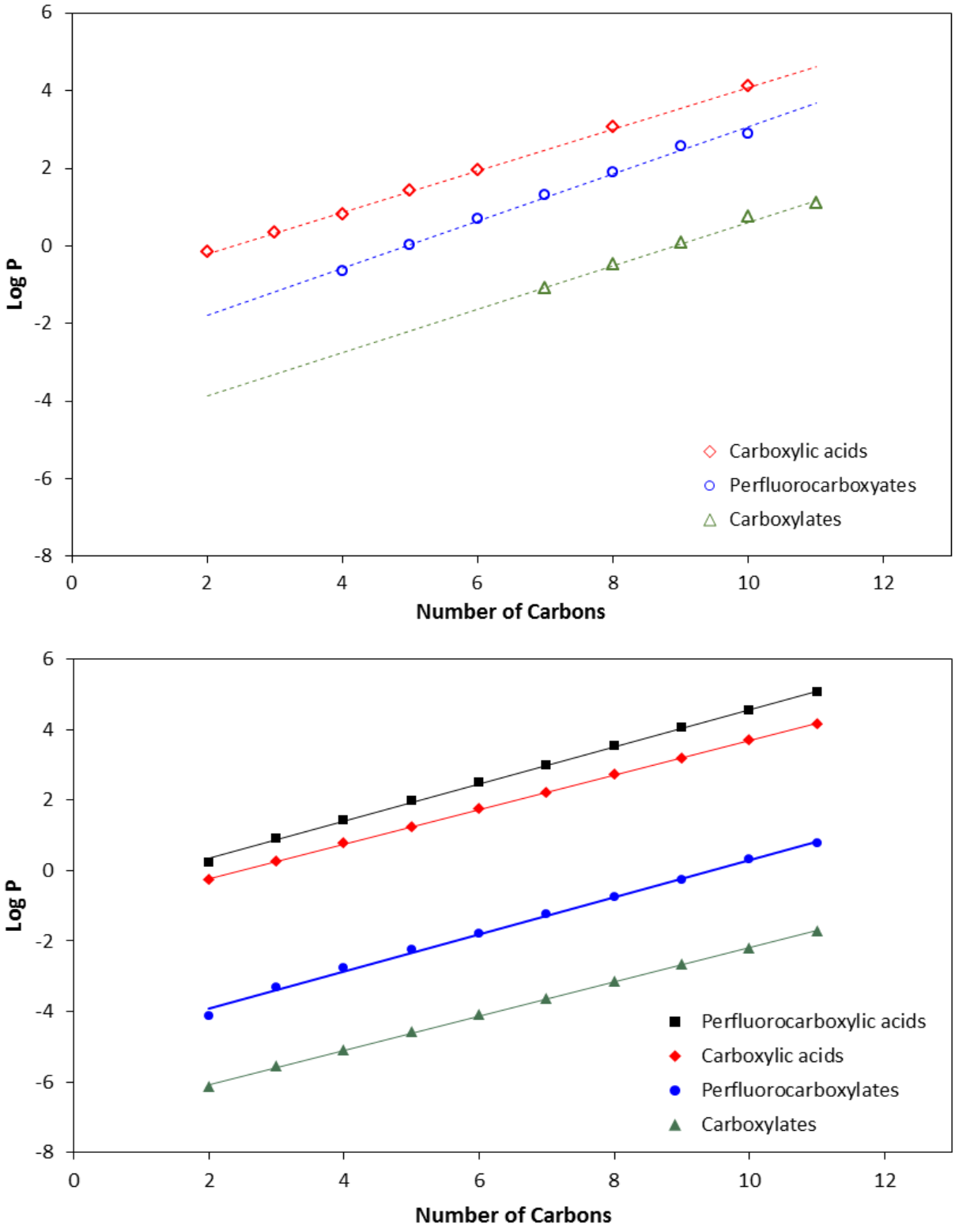


Figure 3.S2. Plots of the experimental (top) and calculated (bottom; using eq. 3.4) Log P values (reported in Table 3.1) with the number of carbon atoms for carboxylic acids, perfluorocarboxylic acids, and their conjugate bases.

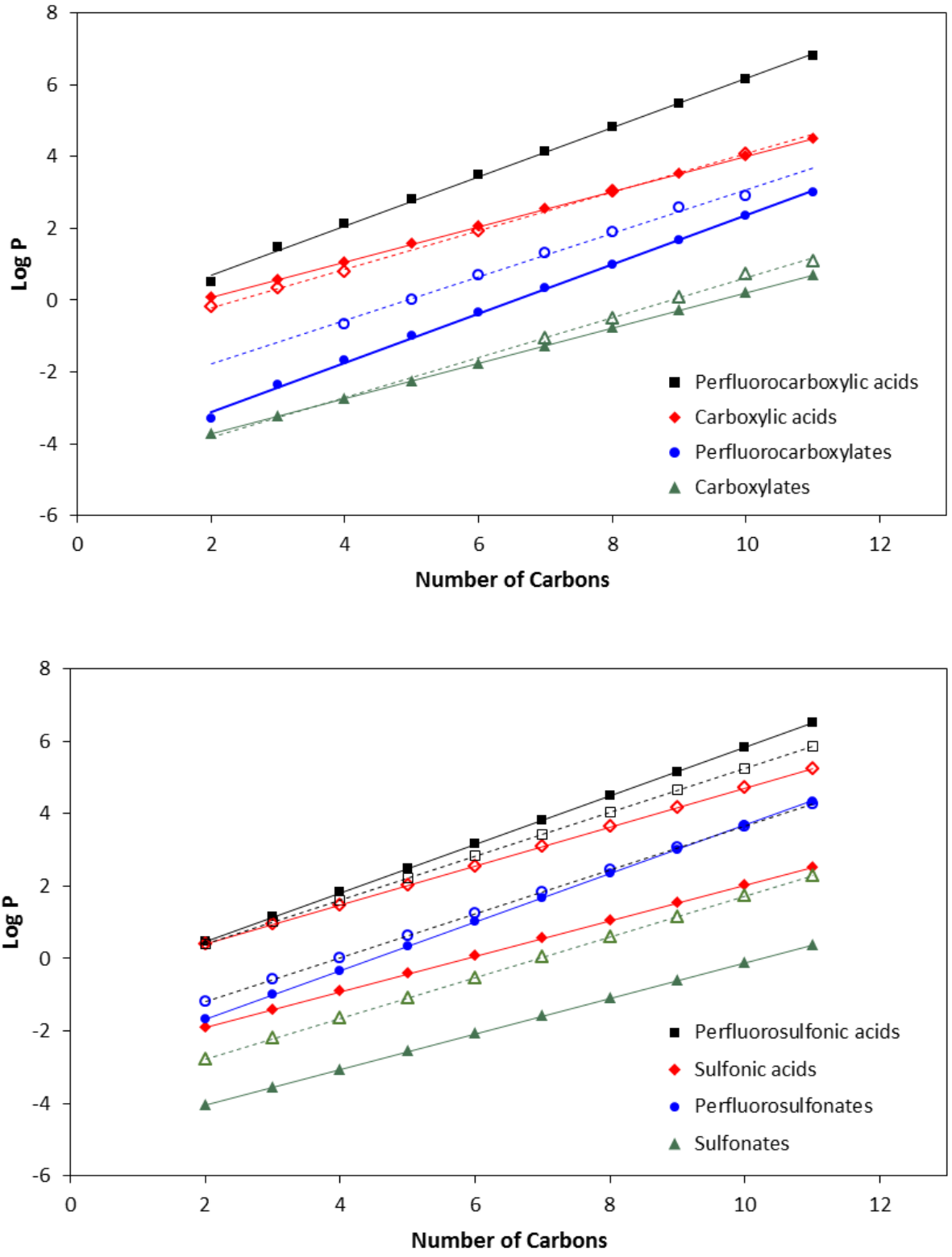


Figure 3.S3. Plots of the experimental/predicted (broken lines and unfilled markers) and calculated (using EPI Suite, solid lines and filled markers) Log P values with the number of carbon atoms for carboxylic acids, perfluorocarboxylic acids, and their conjugate bases (top, from Table 3.1), and for sulfonic acids, perfluorosulfonic acids, and their conjugate bases (bottom, from Table 3.2).

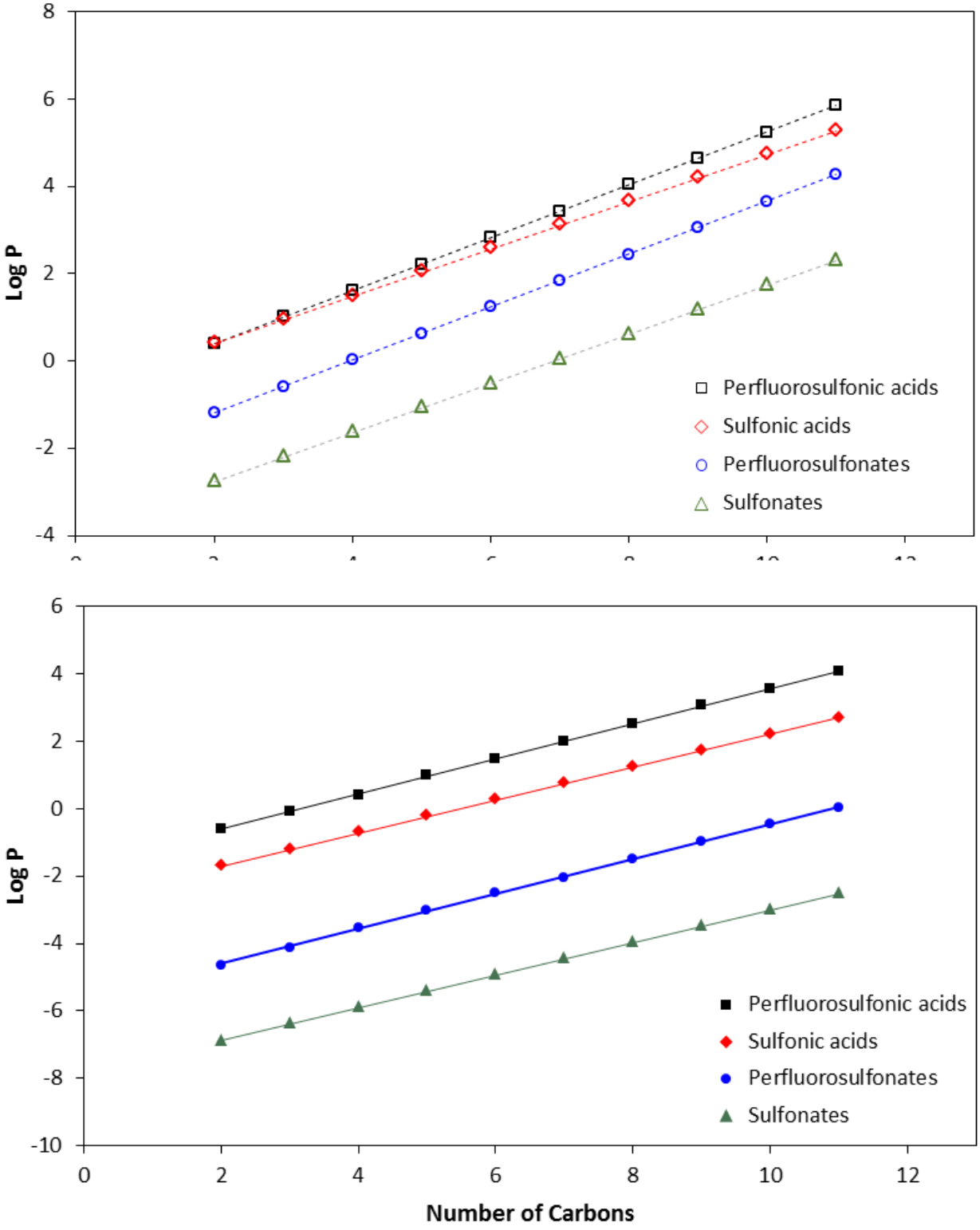


Figure 3.S4. Plot of the predicted (top) and calculated (bottom, using eq. 3.4) Log P values (reported in Table 3.2) with the number of carbon atoms for sulfonic acids, perfluorosulfonic acids, and their conjugate bases.

Table 3.S1. Compilation of previous calculations and predicted values for PFCAs

N [a]	SPARC 2009[b]	EPI Suite 2006[c]	EPI Suite 2009[b]	SPARC 2006[c]	EPI Suite 2015 (this work)	COSMO therm[c]	Kelly et. al.[d]	Predicted (this work)
2					0.50			-0.20
3					1.47			0.41
4	2.91		2.43		2.14			1.01
5	3.69		3.40		2.81			1.62
6	4.50	4.37	4.37	3.12	3.48	3.26		2.22
7	5.36	5.33	5.33	3.82	4.15	3.82	2.80	2.83
8	6.26	6.30	6.30	4.59	4.81	4.30	3.60	3.44
9	7.23	7.27	7.27	5.45	5.48	4.84	4.50	4.04
10	8.26	8.23	8.23	6.38	6.15	5.30	5.40	4.65
11		9.20		7.40	6.82	5.76	6.40	5.25
slope	0.889	0.966	0.966	0.855	0.685	0.499	0.900	0.606
intercept	-0.764	-1.430	-1.430	-2.145	-0.671	0.302	-3.560	-1.412

[a] Number of carbon atoms; [b] From Ref. 24; [c] From Ref. 22; [d] From Ref. 23.

Table 3.S2a. Calculated energies in solution (in water, E_w, and octanol, E_o, in Hartrees) and Log P values for the alkyl carboxylates and carboxylic acids studied at the B3LYP-SMD/6-31++G(d,p)//B3LYP/6-31++G(d,p) level of theory.

	Carboxylates			**Carboxylic acids**		
N[a]	**E_w**	**E_o**	**Log P**	**E_w**	**E_o**	**Log P**
2	-228.65639	-228.64303	-6.15	-229.11651	-229.11595	-0.26
3	-267.97228	-267.96018	-5.57	-268.43392	-268.43447	0.25
4	-307.28900	-307.27793	-5.10	-307.75077	-307.75247	0.78
5	-346.60597	-346.59599	-4.59	-347.06807	-347.07078	1.24
6	-385.92300	-385.91407	-4.11	-386.38515	-386.38894	1.74
7	-425.24018	-425.23230	-3.63	-425.70229	-425.70711	2.22
8	-464.55723	-464.55039	-3.15	-465.01934	-465.02525	2.72
9	-503.87439	-503.86858	-2.67	-504.33646	-504.34340	3.19
10	-543.19145	-543.18668	-2.20	-543.65352	-543.66153	3.69
11	-582.50855	-582.50483	-1.71	-582.97063	-582.97969	4.17

[a] Number of carbon atoms

Table 3.S2b. Calculated energies in solution (in water, E_w, and octanol, E_o, in Hartrees) and Log P values for the perfluorocarboxylates and perfluorocarboxylic acids studied at the B3LYP-SMD/6-31++G(d,p)//B3LYP/6-31++G(d,p) level of theory.

	Perfluorocarboxylates			**Perfluorocarboxylic acids**		
N[a]	**E_w**	**E_o**	**Log P**	**E_w**	**E_o**	**Log P**
2	-526.39193	-526.38299	-4.12	-526.82989	-526.83041	0.24
3	-764.18523	-764.17802	-3.32	-764.62347	-764.62544	0.91
4	-1001.97656	-1001.97053	-2.78	-1002.41466	-1002.41776	1.43
5	-1239.76708	-1239.76218	-2.25	-1240.20539	-1240.20969	1.98
6	-1477.55758	-1477.55371	-1.78	-1477.99586	-1478.00128	2.49
7	-1715.34812	-1715.34543	-1.23	-1715.78648	-1715.79300	3.00
8	-1953.13885	-1953.13720	-0.76	-1953.57709	-1953.58476	3.53
9	-2190.92925	-2190.92871	-0.25	-2191.36765	-2191.37647	4.06
10	-2428.71971	-2428.72039	0.31	-2429.15833	-2429.16822	4.55
11	-2666.51042	-2666.51213	0.79	-2666.94898	-2666.96001	5.08

[a] Number of carbon atoms

Table 3.S2c. Calculated energies in solution (in water, E_w, and octanol, E_o, in Hartrees) and Log P values for the alkyl sulfonates and sulfonic acids studied at the B3LYP-SMD/6-31++G(d,p)//B3LYP/6-31++G(d,p) level of theory.

	Sulfonates			**Sulfonic acids**		
N[a]	**E_w**	**E_o**	**Log P**	**E_w**	**E_o**	**Log P**
2	-703.24109	-703.22611	-6.90	-703.67186	-703.66814	-1.71
3	-742.55817	-742.54431	-6.38	-742.98928	-742.98660	-1.23
4	-781.87541	-781.86255	-5.92	-782.30657	-782.30500	-0.72
5	-821.19253	-821.18077	-5.41	-821.62384	-821.62333	-0.23
6	-860.50968	-860.49891	-4.95	-860.94093	-860.94148	0.25
7	-899.82677	-899.81707	-4.46	-900.25806	-900.25967	0.74
8	-939.14386	-939.13521	-3.98	-939.57515	-939.57781	1.22
9	-978.46094	-978.45334	-3.50	-978.89224	-978.89596	1.71
10	-1017.77802	-1017.77149	-3.01	-1018.20933	-1018.21411	2.20
11	-1057.09509	-1057.08961	-2.52	-1057.52641	-1057.53224	2.68

[a] Number of carbon atoms

Table 3.S2d. Calculated energies in solution (in water, E_w, and octanol, E_o, , in Hartrees) and Log P values for the perfluorosulfonates and perfluorosulfonic acids studied at the B3LYP-SMD/6-31++G(d,p)//B3LYP/6-31++G(d,p) level of theory.

	Perfluorosulfonates			**Perfluorosulfonic acids**		
N[a]	**E_w**	**E_o**	**Log P**	**E_w**	**E_o**	**Log P**
2	-1199.43273	-1199.42267	-4.63	-1199.84280	-1199.84150	-0.60
3	-1437.22356	-1437.21460	-4.12	-1437.63410	-1437.63390	-0.09
4	-1675.01413	-1675.00641	-3.55	-1675.42487	-1675.42579	0.42
5	-1912.80452	-1912.79795	-3.03	-1913.21534	-1913.21748	0.99
6	-2150.59519	-2150.58975	-2.50	-2151.00609	-2151.00932	1.49
7	-2388.38582	-2388.38140	-2.03	-2388.79665	-2388.80097	1.99
8	-2626.17635	-2626.17312	-1.49	-2626.58737	-2626.59281	2.51
9	-2863.96701	-2863.96489	-0.98	-2864.37778	-2864.38445	3.07
10	-3101.75741	-3101.75640	-0.46	-3102.16870	-3102.17641	3.55
11	-3339.54823	-3339.54829	0.03	-3339.95908	-3339.96795	4.08

[a] Number of carbon atoms

Table 3.S3a. Calculated Mulliken atomic charges on the charged oxygen atoms of the anions and on the OH oxygen atom of the acids (CAs and PFCAs) in the gas phase (B3LYP/6-31++G(d,p)) and in solution (B3LYP-SMD/6-31++G(d,p)//B3LYP/6-31++G(d,p)).

Gas Phase

	Carboxylic acids			Perfluorocarboxylic acids		
	Anion		Neutral	Anion		Neutral
N[a]	O1	O2	O2	O1	O2	O2
2	-0.618481	-0.636716	-0.403217	-0.603829	-0.607824	-0.404956
3	-0.626895	-0.620511	-0.413639	-0.591953	-0.597315	-0.390934
4	-0.624000	-0.612998	-0.415313	-0.570675	-0.584923	-0.399863
5	-0.617665	-0.609303	-0.413159	-0.564606	-0.574406	-0.398156
6	-0.612348	-0.605288	-0.410851	-0.562362	-0.570606	-0.397162
7	-0.610249	-0.603574	-0.410545	-0.560885	-0.567967	-0.397199
8	-0.607941	-0.602242	-0.409784	-0.560480	-0.566461	-0.396106
9	-0.606404	-0.601720	-0.408486	-0.559965	-0.565027	-0.395865
10	-0.605578	-0.601147	-0.408257	-0.560095	-0.564647	-0.395394
11	-0.604820	-0.601084	-0.407541	-0.559919	-0.563997	-0.395605

Octanol phase

	Carboxylic acids			Perfluorocarboxylic acids		
	Anion		Neutral	Anion		Neutral
N	O1	O2	O2	O1	O2	O2
2	-0.728703	-0.747571	-0.450019	-0.675776	-0.675860	-0.446797
3	-0.743930	-0.737045	-0.462660	-0.662678	-0.674480	-0.423714
4	-0.745248	-0.731726	-0.465659	-0.649487	-0.663746	-0.431914
5	-0.741150	-0.729803	-0.463938	-0.645281	-0.656201	-0.430341
6	-0.737454	-0.726759	-0.462287	-0.643587	-0.654220	-0.428691
7	-0.735914	-0.726186	-0.461741	-0.642724	-0.652554	-0.428259
8	-0.734553	-0.724951	-0.461321	-0.643075	-0.651462	-0.427264
9	-0.733227	-0.724970	-0.459793	-0.642458	-0.650419	-0.426823
10	-0.732837	-0.724460	-0.459765	-0.643084	-0.649998	-0.426248
11	-0.732257	-0.724558	-0.458884	-0.642895	-0.649572	-0.426519

Water phase

	Carboxylic acids			Perfluorocarboxylic acids		
	Anion		Neutral	Anion		Neutral
N	O1	O2	O2	O1	O2	O2
2	-0.752432	-0.771204	-0.457706	-0.693007	-0.691983	-0.451386
3	-0.768098	-0.763384	-0.471331	-0.680362	-0.692870	-0.427335
4	-0.770004	-0.759167	-0.473757	-0.668217	-0.681757	-0.435625
5	-0.766484	-0.757148	-0.472653	-0.664384	-0.674612	-0.433232
6	-0.762929	-0.754479	-0.470712	-0.663408	-0.672453	-0.432093
7	-0.761534	-0.753820	-0.470574	-0.662561	-0.670659	-0.431418
8	-0.760300	-0.752740	-0.469925	-0.662573	-0.669987	-0.429782
9	-0.759090	-0.752527	-0.468701	-0.662119	-0.668832	-0.429670
10	-0.758821	-0.752075	-0.468505	-0.662457	-0.668677	-0.429329
11	-0.758293	-0.752073	-0.467832	-0.662477	-0.668177	-0.429448

[a] Number of carbon atoms.

Table 3.S3b. Calculated Mulliken atomic charges on the charged oxygen atoms of the anions and on the OH oxygen atom of the acids (SAs and PFSAs) in the gas phase (B3LYP/6-31++G(d,p)) and in solution (B3LYP-SMD/6-31++G(d,p)//B3LYP/6-31++G(d,p)).

Gas Phase	**Sulfonic acids**				**Perfluorinated sulfonic acids**			
	Anion			Neutral	Anion			Neutral
N	O1	O2	O3	O2	O1	O2	O3	O2
2	-0.700754	-0.708087	-0.700711	-0.590908	-0.653860	-0.677887	-0.660597	-0.566387
3	-0.702548	-0.699329	-0.702467	-0.592075	-0.638985	-0.671696	-0.674246	-0.564227
4	-0.698780	-0.694952	-0.698745	-0.590193	-0.633039	-0.664494	-0.672768	-0.559758
5	-0.695406	-0.690102	-0.695387	-0.584254	-0.630404	-0.659041	-0.666897	-0.554996
6	-0.689612	-0.689334	-0.689602	-0.583466	-0.627970	-0.655646	-0.664302	-0.551797
7	-0.687232	-0.687203	-0.687232	-0.581590	-0.626835	-0.652811	-0.661873	-0.548898
8	-0.683720	-0.685734	-0.683688	-0.579946	-0.625650	-0.651963	-0.659900	-0.548008

Octanol phase	**Sulfonic acids**				**Perfluorinated sulfonic acids**			
	Anion			Neutral	Anion			Neutral
N	O1	O2	O3	O2	O1	O2	O3	O2
2	-0.780367	-0.785540	-0.780304	-0.626671	-0.701852	-0.726885	-0.707664	-0.593376
3	-0.783443	-0.780739	-0.783334	-0.627912	-0.689344	-0.723053	-0.723362	-0.591295
4	-0.781403	-0.776965	-0.781350	-0.625358	-0.684563	-0.717546	-0.723221	-0.587149
5	-0.778799	-0.773092	-0.778774	-0.619348	-0.682222	-0.713477	-0.717677	-0.582315
6	-0.774277	-0.771976	-0.774253	-0.618397	-0.680379	-0.710723	-0.715564	-0.578856
7	-0.772349	-0.770662	-0.772344	-0.616421	-0.679788	-0.708177	-0.713480	-0.575921
8	-0.769474	-0.769130	-0.769437	-0.614819	-0.678625	-0.707413	-0.711771	-0.575357

Water phase	**Sulfonic acids**				**Perfluorinated sulfonic acids**			
	Anion			Neutral	Anion			Neutral
n	O1	O2	O3	O2	O1	O2	O3	O2
2	-0.796223	-0.801283	-0.796155	-0.631842	-0.712273	-0.736659	-0.718703	-0.596277
3	-0.799785	-0.796538	-0.799668	-0.633006	-0.700252	-0.733885	-0.734444	-0.594122
4	-0.797785	-0.793173	-0.797727	-0.630485	-0.695574	-0.728504	-0.733693	-0.590135
5	-0.795307	-0.789135	-0.795279	-0.624404	-0.693474	-0.724192	-0.728422	-0.585273
6	-0.790931	-0.788458	-0.790904	-0.623574	-0.691775	-0.721260	-0.726559	-0.581617
7	-0.789086	-0.787070	-0.789080	-0.621534	-0.691054	-0.718844	-0.724901	-0.578594
8	-0.786337	-0.785810	-0.786300	-0.620036	-0.690111	-0.718025	-0.722598	-0.578024

Section 3.S1.
Determination of experimental partition coefficients of perfluorocarboxylates, carboxylates and perfluorooctanesulfonates .

Jing et al. (Ref. 26) published the first set of experimental Log P values for a group of linear perfluoalkyl carboxylates. The Log P values, calculated using eq. 3.S1, were not explicitly reported; hence, we decided to do so in this section (see Table 3.SS1) as we found some differences with the Lop P *versus* N slopes reported.

$$\text{Log P} = \frac{z_i \, F \, \Delta^{\circ}{}_{w}\emptyset^{0\prime}}{\ln(10) \, R \, T \, 1000} \qquad (3.S1)$$

In eq 3.S1, $\Delta^{\circ}{}_{w}\emptyset^{0\prime}$ is the formal ion transfer potential, z_i is the charge of the molecule, R is the ideal gas constant and F is Faraday's constant.

Table 3.SS1. Experimental log P values determined according to Jing et al. (Ref. 26).

Compounds	**N**[a]	**$\Delta^{\circ}{}_{w}\emptyset^{0\prime}$ (mV)**[b]	**Log P**
Carboxylates	7	63 ± 6	-1.1 ± 0.1
	8	30 ± 5	-0.51 ± 0.08
	9	4 ± 4	0.07 ± 0.07
	10	44 ± 5	0.74 ± 0.08
	11	64 ± 5	1.08 ± 0.08
Perfluorocarboxylates	2		-1.67[c]
(PFCs)	3		-1.0[c]
	4	39 ± 5	-0.66 ± 0.08
	5	2 ± 5	0.03 ± 0.08
	6	41 ± 6	0.7 ± 0.1
	7	77 ± 5	1.30 ± 0.08
	8	112 ± 6	1.9 ± 0.1
	9	152 ± 4	2.57 ± 0.07
	10	174 ± 8	2.9 ± 0.1
Perfluorooctanesulfonate	8	145 ± 5	2.45 ± 0.08
Octanesulfonate	8	34 ± 6	0.6 ± 0.1

[a] Number of carbon atoms; [b] Values reported in Table 3.S1 of Ref. 26;
[c] Obtained by extrapolation from the curve of Log P *versus* N.

Section 3.S2.
Cartesian coordinates of the perfluorinated species studied (PFCA, PFC, PFSA, PFS) calculated at the B3LYP/6-31++G(d,p) level of theory.

Perfluorocarboxylic acids

```
Trifluoroethanoic acid
 Charge =  0 Multiplicity = 1
 C,0,3.5427366207,-0.4179018418,0.3553517994
 C,0,4.8246510135,0.0903416318,-0.3542747703
 O,0,5.5316764853,-0.6092967072,-1.0304170679
 O,0,5.004586402,1.3915614397,-0.096835719
 H,0,5.8131463059,1.6834774206,-0.5529427057
 F,0,3.3539779494,-1.7168115352,0.1063465749
 F,0,3.6433627579,-0.2461614401,1.689293408
 F,0,2.4629092154,0.2642163021,-0.0783650694


Perfluoropropanoic acid
 Charge =  0 Multiplicity = 1
 C,0,2.226370581,0.3135549608,-0.1882715124
 C,0,3.5219060833,-0.3915227444,0.3109104682
 C,0,4.8259700797,0.1199452606,-0.3613182729
 O,0,5.4847298162,-0.5502975747,-1.111010659
 O,0,5.0891757181,1.3767410261,0.0186488959
 H,0,5.9101002267,1.6616503247,-0.4200110117
 F,0,2.196548896,1.5963198669,0.2004349082
 F,0,2.1819086956,0.271264234,-1.5341479546
 F,0,3.3953833362,-1.71031954,0.0540206655
 F,0,3.6053837969,-0.2152122117,1.6585842899
 F,0,1.1443600904,-0.3077684621,0.2992211929


Perfluorobutanoic acid
 Charge =  0 Multiplicity = 1
 C,0,0.8941573872,-0.445575055,0.1977622458
 C,0,2.2299802778,0.2794769182,-0.1587074395
 C,0,3.5379395992,-0.428388023,0.3157820511
 C,0,4.8168467411,0.1187683043,-0.3823757837
 O,0,5.4907898288,-0.5418408978,-1.1264850086
 O,0,5.0416593803,1.3880823639,-0.021603313
 H,0,5.8479601361,1.6947735751,-0.4725689389
 F,0,0.763131861,-1.5836871318,-0.4951699415
 F,0,0.8470415469,-0.7236890449,1.5103381276
 F,0,2.180506827,1.5195072261,0.3790571745
 F,0,2.2870499763,0.3955348969,-1.5138796876
 F,0,3.44069539,-1.7489818721,0.0449137155
 F,0,3.6622866263,-0.2707882987,1.6616884839
 F,0,-0.1346165779,0.3605015088,-0.1082162057


Perfluoropentanoic acid
 Charge =  0 Multiplicity = 1
 C,0,-0.3939598693,0.4677715382,0.0077057354
 C,0,0.891526244,-0.4091737692,0.1667574539
 C,0,2.2357672823,0.3246300324,-0.1530259972
 C,0,3.5254924371,-0.413273227,0.3368722798
 C,0,4.8176383046,0.0973686582,-0.3657134516
 O,0,5.4835710315,-0.5894737342,-1.0928809203
 O,0,5.0638808553,1.3690931581,-0.0274614346
 H,0,5.8781535425,1.652248326,-0.4795034134
 F,0,-0.4597200756,1.4045283383,0.9627169912
 F,0,-0.4136675111,1.0667538942,-1.193990535
 F,0,0.7638396778,-1.4693232447,-0.6629690965
 F,0,0.9227431934,-0.8519351938,1.448159003
```

F,0,2.2035504807,1.558209399,0.4062087181
F,0,2.3344260533,0.4661489673,-1.5030949267
F,0,3.398619028,-1.7332966078,0.079241293
F,0,3.6544098731,-0.2420634237,1.6798746858
F,0,-1.4717851977,-0.3234751311,0.1119542651

Perfluorohexanoic acid
Charge = 0 Multiplicity = 1
C,0,-1.7335370519,-0.3738884745,-0.041760232
C,0,-0.3910636364,0.4267794644,0.0194797292
C,0,0.8969360803,-0.4569478864,0.154359045
C,0,2.2298396541,0.3014606761,-0.1724451407
C,0,3.5304120111,-0.4082183598,0.3319958315
C,0,4.8161954504,0.1212947481,-0.3685089242
O,0,5.4953328179,-0.5567261758,-1.091715204
O,0,5.0402001896,1.3977589563,-0.0329278763
H,0,5.8510836206,1.6937496346,-0.482843978
F,0,-1.8433123725,-1.0430802726,-1.1965159763
F,0,-1.8134767248,-1.2428060207,0.977886209
F,0,-0.4624646733,1.2576241125,1.0842864727
F,0,-0.3106146066,1.1685400884,-1.1131452914
F,0,0.7864886111,-1.513419552,-0.686469424
F,0,0.9579368891,-0.917013724,1.4276245796
F,0,2.1742664055,1.5403271296,0.3715681769
F,0,2.3338221012,0.4247627539,-1.5231553114
F,0,3.4299465978,-1.7326431444,0.0843577085
F,0,3.6497682879,-0.222933682,1.673845037
F,0,-2.7547524409,0.4911449082,0.0482768889

Perfluoroheptanoic acid
Charge = 0 Multiplicity = 1
C,0,-3.0223883155,0.5016335373,0.2122877138
C,0,-1.7294878641,-0.3398026649,-0.0495293862
C,0,-0.3894719296,0.4682652056,0.0474016565
C,0,0.8905796555,-0.4333409454,0.1790148793
C,0,2.2291326061,0.3115411406,-0.158578841
C,0,3.5247153378,-0.4095993895,0.3435406814
C,0,4.8110315097,0.0914080274,-0.3766248022
O,0,5.476800125,-0.608177114,-1.0916477124
O,0,5.0524558095,1.371369781,-0.0672194566
H,0,5.8631891493,1.6490373609,-0.5289295455
F,0,-3.1157899758,0.8509000591,1.5016509196
F,0,-3.0280597515,1.6110039785,-0.5435368281
F,0,-1.831259272,-0.865378133,-1.2913979118
F,0,-1.7132908408,-1.3479763212,0.8567404985
F,0,-0.4522461114,1.2830496582,1.1281794326
F,0,-0.2792919938,1.2313373095,-1.0675118522
F,0,0.7650526163,-1.4898764253,-0.658541528
F,0,0.9579745762,-0.8870307458,1.4536671359
F,0,2.1887948712,1.5529182003,0.3812285116
F,0,2.3285309987,0.4282104879,-1.5100884852
F,0,3.403565122,-1.7359236185,0.1164910357
F,0,3.6596776996,-0.2066124077,1.6812321234
F,0,-4.0915060923,-0.2423089213,-0.106649889

Perfluorooctanoic acid
Charge = 0 Multiplicity = 1
C,0,-4.3612246387,-0.1889246143,-0.2122449151
C,0,-3.0192601326,0.4891001972,0.220331202
C,0,-1.7331578363,-0.3647898913,-0.0544431948
C,0,-0.395278145,0.4562413,0.0188740077
C,0,0.8882288925,-0.437435858,0.1757101209
C,0,2.2254228957,0.3074131417,-0.1682047694
C,0,3.5219464906,-0.4023684809,0.3475279931

C,0,4.8098933123,0.1018015649,-0.3675560744
O,0,5.4828887264,-0.5976771965,-1.0759239485
O,0,5.0437726166,1.3842125542,-0.0625106607
H,0,5.8558148092,1.6632443502,-0.5210940326
F,0,-5.3825522005,0.5465701596,0.2507702753
F,0,-4.4576613973,-0.2595065251,-1.5460286918
F,0,-4.4531531387,-1.42580725,0.3002391328
F,0,-3.1002962061,0.7384301101,1.5470048016
F,0,-2.9281324179,1.6669575921,-0.4449603708
F,0,-1.831843395,-0.9110659695,-1.2903442593
F,0,-1.6902032934,-1.3624954797,0.8612238766
F,0,-0.4605298869,1.3005558434,1.0757487315
F,0,-0.2845766937,1.1838714109,-1.1186791681
F,0,0.772128472,-1.5097130419,-0.6433030486
F,0,0.9522439908,-0.8664634589,1.4589669365
F,0,2.1791790613,1.5555707318,0.3552374
F,0,2.3295620251,0.4065095966,-1.5207344678
F,0,3.4104493261,-1.7308246748,0.1283742084
F,0,3.6471887637,-0.1901501117,1.6846989155

Perfluorononanoic acid
Charge = 0 Multiplicity = 1
C,0,-4.3405423106,-0.105501911,-0.2296346473
C,0,-2.9972424425,0.5641609034,0.2237667466
C,0,-1.7245672909,-0.3210221508,-0.0334316458
C,0,-0.3758015469,0.4860557939,0.0073684026
C,0,0.8963777159,-0.4175529188,0.1971477576
C,0,2.2421294493,0.295015086,-0.1803399755
C,0,3.5306871911,-0.4087352539,0.3625703017
C,0,4.824090219,0.0529047075,-0.3712418711
O,0,5.488593582,-0.6807269457,-1.0525447193
O,0,5.0729856251,1.3431906086,-0.1151880865
H,0,5.8881548267,1.595082365,-0.583844022
F,0,-4.4235998372,-0.0434631239,-1.5779876895
F,0,-3.0717993807,0.8290283347,1.5503029336
F,0,-2.8649745762,1.7336752283,-0.4480013489
F,0,-1.8372036451,-0.9016757198,-1.2514516199
F,0,-1.6858725899,-1.2885846727,0.9133423503
F,0,-0.4281553545,1.3695467397,1.0326873308
F,0,-0.2567766765,1.1694127877,-1.156245652
F,0,0.7638244841,-1.5209631276,-0.576727275
F,0,0.9586769945,-0.7942427538,1.496702909
F,0,2.2129105454,1.5649210513,0.2894633731
F,0,2.3445315601,0.3347636718,-1.5360309239
F,0,3.4038147847,-1.7432172206,0.1940745259
F,0,3.6590751098,-0.1468821699,1.6907052189
C,0,-5.6319436743,0.5591372014,0.3523650256
F,0,-4.3468196681,-1.405856874,0.153785183
F,0,-5.7411298901,0.3275510448,1.6666344081
F,0,-5.619720064,1.8844961785,0.1403023005
F,0,-6.7009293903,0.03399798,-0.2636088908

Perfluorodecanoic acid
Charge = 0 Multiplicity = 1
C,0,-4.3303594493,-0.1517560196,-0.1995196017
C,0,-2.990598789,0.5514940425,0.2244234697
C,0,-1.7129759464,-0.3385583921,0.0056835749
C,0,-0.3685307572,0.4766067169,0.0083287349
C,0,0.9097600418,-0.4121908028,0.2260364688
C,0,2.2490790345,0.2922035212,-0.1880152185
C,0,3.5446217504,-0.380482555,0.3772803831
C,0,4.8307367728,0.0545939961,-0.3850459993
O,0,5.494120248,-0.7047333748,-1.0387262388
O,0,5.0746993121,1.3559721674,-0.1869211299
H,0,5.8852846874,1.5915104752,-0.6717536821
F,0,-4.4114422262,-0.1359673804,-1.5518228068

```
 F,0,-3.0657538336,0.8749062427,1.5372279307
 F,0,-2.8624123543,1.6874025347,-0.5022812025
 F,0,-1.8237705684,-0.9726542551,-1.1858304862
 F,0,-1.6664430567,-1.2627103897,0.9943323009
 F,0,-0.4208183061,1.3984114357,0.999267213
 F,0,-0.2582347438,1.1151310935,-1.1814407953
 F,0,0.7793757035,-1.5461110742,-0.5027027662
 F,0,0.9821035028,-0.7371986019,1.5389134568
 F,0,2.214639274,1.5806341334,0.2278145117
 F,0,2.3442819186,0.2755825228,-1.5446304075
 F,0,3.4237407055,-1.7218580874,0.2694378453
 F,0,3.6798183296,-0.0586054368,1.6914851733
 C,0,-5.6173385866,0.5248939817,0.3875733711
 F,0,-4.3052019345,-1.439409931,0.2212886947
 F,0,-5.7198655584,0.20174439,1.6965828254
 F,0,-5.5097078962,1.8714946336,0.2730590984
 C,0,-6.9541960264,0.1024789384,-0.3069317279
 F,0,-7.9806509746,0.5880588529,0.4061857364
 F,0,-7.0588803213,-1.234539191,-0.3588056821
 F,0,-7.0277980219,0.5957984731,-1.5496690741


Perfluoroundecanoic acid
 Charge =  0 Multiplicity = 1
 C,0,-4.3142213146,-0.075622475,-0.1857345611
 C,0,-2.9630121766,0.6307828528,0.1982864046
 C,0,-1.6996751424,-0.2901315014,0.029426733
 C,0,-0.3426824386,0.5027432661,-0.0160548401
 C,0,0.9216788864,-0.3920184389,0.2520225321
 C,0,2.2716932562,0.2664866744,-0.2010069043
 C,0,3.5562361455,-0.3917836477,0.405285744
 C,0,4.8486900154,-0.029471254,-0.3837678099
 O,0,5.5001303254,-0.8415427242,-0.9838580356
 O,0,5.1129069884,1.2784001916,-0.2738902831
 H,0,5.9268715832,1.4680278764,-0.7729675999
 F,0,-4.4013768297,-0.1229757091,-1.5361914374
 F,0,-3.0309323556,1.0271815851,1.4915090052
 F,0,-2.8175353286,1.7223435066,-0.5900623789
 F,0,-1.8227977604,-0.9900409897,-1.1234385894
 F,0,-1.6650699023,-1.1561156728,1.0698427588
 F,0,-0.3790523545,1.4809694243,0.9200376432
 F,0,-0.2237482748,1.0692752516,-1.2409731941
 F,0,0.7730904689,-1.5630728384,-0.4116149592
 F,0,0.9899923888,-0.6432748972,1.5812684498
 F,0,2.2570827256,1.577440456,0.1381810175
 F,0,2.367134195,0.1688323149,-1.554208142
 F,0,3.4116265141,-1.7349280069,0.3845727798
 F,0,3.6991592586,0.0116873547,1.6959326803
 C,0,-5.5888462934,0.650446648,0.3777439398
 F,0,-4.3007182408,-1.340113769,0.2989357053
 F,0,-5.6903493201,0.369469355,1.6990052985
 F,0,-5.4384200234,1.9886192106,0.2268048279
 C,0,-6.924018366,0.2297588949,-0.3287175579
 F,0,-6.9418326998,-1.1160300859,-0.4918809914
 F,0,-6.9774245194,0.8214128017,-1.5435299896
 C,0,-8.2265682431,0.6235295269,0.4434347422
 F,0,-9.2825069503,0.388299114,-0.3487904597
 F,0,-8.3618351226,-0.1022288511,1.5605334123
 F,0,-8.2106038745,1.9262517759,0.7660469293
```

Perfluorocarboxylates

```
Trifluoroethanoate
 Charge = -1 Multiplicity = 1
 C,0,1.9234958757,2.4568359134,4.2782630001
 C,0,2.593743328,3.6682558796,5.056187674
 O,0,2.0348928847,3.8979559876,6.1484490386
 O,0,3.55857312,4.1965515611,4.4689255384
 F,0,2.4939904336,2.1588369459,3.0768506564
```

F,0,1.9621346514,1.2919479296,4.9994268878
F,0,0.5991841666,2.6834590527,4.0071053947

Perfluoropropanoate
Charge = -1 Multiplicity = 1
C,0,0.4048923268,2.7801584548,3.907167994
C,0,1.9168321723,2.5761899633,4.1783697512
C,0,2.6501806782,3.6583448743,5.086253985
O,0,1.872211418,4.3814585984,5.7440279949
O,0,3.8908911374,3.5929708328,5.0136697058
F,0,-0.3449752973,2.6862323382,5.0177542879
F,0,0.1627949719,3.9694062034,3.3192978878
F,0,2.4946452106,2.4779018523,2.9325276654
F,0,2.020893091,1.3222926068,4.7540749589
F,0,-0.0618635188,1.8225475056,3.0474150093

Perfluorobutanoate
Charge = -1 Multiplicity = 1
C,0,-0.344094422,1.5811075503,3.2534224212
C,0,0.3720762014,2.4906249183,4.3035337336
C,0,1.9283154358,2.4763757036,4.2889833716
C,0,2.6190237694,3.6818779336,5.0796890022
O,0,2.1653579746,3.8075282858,6.2352987543
O,0,3.5020563633,4.2774412278,4.4390980018
F,0,-0.1925569773,2.0290463259,1.9952022269
F,0,0.1004514423,0.3108184518,3.3076321534
F,0,-0.1053457991,2.0981174612,5.5113213816
F,0,-0.0731987485,3.7574002425,4.0507651442
F,0,2.2960088965,2.4250675614,2.9629694279
F,0,2.3199569442,1.2683698315,4.8342975134
F,0,-1.6762965307,1.5536285563,3.507176928

Perfluoropentanoate
Charge = -1 Multiplicity = 1
C,0,-1.7218883289,1.9735303988,2.5774936283
C,0,-0.1657235405,1.9062528159,2.7184433206
C,0,0.447705146,2.8074514826,3.8466721128
C,0,1.921787967,2.4933813138,4.2418858271
C,0,2.650201254,3.6564121171,5.0648855393
O,0,1.9813030575,4.0227076763,6.052242786
O,0,3.7589449988,3.9873400358,4.6122245812
F,0,-2.347153817,1.3854540208,3.6092501154
F,0,-2.158813645,3.24014946,2.4755696562
F,0,0.3376368814,2.2656736786,1.5095099788
F,0,0.1331318145,0.5976778656,2.9379977918
F,0,-0.3747114812,2.68912824,4.9232100728
F,0,0.370894646,4.0902951569,3.3871646432
F,0,2.5716725666,2.1775903176,3.0707749504
F,0,1.8984287886,1.3323055219,4.9889052618
F,0,-2.0917090778,1.3182650182,1.4530953444

Perfluorohexanoate
Charge = -1 Multiplicity = 1
C,0,-2.2544567891,1.3725284359,1.2035957774
C,0,-1.6942786076,1.9475899748,2.5461602179
C,0,-0.1320927283,1.8939127834,2.6889135713
C,0,0.4547887648,2.8140853171,3.8195903075
C,0,1.9191723357,2.5029919515,4.2525900247
C,0,2.6273606877,3.6739857308,5.0834494039
O,0,1.9324723227,4.051830536,6.0480018899
O,0,3.7490760428,3.996602869,4.657914206
F,0,-1.9710574445,2.1707858146,0.1635492887
F,0,-1.7681424238,0.1455808846,0.9516372083

F,0,-2.2661998659,1.2264187197,3.541979329
F,0,-2.1372541868,3.2276552016,2.626739812
F,0,0.3916576422,2.2509893827,1.4845913092
F,0,0.1900954787,0.5952413853,2.924437037
F,0,-0.392465042,2.7100862145,4.8773004078
F,0,0.3952229173,4.0892467988,3.3390018354
F,0,2.5966856712,2.1795724178,3.0991006008
F,0,1.8802790474,1.348773427,5.0088415188
F,0,-3.5975389326,1.2776411549,1.2946541144

Perfluoroheptanoate
Charge = -1 Multiplicity = 1
C,0,-3.808932129,1.0856183756,1.2094064664
C,0,-2.2762674395,1.3981210997,1.2120285646
C,0,-1.7182160497,1.9545995793,2.5690297647
C,0,-0.1529612218,1.8826572097,2.7010192394
C,0,0.4493576966,2.8111135495,3.8177739791
C,0,1.9115295455,2.4861402158,4.2485652007
C,0,2.6390822191,3.661896037,5.0558771237
O,0,1.9569418596,4.059711082,6.0214479845
O,0,3.7591724094,3.9681069759,4.6145449701
F,0,-4.0961582938,0.0160939659,1.9651425104
F,0,-4.5223449963,2.1336377291,1.6516546416
F,0,-2.0620625057,2.3082345872,0.2315445764
F,0,-1.6456857092,0.242991416,0.8812414073
F,0,-2.2862114049,1.2330416508,3.5706898951
F,0,-2.1404875401,3.2388119112,2.6719092424
F,0,0.3667504025,2.2209166814,1.4904025644
F,0,0.1568786766,0.5851384284,2.9540848892
F,0,-0.3942566446,2.7310155296,4.8807897609
F,0,0.4040701173,4.0805037635,3.3217529121
F,0,2.5787159657,2.1336243021,3.0976616841
F,0,1.8596918791,1.3459386059,5.0246561846
F,0,-4.1955623664,0.8166263143,-0.0532867614

Perfluorooctanoate
Charge = -1 Multiplicity = 1
C,0,-4.43917909,0.88385428,-0.19777004
C,0,-3.79783696,1.07523142,1.2162204
C,0,-2.26138406,1.39245451,1.20365714
C,0,-1.71261923,1.97011908,2.55891211
C,0,-0.14877408,1.8812856,2.70639477
C,0,0.45354314,2.82022838,3.81453426
C,0,1.90911576,2.48740145,4.26154392
C,0,2.64192738,3.66731555,5.05809088
O,0,1.95232137,4.09190557,6.00676757
O,0,3.77250431,3.9492041,4.62753812
F,0,-5.69136564,0.41375228,-0.04600213
F,0,-4.50906116,2.04361493,-0.86568341
F,0,-3.74333916,0.00043092,-0.93160119
F,0,-4.01071666,-0.0716529,1.90426469
F,0,-4.47752826,2.08101805,1.82070877
F,0,-2.0324608,2.2923789,0.21313023
F,0,-1.61764375,0.2393076,0.89672323
F,0,-2.29843743,1.27326526,3.56682615
F,0,-2.11544235,3.26183928,2.63220162
F,0,0.38539901,2.19653456,1.49568477
F,0,0.14500768,0.58487449,2.98225603
F,0,-0.39906798,2.76279699,4.87159455
F,0,0.4241226,4.08267212,3.30013007
F,0,2.58207223,2.11147393,3.12142055
F,0,1.84011217,1.35910634,5.05336718

Perfluorononanoate

Charge = -1 Multiplicity = 1
C,0,-4.4497518687,0.8813381032,-0.1391469292
C,0,-3.8146741448,1.0991155927,1.2786442649
C,0,-2.265944221,1.3674746563,1.2533158104
C,0,-1.7084750443,2.0057478812,2.5788135106
C,0,-0.1502283353,1.8710292776,2.7475799056
C,0,0.4750901922,2.8446186189,3.8124117474
C,0,1.9161220797,2.4877264613,4.287021156
C,0,2.679557504,3.6798031908,5.0356303342
O,0,1.997605365,4.1669687564,5.9593941177
O,0,3.8205968372,3.9079675077,4.6009573158
F,0,-4.5626584656,2.0773967384,-0.7627737059
F,0,-3.6556554023,0.0717811827,-0.8830284267
F,0,-4.0552882242,-0.0115578777,2.0200831039
F,0,-4.4532625725,2.1483819126,1.8509762241
F,0,-2.005247062,2.2021456186,0.2157425256
F,0,-1.65531317,0.180317654,1.0210436268
F,0,-2.3268089966,1.3901709305,3.6199361816
F,0,-2.0647910914,3.3128206941,2.5721710389
F,0,0.4045880627,2.1041305541,1.5275722546
F,0,0.095875178,0.5816613763,3.094140748
F,0,-0.3857985271,2.8677098708,4.8639960476
F,0,0.490904373,4.0802190442,3.2358177494
F,0,2.5851025331,2.0400406973,3.1708891143
F,0,1.8067493649,1.3992373769,5.128500833
C,0,-5.8740279331,0.2346370197,-0.1271081911
F,0,-6.6995808276,0.9000704213,0.6961884649
F,0,-5.8247799874,-1.0499187708,0.2511170663
F,0,-6.382932916,0.2859837409,-1.371132179

Perfluorodecanoate
Charge = -1 Multiplicity = 1
C,0,-4.4384286931,0.8894929801,-0.1494874185
C,0,-3.8118243704,1.1129083141,1.2744633187
C,0,-2.2585703489,1.3602693689,1.2535882113
C,0,-1.7008836934,2.0134198179,2.5717079692
C,0,-0.1453649345,1.8612407046,2.7523774098
C,0,0.4866186793,2.8500302421,3.7989577004
C,0,1.9195357787,2.4845048945,4.2908976714
C,0,2.6936350224,3.6816073396,5.0201875486
O,0,2.0091777161,4.2018118055,5.9238715721
O,0,3.8433902079,3.8803667738,4.5941555911
F,0,-4.5415923087,2.0891449645,-0.7738194769
F,0,-3.6290612668,0.0867374833,-0.8824567876
F,0,-4.0706512718,0.0126511853,2.0240726009
F,0,-4.435803023,2.1781955135,1.8315008134
F,0,-1.9812881806,2.1756219996,0.2048390407
F,0,-1.6612961382,0.162369987,1.0442732443
F,0,-2.3335498864,1.4235678549,3.6190561749
F,0,-2.0400634906,3.324618796,2.5408961907
F,0,0.4197836919,2.0590318124,1.530878375
F,0,0.0809620412,0.5768379288,3.1290854497
F,0,-0.3810499197,2.9085439312,4.8435984152
F,0,0.5235914197,4.0717245678,3.1943086405
F,0,2.5898126184,2.0057517222,3.1883696356
F,0,1.790439056,1.4149397395,5.1537341586
C,0,-5.8609758451,0.2292401007,-0.1244785838
C,0,-6.6647963259,0.3548988374,-1.4607186834
F,0,-7.0581447435,1.617404999,-1.6750750246
F,0,-5.929800857,-0.056774899,-2.5060417579
F,0,-6.6162146083,0.7994778082,0.8466080798
F,0,-5.7304725713,-1.0915619575,0.1403097434
F,0,-7.7607943944,-0.4191830059,-1.3795004124

Perfluoroundecanoate
Charge = -1 Multiplicity = 1

C,0,-4.464761228,0.8927813187,-0.085144644
C,0,-3.8310373357,1.1656401254,1.3280259868
C,0,-2.2704697209,1.3605035825,1.2969668555
C,0,-1.6897803941,2.0492259859,2.5869161487
C,0,-0.1395624244,1.8546882905,2.7725878847
C,0,0.5256084312,2.8629840643,3.7792203134
C,0,1.9466051467,2.4706611536,4.285046336
C,0,2.7604735941,3.6700358045,4.9656791044
O,0,2.0952656509,4.2467566746,5.8492107846
O,0,3.9148420343,3.8151629859,4.5305919836
F,0,-4.5291555153,2.0621585315,-0.7678252798
F,0,-3.6810820716,0.0271427527,-0.7717272826
F,0,-4.1252746923,0.111676747,2.1296734923
F,0,-4.4182204316,2.2769773521,1.8321262399
F,0,-1.9685530241,2.1218989511,0.2150628927
F,0,-1.7125826054,0.1360945291,1.1384647557
F,0,-2.3386949522,1.5230328296,3.6579479756
F,0,-1.9870142268,3.3682525681,2.5031074018
F,0,0.4295102231,1.9862975321,1.5440605579
F,0,0.0463413778,0.5794215116,3.1990893528
F,0,-0.3380993953,2.9912555037,4.8208757773
F,0,0.6013354782,4.05786632,3.1266781051
F,0,2.5992403923,1.9262022975,3.2025106595
F,0,1.7837524551,1.4415933482,5.1903725592
C,0,-5.9109607985,0.2801332058,-0.0239658777
C,0,-6.7102890108,0.397830826,-1.3681650941
C,0,-7.973506932,-0.5200611796,-1.4635596423
F,0,-8.7681128138,-0.3559150096,-0.3942551246
F,0,-7.6310938417,-1.8117496723,-1.5580891122
F,0,-7.1320584553,1.674601339,-1.5188585064
F,0,-5.9046123833,0.0748488679,-2.4098360574
F,0,-6.6292816773,0.9102425782,0.9367600634
F,0,-5.8133698524,-1.0334731679,0.2977482152
F,0,-8.6659763811,-0.1855660874,-2.5654776149

Perfluorosulfonic acids

Pentafluoroethanesulfonic acid
 Charge = 0 Multiplicity = 1
C,0,2.4088193177,0.3273796305,0.1073223766
C,0,3.7028147247,-0.3975868728,-0.3664293926
F,0,3.7635847697,-0.3383725445,-1.7158391553
F,0,3.6531709396,-1.6823894222,0.0212407704
F,0,2.3729311513,0.3872596757,1.4449512089
F,0,2.353725027,1.5672310387,-0.3909761684
S,0,5.3130165884,0.3492542192,0.2984808378
O,0,5.4594724057,-0.0582637663,1.6785123792
O,0,6.3563720193,-0.5478615049,-0.5716162878
O,0,5.3728747333,1.7304140288,-0.1571999845
H,0,6.552854748,-0.0920053035,-1.4103763695
F,0,1.3426029654,-0.3620941387,-0.3270429649

Perfluoropropanesulfonic acid
 Charge = 0 Multiplicity = 1
C,0,1.0864927358,-0.4969679624,-0.1720484942
C,0,2.4118057883,0.2946711142,0.0772081172
C,0,3.7103900833,-0.4485770965,-0.3628471782
F,0,3.8123791143,-0.4170042978,-1.7097239496
F,0,3.6797618039,-1.7284896755,0.0482452404
F,0,2.4913166138,0.5614069109,1.4026475635
F,0,2.3311972056,1.4576319061,-0.6045163853
F,0,1.0258193876,-0.9132641417,-1.4478434184
F,0,1.0036795897,-1.5596300158,0.6377505734
S,0,5.2984561343,0.3374596089,0.3305422713
O,0,5.4683130518,-0.1120867798,1.6945368443

O,0,6.3723669202,-0.4917949402,-0.5704774374
O,0,5.3048101203,1.7338138159,-0.0805823098
H,0,6.5393683046,-0.0093563344,-1.4006568437
F,0,0.0459753465,0.3110418682,0.0693806767

Perfluorobutanesulfonic acid
Charge = 0 Multiplicity = 1
C,0,-0.2171400729,0.400582572,-0.0452411019
C,0,1.0877264636,-0.4569999836,-0.1376987034
C,0,2.4192574288,0.3414656853,0.0710242351
C,0,3.6992742371,-0.4338054472,-0.3810649884
F,0,3.8066877185,-0.3863278881,-1.7260945669
F,0,3.6386397614,-1.716350625,0.0153180128
F,0,2.5409243079,0.6349079767,1.3871995445
F,0,2.3540325453,1.4949874187,-0.6324357864
F,0,1.1101638732,-1.0346383363,-1.3655580815
F,0,1.0110189098,-1.4251398054,0.801849373
F,0,-0.3240402676,1.2240359228,-1.0956740669
F,0,-0.2273616195,1.125263493,1.083616558
S,0,5.3041240764,0.3080052407,0.3267415376
O,0,5.4720489206,-0.1781678011,1.6783401806
O,0,6.3614601177,-0.516579161,-0.5980727523
O,0,5.3321853452,1.7139524353,-0.0502123011
H,0,6.5311257133,-0.0189854095,-1.4186539776
F,0,-1.2734381289,-0.4248454475,-0.0393169651

Perfluoropentanesulfonic acid
Charge = 0 Multiplicity = 1
C,0,-0.2133739238,0.3581949327,-0.0466066836
C,0,1.0939744154,-0.5039482297,-0.1125371575
C,0,2.4148664686,0.3193170315,0.0952617049
C,0,3.7032002272,-0.4330222396,-0.3735756034
F,0,3.8003620765,-0.3752707795,-1.7189469081
F,0,3.6661336172,-1.7188337788,0.0160575439
F,0,2.54500981,0.5999467263,1.4126986355
F,0,2.3269419476,1.4769010701,-0.5977306298
F,0,1.144934648,-1.1020423036,-1.3288057831
F,0,1.0357878167,-1.4626675134,0.8414134599
C,0,-1.5325821511,-0.4644614915,0.1275126745
F,0,-0.3234396161,1.0655433889,-1.1938497528
F,0,-0.129154776,1.2187184742,0.9968053417
F,0,-1.5996379098,-1.0140239173,1.3463360705
F,0,-1.6076719448,-1.4352905332,-0.7964828633
S,0,5.3027993909,0.3292212142,0.3252867223
O,0,5.48796164,-0.1577156511,1.6743727177
O,0,6.3640007917,-0.4788636805,-0.6097243308
O,0,5.3091729018,1.7362243809,-0.0484869508
H,0,6.5187212214,0.0221448157,-1.4312222164
F,0,-2.5772405414,0.3610273635,-0.0277492211

Perfluorohexanesulfonic acid
Charge = 0 Multiplicity = 1
C,0,-0.2111623338,0.3953072872,-0.0616333609
C,0,1.0876349869,-0.4853629243,-0.1303386609
C,0,2.4159072465,0.3240636871,0.0902964078
C,0,3.6987997471,-0.4366785909,-0.3800324507
F,0,3.8001681269,-0.3718336252,-1.7247375095
F,0,3.6501777906,-1.7243681812,0.0016001822
F,0,2.54494319,0.5930626161,1.4101982589
F,0,2.3422900282,1.4876946249,-0.5945758478
F,0,1.1415375469,-1.0707667204,-1.3520492016
F,0,1.015519033,-1.4497693026,0.8159682447
C,0,-1.528893448,-0.4304070789,0.1385817899
F,0,-0.3099919162,1.0981114823,-1.2156712072

F,0,-0.0975779413,1.2640983586,0.9711546855
C,0,-2.846433647,0.3546281238,-0.1712754982
F,0,-1.5917686714,-0.8424312112,1.4245038467
F,0,-1.5042415502,-1.5168942798,-0.6722494265
F,0,-2.9676829038,0.5884608487,-1.4842838994
F,0,-2.8666615025,1.5241678212,0.48641868
S,0,5.3027169741,0.3087875565,0.3272079934
O,0,5.4784391098,-0.1835112153,1.6755746605
O,0,6.359911984,-0.5064716939,-0.606278378
O,0,5.3232932954,1.7167277125,-0.0426060567
H,0,6.5204879825,-0.0052711695,-1.4265213388
F,0,-3.8909138777,-0.384149596,0.2291405366

Perfluoroheptanesulfonic acid
Charge = 0 Multiplicity = 1
C,0,-0.2148597721,0.3821687846,-0.0412000762
C,0,1.0885474433,-0.4921593925,-0.1288894545
C,0,2.4133396125,0.3220868693,0.0938986661
C,0,3.6981156705,-0.426270451,-0.3913909037
F,0,3.7972074689,-0.3383876707,-1.7349897914
F,0,3.6546098935,-1.7203486907,-0.0312724555
F,0,2.5478603534,0.5759461431,1.4162923012
F,0,2.3293370666,1.4928912873,-0.5773705089
F,0,1.1386019544,-1.0623530163,-1.3576075331
F,0,1.0285055535,-1.4681241083,0.8066282943
C,0,-1.523239332,-0.4588494301,0.1817833385
F,0,-0.3348592871,1.0814176434,-1.1943648939
F,0,-0.0885620339,1.2508777807,0.9893630861
C,0,-2.84337272,0.3165845292,-0.156403578
F,0,-1.565244864,-0.8437205459,1.4795687486
F,0,-1.4735070483,-1.5644187305,-0.6004208669
C,0,-4.1481024884,-0.3344757837,0.4107913173
F,0,-2.973587608,0.3849059896,-1.5006857106
F,0,-2.7662935997,1.5739663903,0.3442270738
F,0,-4.2009115346,-0.2220769044,1.7438057816
F,0,-4.211988299,-1.6329145561,0.0769301059
S,0,5.3001748366,0.3123425508,0.3271820388
O,0,5.4832547443,-0.2098663193,1.6632871633
O,0,6.3593728787,-0.474950742,-0.6277845427
O,0,5.3113902972,1.7285115826,-0.0101773272
H,0,6.512038839,0.0441470342,-1.438336464
F,0,-5.2071730353,0.2984882164,-0.113653869

Perfluorooctanesulfonic acid
Charge = 0 Multiplicity = 1
C,0,-0.2169924002,0.3874056803,-0.0307798285
C,0,1.0844305356,-0.4881316353,-0.1320988887
C,0,2.411394357,0.3201953027,0.1009292845
C,0,3.6940554917,-0.4250234422,-0.3944937724
F,0,3.7896616248,-0.3245916527,-1.7373640423
F,0,3.6497101147,-1.7225599176,-0.0467426024
F,0,2.5467549687,0.5574060364,1.4261192438
F,0,2.330708384,1.4998159352,-0.5551208048
F,0,1.1331786235,-1.0417093485,-1.3685307937
F,0,1.0226318102,-1.4764940923,0.7901767691
C,0,-1.5294698295,-0.4556566873,0.1650444544
F,0,-0.3292213523,1.1125296148,-1.1689550701
F,0,-0.0920628553,1.2315609148,1.0199699045
C,0,-2.8450980612,0.3394617041,-0.1604080847
F,0,-1.5788647534,-0.8735637839,1.4516664731
F,0,-1.477080392,-1.5377380981,-0.6482700473
C,0,-4.1455132893,-0.3194497959,0.4171614595
F,0,-2.9657899689,0.4305192045,-1.5067063528
F,0,-2.7432624105,1.5885853042,0.354142763
C,0,-5.480176388,0.2158763921,-0.1991992944
F,0,-5.5224344777,1.5561567792,-0.1440553631

F,0,-6.5074989373,-0.2777267083,0.5066899151
F,0,-5.6117444101,-0.1741716837,-1.473496051
F,0,-4.1925818502,-0.0922899845,1.7491044046
F,0,-4.1061105065,-1.6569232577,0.1988310837
S,0,5.2998151469,0.3043576396,0.3246666695
O,0,5.4787787227,-0.2164699966,1.6618645842
O,0,6.3539682326,-0.4913949544,-0.6288675901
O,0,5.3206593049,1.7198132946,-0.015339103
H,0,6.5140157701,0.0281165184,-1.4377581994

Perfluorononanesulfonic acid
Charge = 0 Multiplicity = 1
C,0,-0.2087321695,0.3633084117,-0.0060612489
C,0,1.1000794347,-0.4955578765,-0.1469436348
C,0,2.4206776781,0.3160263977,0.1091721261
C,0,3.7077927598,-0.3997266507,-0.4169963021
F,0,3.7954821592,-0.2538531969,-1.7561421025
F,0,3.6774967636,-1.7083839794,-0.1122488623
F,0,2.5600071022,0.5079263887,1.4413676193
F,0,2.326069905,1.5168292424,-0.5054149036
F,0,1.1473676872,-1.0013918893,-1.4036858989
F,0,1.0523554903,-1.5184884687,0.7378076283
C,0,-1.512629616,-0.4986294342,0.1645352367
F,0,-0.3336408626,1.1302641717,-1.1151366849
F,0,-0.0856586411,1.167896199,1.0754129871
C,0,-2.8364622268,0.2962283223,-0.131622654
F,0,-1.5537297997,-0.958341457,1.4372033686
F,0,-1.4520513439,-1.5531397313,-0.683246473
C,0,-4.1272497663,-0.3907437442,0.4435039901
F,0,-2.9682820738,0.4173576042,-1.4737987543
F,0,-2.7358497097,1.5315129963,0.4141823719
C,0,-5.4622123803,0.135594256,-0.1884241587
F,0,-5.4122692857,1.4871473741,-0.2822443861
F,0,-5.5914244523,-0.3872866505,-1.4287782585
F,0,-4.1653260262,-0.1743302064,1.7801330829
F,0,-4.0537263003,-1.725004398,0.2188592233
S,0,5.3100864139,0.3197456242,0.3200112526
O,0,5.502748108,-0.2523506592,1.63419254
O,0,6.3675203739,-0.4252899917,-0.6700211144
O,0,5.3134167617,1.7479033727,0.0371945006
H,0,6.5212217773,0.1291901032,-1.4566626204
C,0,-6.7548451065,-0.2293970894,0.6141514798
F,0,-7.8250525072,0.0932563261,-0.1261053119
F,0,-6.792937806,-1.5446993448,0.8786185622
F,0,-6.8124455909,0.4504984678,1.7661332298

Perfluorodecanesulfonic acid
Charge = 0 Multiplicity = 1
C,0,-0.1974662005,0.3764232588,0.0191873968
C,0,1.1056555015,-0.4847091211,-0.1549929934
C,0,2.4325339954,0.3089642973,0.1244798029
C,0,3.7115546123,-0.3954642751,-0.435968572
F,0,3.7940639082,-0.1956072978,-1.7684421786
F,0,3.6714791995,-1.7153098437,-0.1846361752
F,0,2.5799776331,0.4499677535,1.4619510326
F,0,2.3432280478,1.5328935322,-0.4433939854
F,0,1.1460301129,-0.9478783414,-1.4283515524
F,0,1.054383932,-1.5369155812,0.6944001307
C,0,-1.5065231715,-0.483548374,0.1584169553
F,0,-0.3183554049,1.1844589354,-1.0607868349
F,0,-0.067904356,1.1396760992,1.129608709
C,0,-2.8262591788,0.3301413701,-0.1027616483
F,0,-1.5485531375,-0.9931705505,1.4119252335
F,0,-1.453071627,-1.5034212808,-0.7312564171
C,0,-4.121136409,-0.3779659519,0.4395594835
F,0,-2.9555635343,0.512005042,-1.438609302
F,0,-2.719710213,1.5385712057,0.498637056

```
 C,0,-5.4527479575,0.1818224283,-0.1791551555
 F,0,-5.3764098037,1.5331477953,-0.2418007743
 F,0,-5.5763493093,-0.3066891632,-1.4365825312
 F,0,-4.1629492249,-0.2175599899,1.7832007433
 F,0,-4.0472573899,-1.7003025141,0.1561997516
 S,0,5.3238106274,0.280113745,0.320109006
 O,0,5.5135292988,-0.3355809986,1.6148897269
 O,0,6.3697126496,-0.4450684934,-0.6968144148
 O,0,5.3429806272,1.7164000704,0.082827578
 H,0,6.5295113523,0.134010294,-1.4642598663
 C,0,-6.7389544392,-0.1949636246,0.6346702398
 F,0,-6.6725873674,-1.4985648733,1.0012179703
 F,0,-6.7894377791,0.5732074094,1.7462768722
 C,0,-8.0852199493,0.0054157994,-0.1369460232
 F,0,-8.2108790945,-0.8888139126,-1.125688174
 F,0,-8.1555550038,1.2424272429,-0.6528542714
 F,0,-9.1008242471,-0.1623509014,0.7220695312

Perfluoroundecanesulfonic acid
Charge =  0 Multiplicity = 1
 C,0,1.2554412545,-0.2810936507,-0.39775135
 C,0,2.600950434,0.1661811209,0.2785308968
 C,0,3.8733840317,-0.2095571673,-0.5497568357
 F,0,4.0256581407,0.6596638928,-1.5714564711
 F,0,3.7678659798,-1.4572456423,-1.0379474256
 F,0,2.6962538365,-0.4293624062,1.4899245268
 F,0,2.5872816715,1.5082570491,0.4431005495
 F,0,1.3289997927,0.0023251728,-1.7213051835
 F,0,1.1263724882,-1.619043399,-0.240797903
 S,0,5.474290483,-0.1333365612,0.4797701153
 O,0,5.588404437,-1.360500864,1.2363830616
 O,0,6.5375681722,-0.2450761279,-0.7491670809
 O,0,5.5510740858,1.1997123392,1.0600517745
 H,0,6.7433338301,0.6478990488,-1.0809918815
 C,0,-0.0171830059,0.4277748364,0.1925216056
 C,0,-1.3646874676,-0.301535873,-0.1596586597
 C,0,-2.6398063655,0.5954696036,0.0455891227
 C,0,-3.9801682765,-0.2233241435,0.1211993841
 C,0,-5.2666002169,0.6506092378,-0.1103026638
 C,0,-6.5924025113,-0.0351155824,0.3809253245
 C,0,-7.8960765011,0.6069198513,-0.2079054306
 C,0,-9.2142022267,0.2146495085,0.5382521298
 F,0,0.1008843898,0.4788711418,1.5399881021
 F,0,-0.0634296833,1.6903178888,-0.2950224928
 F,0,-1.4715422466,-1.3986527187,0.626314108
 F,0,-1.3220995586,-0.689984796,-1.456479179
 F,0,-2.5018642317,1.2921235065,1.1983797944
 F,0,-2.7176799685,1.4657873534,-0.9890185209
 F,0,-4.057774414,-0.7984205221,1.3445463244
 F,0,-3.9519220412,-1.1948224317,-0.821845518
 F,0,-5.124841562,1.8216891684,0.5550553731
 F,0,-5.3739337402,0.907281416,-1.4354825211
 F,0,-6.640198482,0.0483776999,1.7321305757
 F,0,-6.5706100698,-1.3422262835,0.0246180298
 F,0,-7.7915894953,1.957846508,-0.1622334919
 F,0,-8.0275344073,0.2191085275,-1.4966524037
 F,0,-10.2590091972,0.6609768752,-0.1735546286
 F,0,-9.3113286542,-1.1185630227,0.6585300482
 F,0,-9.2603493742,0.7685846659,1.7563938047
```

Perfluorosulfonates

Pentafluoroethanesulfonate
 Charge = -1 Multiplicity = 1
 C,0,2.4512510264,0.31581666,0.1277353317
 C,0,3.7371900608,-0.3936723323,-0.3700032365
 F,0,3.6866738321,-0.3538628156,-1.7357998116
 F,0,3.618911166,-1.7035704517,0.0032210865
 F,0,2.3467902864,0.2987477707,1.4662805113
 F,0,2.3817319127,1.5901831248,-0.2893989119
 S,0,5.416364384,0.2865558019,0.2264220853
 O,0,5.3422572149,0.0939346258,1.6931758665
 O,0,6.3613395658,-0.5993206079,-0.489999983
 O,0,5.3785575743,1.6936955807,-0.2356070101
 F,0,1.3520048467,-0.3245096563,-0.3660627184

Pefluoropropanesulfonate
 Charge = -1 Multiplicity = 1
 C,0,1.1169453243,-0.4961569488,-0.163795625
 C,0,2.4463212759,0.2930554945,0.0745605783
 C,0,3.7499565891,-0.4336515429,-0.3707430483
 F,0,3.7558484221,-0.4246817907,-1.7363052196
 F,0,3.6442347764,-1.7422155916,0.0204313672
 F,0,2.4766328104,0.5726417635,1.4017601735
 F,0,2.3164422438,1.4583427535,-0.61094061
 F,0,1.0087440055,-0.9228049197,-1.4359637478
 F,0,1.0067504955,-1.5592488711,0.6502600247
 S,0,5.4013004908,0.2842857436,0.2779410097
 O,0,5.3756200953,-0.0728056379,1.7140852405
 O,0,6.3801509997,-0.4580794839,-0.5475077747
 O,0,5.261913112,1.7270428461,-0.028994185
 F,0,0.0621040392,0.3141628254,0.0857630464

Perfluorobutanesulfonate
 Charge = -1 Multiplicity = 1
 C,0,-0.1896651779,0.4027764335,-0.0428917166
 C,0,1.1133232614,-0.4572789636,-0.1297933861
 C,0,2.4537019001,0.3352731355,0.0692353017
 C,0,3.7379880909,-0.4203546415,-0.3926715957
 F,0,3.7468213351,-0.3884951899,-1.7566791186
 F,0,3.6012876477,-1.7305577223,-0.0197511527
 F,0,2.5256188979,0.6381522014,1.388302644
 F,0,2.3343906102,1.4955724386,-0.6322858952
 F,0,1.0892459591,-1.0564378652,-1.3498640612
 F,0,1.0043549362,-1.4168363699,0.8231276373
 F,0,-0.3230537814,1.2140839987,-1.1033744555
 F,0,-0.2220327853,1.1458672547,1.0751059712
 S,0,5.4041970809,0.2529494592,0.2699848654
 O,0,5.3805407842,-0.1489878215,1.6940101829
 O,0,6.3676663831,-0.4769731272,-0.5840659206
 O,0,5.2826894091,1.7063724392,0.0081955383
 F,0,-1.2595527412,-0.4227321597,-0.0235827287

Perfluoropentanesulfonate
 Charge = -1 Multiplicity = 1
 C,0,-0.1911370662,0.3576232501,-0.0484142683
 C,0,1.1190711546,-0.50264913,-0.1177170099
 C,0,2.4475316176,0.3129191339,0.0924759776
 C,0,3.7418028085,-0.4149958228,-0.386444884
 F,0,3.7405864652,-0.3722933083,-1.7499790219
 F,0,3.6323387177,-1.730112522,-0.0212130172

F,0,2.5220400937,0.5910207799,1.4159576179
F,0,2.3059054511,1.4813000033,-0.5898067824
F,0,1.1247424043,-1.1085616387,-1.3331236494
F,0,1.0251379236,-1.4658603061,0.8372384465
C,0,-1.5094397586,-0.4630323652,0.1382408844
F,0,-0.3317542461,1.0574879437,-1.2010232373
F,0,-0.131666444,1.2309903263,0.9873554425
F,0,-1.5894381141,-1.0030657969,1.3629103905
F,0,-1.6097666836,-1.4436977349,-0.7745720757
S,0,5.4013862147,0.2845918442,0.2681296031
O,0,5.3925180278,-0.1186977642,1.6918732278
O,0,6.3700622512,-0.4300060903,-0.5927863683
O,0,5.2552442207,1.7358552859,0.0080754612
F,0,-2.5635664481,0.3633158523,-0.018214007

Perfluorohexanesulfonate
Charge = -1 Multiplicity = 1
C,0,-0.1887318537,0.393792272,-0.0618724557
C,0,1.1118661283,-0.4857565391,-0.1325333372
C,0,2.4479179614,0.3158534326,0.0893661978
C,0,3.736194459,-0.4202906412,-0.3933860938
F,0,3.7388906646,-0.3639813758,-1.756281182
F,0,3.6130259572,-1.7377966369,-0.041770432
F,0,2.5218992623,0.5819086852,1.4151530424
F,0,2.3196509863,1.4911806596,-0.5838821958
F,0,1.119351946,-1.0808206784,-1.3524127841
F,0,1.0024955847,-1.4518909473,0.816760158
C,0,-1.5093602185,-0.4266547864,0.1491239722
F,0,-0.3185234904,1.089331591,-1.2216394857
F,0,-0.1009158903,1.2763056815,0.9626816749
C,0,-2.8258523968,0.3548779,-0.1719601255
F,0,-1.590751554,-0.8196779093,1.4426290434
F,0,-1.5090224747,-1.5282572996,-0.6430668654
F,0,-2.9638549824,0.5646081696,-1.4888234444
F,0,-2.8589437574,1.5378103139,0.4622221741
S,0,5.4009530786,0.2577565174,0.2713594333
O,0,5.3878849883,-0.1628386183,1.6899644571
O,0,6.3641948665,-0.4541589721,-0.5977601033
O,0,5.2665775925,1.7131703038,0.0288011811
F,0,-3.8776151275,-0.3762439322,0.2446555808

Perfluoroheptanesulfonate
Charge = -1 Multiplicity = 1
C,0,-0.1941000929,0.3799331247,-0.0397298604
C,0,1.1123150326,-0.4909114553,-0.1325641894
C,0,2.444356429,0.3164117794,0.0921500961
C,0,3.7355918377,-0.4075397903,-0.401490938
F,0,3.7340260049,-0.3399956368,-1.7638180197
F,0,3.6216660992,-1.7286451553,-0.060348131
F,0,2.5219712013,0.5695180724,1.4203177207
F,0,2.3061800361,1.4970504375,-0.5697220575
F,0,1.1159099639,-1.0678682942,-1.3607815236
F,0,1.0161822068,-1.4710740924,0.8040254105
C,0,-1.5050010199,-0.459325863,0.1808352745
F,0,-0.3427998204,1.082367365,-1.1921686218
F,0,-0.0990257284,1.2520804719,0.9918624854
C,0,-2.8266931315,0.3159356205,-0.1554357088
F,0,-1.5674441746,-0.8458708744,1.4801442747
F,0,-1.4800556739,-1.5680735458,-0.5989560898
C,0,-4.1305488918,-0.3325544254,0.4157945222
F,0,-2.974228327,0.3800953032,-1.4999417579
F,0,-2.765570359,1.5768534211,0.3395220974
F,0,-4.1912772289,-0.2191071683,1.7495367519
F,0,-4.2098430481,-1.6315204944,0.0851474301
S,0,5.3977108786,0.2751131802,0.2655985482

O,0,5.3921825631,-0.1628897312,1.6788970847
O,0,6.3635204907,-0.4189101404,-0.615150958
O,0,5.2517535084,1.7323307796,0.0412835956
F,0,-5.1952912861,0.3030482318,-0.1068615362

Perflurooctanesulfonate
Charge = -1 Multiplicity = 1
C,0,-0.1965952853,0.3878124429,-0.0325773375
C,0,1.1069348609,-0.4857129327,-0.1412520336
C,0,2.4415153916,0.3126846914,0.1013453245
C,0,3.7299808144,-0.4035015656,-0.4104591723
F,0,3.7274033816,-0.3022639081,-1.7707394104
F,0,3.6113541929,-1.7321089538,-0.1014502604
F,0,2.5202586266,0.5346142073,1.4348198408
F,0,2.3066563195,1.5091541255,-0.532164049
F,0,1.110248381,-1.0383570627,-1.3804847138
F,0,1.0061564367,-1.4839131589,0.7755243422
C,0,-1.5111471831,-0.4522876684,0.1687132131
F,0,-0.3408555579,1.112377358,-1.1719075107
F,0,-0.0993279123,1.2392901837,1.0156864864
C,0,-2.8286231403,0.3391009617,-0.1602455045
F,0,-1.580452134,-0.8599521048,1.4604866046
F,0,-1.483964719,-1.5443899446,-0.6330984259
C,0,-4.1290511496,-0.3128931439,0.42665478
F,0,-2.9688578857,0.4151580348,-1.5076514581
F,0,-2.7437175301,1.596090395,0.338581277
C,0,-5.4638232862,0.2098557679,-0.199686833
F,0,-5.5149579847,1.5511867898,-0.177476016
F,0,-6.4947673348,-0.2669312395,0.5200941816
F,0,-5.6065609848,-0.210408734,-1.4639602108
F,0,-4.1884271774,-0.0640167118,1.7555877868
F,0,-4.101213848,-1.6547315909,0.2323055616
S,0,5.3956291687,0.2570152117,0.2692698494
O,0,5.3860196932,-0.2016578648,1.6760129403
O,0,6.3573772855,-0.4305093107,-0.6209688954
O,0,5.2595022408,1.7182336854,0.0661567035

Perfluorononanesulfonate
Charge = -1 Multiplicity = 1
C,0,-0.1873555199,0.3692798939,-0.0129230707
C,0,1.1243352283,-0.4871707566,-0.1545246013
C,0,2.4521953783,0.3176981472,0.102771562
C,0,3.7457379116,-0.3738406771,-0.4297675491
F,0,3.7370636803,-0.2423256168,-1.7873020344
F,0,3.6418082465,-1.7102126206,-0.1505838154
F,0,2.5337881365,0.5091574872,1.4408296993
F,0,2.303739469,1.5272152893,-0.502144747
F,0,1.1261169534,-1.0041501925,-1.4091417157
F,0,1.0390536359,-1.5118091499,0.7342574417
C,0,-1.4929522636,-0.4900939272,0.1641598674
F,0,-0.3434076435,1.130064997,-1.126822249
F,0,-0.0941169341,1.1855917924,1.0632563712
C,0,-2.8197868668,0.3022306445,-0.1274593912
F,0,-1.5506887746,-0.945703886,1.4406590172
F,0,-1.4599622683,-1.5511325294,-0.6776642299
C,0,-4.109466656,-0.3854217238,0.4509248692
F,0,-2.972146286,0.4222045356,-1.4695590435
F,0,-2.7381685296,1.5401075682,0.4157367635
C,0,-5.4474085242,0.1365000187,-0.1795009857
F,0,-5.4117967211,1.4883423151,-0.2784908424
F,0,-5.5862283942,-0.3908682757,-1.4181256349
F,0,-4.1579654946,-0.1655752574,1.7879996778
F,0,-4.0488578373,-1.72163788,0.2330041169
S,0,5.4073397243,0.2878182674,0.2590692276
O,0,5.4079348647,-0.2039113968,1.6546177861
O,0,6.372226474,-0.3690688811,-0.6506455594

O,0,5.2557757017,1.7519643046,0.0909389105
C,0,-6.7384096916,-0.229770327,0.624383127
F,0,-7.8126648289,0.1016266396,-0.1122905405
F,0,-6.7876484964,-1.5465610431,0.8807524225
F,0,-6.7995625839,0.4419703106,1.78171498

Perflurodecanesulfonate
Charge = -1 Multiplicity = 1
C,0,-0.1760174629,0.3783675514,0.0122115454
C,0,1.1306636285,-0.4776835278,-0.1709049817
C,0,2.4636759555,0.3077773273,0.1171440724
C,0,3.7520010246,-0.3680224611,-0.4470382148
F,0,3.7407018398,-0.1811826518,-1.7981110173
F,0,3.641640092,-1.7140809276,-0.2221898395
F,0,2.5495975218,0.4411740634,1.4620378758
F,0,2.3207685566,1.542687768,-0.4356078804
F,0,1.1259226039,-0.938204518,-1.4472781906
F,0,1.0420799981,-1.5403289181,0.6718147074
C,0,-1.4856914374,-0.4816282795,0.1551172165
F,0,-0.3306786085,1.1883981425,-1.066687465
F,0,-0.076167928,1.1462123406,1.1227587808
C,0,-2.8081297635,0.3276128273,-0.109798299
F,0,-1.5475426425,-0.9835774401,1.4137483155
F,0,-1.4558749101,-1.5112710173,-0.7247526691
C,0,-4.1021867218,-0.3738033902,0.443723925
F,0,-2.95845417,0.4927283393,-1.4475220498
F,0,-2.7192903878,1.5457692298,0.4747941169
C,0,-5.4363797081,0.1784201825,-0.1767752468
F,0,-5.3709109895,1.5294178102,-0.2581951981
F,0,-5.5753299631,-0.3267234705,-1.4273919073
F,0,-4.1532336654,-0.195851338,1.7863604314
F,0,-4.043420664,-1.7009703342,0.1792506832
S,0,5.4186133638,0.2559890893,0.2651093493
O,0,5.4239932916,-0.3044399572,1.6344681046
O,0,6.3776911783,-0.3569639425,-0.6806580254
O,0,5.2700838589,1.7270957988,0.1706893728
C,0,-6.72078078,-0.1867028305,0.6456810451
F,0,-6.6633696723,-1.4855375099,1.0305461782
F,0,-6.7742870045,0.5959615389,1.7479277971
C,0,-8.0689978379,0.0046287459,-0.1247527225
F,0,-8.2086731599,-0.9104146683,-1.0930838507
F,0,-9.0849168234,-0.1398592586,0.7424627201
F,0,-8.1422685026,1.230075516,-0.6677309999

Perfluroundecanesulfonate
Charge = -1 Multiplicity = 1
C,0,-0.1638256683,0.3607205144,0.0218553582
C,0,1.1535322429,-0.4685770387,-0.2037847796
C,0,2.4759222238,0.3188874657,0.1249378239
C,0,3.7733781979,-0.308711381,-0.4728832539
F,0,3.7599363721,-0.0515744512,-1.8124383492
F,0,3.6815828971,-1.6660699125,-0.3185801949
F,0,2.560490353,0.3831531779,1.4749337396
F,0,2.3159379245,1.5788833747,-0.362955795
F,0,1.1548418859,-0.8638808263,-1.5018034464
F,0,1.0788520122,-1.573843021,0.5835540964
C,0,-1.4623943561,-0.5210207194,0.1237629314
F,0,-0.3305684206,1.2202963627,-1.01602806
F,0,-0.0714470915,1.0747836627,1.1683881778
C,0,-2.7959294788,0.2863521901,-0.0867669602
F,0,-1.5103775888,-1.0936874869,1.3524545529
F,0,-1.4260196189,-1.49895409,-0.8130831933
C,0,-4.0779585944,-0.4607655999,0.434255487
F,0,-2.9576433654,0.5251202382,-1.4119697471
F,0,-2.7166967964,1.4702103135,0.5657433266
C,0,-5.4234662537,0.114437224,-0.14209678
F,0,-5.3659588153,1.4674629255,-0.1492004381
F,0,-5.5728626332,-0.3251913319,-1.4153368624

F,0,-4.119100618,-0.3627293674,1.7855747271
F,0,-4.0071239733,-1.7688764159,0.0907927074
S,0,5.4304438052,0.3007306097,0.2732951262
O,0,5.4391493425,-0.3232970438,1.6148460271
O,0,6.399306288,-0.255494987,-0.6971972376
O,0,5.2639064417,1.7726630453,0.2476395368
C,0,-6.6949900187,-0.3075414398,0.6795575023
F,0,-6.5968730665,-1.6156081103,1.0192097468
F,0,-6.7431237251,0.4340775293,1.8131300402
C,0,-8.0458872864,-0.1154134776,-0.0934872763
F,0,-8.1705317384,-1.1017478923,-1.0110338494
F,0,-8.040385113,1.0809175792,-0.7314395593
C,0,-9.3259835182,-0.1533029146,0.8049603609
F,0,-9.4016742633,0.9301709473,1.58870841
F,0,-10.4086934173,-0.1771171021,0.0106566407
F,0,-9.3367859073,-1.2522347207,1.5756338634

Chapter 4. Thermodynamic Stability of Neutral and Anionic PFOAs

4.1. Introduction

Perfluorinated acids (PFAs) have been produced for over six decades for use, among other applications, as protective coatings for different materials, for the semi-conductors industry or incorporated as a component of fire-fighting foams.[1] Unfortunately, their physico-chemical properties make them a burden for the environment and they can be found near production zones or far from these areas. PFAs have been found in wildlife thousands of miles away from discharging zones, and also in the atmosphere.[2,3] Perfluorinated carboxylic acids (PFCAs), perfluorinated sulfonic acids and their anionic counterparts, perfluorinated carboxylates and perfluorinated sulfonates, are the most studied PFAs not only due to their persistence in the environment but also due to their relation to health disorders, including cancer.[4-7] Perfluorooctane sulfonic acid, perfluorooctane carboxylic acid and their salts were declared persistent organic pollutants several years ago and their production has been under scrutiny in some countries and by international agencies.[8,9] The company 3M, which was the main producer of these chemicals in the past century, phased out its production in 2002. However, more than 50 years after being synthesized there is a clear need for a better understanding, linked to the knowledge of accurate physico-chemical properties of these compounds, of their environmental transport and distribution.

The acronym PFOSs is used in this work to identify the group of 89 structural isomers of perfluorooctane sulfonic acid (PFOS **n**, **n** = **1** to **89**), while PFOAs identifies the 39 structural isomers of perfluorooctane carboxylic acid (PFOA **n**, **n** = **1** to **39**). The nomenclature system proposed by Rayne *et al.*[10] is used in this study (see Table 4.S1 of the Supporting Information (SI), section 4.6). This system assigns lower numbers to more branched isomers, while higher **n** values are assigned to less branched ones.

Though the synthesis of PFOAs can be performed using several procedures, two industrial methods became widely used: electrochemical fluorination (ECF, first used in 1947 by the 3M Company)[11] and telomerization (introduced in mid 1960s).[12] ECF generates not only the linear PFOA isomer (PFOA **39**), but a mixture that has traditionally been reported as containing 78% straight chain, 13% terminally branched, and 9% internally branched structural isomers.[11,13] Telomerization, the

preferred method for synthesizing PFOAs since 2002, generates a higher proportion of the linear isomer.[14] The presence of PFCAs in the environment has been demonstrated not to be exclusively linked to their large-scale synthesis. Many recognized precursors can degrade generating these compounds before any further transformation takes place.[15,16]

Some authors agree that the predominance of linear isomers of PFAs in human and wildlife blood samples could point to telomerization-based processes as their major source in the environment.[14,17,18] Similarly, ECF synthesis is the assumed source when the proportion of branched isomers becomes significant. The much greater proportion of linear isomers has also been explained by differences in biological retention[14, 19 - 21] or in the physico-chemical partition mechanisms associated with both local and global transport.[22,23] It has become a common practice to assume that the analysis of aqueous samples is the ultimate source of information about possible sources of PFOA isomers.[14,16,24] This practice assumes that non-biotic factors play no role on the stability of these compounds.

Whether the linear PFOA isomer (PFOA **39**) is more thermodynamically stable than the branched isomers or not, remains a topic of discussion to this date. However, the well-established experimental fact of the greater thermodynamic stability of branched alkane isomers over linear ones must be seriously considered.[25] This pattern has been theoretically observed for alkanes[26] and at some level for PFOSs (after studying the 89 structural isomers in the gas phase, *n*-octanol and water) when using the M06-2X functional,[27] but not with B3LYP.[28] Wiberg[29] and Ess *et al.*[26] indicated that electron correlation determines the stability differences between branched and linear isomers. Thus, for properly describing the thermodynamic stability within a family of structural isomers, the choice of the functional is very important, especially so when there is no experimental data to validate such a study. The B3LYP functional has been known to improperly reproduce heats of formation and bond energies in molecules with more than four carbon atoms,[30-36] probably due to its inability to properly describe medium-range dispersion-like forces; thus, it seems unfit for this purpose. However, the functional M06-2X is able to represent medium-range (less than 5 Å) electron correlation energies which allows a better description of intramolecular non-covalent interactions.[37]

In practice, the observed synthesis-based profiling of the PFOA family of isomers seems to be kinetically determined rather than driven by thermodynamic stability. This idea has been proposed in previous studies with PFAs as a possible mechanism to justify their observed relative proportions.[28,38-41]

The thermodynamic stability of the 39 structural PFOA isomers in the gas phase, *n*-octanol and water, taking into account both the neutral and anionic forms, is theoretically studied in this work. In the absence of experimental data, several methods are applied and the results discussed. A previous thermodynamic stability study on PFOAs focused on the linear (PFOA **39**) and the monomethylated isomers (PFOAs **34**-**38**).[42] However, to the best of our knowledge, this is the first in-depth thermodynamic stability study of a complete family of structural isomers of perfluorinated carboxylic acids in the gas phase, *n*-octanol, and water. Whenever possible, comparisons are made with the PFOSs results previously reported.[27,28]

Accurate standard Gibbs free energies of formation need to be calculated to properly describe and understand the relative thermodynamic stability of these compounds. These data are also required for the calculation of accurate acid dissociation constants in different media and to determine various partition coefficients for PFOAs. Moreover, accurate physico-chemical properties are required to properly predict the environmental fate of these species, *i.e.*, to better model their environmental distribution and transport between different media; hence, the relevance of this study.

4.2. Methodology

Electronic structure calculations were performed with the Gaussian 09 software package.[43] Density functional theory (DFT) calculations were initially performed using the B3LYP functional.[44,45] Additional functionals such as B97D,[34] LC-ωPBE[46] and M06-2X,[47] and the semi-empirical PM6[48] method were also applied. The 6-31++G(d,p) basis set was employed with all the functionals. Additional M06-2X calculations were performed using the 6-311++G(3df,3p) basis set.

The B97D functional, a semi-empirical generalized gradient approximation functional proposed to overcome the difficulties associated with B3LYP, belongs to the group of DFT methods that includes dispersion corrections. This method employs an empirical term of the form C_6/r^6 to account for a correction associated with dispersion. It restricts functional density analysis to short-range

electron correlation, and uses the C_6/r^6 empirical parameter to describe large- to medium-range interatomic interactions. LC-ωPBE is a corrected functional that optimizes the previous functional PBE[49,50] to deal with the long-range asymptote of the exchange-correlation potential. M06-2X is a global hybrid meta-exchange-correlation functional with 54% Hartree-Fock exchange. Its empirical parameterization allows an increased response to dispersion forces and enhances its ability to describe medium-range electron correlation and van der Waals interactions much more effectively than B3LYP.[47,51]

Rayne and Forest[42] studied the relative gas-phase enthalpies of several fragments of families of structural isomer involving linear and branched alkanes and some alcohols. They found that the PM6 calculations were consistently in better agreement with experiment than the B3LYP calculations. The experimental data they compiled clearly showed that the more branched an isomer, the lower its relative enthalpy (and as we learn in basic organic chemistry, the greater its thermodynamic stability, *i.e.*, the lower its relative Gibbs free energy of formation value). They also studied the series PFOSs **83**-**89** and PFOAs **34**-**39** previously discussed, which includes the linear and the mono-methylated isomers, and found that the M05-2X[30,52] functional yielded results in agreement with PM6 thermodynamic conclusions for this incomplete families of isomers. The M06 family of functionals succeeded the M05 group of functionals, hence our choice of the M06-2X functional for this and previous related works.[27,28]

As previously performed, when studying the 89 isomers of the PFOSs family,[27,28] geometry optimizations and frequency calculations were performed in the gas phase, water and *n*-octanol for all levels of theory. Solvent effects were accounted for (on geometries and frequencies) by means of the IEF-PCM (with B3LYP only) and SMD continuum solvation methods.[53] UAHF atomic radii were used with PCM calculations to construct the solvent cavity. Stationary points were verified as minima by a harmonic frequency calculation at the same level of theory. Unless otherwise indicated, the M06-2X calculations discussed in this study make use of the 6-311++G(3df,3p) basis set, and calculations in solution apply the SMD method.

As previously seen (experimentally and theoretically) for the linear PFOS isomer,[27,28] the most stable structure of PFOA **39**, instead of being zig-zag (as would be the case for octanoic acid, its non-fluorinated analogue), is helical.[54] This geometry minimizes the electrostatic repulsion between

fluorine atoms, and is well reproduced with the B3LYP functional and each of the other methods applied in this study (the LC-ωPBE, M06-2X and B97D functionals, and the PM6 method). Figure 4.S1 shows a compilation of frontal views of the optimized structure of the neutral and anionic PFOA **39** at each of the levels of theory considered in this study, in the gas phase, *n*-octanol and water. The PM6 structures show less helical shape than the others, especially when calculated in water, but they are definitely not zig-zag conformations.

The methodology used to obtain the initial geometry to optimize the other 38 isomers was based on making the corresponding chain changes on the optimized gas-phase B3LYP helical structure of PFOA **39**. Because B3LYP was the functional initially used in this study, the optimized B3LYP/ 6-31++G(d,p) gas-phase geometries were used as starting point for the other calculations on each isomer. Since the same procedure is followed for the set of isomers with all the methods applied, we expect the stability comparison to be meaningful. However, we cannot claim to be working with the global minimum geometries of these compounds.

4.3. Results and Discussion

The relative standard Gibbs free energies of formation (relative G, in kJ/mol at 298.15 K) for the neutral PFOAs in the gas phase at six levels of theory (using the LC-ωPBE, M06-2X, B3LYP and B97D functionals, and the PM6 method) are shown in Table 4.1 in order of stability. Table 4.2 displays the same information for the anions. Relative G values listed following the naming label (*i.e.*, from PFOA **1** to PFOA **39**) in the gas phase, *n*-octanol and water, at the different levels of theory considered, appear in Tables 4.S2 to 4.S2e for neutral species and in Tables 4.S3 to 4.S3e for anions.

4.3.1. Method comparison

Various similarities can be observed between the PFOA family and that of the 89 PFOS isomers (previously studied with the B3LYP and M06-2X functionals).[27,28] In both cases, the stability ranking of neutral species at any of the levels of theory applied is very little affected by the phase considered (gas phase, *n*-octanol and water). The variability between environments is relatively higher for anions than for neutral species, but the changes are generally within three ranking positions. Differences in G values between pairs of environments (gas-octanol, gas-water and

Table 4.1. Stability order of the 39 neutral PFOA isomers calculated at the M06-2X, PM6, LC-ωPBE, B97D, B3LYP and levels of theory in the gas phase.[a]

Stability Order	M06-2X/ 6-311++G(3df,3p)		M06-2X/ 6-31++G(d,p)		PM6		LC-ωPBE/ 6-31++G(d,p)		B97D/ 6-31++G(d,p)		B3LYP/ 6-31++G(d,p)	
1	**24**	*0.0*	**24**	*0.0*	**5**	*0.0*	**24**	*0.0*	**24**	*0.0*	**24**	*0.0*
2	**5**	*0.4*	**5**	*3.1*	**24**	*12.3*	**13**	*12.4*	**13**	*14.5*	**13**	*15.9*
3	**13**	*4.8*	**13**	*4.5*	**13**	*13.3*	**16**	*15.7*	**16**	*15.9*	**34**	*17.0*
4	**16**	*4.9*	**16**	*6.2*	**3**	*17.6*	**33**	*18.3*	**33**	*16.9*	**33**	*18.3*
5	**3**	*7.1*	**3**	*8.6*	**16**	*20.0*	**3**	*22.8*	**6**	*18.3*	**6**	*19.3*
6	**33**	*15.0*	**33**	*16.3*	**12**	*28.4*	**6**	*26.9*	**3**	*20.2*	**16**	*19.5*
7	**12**	*22.3*	**6**	*20.6*	**33**	*31.0*	**34**	*28.5*	**27**	*22.6*	**27**	*20.6*
8	**6**	*23.0*	**12**	*22.7*	**2**	*32.7*	**27**	*28.5*	**34**	*25.8*	**20**	*22.3*
9	**2**	*28.6*	**2**	*26.9*	**6**	*34.1*	**5**	*31.4*	**21**	*27.5*	**21**	*23.0*
10	**28**	*28.8*	**28**	*28.9*	**14**	*35.7*	**21**	*34.2*	**20**	*27.5*	**3**	*28.3*
11	**27**	*32.8*	**27**	*32.1*	**28**	*36.0*	**12**	*34.6*	**5**	*31.0*	**39**	*29.5*
12	**1**	*35.8*	**1**	*32.8*	**27**	*42.5*	**28**	*35.9*	**28**	*31.0*	**8**	*32.4*
13	**4**	*38.2*	**4**	*37.5*	**4**	*45.6*	**20**	*36.1*	**12**	*31.7*	**38**	*32.6*
14	**14**	*38.5*	**31**	*38.0*	**18**	*48.4*	**8**	*40.1*	**26**	*35.9*	**26**	*33.0*
15	**31**	*38.7*	**14**	*40.6*	**1**	*49.8*	**26**	*40.3*	**8**	*36.2*	**28**	*35.5*
16	**18**	*40.2*	**26**	*41.8*	**31**	*50.6*	**2**	*41.9*	**2**	*38.5*	**12**	*37.3*
17	**26**	*42.9*	**18**	*42.2*	**17**	*50.8*	**38**	*44.6*	**38**	*38.6*	**30**	*39.4*
18	**8**	*43.9*	**8**	*42.8*	**34**	*52.9*	**1**	*44.9*	**14**	*39.0*	**25**	*39.7*
19	**30**	*44.9*	**34**	*43.2*	**26**	*53.2*	**30**	*45.1*	**30**	*40.4*	**35**	*39.9*
20	**7**	*45.0*	**30**	*43.7*	**8**	*54.6*	**25**	*45.2*	**39**	*40.5*	**36**	*43.3*
21	**34**	*45.8*	**7**	*44.5*	**25**	*56.9*	**14**	*45.2*	**7**	*41.1*	**37**	*43.9*
22	**25**	*47.1*	**20**	*44.8*	**20**	*57.9*	**39**	*45.6*	**31**	*41.3*	**31**	*44.2*
23	**20**	*47.2*	**25**	*46.0*	**38**	*58.0*	**31**	*47.2*	**25**	*42.2*	**2**	*44.3*
24	**21**	*48.8*	**21**	*46.6*	**21**	*58.3*	**4**	*49.0*	**4**	*42.4*	**7**	*45.5*
25	**17**	*51.4*	**38**	*50.0*	**19**	*58.9*	**7**	*50.3*	**35**	*44.0*	**5**	*45.5*
26	**38**	*52.0*	**17**	*52.3*	**30**	*59.1*	**35**	*51.9*	**1**	*46.5*	**14**	*46.7*
27	**19**	*54.8*	**19**	*52.8*	**15**	*61.6*	**36**	*54.6*	**37**	*49.2*	**4**	*46.9*
28	**10**	*55.4*	**10**	*54.2*	**35**	*62.9*	**19**	*55.0*	**19**	*49.3*	**1**	*47.0*
29	**9**	*59.6*	**35**	*56.7*	**39**	*68.5*	**37**	*56.0*	**36**	*49.6*	**19**	*48.3*
30	**35**	*60.1*	**9**	*57.7*	**7**	*68.7*	**18**	*62.2*	**18**	*55.2*	**9**	*56.2*
31	**36**	*60.6*	**36**	*58.6*	**37**	*69.3*	**9**	*62.8*	**9**	*55.8*	**22**	*60.2*
32	**37**	*62.2*	**39**	*59.5*	**10**	*69.7*	**15**	*64.2*	**22**	*61.1*	**18**	*64.6*
33	**39**	*62.5*	**37**	*59.6*	**36**	*69.8*	**10**	*68.6*	**10**	*62.6*	**23**	*66.9*
34	**15**	*67.6*	**15**	*67.0*	**32**	*77.1*	**17**	*71.8*	**17**	*65.6*	**10**	*67.6*
35	**32**	*72.2*	**32**	*71.4*	**9**	*77.9*	**22**	*74.5*	**32**	*70.6*	**32**	*69.9*
36	**29**	*77.6*	**29**	*75.4*	**22**	*79.2*	**32**	*78.1*	**15**	*72.1*	**15**	*73.1*
37	**22**	*78.8*	**22**	*76.6*	**11**	*84.2*	**23**	*79.7*	**23**	*73.3*	**17**	*74.9*
38	**23**	*82.9*	**23**	*79.6*	**29**	*84.3*	**29**	*86.2*	**29**	*76.1*	**29**	*76.3*
39	**11**	*95.8*	**11**	*94.5*	**23**	*86.3*	**11**	*102.2*	**11**	*94.4*	**11**	*92.9*

[a] PFOAs labels shown in bold, relative G values (in kJ/mol at 298.15 K) shown in italics.

Table 4.2. Stability order of the 39 anionic PFOA isomers calculated at the M06-2X, PM6, LC-ωPBE, B97D, B3LYP levels of theory in the gas phase.[a]

Stability Order	M06-2X/ 6-311++G(3df,3p)		M06-2X/ 6-31++G(d,p)		PM6		LC-ωPBE/ 6-31++G(d,p)		B97D/ 6-31++G(d,p)		B3LYP/ 6-31++G(d,p)	
1	**5**	*0.0*[b]	**24**	*0.0*[b]	**5**	*0.0*[b]	**24**	*0.0*[b]	**24**	*0.0*[b]	**24**	*0.0*[b]
2	**24**	*0.0*[b]	**3**	*1.7*	**13**	*25.0*[b]	**13**	*11.9*[b]	**13**	*15.3*[b]	**21**	*19.2*
3	**3**	*0.0*	**5**	*3.0*[b]	**24**	*29.6*[b]	**3**	*13.8*	**3**	*18.7*	**20**	*19.9*
4	**13**	*5.9*[b]	**13**	*6.6*[b]	**3**	*40.4*	**16**	*18.1*	**16**	*18.9*	**3**	*20.8*
5	**16**	*11.7*	**16**	*13.4*	**12**	*43.4*[b]	**6**	*27.3*[b]	**6**	*19.8*[b]	**13**	*21.0*[b]
6	**12**	*22.4*[b]	**6**	*22.0*[b]	**2**	*45.2*[b]	**27**	*30.2*	**21**	*26.8*	**6**	*21.1*[b]
7	**6**	*23.7*[b]	**12**	*22.7*[b]	**6**	*47.1*[b]	**5**	*30.4*[b]	**27**	*28.6*	**16**	*21.2*
8	**14**	*26.8*	**14**	*26.2*	**16**	*47.4*	**21**	*31.2*	**20**	*28.8*	**34**	*21.3*
9	**1**	*31.4*[b]	**1**	*28.8*[b]	**4**	*65.4*	**34**	*33.0*	**34**	*32.4*	**27**	*22.8*
10	**4**	*32.7*	**4**	*31.9*	**1**	*65.6*[b]	**20**	*33.1*	**12**	*35.2*[b]	**8**	*29.6*
11	**2**	*33.9*[b]	**2**	*34.4*[b]	**14**	*66.7*	**33**	*33.1*	**8**	*35.5*	**33**	*33.8*
12	**33**	*34.5*	**33**	*36.5*	**28**	*75.8*	**8**	*37.3*	**5**	*37.2*[b]	**26**	*35.0*
13	**27**	*40.7*	**27**	*39.3*	**27**	*81.0*	**12**	*37.8*[b]	**33**	*37.7*	**4**	*38.0*
14	**8**	*42.7*	**28**	*41.9*	**17**	*82.2*	**14**	*37.9*	**4**	*39.5*	**12**	*39.2*[b]
15	**28**	*43.1*	**8**	*42.3*	**33**	*85.3*	**4**	*39.1*	**14**	*40.1*	**7**	*41.1*
16	**7**	*45.8*	**20**	*44.8*	**9**	*88.1*	**1**	*41.2*[b]	**7**	*41.5*	**25**	*42.2*
17	**20**	*46.9*	**21**	*45.2*	**26**	*88.3*	**26**	*42.1*	**26**	*41.7*	**28**	*42.8*
18	**26**	*48.7*	**7**	*45.4*	**18**	*89.2*	**28**	*43.7*	**28**	*44.6*	**14**	*43.7*
19	**21**	*48.7*	**26**	*47.4*	**8**	*89.4*	**7**	*46.0*	**19**	*49.2*	**1**	*44.9*[b]
20	**34**	*49.2*	**34**	*49.0*	**25**	*90.2*	**25**	*48.2*	**25**	*49.6*	**19**	*45.0*
21	**25**	*53.1*	**25**	*51.6*	**34**	*95.4*	**2**	*50.3*[b]	**1**	*53.5*[b]	**39**	*46.5*
22	**15**	*57.7*	**19**	*56.6*	**7**	*95.8*	**19**	*53.4*	**2**	*53.8*[b]	**5**	*47.2*[b]
23	**31**	*57.9*	**15**	*56.6*	**20**	*95.9*	**30**	*56.5*	**30**	*58.7*	**38**	*49.2*
24	**19**	*58.1*	**31**	*58.6*	**21**	*96.6*	**38**	*58.9*	**15**	*60.0*	**2**	*49.3*[b]
25	**18**	*59.6*	**30**	*61.3*	**19**	*96.7*	**39**	*60.6*	**38**	*60.4*	**30**	*52.4*
26	**17**	*61.0*	**9**	*61.9*	**31**	*97.4*	**15**	*61.5*	**31**	*60.9*	**35**	*52.8*
27	**30**	*62.5*	**17**	*62.3*	**30**	*102.0*	**31**	*61.9*	**9**	*61.4*	**36**	*57.9*
28	**9**	*64.0*	**18**	*62.3*	**10**	*106.1*	**9**	*63.4*	**39**	*62.2*	**9**	*58.4*
29	**10**	*69.1*	**10**	*67.4*	**15**	*106.2*	**35**	*63.4*	**35**	*63.0*	**15**	*58.6*
30	**38**	*73.2*	**38**	*70.9*	**11**	*114.4*	**36**	*67.5*	**36**	*69.6*	**31**	*59.9*
31	**35**	*78.1*	**35**	*77.0*	**35**	*114.8*	**37**	*71.2*	**37**	*70.8*	**37**	*60.6*
32	**36**	*78.2*	**36**	*78.4*	**38**	*119.2*	**18**	*76.4*	**18**	*74.7*	**22**	*69.5*
33	**39**	*82.7*	**39**	*80.5*	**22**	*120.5*	**10**	*78.4*	**10**	*76.9*	**10**	*77.8*
34	**37**	*84.1*	**37**	*82.0*	**36**	*127.0*	**17**	*78.5*	**22**	*78.0*	**18**	*79.0*
35	**22**	*90.7*	**22**	*85.7*	**37**	*129.1*	**22**	*83.8*	**17**	*79.1*	**23**	*79.0*
36	**32**	*92.3*	**32**	*90.8*	**29**	*129.3*	**32**	*90.6*	**23**	*90.0*	**17**	*82.5*
37	**29**	*93.6*	**29**	*92.2*	**39**	*132.1*	**23**	*91.2*	**32**	*90.1*	**32**	*83.6*
38	**23**	*98.2*	**23**	*94.5*	**32**	*133.8*	**29**	*96.9*	**29**	*92.8*	**29**	*88.8*
39	**11**	*114.8*	**11**	*112.7*	**23**	*140.5*	**11**	*111.9*	**11**	*113.3*	**11**	*104.7*

[a] PFOAs labels shown in bold, relative G values (in kJ/mol at 298.15 K) shown in italics; [b] Estimated value using the corresponding gas-octanol correlation (M06-2X, B3LYP, PM6) or gas-water correlation (B97D) with details shown in Table 4.S5 (some anions became decarboxylated during the gas-phase optimization).

octanol-water) for both the neutral and anionic species are also very similar when comparing the results obtained at the different levels of theory considered with the same solvation method (see Tables 4.S4 to 4.S4e, and in particular the mean absolute differences, MAD, reported). Figures 4.S2 (data from Table 4.S2) and 4.S3 (data from Table 4.S3) show the M06-2X results for neutrals and anions, respectively, in the three phases considered, while Figures 4.S4 to 4.S6 display the M06-2X results in each solvent, comparing the relative G values of neutrals and anions. Given the similarities observed, comparisons between methods will focus on the results obtained for the neutral PFOAs in the gas phase, unless otherwise indicated.

Various linear correlations were explored (between neutral and anionic species in each environment, and between pairs of environments for each type of species); these results are shown in Table 4.S5. Strong correlations (with R^2 values between 0.985 and 0.998) were found when considering neutral PFOAs in any pair of environments, with the exception of the B3LYP-PCM results in gas-octanol (R^2 = 0.973) and gas-water (R^2 = 0.955). The only strong correlations involving anions were obtained when considering the G values in octanol and water with R^2 values of 0.990-0.996 (PM6 values lead to an R^2 value of 0.978). The gas-octanol correlations between anions were usually better (*i.e.*, with a higher R^2 value) than the gas-water correlations. In cases where geometry optimizations could not be performed for a particular species (*e.g.*, some anions decarboxylated when optimized in the gas phase; this was never the case when using the LC-ωPBE functional), these correlations provided a way to estimate relative G values. Similar good correlations were also found when studying the 89 PFOS isomers.[27,28]

Interesting observations from Table 4.1 are that PFOA **24** is predicted as the most stable neutral species by all methods (except PM6, for which it comes up as the second most stable), while PFOA **11** appears the least stable (PM6 predicts it as the third least stable). PFOA **24** is also predicted as the most stable for the anions (see Table 4.2), (except regarding PM6, for which it comes up as the third most stable). Using M06-2X, the difference between the most stable anion (PFOA **24**) and the second most stable anion (PFOA **3**) is only 1.7 kJ/mol with the 6-31++G(d,p) basis set (with the 6-311++G(3df,3p) basis set, PFOAs **5**, **24** and **3** have the same relative G value (0.0 kJ/mol), followed by PFOA **13** with a relative G of 5.9 kJ/mol). This difference is more significant for the other methods (11.9-25.0 kJ/mol).

Because it would be overwhelming to discuss the data gathered in extreme detail, we have organized the 39 isomers into three groups of 13 members each. Group A contains the 13 most stable isomers, Group B is made up of the 13 isomers with intermediate stability and Group C contains the 13 least stable isomers. Analysis of the results for the 39 neutral and anionic isomers using Tables 4.1 and 4.2 is relatively incomplete when focused only upon comparison of the least branched isomers (PFOAs **34**-**39**). Little information can be obtained about the relative stability of the entire family of 39 isomers if all of them are not considered. The relative stability distribution of PFOAs **34-39** among groups {A,B,C} depends on the method applied. The M06-2X distribution of these six isomers is {0,1,5}[a] with the largest basis set (with the smaller basis set the distribution is very similar {0,2,4}). PM6 is the method that most resembles the M06-2X distribution {0,2,4}. Next are LC-ωPBE {1,2,3} and B97D {1,3,2}. They are ranked as much more stable by B3LYP than by any of the other methods {2,4,0}. The results obtained for the seven least branched PFOSs (PFOSs **83**-**89**), if arranged in groups {A,B,C} of 30 isomers, have a lot in common with the PFOA results. M06-2X {2,5,0} predicts these isomers to be much less stable than does B3LYP {7,0,0}.[27]

Given that the PFOA label (**n**) used to identify these isomers is related to their degree of branching, we can use the average of the labels of the isomers in a particular group {A,B,C} to get an overall idea of the performance of the different methods applied to the 39 PFOA isomers. The larger the label **n**, the less branched the PFOA isomer in general, and the larger the aliphatic chain attached to the head group (see Table 4.S1). However, there are groups of isomers that have very similar degrees of branching and differ only regarding the position of the same type of substituents, *e.g.*, PFOAs **6-11**, **12-18**, **21-23**, **24-33** and **34-38**), but without doubt, the group of PFOAs **12-18** has a much greater degree of branching than PFOAs **34-38**. Table 4.3 displays this information for neutral and anionic PFOAs in the gas phase at different levels of theory. The same overall tendencies previously noticed for the reduced group of least branched PFOA isomers can be observed. The M06-2X distribution of average labels of neutral isomers per group {13,22,24}[b] is very similar to the PM6 distribution {14,22,23}, which indicates that these methods predict more branched isomers to be more thermodynamically stable than less branched ones. This stability ranking resembles that of alkanes. The opposite general prediction is made by B3LYP {22,22,16}, while an intermediate situation is equally described by LC-ωPBE and B97D {19,20,21}. Somehow similar M06-2X and

[a] The values in brackets represent how many of the PFOAs **34**-**39** are in each group, *e.g.*, {0,1,5} means that none of these six isomers are in group A, while 1 and 5 of them are in groups B and C, respectively.
[b] The notation {13,22,24} indicates that 13, 22, and 24 are the averages of the labels of the PFOAs in groups A, B and C, respectively.

Table 3. Average label identifying the 39 PFOA isomers (neutrals and anions) in each of the three stability groups in the gas phase.

	M06-2X/ 6-311++G(3df,3p)		M06-2X/ 6-31++G(d,p)		PM6		LC-ωPBE/ 6-31++G(d,p)		B97D/ 6-31++G(d,p)		B3LYP/ 6-31++G(d,p)	
	Neutral	Anion	Neutral	Anion	Neutral	Anion	Neutral	Anion	Neutral	Anion	Neutral	Anion
Group A [a]	13 [d]	12	13	12	14	12	19	14	19	17	22	19
Group B [b]	22	21	22	21	22	21	20	22	20	18	22	19
Group C [c]	24	27	24	27	23	27	21	24	21	23	16	22

[a] Thirteen most stable PFOA isomers; [b] Thirteen PFOA isomers with intermediate stability; [c] Thirteen least stable PFOA isomers; [d] 13 is the average label of the thirteen most-stable neutral PFOAs at the M06-2X/6-31++G(d,p) level of theory (labels in this group: **24**, **5**, **13**, **16**, **3**, **33**, **12**, **6**, **2**, **28**, **27**, **1**, **4**; see Table 4.1).

B3LYP behaviours can be observed when examining the PFOSs data for the 89 neutral isomers in the gas phase when arranged in groups of 30 isomers, as previously described.[27] In the PFOSs case, the PM6 results[39] {43,47,46} are in between the M06-2X {52,51,32} and B3LYP {66,46,23} results, perhaps because the PM6 optimized structures were obtained by another group following a different procedure than the one followed in present and previous studies.[27,28]

Figures 4.1 and 4.2 display the gas-phase relative G values for neutral and anionic PFOAs, respectively, as calculated using the M06-2X, PM6, LC-ωPBE, B3LYP and B97D methods. Another point of view for comparisons comes from visualizing differences in relative G values between a particular method (M06-2X is the chosen one in this study) and the others. Tables 4.S6 to 4.S6c show the calculated differences in relative G values between M06-2X and other methods (PM6, LC-ωPBE, B3LYP and B97D) for neutral and anionic PFOAs in the three environments considered. Figures 4.3 and 4.4 display these values in the gas phase for neutral and anionic PFOAs, respectively. The M06-2X and B3LYP comparisons in *n*-octanol and water are also shown, and it can be seen how similar these curves are to that in the gas phase in both cases (neutrals and anions), a result in agreement with our previous discussion and the previous PFOSs study.[27] The mean absolute differences (MADs) of the calculated differences are 13.4-14.9 kJ/mol (see Table 4.S6b). These values are 8.6-9.8 and 9.4-10.4 kJ/mol when comparing M06-2X with LC-ωPBE (see Table 4.S6a) and with B97D (see Table 4.S6c), respectively. The M06-2X, LC-ωPBE, B97D and B3LYP methods predict consistent average differences in relative G values for neutrals and anions in the three environments.

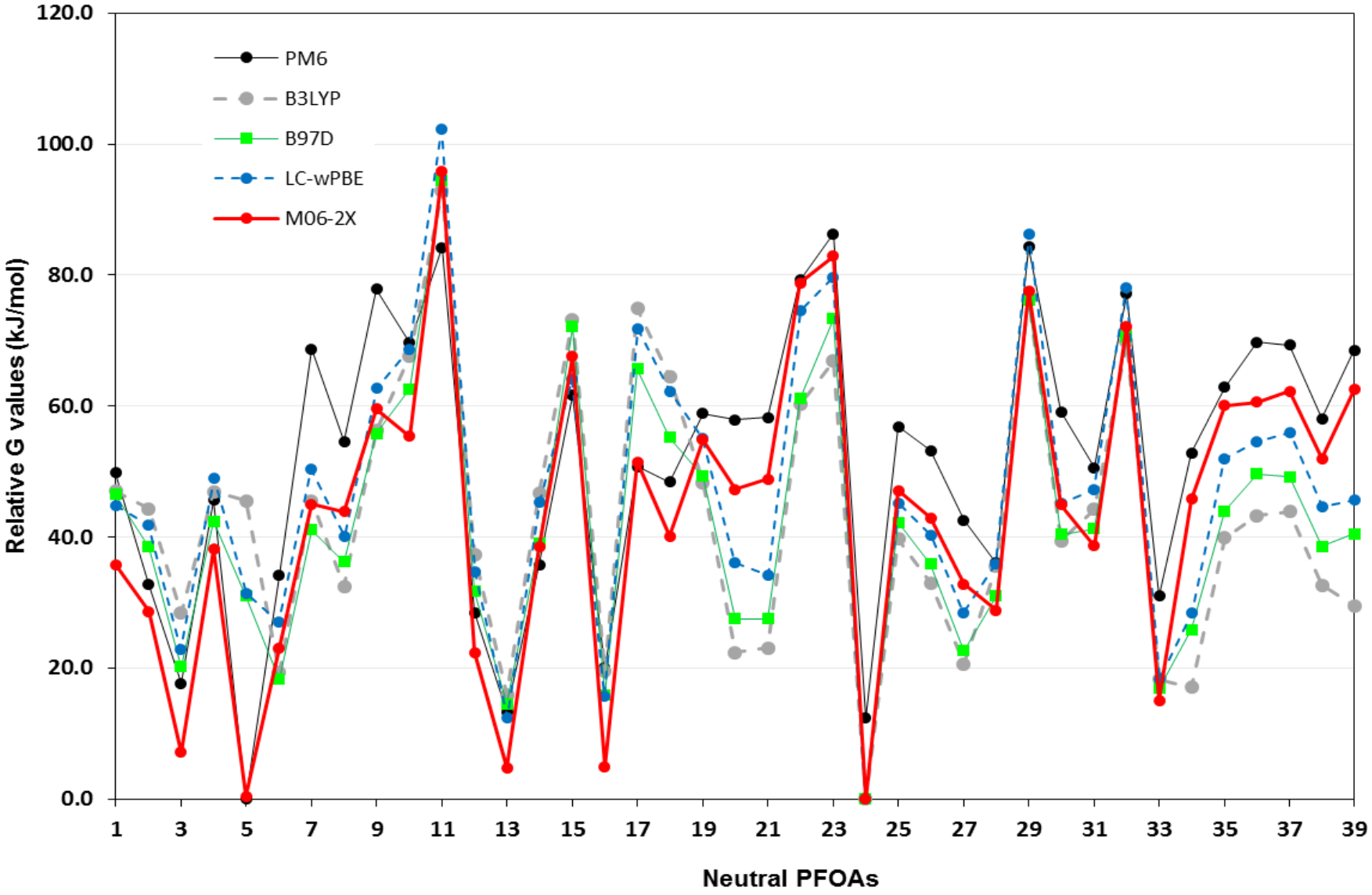


Figure 4.1. Comparison of relative G values of neutral PFOA isomers in the gas phase using several methods.

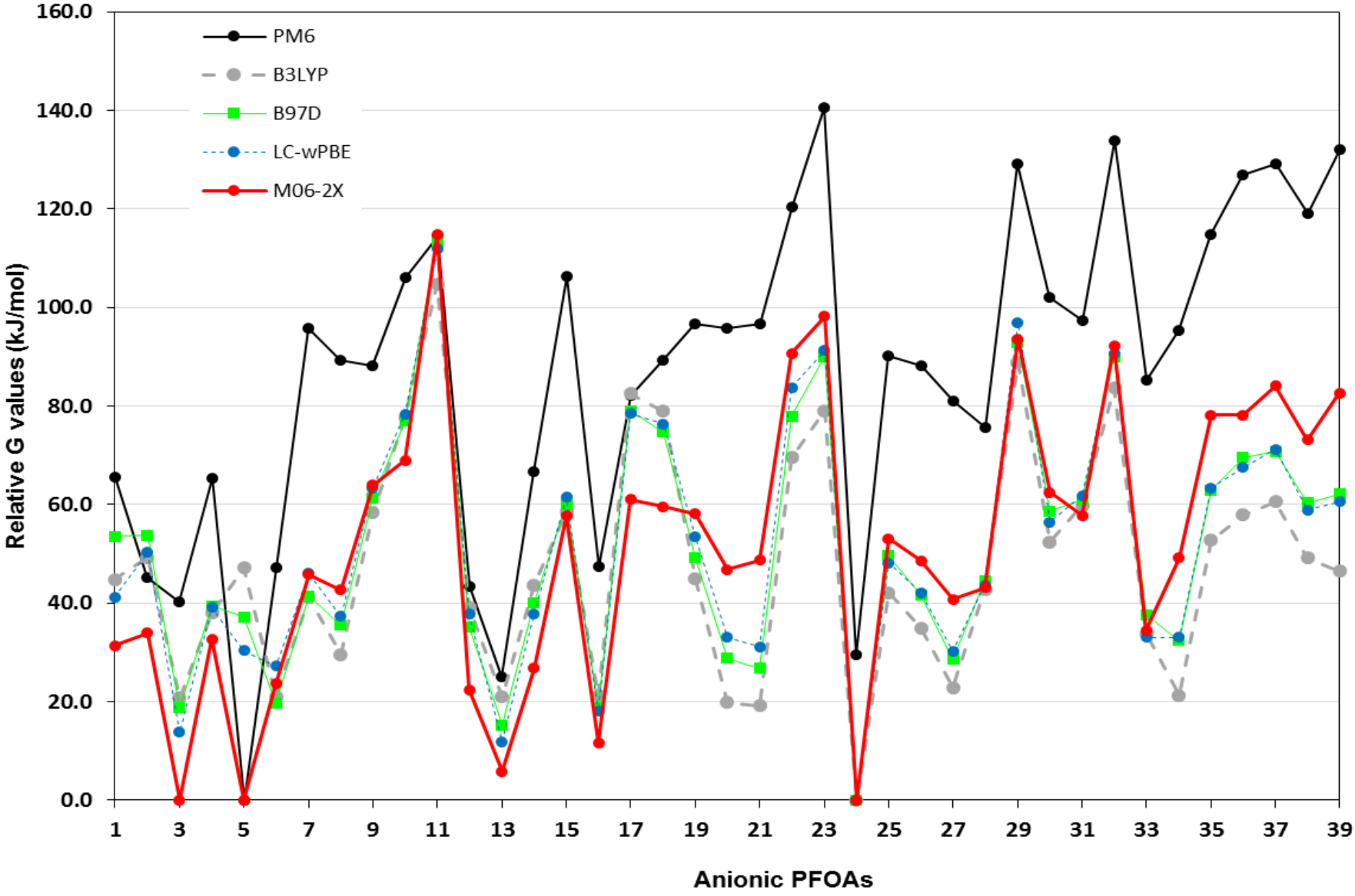


Figure 4.2. Comparison of relative G values of anionic PFOA isomers in the gas phase using several methods.

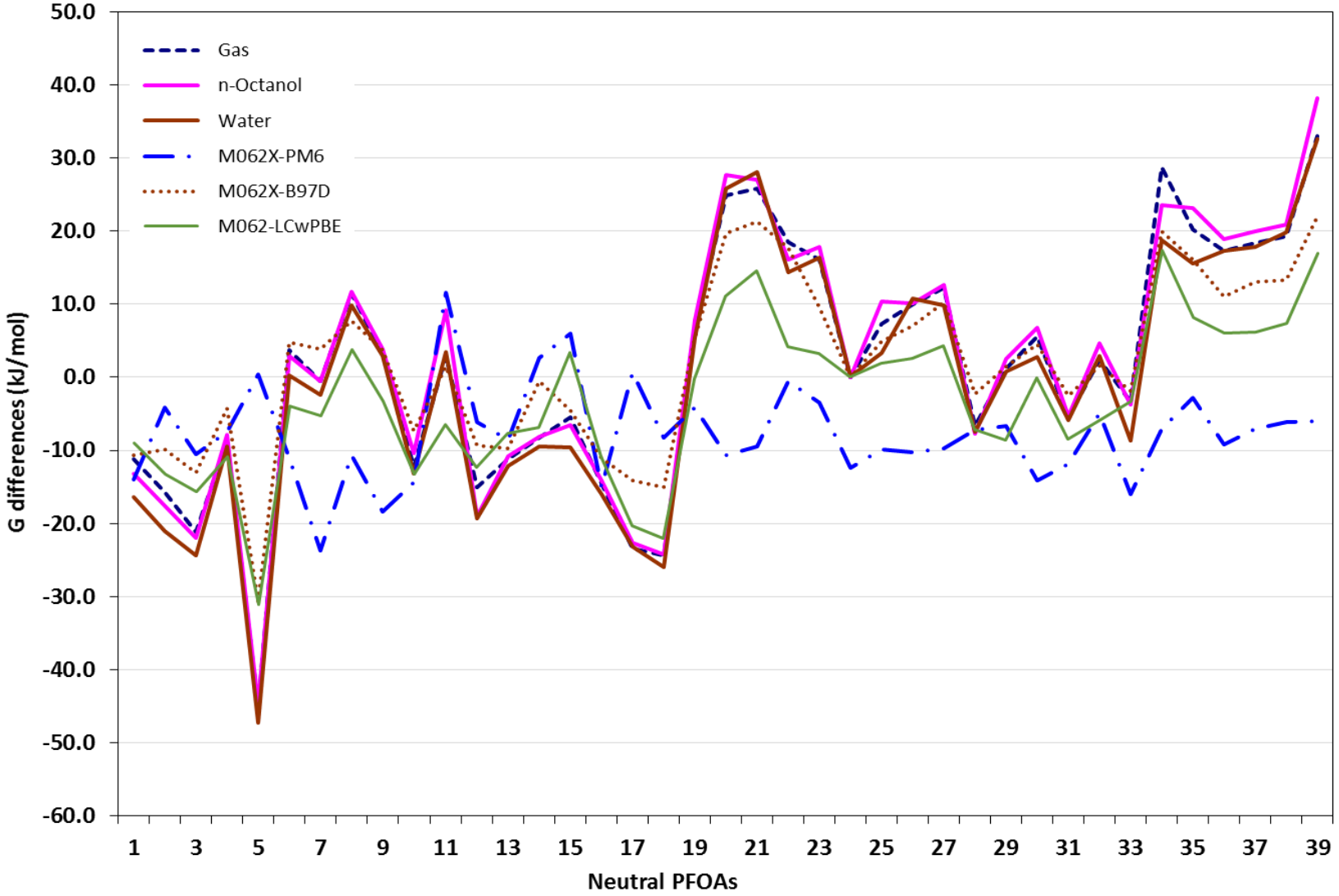


Figure 4.3. Relative G differences between isomers of neutral PFOA calculated by M06-2X and B3LYP methods in three environments, shown along with gas-phase differences between M06-2X and LC-ωPBE, B97D and PM6 for comparison.

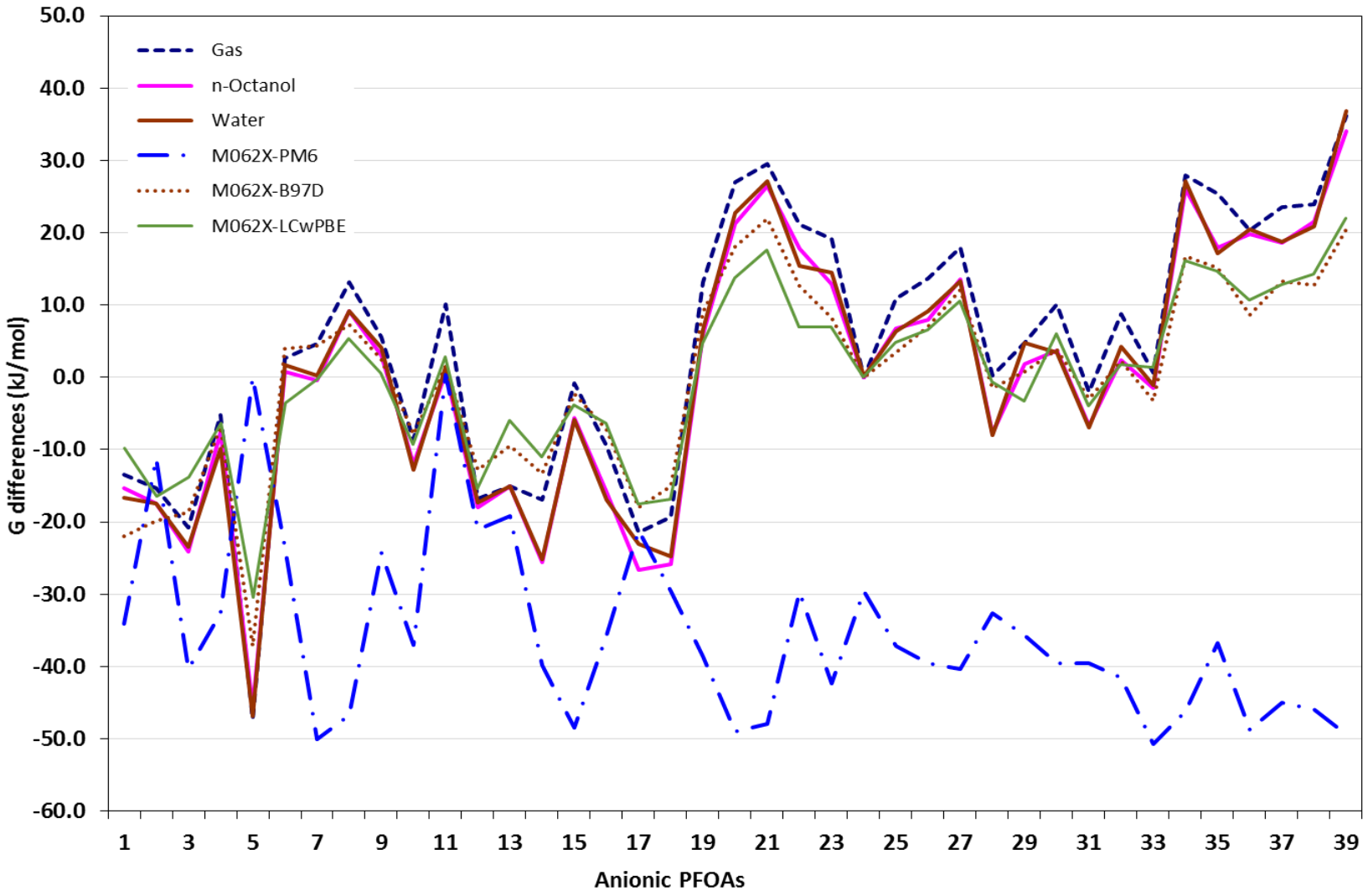


Figure 4.4. Relative G differences between isomers of anionic PFOA calculated by M06-2X and B3LYP methods in three environments, shown along with gas-phase differences between M06-2X and LC-ωPBE, B97D and PM6 for comparison.

The main difference between Figures 4.1 and 4.2 (and Figures 4.3 and 4.4) has to do with the PM6 calculations. The PM6 relative G values are larger than the M06-2X values in most cases (see Table 4.S6). These two methods are closest in performance for neutral PFOAs with MADs of 8.8-11.0 kJ/mol in the three environments, a result somewhat in agreement with the previously mentioned observations by Rayne and Forest regarding the PFOSs **83**-**89** family.[42] However, when considering anions, the MAD values are significantly greater (24.7-35.4 kJ/mol) than the MADs between M06-2X and any of the other methods applied.

The LC-ωPBE, B97D and B3LYP methods tend to yield consistent, similar differences relative to the M06-2X calculations (see Figures 4.1 to 4.4), while the LC-ωPBE and B97D results fall between the B3LYP and M06-2X calculations. The calculated differences in relative G values of these three functionals relative to M06-2X reveal three regions, shown in Figures 4.3 and 4.4. One region contains the most branched isomers (PFOAs **1** to **18**), which generally display lower relative G differences. The calculated differences generally increase in relation to the second (made of PFOAs **19** to **33**) and third regions (made of the linear and monomethyl isomers, PFOAs **34** to **39**). A similar general pattern was previously identified when comparing M06-2X and B3LYP relative G differences in PFOSs.[27] Ignoring the PM6 calculations, the B3LYP results for both neutral and anionic PFOAs show the largest differences with M06-2X. Hence, the next paragraph will deal briefly with their comparison for neutral PFOAs in the gas phase.

B3LYP relative G values are consistently higher than the M06-2X prediction (with the exception of PFOAs **6**, **8**, **9** and **11**, see Figures 4.1, 4.3, and Table 4.S6b) for almost the first half of the PFOA family, from PFOS **1** to PFOS **18**, the most branched PFOAs. However, the opposite situation is observed (with the exception of PFOAs **28**, **31** and **33**) for the remaining, least branched PFOAs (PFOA **19** to PFOA **39**). As previously seen with the PFOS family,[27] M06-2X consistently calculates more branched (least branched) isomers as more (less) thermodynamically stable than does B3LYP, which modestly aligns with the well-accepted (although not clearly understood and still in debate) idea that degree of branching is inversely related to thermodynamic stability. Figure 4.5 combines the gas-phase relative G values of neutral PFOAs and PFOSs[27] using both the M06-2X and B3LYP functionals.

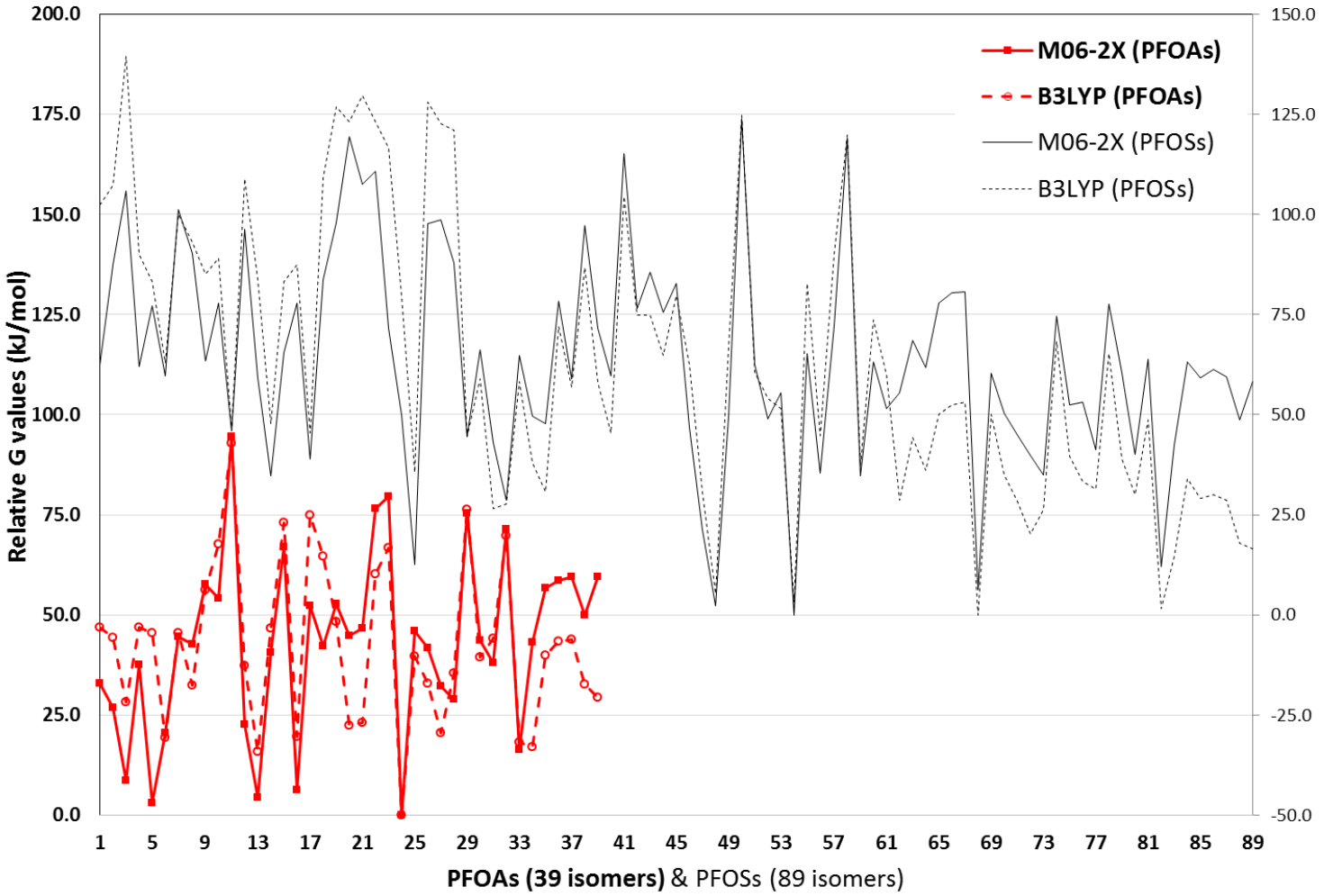


Figure 4.5. Relative G values of neutral PFOA (left y-axis) and PFOS (right y-axis, taken from Ref. 27) isomers in the gas phase using the M06-2X and B3LYP functionals.

To explore the effectiveness of the continuum solvation method used, B3LYP calculations were performed using the PCM and SMD methods (PCM and SMD results are jointly reported in Tables 4.S2b, 4.S3b, 4.S4b and 4.S5). The PCM correlations between relative G values of neutrals and anions in each of the three solvents (see the first three columns of Table 4.S5) are similar to the SMD correlations. However, gas-octanol and gas-water correlations for both neutrals and anions are significantly weaker with PCM (with R^2 values of 0.973, 0.955, 0.924 and 0.896, respectively) than with SMD (with R^2 values of 0.993, 0.991, 0.949 and 0.934, respectively). Furthermore, the MADs of the differences of G values for neutrals (gas-octanol and gas-water) and anions are significantly greater than the SMD values (see Table 4.S4b). However, the relative G values are very similar for neutral and anionic PFOAs regardless of the solvation method used (see Figure 4.S7).

M06-2X calculations were performed with the 6-311+G(3df,3p) and 6-31++G(d,p) basis sets. Table 4.S7 shows the relative G values for the neutral and anionic PFOAs in the gas phase at these two levels of theory, together with the absolute differences (ADs) for each PFOA (from 0.1 to 3.3 kJ/mol for the neutrals, and from 0.2 to 5.0 kJ/mol for the anions) and the MADs. The ADs are negligible in most cases and the MADs values are 1.6 kJ/mol for both neutrals and anions. Hence, the effect on the relative thermodynamic stability of this family of compounds of the basis set used is not significant.

Further proof against the need to work with a basis set larger than 6-31++G(d,p) was discussed for PFOS after examining calculations of relative G values for the least branched isomers, PFOSs **83**-**89**.[28] We have compiled the gas-phase thermodynamic information (relative standard Gibbs free energies and enthalpies of formation) for the equivalent PFOA series, **34**-**39**, at different levels of theory in Tables 4.4 (for neutrals) and 4.5 (for anions). For comparison, previous calculations for the neutrals using the B3LYP and PM6 methods from Ref. 42 are also shown. Taking into account both the M06-2X and B3LYP calculations, our previous comments and conclusions regarding the size of the basis set apply. All methods predict PFOA **34** (neutral or anionic) as the most stable of this series. Using the M06-2X method, the linear (least branched) isomer, PFOA **39**, closely followed by PFOA **37**, is predicted as the least stable (neutral and anion) of this series. The PM6 relative G values reported in this work are consistently smaller (by 2.4 kJ/mol or less) than the values reported in Ref. 42. These differences are not significant and could be related to the procedure used to generate the initial geometries to be optimized.

Table 4.4. Relative standard Gibbs free energies and enthalpies of formation (relative G and H) values (in kJ/mol at 298.15 K) for the least branched neutral PFOA isomers (PFOS **34** to **39**) calculated at different levels of theory (using the 6-31++G(d,p) basis set when applicable, unless otherwise indicated) in the gas phase.

PFOA n	**Relative G** [Order]						**Relative H** [Order]					
n	**B3LYP**[a]	**B3LYP**	**M06-2X**[b]	**M06-2X**	**PM6**[a]	**PM6**	**B3LYP**[a]	**B3LYP**	**M06-2X**[b]	**M06-2X**	**PM6**[a]	**PM6**
34	0.0 [1]	0.0 [1]	0.0 [1]	0.0 [1]	0.0 [1]	0.0 [1]	0.0 [1]	0.0 [1]	0.0 [1]	0.0 [1]	0.0 [1]	0.0 [1]
35	22.9 [4]	22.8 [4]	14.3 [3]	13.5 [3]	11.4 [3]	10.0 [3]	20.9 [4]	20.2 [4]	12.6 [3]	13.1 [3]	8.6 [3]	10.3 [3]
36	27.0 [6]	26.3 [5]	14.8 [4]	15.4 [4]	18.2 [5]	16.9 [6]	24.0 [6]	22.3 [5]	13.9 [5]	14.0 [5]	15.9 [5]	15.0 [5]
37	27.0 [5]	26.8 [6]	16.4 [5]	16.5 [6]	18.8 [6]	16.4 [5]	23.9 [5]	22.3 [6]	13.6 [4]	13.9 [4]	15.8 [4]	14.8 [4]
38	16.1 [3]	15.6 [3]	6.2 [2]	6.9 [2]	7.4 [2]	5.2 [2]	14.6 [2]	12.8 [2]	5.9 [2]	6.9 [2]	8.3 [2]	8.2 [2]
39	14.6 [2]	12.5 [2]	16.7 [6]	16.3 [5]	18.0 [4]	15.6 [4]	16.5 [3]	13.5 [3]	20.9 [6]	20.7 [6]	21.8 [6]	21.7 [6]

[a] From Ref. 42 (B3LYP/6-311++G(d,p) and PM6); [b] Using the 6-311++G(3df,3p) basis set.

Table 4.5. Relative standard Gibbs free energies and enthalpies of formation (relative G and H) (in kJ/mol at 298.15 K) for the least branched anionic PFOA isomers (PFOS **34** to **39**) calculated at different levels of theory (using the 6-31++G(d,p) basis set when applicable, unless otherwise indicated) in the gas phase.

PFOA n	**Relative G** [Order]				**Relative H** [Order]			
n	**B3LYP**	**M06-2X**[a]	**M06-2X**	**PM6**	**B3LYP**	**M06-2X**[b]	**M06-2X**	**PM6**
34	0.0 [1]	0.0 [1]	0.0 [1]	0.0 [1]	0.0 [1]	0.0 [1]	0.0 [1]	0.0 [1]
35	22.8 [4]	14.3 [3]	13.5 [3]	10.0 [3]	20.2 [4]	12.6 [3]	13.1 [3]	10.3 [3]
36	26.3 [5]	14.8 [4]	15.4 [4]	16.9 [6]	22.3 [5]	13.9 [5]	14.0 [5]	15.0 [5]
37	26.8 [6]	16.4 [5]	16.5 [6]	16.4 [5]	22.3 [6]	13.6 [4]	13.9 [4]	14.8 [4]
38	15.6 [3]	6.2 [2]	6.9 [2]	5.2 [2]	12.8 [2]	5.9 [2]	6.9 [2]	8.2 [2]
39	12.5 [2]	16.7 [6]	16.3 [5]	15.6 [4]	13.5 [3]	20.9 [6]	20.7 [6]	21.7 [6]

[a] Using the 6-311++G(3df,3p) basis set.

4.3.2. Structure and relative stability of PFOA isomers: M06-2X predictions

The fact that some subgroups of isomers with an apparently similar degree of branching (*e.g.*, PFOAs **6** to **11**, **12** to **18**, **21** to **23**, **24** to **33** and **34** to **38**) have different relative thermodynamic stabilities, impels us to explore the relationship between relative G-values trends and patterns of substitution (indicated by the types and positions of the substituents) on the main chain that contains the head group (–COOH or $–COO^-$) within this family of 39 isomers. Except for PM6, these trends are qualitatively very similar for both neutrals and anions in the three environments under all tested methods. As previously mentioned, to facilitate data analysis, the 39 PFOA isomers are divided into three groups (A, B and C), each containing thirteen isomers. The following discussion will concentrate on trends within groups A and C rather than on local differences between isomers, focusing on the M06-2X/6-311+G(3df,3p) results.

Table 4.6 combines the stability order of neutral PFOA isomers in the gas phase, the length of the main chain and the type of substitution (taking both type and positions of substituents into account) in each isomer. Table 4.S8 displays the same information for anions. The averages of chain length (defined here as the average of the longest linear backbone for each isomer, ignoring substituents) for the neutrals (anions) in groups A, B and C are 3.9, 4.7 and 5.0 (3.8, 4.5 and 5.2), respectively. These observations agree with previous discussions indicating that with M06-2X, the most branched isomers (with a smaller chain length) are in general ranked as more thermodynamically stable than the least branched isomers, in agreement with what is well accepted for alkanes.

The thirteen most stable (group A, see Table 4.1) neutral PFOAs in the gas phase are predicted to be **24**>**5**>**13**>**16**>**3**>**33**>**12**>**6**>**2**>**28**>**27**>**1**>**4** (**4** has relative G values of 38.2, 39.1 and 38.6 kJ/mol in the gas phase, *n*-octanol and water, respectively, as shown in Table 4.S2). The thirteen least stable (group C, see Table 4.1) neutral PFOAs in the gas phase are **11**<**23**<**22**<**29**<**32**<**15**<**39**<**37**<**36**<**35**<**9**<**10**<**19** (**11** has relative G values of 95.8, 97.7 and 95.1 kJ/mol in the gas phase, *n*-octanol and water, respectively, as shown in Table 4.S2). Figures 4.6 and 4.7 display the structures of the nine most and least stable neutral isomers in the gas phase, respectively; relative G values are shown in parentheses.

Table 4.6. Stability order and substitution pattern of the 39 neutral PFOA isomers in the gas phase (M06-2X).[a]

				Type of substitution (*Position of the substitution*)									
PFOA n n	**Stability order**	**Chain length** [b]	ACL[c]	CH_3 (α)	CH_3 (β)	CH_3 (γ)	CH_3 (δ)	CH_3 (ε)	CH_3CH_2 (α)	CH_3CH_2 (β)	CH_3CH_2 (γ)	$(CH_3)_2CH_2$ (α)	$CH_3CH_2CH_2$ (α)
24	1	5		2									
5	2	3		2	2								
13	3	4		2		1							
16	4	4		1		2							
3	5	3			2				1				
33	6	5					2						
12	7	4	3.9	2	**1**								
6	8	4		1					1				
2	9	3		1	1				2				
28	10	5			**2**								
27	11	5		1			1						
1	12	3							2				
4	13	3			1							1	
14	14	4		1	**2**								
31	15	5				**2**							
18	16	4			**1**	2							
26	17	5		1		**1**							
8	18	4				1			1				
30	19	5			**1**		1						
7	20	4	4.7		1				1				
34	21	6		1									
25	22	5		1	**1**								
20	23	4											1
21	24	5							1				
17	25	4			**2**	1							
38	26	6						1					
19	27	4										1	
10	28	4			**1**					**1**			
9	29	4		1						**1**			
35	30	6			**1**								
36	31	6				**1**							
37	32	6					**1**						
39	33	7	5.0										
15	34	4		1	**1**	1							
32	35	5				**1**	1						
29	36	5			**1**	**1**							
22	37	5								**1**			
23	38	5									**1**		
11	39	4				1				**1**			

[a] The position of the substitution is represented by α (carbon next to the -COOH group, position one), β, γ, δ and ε (positions 2, 3, 4 and 5 after the -COOH group, respectively); coloured numbers represent the number of substitutions (yellow and clear background represents a substitution either in position α or at the tail, and blue represents a substitution elsewhere); [b] Length of the unsubstituted backbone; [c] Average chain length.

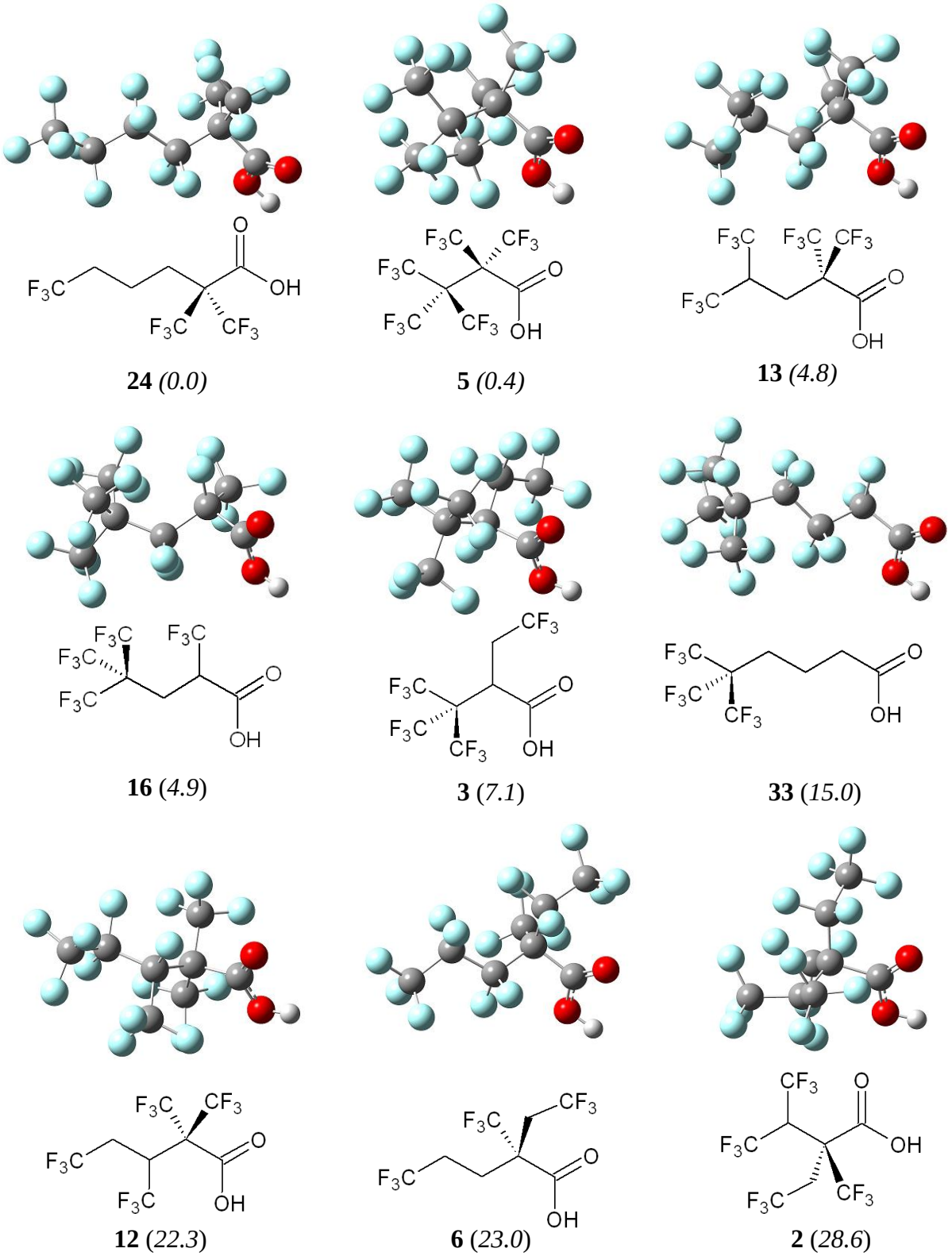
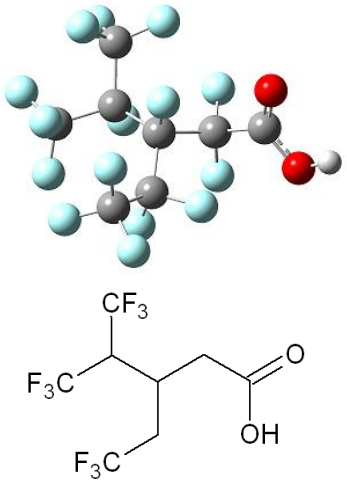
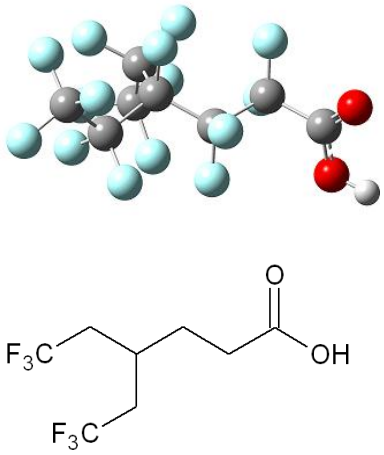


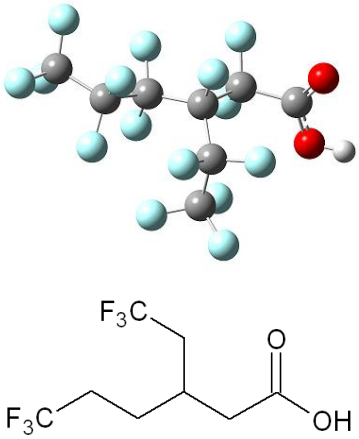
Figure 4.6. Most stable gas-phase neutral isomers with their relative G values in kJ/mol at 298.15 K (M06-2X/6-311++G(3df,3p)) results; all main-chain carbons are perfluorinated but depicted as simple carbons for simplicity).



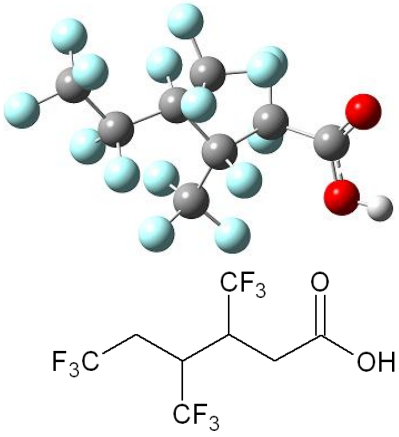
11 (*95.8*)



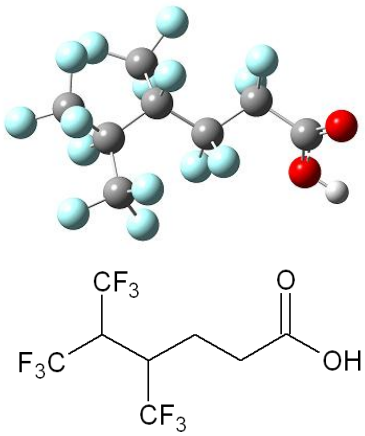
23 (*82.9*)



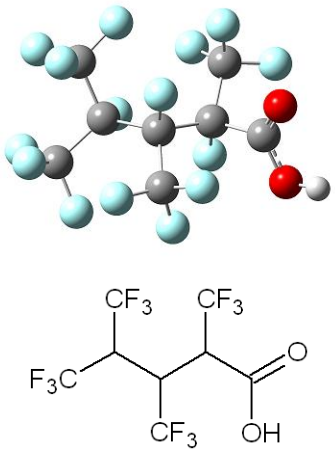
22 (*78.8*)



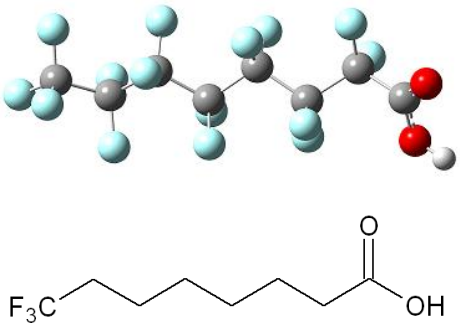
29 (*77.6*)



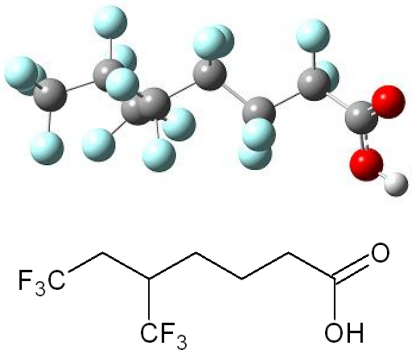
32 (*72.2*)



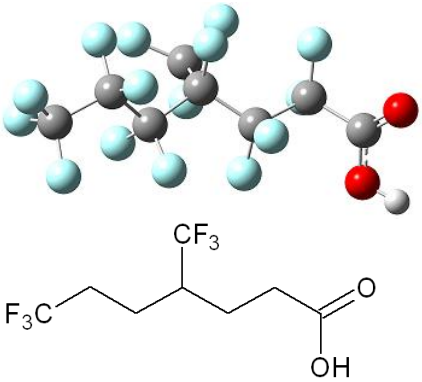
15 (*67.6*)



39 *(62.5)*



37 *(62.2)*



36 *(60.6)*

Figure 4.7. Least stable gas-phase neutral isomers with their relative G values in kJ/mol at 298.15 K (M06-2X/6-311++G(3df,3p)) results; all main-chain carbons are perfluorinated but depicted as simple carbons for simplicity).

There are no major differences when the most stable anions and neutrals in the three media considered are compared. The thirteen most stable anions (see Table 4.2) in the gas phase are **24≈5≈3>13**>**16**>**12**>**6**>**14**>**1**>**4**>**2**>**33**>**27** (**27** has relative G values of 40.7, 35.6 and 34.3 kJ/mol in the gas phase, *n*-octanol and water, respectively, as shown in Table 4.S3), while the thirteen least stable are **11**<**23**<**29**<**32**<**22**<**37**<**39**<**36**<**35**<**38**<**10**<**9**<**30** (**11** has relative G values of 114.0, 104.0 and 100.0 kJ/mol in the gas phase, *n*-octanol and water, respectively, as shown in Table 4.S3).

The most stable isomers (group A) have a predominance of (at least one but sometimes several) substituents (mostly methyl groups, but also ethyl and isopropyl) next to the head group (α position) or at the tail (see Figure 4.6 and the yellow-coloured cells shown in Tables 4.6 and 4.S8). Because this type of substitution sometimes appears in isomers in groups B or C, it does not seem to significantly increase thermodynamic stability. However, substitutions which occur somewhere in the middle of the main chain (see Figure 4.7 and the blue-coloured cells shown in Tables 4.6 and 4.S8) predominate in the least stable group of isomers (group C). This type of substitution is almost absent in isomers of group A (PFOAs **12** and **28** are exceptions). Isomers with ethyl substitutions other than next to the head group or the tail (such as PFOAs **9**, **10**, **11**, **22** and **23**) belong to group C. The protobranching effect,[55] which can describe differences in thermodynamic stability between structural isomers due to branching through electron correlation, could be used to explain the observed relative stability among the 39 PFOA isomers.

The general relationships previously mentioned between thermodynamic stability and patterns of substitution were also observed in the family of 89 PFOSs isomers.[27] Significant deviations from the helical conformation of the main chain due to the nature and position of substituents were identified as a feature present in the least stable PFOSs when studied with the B3LYP functional.[28] However, inspecting the M06-2X structures of PFOSs[27] and PFOAs does not seem to reveal any significant relationship between helical shape and stability.

4.3.2.1. Enthalpy and entropy contributions to the Gibbs free energies

In order to explore how the enthalpy (H) and entropy (S) contributions affect the calculated standard Gibbs free energies of the neutral PFOAs in the gas phase, Figures 4.S8 to 4.S10 have been added the SI section. Figure 4.S8 displays the relative S values when using the M06-2X, B97D and B3LYP functionals. In general terms, the three graphs are very similar. These methods predict a

graph containing three regions, which closely resemble the three regions of Figures 4.3 and 4.4 when plotting relative G differences. One region contains the most branched isomers (PFOAs **1** to **18**), which generally display lower S values. Relative entropies generally increase for the second (made of PFOAs **19** to **33**) and third regions (made of the linear and monomethyl isomers, PFOAs **34** to **39**). Similar results were observed for the PFOSs.[27]

Figures 4.S9 and 4.S10 display the relative H, S and G values using the M06-2X and B3LYP functionals, respectively. Similar to what was observed for PFOSs,[27] the curves of relative G and H values follow a very similar general pattern at both levels of theory. The relative S values are also quantitatively similar for both functionals. The previous observations suggest that, similar to what was found for the PFOSs,[27] the difference in thermodynamic stability within this family of isomers is mostly enthalpic.

4.4. Conclusions

The relative thermodynamic stability of the family of 39 PFOAs isomers (neutrals and anions) has been studied in the gas phase, *n*-octanol and water using several methods (M06-2X, LC-ωPBE, B97D, B3LYP and PM6). The PM6 results closely resemble the M06-2X results for neutral PFOAs, while the discrepancies between these methods when studying the anions are huge. However, LC-ωPBE and B97D follow the MO6-2X and B3LYP results qualitatively, and from a quantitative point of view, the LC-ωPBE and B97D results are somewhere in between the MO6-2X and B3LYP stability results.

Various similarities with the PFOS study[27] applying the M06-2X and B3LYP functionals have been identified. The general stability trends are independent of the type of species (neutral or anionic) and the environment (gas phase, *n*-octanol or water). M06-2X seems to produce results that could be better trusted: more branched isomers tend to be predicted as more stable in general. These isomers are calculated to have lower M06-2X relative standard Gibbs free energies of formation than predicted with B3LYP, and the opposite is observed for the least branched isomers, which in a way resembles well known trends for alkanes. The M06-2X results emphasize isomers with substituents close to the head group and tail ends of the molecule as a factor in stability, while

substitution patterns on the middle carbons tend to decrease stability within the PFOA family of isomers. The difference in stability for these compounds is mostly enthalpic.

The calculation of various physico-chemical quantities of PFOAs (acid dissociation constants and various partition coefficients), work currently in progress, will reveal any obvious structure-property patterns and help us to compare the thermodynamic data generated by the methods applied here.

4.5. References

[1] Tsai, W. T.; Chen, H. P.; Hsien. W. Y. A review of uses, environmental hazards and recovery/recycle technologies of perfluorocarbons (PFCs) emissions from the semiconductor manufacturing processes. *J. Loss Prev. Process Ind.* **2002**. *15*, 65–75. (b) Lindstrom, A. B.; Strynar, M. J.; Libelo, E. L. Polyfluorinated compounds, past, present, and future. *Environ. Sci. Technol.* **2011**, *45*, 7954–7961.

[2] Martin, J. W.; Smithwick, M. M.; Braune, B. M.; Hoekstra, P. F.; Muir, D. C. G.; Mabury, S. A. Identification of long-chain perfluorinated acids in biota from the Canadian Arctic. *Environ. Sci. Technol.* **2004**, *38*, 373-380.

[3] Ellis, D. A.; Martin, J. W.; De Silva, A. O.; Mabury, S. A.; Hurley, M. D.; Andersen, M. P. S.; Wallington, T. J. Degradation of fluorotelomer alcohols: A likely atmospheric source of perfluorinated carboxylic acids. *Environ. Sci. Technol.* **2004**, *38*, 3316-3321.

[4] Domingo, J. L. Health risks of dietary exposure to perfluorinated compounds. *Environ. Int.* **2012**, *40*, 187-195.

[5] Lau, C.; Anitole, K.; Hodes, C.; Lai, D.; Pfahles-Hutchens, A.; Seed, J. Perfluoroalkyl acids: A review of monitoring and toxicological findings. *Toxicol. Sci.* **2007**, *99*, 366-394.

[6] Jacquet, N.; Maire, M. A.; Landkocz, Y.; Vasseur P. Carcinogenic potency of perfluorooctane sulfonate (PFOS) on Syrian hamster embryo (SHE) cells. *Arch. Toxicol*. **2012**, *86*, 305-314.

[7] *Perfluorinated Compounds (PFCs) and Human Health Concerns: Human Health and Safety initiative.* Global health and safety initiative, 2009*;* http://www.healthybuilding.net/healthcare /2009-04-20PFCs_fact_sheet.

[8] *Environment Program Secretariat of the Stockholm Convention on Persistent Organic Pollutants. Conference: The Nine New POPs; An Introduction to the Nine Chemicals Added to the Stockholm Convention by the Conference of the Parties at Its Fourth Meeting Date.* United Nations, 2010; http://chm.pops.int/programmes/newpops/publications/tabid/695/language/en-us/default.aspx.

[9] *Perfluorooctanoic Acid (PFOA) and Fluorinated Telomers*. United States Environmental Protection Agency; http://www.epa.gov/oppt/pfoa/

[10] Rayne, S.; Forest, K.; Friesen, K. J. Congener-specific numbering systems for the environmentally relevant C(4) through C(8) perfluorinated homologue groups of alkyl sulfonates, carboxylates, telomer alcohols, olefins, and acids, and their derivatives. *J. Environ. Sci. Health, Part A Tox./Hazard. Subst. Environ. Eng.*, **2008**, *43*, 1391–1401.

[11] Savu, P. *Kirk-Othmer Encyclopedia of Chemical Terminology*, John Wiley & Sons, Inc. 1994.

[12] U.S. Pat. 3,132,185 (May 5, 1964), Parsons R. E.; U.S. Pat. 3,226,449 (Dec. 28, 1965), W. A. Blanchard and J. C. Rhode; U.S. Pat. 3,234,294 (Feb. 8, 1966), R. E. Parsons; U.S. Pat. 4,425,199 (Jan. 10, 1984), M. Hamada, J. Ohmura, and F. Muranaka.

[13] Reagen, W. K.; Lindstrom, K. R.; Jacoby, C. B.; Purcell, R. G.; Kestner, T. A.; Payfer, R. M.; Miller, J. W. *Society of Environmental Toxicology and Chemistry*: *28th North American meeting*, Milwaukee, WI, 2007.

[14] Benskin, J. P.; Yeung, L. W. Y; Yamashita, N.; Taniyasu, S.; Lam, P. K. S; Martin, J. W. Perfluorinated acid isomer profiling in water and quantitative assessment of manufacturing source. *Environ. Sci. Technol.* **2010**, *44*, 9049-9054.

[15] Prevedouros K.; Cousins I. T.; Buck R. C.; Korzeniowski S. H. Sources, fate and transport of perfluorocarboxylates. *Environ. Sci. Technol.* **2006**, *40*, 32–44.

[16] Benskin, J. P.; Ahrens, L.; Muir, D. C. G.; Scott, B. F.; Spencer, C.; Rosenberg, B.; Tomy, G; Kylin, H.; Lohmann, R.; Martin, J. W. Manufacturing origin of perfluorooctanoate (PFOA) in Atlantic and Canadian arctic seawater. *Environ. Sci. Technol.* **2012**, *46*, 677-685.

[17] De Silva, A. O.; Mabury, S. A. Isolating isomers of perfluorocarboxylates in polar bears (*Ursus maritimus*) from two geographical locations. *Environ. Sci. Technol.* **2004**, *38*, 6538-6545.

[18] De Silva, A. O.; Mabury, S. A. Isomer distribution of perfluorocarboxylates in human blood: Potential correlation to source. *Environ. Sci. Technol.* **2006**, *40*, 2903-2909.

[19] Benskin, J. P.; De Silva, A. O.; Martin, L. J.; Arsenault, G.; McCrindle, R.; Riddell, N.; Mabury, S. A.; Martin, J. W. Disposition of perfluorinated acid isomers in Sprague-Dawley rats; part 1: single dose. *Environ. Toxicol. Chem.* **2009**, *28*, 542-554.

[20] De Silva, A. O.; Benskin, J. P.; Martin, L. J.; Arsenault, G.; McCrindle, R.; Riddell, N.; Martin, J. W.; Mabury, S. A. Disposition of perfluorinated acid isomers in Sprague-Dawley rats; part 2: subchronic dose. *Environ. Toxicol. Chem.* **2009**, *28*, 555-567.

[21] De Silva, A. O.; Tseng, P. J.; Mabury, S. A. Toxicokinetics of perfluorocarboxylate isomers in rainbow trout. *Environ. Toxicol.Chem.* **2009**, *28*, 330-337.

[22] Karrman, A.; Elgh-Dalgren, K.; Lafossas, C.; Moskeland, T. Environmental levels and distribution of structural isomers of perfluoroalkyl acids after aqueous fire-fighting foam (AFFF) contamination. *Environ. Chem.* **2011,** *8*, 372-380.

[23] De Silva, A. O.; Muir, D. C. G.; Mabury, S. A. Distribution of perfluorocarboxylate isomers in select samples from the North American environment. *Environ. Toxicol. Chem.* **2009,** *28*, 1801-1814.

[24] McMurdo, C. J.; Ellis, D. A.; Webster, E.; Butler, J.; Christensen, R. D.; Reid, L. K. Aerosol enrichment of the surfactant PFO and mediation of the water-air transport of gaseous PFOA. *Environ. Sci. Technol.* **2008**, *42*, 3969-3974.

[25] (a) Ipatieff, V. N.; Grosse, A. V. Action of Aluminum Chloride on Paraffins: Autodestructive Alkylation. *Ind. Eng. Chem.* **1936**, *28*, 461-464; (b) Olah, G. A.; Molnur, A. *Hydrocarbon Chemistry*, Wiley: New York, 1995.; (c) Afeefy, H. Y.; Liebman, J. F.; Stein, S. E. *Neutral Thermochemical Data: NIST Chemistry Webbook, NIST Standard Reference Database Number 69*, National Institute of Standards and Technology: Gaithersburg, MD, 1996; (d) Fliszar, S. *Charge Distribution and Chemical Effects*, Springer-Verlag: Berlin, 1983.

[26] Ess, D. H.; Liu, S.; De Proft, F. Density Functional Steric Analysis of Linear and Branched Alkanes. *J. Phys. Chem. A* **2010**, *114*, 12952–12957.

[27] Giroday, T; Montero-Campillo, M. M.; Mora-Diez, N. Thermodynamic stability of PFOS: M06-2X and B3LYP comparison. *Comp. Theor. Chem.* **2014**, *1046*, 81–92.

[28] Montero-Campillo, M. M.; Mora-Diez, N.; Lamsabhi, A. M. Thermodynamic Stability of Neutral and Anionic PFOS: A Gas-Phase, n-Octanol, and Water Theoretical Study. *J. Phys. Chem. A* **2010**, *114*, 10148-10155.

[29] Wiberg, K. B. Substituent effects. 2. n-butyl and tert-butyl derivatives. *J. Org. Chem.* **1991**, *56*, 544-550.

[30] Zhao, Y.; Truhlar, D. G. Density functionals with broad applicability in chemistry. *Acc. Chem. Res.* **2008**, *41*, 157–167.

[31] Raghavachari, K.; Stefanov, B. B.; Curtiss, L. A. Accurate density functional thermochemistry for larger molecules. *Mol. Phys.* **1997**, *91*, 555-559.

[32] Curtiss, L. A.; Raghavachari, K.; Redfern, P. C.; Pople, J. A. Assessment of Gaussian-2 and density functional theories for the computation of enthalpies of formation. *J. Chem. Phys.* **1997**, *106*, 1063-1079.

[33] Saeys, M.; Reyniers, M. F.; Marin, G. B.; van Speybroeck, V.; Waroquier, J. Ab initio calculations for hydrocarbons: Enthalpy of formation, transition state geometry, and activation energy for radical reactions. *J. Phys. Chem. A* **2003**, *107*, 9147-9159.

[34] Grimme, S. Semiempirical GGA-type density functional constructed with a long-range dispersion correction. *J. Comp. Chem.* **2006**, *27*, 1787-1799.

[35] Feng, Y.; Liu, L.; Wang, J. T.; Huang, H.; Guo, Q. X. Assessment of experimental bond dissociation energies using composite ab initio methods and evaluation of the performances of density functional methods in the calculation of bond dissociation energies. *J. Chem. Inf. Comput. Sci.* **2003**, *43*, 2005-2013.

[36] Izgorodina, E. I.; Coote, M. L.; Radom, L. Trends in R-X bond dissociation energies (R = Me, Et, i-Pr, t-Bu; X = H, CH3, OCH3, OH, F): A surprising shortcoming of density functional theory. *J. Phys. Chem. A* **2005**, *109*, 7558-7566.

[37] Schwabe, T.; Grimme, S. Double-hybrid density functionals with long-range dispersion corrections: higher accuracy and extended applicability. Phys. Chem. Chem. Phys. **2007**, *9*, 3397-3406.

[38] Liu, P.; Goddard, J. D.; Arsenault, G.; Gu, J.; McAlees, A.; McCrindle, R.; Robertson, V. Theoretical studies of the conformations and F-19 NMR spectra of linear and a branched perfluorooctanesulfonamide (PFOSAmide). *Chemosphere* **2007**, *69*, 1213–1220.

[39] Rayne, S.; Forest, K.; Friesen, K. J. Relative gas-phase free energies for the C(3) through C(8) linear and branched perfluorinated sulfonic acids: implications for kinetic versus thermodynamic control during synthesis of technical mixtures and predicting congener profile inputs to environmental systems. *J. Mol. Struct.: Theochem* **2008**, *869*, 81-82.

[40] Torres, F. J.; Ochoa-Herrera, V.; Blowers, P.; Sierra-Alvarez, P. Ab initio study of the structural, electronic, and thermodynamic properties of linear perfluorooctane sulfonate (PFOS) and its branched isomers. *Chemosphere* **2009**, *76*, 1143-1149.

[41] Rayne, S.; Forest, K. Comment on "Ab initio study of the structural, electronic, and thermodynamic properties of linear perfluorooctane sulfonate (PFOS) and its branched isomers" by FJ Torres, V. Ochoa-Herrera, P. Blowers, R. Sierra-Alvarez [Chemosphere 76 (8) (2009) 1143-1149]. *Chemosphere* **2009**, *77*, 1455-1456.

[42] Rayne, S.; Forest, K. Comparative semiempirical, ab initio, and density functional theory study on the thermodynamic properties of linear and branched perfluoroalkyl sulfonic acids/sulfonyl fluorides, perfluoroalkyl carboxylic acid/acyl fluorides, and perhydroalkyl sulfonic acids, alkanes, and alcohols. *J. Mol. Struct.: Theochem* **2010**, *941*, 107-118.

[43] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.;

Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A. Jr; Peralta J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09*, revision **A.1**; Gaussian, Inc., Wallingford CT, **2009**.

[44] Becke, A. D. Density functional thermochemistry. 3. The role of exact exchange. *J. Chem. Phys*. **1993**, *98*, 5648-5652.

[45] Lee, C.; Yang, W. T.; Parr, R. G. Development of the Colle-Salvetti correlation-energy formula into a functional of the electron-density. *Phys. Rev*. *B* **1988**, *37*, 785-789.

[46] Vydrov, O. A.; Scuseria, G. E. Assessment of a long-range corrected hybrid functional. *J. Chem. Phys.* **2006**, *125*, 234109.

[47] Zhao, Y.; Truhlar, D. G. The M06 suite of density functionals for main group thermochemistry, thermochemical kinetics, noncovalent interactions, excited states, and transition elements: two new functionals and systematic testing of four M06-class functionals and 12 other functionals. *Theor. Chem. Acc.* **2008**, *120*, 215-241.

[48] Stewart, J. J. P. Optimization of parameters for semiempirical methods V: Modification of NDDO approximations and application to 70 elements. *J. Mol. Model.* **2007**, *13*, 1173-1213.

[49] Perdew, J. P.; Burke, K.; Ernzerhof, M. Generalized gradient approximation made simple. *Phys. Rev. Lett.* **1996**, *77*, 3865-3868.

[50] Perdew, J. P.; Burke, K.; Ernzerhof, M. Generalized gradient approximation made simple (vol 77, pg 3865, 1996). *Phys. Rev. Lett.* **1997**, *78*, 1396-1396.

[51] (a) Zhao, Y.; Truhlar, D. A Density Functional That Accounts for Medium-Range Correlation Energies in Organic Chemistry, *Org. Lett.* **2006**, *8*, 5753-5755; (b) Huenerbein, R.; Schirmer, B.; Moellmann, J.; Grimme, S. Effects of London dispersion on the isomerisation reactions of large organic molecules: a density functional benchmark study, *Phys. Chem. Chem. Phys.* **2010**, *12*, 6940-6948; (c) Rayne, S.; Forest, K. Theoretical studies on the pK_a values of perlfuoroalkyl carboxylic acids, *J. Mol. Struct.: Theochem* **2010**, *948*, 102-107.

[52] Zhao, Y.; Schultz, N. E.; Truhlar, D. G. Design of density functionals by combining the method of constraint satisfaction with parametrization for thermochemistry, thermochemical kinetics, and noncovalent interactions. *J. Chem. Theory Comput.* **2006**, *2*, 364-382.

[53] Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Universal Solvation Model Based on Solute Electron Density and on a Continuum Model of the Solvent Defined by the Bulk Dielectric Constant and Atomic Surface Tensions. *J. Phys. Chem. B*, **2009**, *113*, 6378-6396.

[54] Ellis, D. A.; Denkenberger, K. A.; Burrow, T. E.; Mabury, S. A. The use of F-19 NMR to interpret the structural properties of perfluorocarboxylate acids: A possible correlation with their environmental disposition. *J. Phys. Chem. A.* **2004**, *108*, 10099-10106.

[55] Wodrich, M. D.; Wannere, C. S.; Mo Y.; Jarowski, P. D.; Houk, K. N.; Schleyer, P. V. R. The concept of protobranching and its many paradigm shifting implications for energy evaluations. *Chem. Eur. J.* **2007**, *13*, 7731-7744.

4.6. Supporting Information

Table 4.S1. Names and numbering system used for the 39 PFOA isomers as described in Ref. 10.[a]

PFOA **n n**	**Substitution**	PFOA **n n**	**Substitution**
1	1,1'-diethylpropyl	**21**	1-ethylpentyl
2	1-ethyl-1',2-dimethylpropyl	**22**	2-ethylpentyl
3	1-ethyl-2,2'-dimethylpropyl	**23**	3-ethylpentyl
4	1-isopropyl-2-methylpropyl	**24**	1,1'-dimethylpentyl
5	1,1',2,2'-tetramethylpropyl	**25**	1,2-dimethylpentyl
6	1-ethyl-1'-methylbutyl	**26**	1,3-dimethylpentyl
7	1-ethyl-2-methylbutyl	**27**	1,4-dimethylpentyl
8	1-ethyl-3-methylbutyl	**28**	2,2'-dimethylpentyl
9	2-ethyl-1-methylbutyl	**29**	2,3-dimethylpentyl
10	2-ethyl-2'-methylbutyl	**30**	2,4-dimethylpentyl
11	2-ethyl-3-methylbutyl	**31**	3,3'-dimethylpentyl
12	1,1',2-trimethylbutyl	**32**	3,4-dimethylpentyl
13	1,1',3-trimethylbutyl	**33**	4,4'-dimethylpentyl
14	1,2,2'-trimethylbutyl	**34**	1-methylhexyl
15	1,2,3-trimethylbutyl	**35**	2-methylhexyl
16	1,3,3'-trimethylbutyl	**36**	3-methylhexyl
17	2,2',3-trimethylbutyl	**37**	4-methylhexyl
18	2,3,3'-trimethylbutyl	**38**	5-methylhexyl
19	1-isopropylbutyl	**39**	n-heptyl
20	1-propylbutyl		

[a] This method considers only the perfluoroalkyl moiety; for PFOAs a -COOH/-COO^- group is attached to carbon 1.

Table 4.S2. Relative G values (in kJ/mol at 298.15 K) and stability order of the 39 neutral PFOA isomers calculated at the M06-2X/6-311++(3df,3p) level of theory in the gas phase, octanol and water.

PFOA **n**	**Gas phase**		**n-Octanol**		**Water**	
n	**ΔG**	***Order***	**ΔG**	***Order***	**ΔG**	***Order***
1	35.8	*12*	34.0	*12*	34.1	*12*
2	28.6	*9*	29.9	*9*	28.9	*10*
3	7.1	*5*	7.6	*5*	6.8	*5*
4	38.2	*13*	39.1	*13*	38.6	*15*
5	0.4	*2*	2.3	*2*	0.0	*1*
6	23.0	*8*	23.1	*8*	22.6	*8*
7	45.0	*20*	46.4	*21*	44.6	*21*
8	43.9	*18*	45.0	*19*	44.6	*20*
9	59.6	*29*	60.7	*30*	58.9	*29*
10	55.4	*28*	56.1	*27*	54.0	*27*
11	95.8	*39*	97.7	*39*	95.1	*39*
12	22.3	*7*	21.9	*7*	22.1	*7*
13	4.8	*3*	6.0	*4*	5.2	*4*
14	38.5	*14*	41.6	*17*	41.5	*17*
15	67.6	*34*	66.8	*34*	64.1	*34*
16	4.9	*4*	5.9	*3*	4.2	*3*
17	51.4	*25*	53.2	*26*	50.1	*25*
18	40.2	*16*	40.0	*15*	38.3	*14*
19	54.8	*27*	56.2	*28*	55.1	*28*
20	47.2	*23*	47.7	*23*	48.7	*23*
21	48.8	*24*	48.5	*24*	49.1	*24*
22	78.8	*37*	77.9	*37*	77.1	*37*
23	82.9	*38*	83.2	*38*	82.5	*38*
24	0.0	*1*	0.0	*1*	0.1	*2*
25	47.1	*22*	47.2	*22*	45.7	*22*
26	42.9	*17*	42.9	*18*	42.9	*19*
27	32.8	*11*	33.1	*11*	32.5	*11*
28	28.8	*10*	30.3	*10*	28.3	*9*
29	77.6	*36*	77.9	*36*	75.5	*36*
30	44.9	*19*	45.1	*20*	42.6	*18*
31	38.7	*15*	39.3	*14*	37.6	*13*
32	72.2	*35*	74.5	*35*	72.5	*35*
33	15.0	*6*	14.6	*6*	10.7	*6*
34	45.8	*21*	41.5	*16*	40.9	*16*
35	60.1	*30*	60.1	*29*	59.5	*30*
36	60.6	*31*	61.6	*31*	60.0	*31*
37	62.2	*32*	63.1	*32*	62.2	*33*
38	52.0	*26*	52.5	*25*	51.0	*26*
39	62.5	*33*	64.0	*33*	61.8	*32*

Table 4.S2a. Relative G values (in kJ/mol at 298.15 K) and stability order of the 39 neutral PFOA isomers calculated at the M06-2X/6-31++G(d,p) level of theory the gas phase, octanol and water.

PFOA **n**	**Gas phase**		**n-Octanol**		**Water**	
n	**ΔG**	***Order***	**ΔG**	***Order***	**ΔG**	***Order***
1	32.8	*12*	30.2	*11*	30.8	*11*
2	26.9	*9*	27.4	*9*	25.2	*9*
3	8.6	*5*	7.6	*5*	9.6	*5*
4	37.5	*13*	37.5	*14*	37.7	*13*
5	3.1	*2*	1.9	*2*	4.5	*2*
6	20.6	*7*	19.9	*7*	20.9	*7*
7	44.5	*21*	44.1	*22*	45.2	*24*
8	42.8	*18*	42.1	*19*	43.0	*19*
9	57.7	*30*	55.1	*30*	58.3	*31*
10	54.2	*28*	51.1	*27*	53.9	*27*
11	94.5	*39*	92.2	*39*	95.2	*39*
12	22.7	*8*	21.3	*8*	23.2	*8*
13	4.5	*3*	4.3	*3*	5.5	*3*
14	40.6	*15*	40.5	*18*	41.6	*18*
15	67.0	*34*	62.1	*34*	65.3	*34*
16	6.2	*4*	4.7	*4*	6.4	*4*
17	52.3	*26*	49.8	*26*	53.4	*26*
18	42.2	*17*	38.9	*15*	41.3	*17*
19	52.8	*27*	53.2	*28*	54.2	*28*
20	44.8	*22*	45.3	*23*	45.2	*23*
21	46.6	*24*	45.5	*24*	45.0	*22*
22	76.6	*37*	72.6	*36*	73.9	*36*
23	79.6	*38*	78.2	*38*	78.8	*38*
24	0.0	*1*	0.0	*1*	0.0	*1*
25	46.0	*23*	43.2	*21*	44.8	*21*
26	41.8	*16*	40.2	*17*	40.1	*16*
27	32.1	*11*	30.2	*12*	31.1	*12*
28	28.9	*10*	28.6	*10*	30.2	*10*
29	75.4	*36*	72.7	*37*	75.0	*37*
30	43.7	*20*	39.7	*16*	43.0	*20*
31	38.0	*14*	36.5	*13*	38.5	*14*
32	71.4	*35*	70.2	*35*	72.7	*35*
33	16.3	*6*	12.2	*6*	14.5	*6*
34	43.2	*19*	42.6	*20*	40.1	*15*
35	56.7	*29*	54.2	*29*	56.0	*29*
36	58.6	*31*	55.7	*31*	58.0	*30*
37	59.6	*33*	58.9	*33*	60.0	*33*
38	50.0	*25*	46.4	*25*	48.3	*25*
39	59.5	*32*	57.1	*32*	59.5	*32*

Table 4.S2b. Relative G values (in kJ/mol at 298.15 K) and stability order of the 39 neutral PFOA isomers calculated at the B3LYP/6-31++G(d,p) level of theory in the gas phase, octanol and water (using the PCM and SMD solvation methods).

PFOA **n** **n**	**Gas phase**		**n-Octanol**				**Water**			
			PCM		**SMD**		**PCM**		**SMD**	
	ΔG	***Order***	**ΔG**	***Order***	**ΔG**	***Order***	**ΔG**	***Order***	**ΔG**	***Order***
1	47.0	*28*	51.5	*27*	47.2	*26*	52.0	*27*	46.2	*27*
2	44.3	*23*	49.1	*23*	47.5	*27*	50.4	*25*	47.6	*29*
3	28.3	*10*	35.5	*14*	29.6	*11*	36.2	*14*	29.3	*13*
4	46.9	*27*	51.4	*26*	46.9	*23*	49.7	*24*	46.3	*28*
5	45.5	*25*	53.5	*28*	47.0	*25*	55.0	*28*	44.9	*25*
6	19.3	*5*	23.2	*7*	20.2	*7*	24.2	*9*	18.8	*5*
7	45.5	*24*	49.3	*24*	46.9	*24*	50.4	*26*	43.2	*22*
8	32.4	*12*	28.7	*11*	33.3	*14*	22.4	*7*	28.7	*12*
9	56.2	*30*	58.3	*30*	56.9	*30*	58.6	*30*	55.3	*32*
10	67.6	*34*	72.4	*37*	66.4	*34*	72.9	*36*	65.8	*35*
11	92.9	*39*	93.8	*39*	88.5	*39*	91.8	*39*	89.0	*39*
12	37.3	*16*	42.7	*19*	40.9	*19*	43.5	*21*	34.3	*16*
13	15.9	*2*	20.1	*4*	16.8	*2*	18.6	*3*	16.3	*4*
14	46.7	*26*	54.4	*29*	49.8	*29*	55.9	*29*	46.1	*26*
15	73.1	*36*	72.2	*36*	73.3	*36*	72.3	*35*	55.0	*31*
16	19.5	*6*	24.6	*9*	19.9	*5*	25.5	*11*	19.8	*8*
17	74.9	*37*	79.4	*38*	75.8	*38*	80.3	*38*	73.0	*38*
18	64.6	*32*	68.7	*33*	64.2	*32*	70.1	*34*	64.9	*34*
19	48.3	*29*	49.6	*25*	48.3	*28*	49.3	*23*	44.6	*24*
20	22.3	*8*	23.3	*8*	20.0	*6*	22.8	*8*	19.0	*6*
21	23.0	*9*	22.6	*6*	21.4	*9*	21.9	*6*	20.1	*9*
22	60.2	*31*	62.5	*32*	61.8	*31*	60.6	*32*	53.5	*30*
23	66.9	*33*	62.2	*31*	65.4	*33*	59.6	*31*	64.2	*33*
24	0.0	*1*	0.0	*1*	0.0	*1*	0.0	*1*	0.0	*1*
25	39.7	*18*	43.0	*20*	36.8	*16*	41.4	*18*	39.7	*19*
26	33.0	*14*	33.0	*13*	32.8	*13*	32.3	*13*	31.6	*14*
27	20.6	*7*	21.3	*5*	20.5	*8*	21.0	*5*	19.7	*7*
28	35.5	*15*	39.5	*16*	34.4	*15*	40.0	*16*	33.8	*15*
29	76.3	*38*	72.1	*35*	75.3	*37*	73.9	*37*	72.6	*37*
30	39.4	*17*	40.7	*17*	38.3	*18*	41.2	*17*	38.2	*18*
31	44.2	*22*	48.3	*22*	44.6	*22*	48.0	*22*	42.1	*21*
32	69.9	*35*	69.1	*34*	69.9	*35*	67.7	*33*	69.5	*36*
33	18.3	*4*	17.1	*3*	18.4	*4*	20.6	*4*	15.9	*2*
34	17.0	*3*	16.5	*2*	17.9	*3*	16.3	*2*	16.2	*3*
35	39.9	*19*	38.5	*15*	37.0	*17*	36.2	*15*	35.3	*17*
36	43.3	*20*	43.5	*21*	42.7	*20*	42.7	*20*	41.1	*20*
37	43.9	*21*	41.6	*18*	43.2	*21*	41.5	*19*	43.2	*23*
38	32.6	*13*	29.4	*12*	31.7	*12*	28.3	*12*	28.4	*11*
39	29.5	*11*	25.7	*10*	25.8	*10*	24.4	*10*	27.5	*10*

Table 4.S2c. Relative G values (in kJ/mol at 298.15 K) and stability order of the 39 neutral PFOA isomers calculated at the B97D/6-31++G(d,p) level of theory in the gas phase, octanol and water.

PFOA **n**	**Gas phase**		**n-Octanol**		**Water**	
n	**ΔG**	***Order***	**ΔG**	***Order***	**ΔG**	***Order***
1	46.5	*26*	45.3	*26*	47.0	*26*
2	38.5	*16*	38.8	*19*	41.1	*22*
3	20.2	*6*	20.8	*7*	21.6	*6*
4	42.4	*24*	41.1	*24*	41.2	*23*
5	31.0	*11*	30.0	*11*	29.6	*10*
6	18.3	*5*	17.0	*5*	18.7	*5*
7	41.1	*21*	40.8	*23*	40.6	*21*
8	36.2	*15*	32.8	*14*	33.9	*14*
9	55.8	*31*	54.0	*31*	55.0	*31*
10	62.6	*33*	60.3	*32*	60.5	*32*
11	94.4	*39*	93.4	*39*	92.0	*39*
12	31.7	*13*	32.2	*13*	32.3	*13*
13	14.5	*2*	13.8	*2*	14.4	*2*
14	39.0	*18*	40.8	*22*	41.4	*24*
15	72.1	*36*	69.9	*36*	69.0	*36*
16	15.9	*3*	15.0	*3*	15.6	*3*
17	65.6	*34*	63.8	*34*	64.4	*34*
18	55.2	*30*	52.3	*30*	52.9	*30*
19	49.3	*28*	49.0	*29*	48.9	*28*
20	27.5	*10*	25.6	*10*	29.9	*11*
21	27.5	*9*	25.4	*9*	28.1	*8*
22	61.1	*32*	62.2	*33*	63.7	*33*
23	73.3	*37*	70.2	*37*	69.2	*37*
24	0.0	*1*	0.0	*1*	0.0	*1*
25	42.2	*23*	39.5	*20*	38.7	*16*
26	35.9	*14*	34.7	*15*	35.4	*15*
27	22.6	*7*	19.3	*6*	21.9	*7*
28	31.0	*12*	30.1	*12*	31.5	*12*
29	76.1	*38*	73.5	*38*	72.3	*38*
30	40.4	*19*	37.5	*18*	39.8	*18*
31	41.3	*22*	40.4	*21*	40.1	*19*
32	70.6	*35*	67.7	*35*	68.2	*35*
33	16.9	*4*	16.1	*4*	16.1	*4*
34	25.8	*8*	24.1	*8*	28.3	*9*
35	44.0	*25*	41.8	*25*	42.7	*25*
36	49.6	*29*	47.9	*28*	49.3	*29*
37	49.2	*27*	47.2	*27*	47.3	*27*
38	38.6	*17*	37.4	*17*	39.6	*17*
39	40.5	*20*	36.4	*16*	40.2	*20*

Table 4.S2d. Relative G values (in kJ/mol at 298.15 K) and stability order of the 39 neutral PFOA isomers calculated at the PM6 level of theory in the gas phase, octanol and water.

PFOA **n**	**Gas phase**		**n-Octanol**		**Water**	
n	**ΔG**	***Order***	**ΔG**	***Order***	**ΔG**	***Order***
1	49.8	*15*	52.4	*16*	50.3	*16*
2	32.7	*8*	34.3	*8*	33.0	*9*
3	17.6	*4*	23.4	*5*	19.6	*5*
4	45.6	*13*	50.6	*14*	49.1	*15*
5	0.0	*1*	0.0	*1*	0.0	*1*
6	34.1	*9*	34.7	*9*	31.9	*8*
7	68.7	*30*	70.6	*30*	66.8	*29*
8	54.6	*20*	59.6	*22*	56.9	*21*
9	77.9	*35*	79.9	*34*	76.9	*34*
10	69.7	*32*	69.1	*28*	64.1	*28*
11	84.2	*37*	88.0	*38*	85.7	*39*
12	28.4	*6*	28.2	*6*	25.6	*6*
13	13.3	*3*	12.5	*2*	9.8	*2*
14	35.7	*10*	36.9	*10*	36.0	*10*
15	61.6	*27*	63.8	*24*	61.5	*24*
16	20.0	*5*	21.4	*4*	15.6	*4*
17	50.8	*17*	54.4	*18*	51.9	*17*
18	48.4	*14*	47.9	*13*	49.0	*14*
19	58.9	*25*	63.8	*25*	61.7	*26*
20	57.9	*22*	63.1	*23*	61.6	*25*
21	58.3	*24*	64.3	*27*	63.3	*27*
22	79.2	*36*	81.6	*35*	82.5	*36*
23	86.3	*39*	91.9	*39*	85.3	*38*
24	12.3	*2*	14.7	*3*	13.6	*3*
25	56.9	*21*	59.1	*21*	59.2	*22*
26	53.2	*19*	57.3	*19*	52.9	*18*
27	42.5	*12*	44.6	*12*	43.6	*12*
28	36.0	*11*	39.5	*11*	37.5 [a]	*11*
29	84.3	*38*	87.4	*37*	84.8	*37*
30	59.1	*26*	54.4	*17*	54.4	*19*
31	50.6	*16*	50.9	*15*	47.1	*13*
32	77.1	*34*	81.9	*36*	80.5	*35*
33	31.0	*7*	31.2	*7*	31.3	*7*
34	52.9	*18*	57.9	*20*	54.7	*20*
35	62.9	*28*	69.2	*29*	68.0	*30*
36	69.8	*33*	73.8	*31*	71.9	*31*
37	69.3	*31*	75.5	*33*	73.7	*32*
38	58.0	*23*	64.3	*26*	61.1	*23*
39	68.5	*29*	75.1	*32*	75.5	*33*

[a] This value was estimated using the octanol-water correlation equation (see Table 4.S5).

Table 4.S2e. Relative G values (in kJ/mol at 298.15 K) and stability order of the 39 neutral PFOA isomers calculated at the LC-ωPBE/6-31++G(d,p) level of theory in the gas phase, octanol and water.

PFOA **n**	**Gas phase**		**n-Octanol**		**Water**	
n	**ΔG**	***Order***	**ΔG**	***Order***	**ΔG**	***Order***
1	44.9	*18*	44.2	*20*	43.4	*16*
2	41.9	*16*	44.6	*21*	44.2	*18*
3	22.8	*5*	23.8	*5*	24.2	*5*
4	49.0	*24*	47.5	*24*	48.6	*24*
5	31.4	*9*	31.3	*9*	33.1	*10*
6	26.9	*6*	27.3	*6*	27.6	*7*
7	50.3	*25*	49.7	*25*	52.0	*26*
8	40.1	*14*	39.6	*14*	39.6	*14*
9	62.8	*31*	62.2	*32*	63.9	*32*
10	68.6	*33*	67.2	*33*	68.5	*33*
11	102.2	*39*	97.6	*39*	99.9	*39*
12	34.6	*11*	37.4	*13*	38.4	*13*
13	12.4	*2*	14.3	*2*	14.4	*2*
14	45.2	*21*	45.1	*22*	47.1	*22*
15	64.2	*32*	61.2	*31*	63.6	*31*
16	15.7	*3*	14.8	*3*	16.0	*3*
17	71.8	*34*	72.3	*34*	74.8	*35*
18	62.2	*30*	60.8	*30*	62.2	*30*
19	55.0	*28*	53.1	*28*	55.1	*27*
20	36.1	*13*	37.3	*12*	34.0	*11*
21	34.2	*10*	34.4	*10*	32.0	*9*
22	74.5	*35*	72.7	*35*	72.7	*34*
23	79.7	*37*	78.0	*37*	79.6	*37*
24	0.0	*1*	0.0	*1*	0.0	*1*
25	45.2	*20*	44.1	*19*	43.7	*17*
26	40.3	*15*	40.6	*15*	40.8	*15*
27	28.5	*8*	28.1	*8*	28.8	*8*
28	35.9	*12*	35.0	*11*	37.6	*12*
29	86.2	*38*	84.8	*38*	86.3	*38*
30	45.1	*19*	41.2	*16*	44.4	*19*
31	47.2	*23*	46.4	*23*	48.2	*23*
32	78.1	*36*	77.4	*36*	79.6	*36*
33	18.3	*4*	18.8	*4*	17.3	*4*
34	28.5	*7*	27.9	*7*	26.7	*6*
35	51.9	*26*	50.8	*26*	50.6	*25*
36	54.6	*27*	54.1	*29*	56.1	*29*
37	56.0	*29*	52.6	*27*	55.6	*28*
38	44.6	*17*	43.6	*18*	45.1	*20*
39	45.6	*22*	42.5	*17*	46.2	*21*

Table 4.S3. Relative G values (in kJ/mol at 298.15 K) and stability order of the 39 anionic PFOA isomers calculated at the M06-2X/6-311++(3df,3p) level of theory in the gas phase, octanol and water.

PFOA **n**	**Gas phase**		**n-Octanol**		**Water**	
n	**ΔG**	***Order***	**ΔG**	***Order***	**ΔG**	***Order***
1	31.4 [a]	*9*	28.1	*10*	30.6	*10*
2	33.9 [a]	*11*	30.3	*11*	32.3	*12*
3	0.0	*3*	5.9	*4*	6.4	*5*
4	32.7	*10*	37.8	*14*	37.1	*14*
5	0.0 [a]	*1*	0.0	*1*	0.0	*1*
6	23.7 [a]	*7*	21.2	*7*	23.1	*8*
7	45.8	*16*	45.7	*19*	44.8	*19*
8	42.7	*14*	41.7	*15*	41.9	*15*
9	64.0	*28*	64.3	*30*	61.9	*30*
10	69.1	*29*	61.8	*29*	58.5	*29*
11	114.8	*39*	104.0	*39*	100.0	*39*
12	22.4 [a]	*6*	20.0	*6*	20.7	*7*
13	5.9 [a]	*4*	5.3	*3*	6.3	*4*
14	26.8	*8*	26.5	*9*	24.6	*9*
15	57.7	*22*	54.0	*25*	51.9	*25*
16	11.7	*5*	6.7	*5*	4.2	*3*
17	61.0	*26*	56.5	*27*	53.0	*26*
18	59.6	*25*	47.9	*21*	44.5	*18*
19	58.1	*24*	55.9	*26*	55.3	*27*
20	46.9	*17*	45.8	*20*	48.5	*24*
21	48.7	*19*	48.0	*22*	47.2	*22*
22	90.7	*35*	82.8	*36*	79.2	*36*
23	98.2	*38*	89.5	*38*	87.0	*38*
24	0.0 [a,b]	*2*	0.0	*2*	0.1	*2*
25	53.1	*21*	49.4	*24*	47.5	*23*
26	48.7	*18*	44.7	*17*	43.7	*17*
27	40.7	*13*	35.6	*13*	34.3	*13*
28	43.1	*15*	34.8	*12*	31.8	*11*
29	93.6	*37*	86.0	*37*	82.3	*37*
30	62.5	*27*	49.3	*23*	47.1	*21*
31	57.9	*23*	45.3	*18*	42.7	*16*
32	92.3	*36*	80.0	*35*	78.4	*35*
33	34.5	*12*	23.1	*8*	20.0	*6*
34	49.2	*20*	43.3	*16*	45.3	*20*
35	78.1	*31*	65.3	*31*	64.1	*31*
36	78.2	*32*	69.1	*34*	68.5	*34*
37	84.1	*34*	68.8	*32*	66.2	*32*
38	73.2	*30*	58.6	*28*	58.2	*28*
39	82.7	*33*	68.9	*33*	67.8	*33*

[a] The reported value was estimated using the gas-octanol correlation equation (see Table 4.S5); some species decarboxylated at this level of theory; [b] Since PFOA **24** is the 0.0 value, all gas values are estimated relative to it.

Table 4.S3a. Relative G values (in kJ/mol at 298.15 K) and stability order of the 39 anionic PFOA isomers calculated at the M06-2X/6-31++(d,p) level of theory in the gas phase, octanol and water.

PFOA **n**	**Gas phase**		**n-Octanol**		**Water**	
n	**ΔG**	***Order***	**ΔG**	***Order***	**ΔG**	***Order***
1	28.8 [a]	*9*	30.8	*10*	25.6	*9*
2	34.4 [a]	*11*	34.3	*13*	30.6	*11*
3	1.7	*2*	8.6	*5*	7.5	*4*
4	31.9	*10*	37.9	*14*	36.9	*14*
5	3.0 [a]	*3*	4.5	*2*	2.7	*2*
6	22.0 [a]	*6*	22.9	*7*	19.6	*6*
7	45.4	*18*	46.2	*19*	45.5	*21*
8	42.3	*15*	42.7	*15*	41.0	*15*
9	61.9	*26*	61.4	*30*	62.3	*30*
10	67.4	*29*	58.0	*29*	59.9	*29*
11	112.7	*39*	99.3	*39*	102.1	*39*
12	22.7 [a]	*7*	22.5	*6*	20.2	*7*
13	6.6 [a]	*4*	8.1	*4*	5.9	*3*
14	26.2	*8*	29.4	*9*	27.9	*10*
15	56.6	*23*	53.2	*25*	53.3	*25*
16	13.4	*5*	7.9	*3*	8.3	*5*
17	62.3	*27*	55.7	*26*	58.3	*28*
18	62.3	*28*	47.5	*22*	49.5	*24*
19	56.6	*22*	56.1	*28*	54.9	*26*
20	44.8	*16*	48.3	*24*	44.1	*18*
21	45.2	*17*	46.3	*20*	44.5	*19*
22	85.7	*35*	78.3	*35*	80.7	*36*
23	94.5	*38*	84.7	*38*	85.2	*38*
24	0.0 [a,b]	*1*	0.0	*1*	0.0	*1*
25	51.6	*21*	47.7	*23*	47.6	*22*
26	47.4	*19*	44.1	*18*	42.8	*16*
27	39.3	*13*	34.0	*12*	34.8	*13*
28	41.9	*14*	33.1	*11*	33.4	*12*
29	92.2	*37*	82.2	*37*	84.1	*37*
30	61.3	*25*	46.4	*21*	48.2	*23*
31	58.6	*24*	44.1	*17*	44.5	*20*
32	90.8	*36*	78.7	*36*	79.5	*35*
33	36.5	*12*	23.6	*8*	24.4	*8*
34	49.0	*20*	43.9	*16*	42.8	*17*
35	77.0	*31*	65.0	*31*	64.5	*32*
36	78.4	*32*	66.1	*34*	65.3	*33*
37	82.0	*34*	65.6	*33*	67.0	*34*
38	70.9	*30*	55.7	*27*	56.4	*27*
39	80.5	*33*	65.4	*32*	63.3	*31*

[a] The reported value was estimated using the gas-octanol correlation equation (see Table 4.S5); some species decarboxylated at this level of theory; [b] Since PFOA **24** is the 0.0 value, all gas values are estimated relative to it.

Table 4.S3b. Relative G values (in kJ/mol at 298.15 K) and stability order of the 39 anionic PFOA isomers calculated at the B3LYP/6-31++G(d,p) level of theory in the gas phase, octanol and water (using the PCM and SMD methods).

PFOA **n**	**Gas phase**				**n-Octanol**				**Water**			
	PCM		**SMD**		**PCM**		**SMD**		**PCM**		**SMD**	
	ΔG	***Order***	**ΔG**	***Order***	**ΔG**	***Order***	**ΔG**	***Order***	**ΔG**	***Order***	**ΔG**	***Order***
1	48.9 [a]	*22*	44.9 [a]	*19*	46.8	*20*	43.4	*18*	48.5	*25*	47.2	*23*
2	52.7 [a]	*26*	49.3 [a]	*24*	50.4	*27*	47.8	*24*	52.3	*28*	49.7	*28*
3	19.6	*5*	20.8	*4*	32.6	*12*	30.0	*10*	33.2	*14*	29.9	*10*
4	36.9	*13*	38.0	*13*	49.0	*25*	45.4	*19*	48.4	*24*	46.9	*21*
5	52.4 [a]	*25*	47.2 [a]	*22*	50.2	*26*	45.7	*21*	51.9	*27*	46.8	*20*
6	22.6 [a]	*9*	21.1 [a]	*6*	21.7	*4*	20.4	*4*	22.2	*7*	21.5	*8*
7	40.0	*14*	41.1	*15*	47.2	*22*	46.1	*22*	45.7	*22*	44.6	*19*
8	28.5	*10*	29.6	*10*	23.9	*10*	32.6	*11*	22.3	*8*	32.8	*12*
9	57.2	*28*	58.4	*28*	56.7	*30*	61.3	*31*	57.8	*30*	57.8	*31*
10	76.7	*33*	77.8	*33*	75.1	*36*	73.8	*34*	74.0	*36*	71.3	*34*
11	103.6	*39*	104.7	*39*	98.1	*39*	103.4	*39*	92.9	*39*	98.6	*39*
12	41.2 [a]	*16*	39.2 [a]	*14*	39.4	*15*	37.9	*15*	40.1	*16*	38.1	*15*
13	17.2 [a]	*2*	21.0 [a]	*5*	16.5	*3*	20.3	*3*	15.7	*3*	21.4	*7*
14	42.6	*18*	43.7	*18*	52.9	*29*	52.0	*29*	53.7	*29*	49.9	*29*
15	57.4	*29*	58.6	*29*	60.6	*31*	59.7	*30*	60.1	*31*	57.8	*30*
16	20.1	*6*	21.2	*7*	23.5	*8*	22.6	*7*	23.8	*10*	21.1	*5*
17	81.4	*36*	82.5	*36*	83.1	*38*	83.1	*37*	81.6	*38*	76.1	*37*
18	77.8	*34*	79.0	*34*	73.8	*34*	73.8	*33*	72.3	*35*	69.3	*33*
19	43.8	*19*	45.0	*20*	47.1	*21*	50.0	*26*	46.8	*23*	48.7	*26*
20	18.8	*4*	19.9	*3*	22.9	*7*	24.5	*8*	21.8	*6*	25.8	*9*
21	18.1	*3*	19.2	*2*	22.3	*5*	21.6	*5*	20.2	*4*	20.0	*3*
22	68.4	*32*	69.5	*32*	62.8	*32*	65.0	*32*	61.2	*32*	63.9	*32*
23	77.9	*35*	79.0	*35*	70.3	*33*	76.5	*35*	66.6	*33*	72.6	*35*
24	0.0 [a,b]	*1*	0.0 [a]	*1*	0.0	*1*	0.0	*1*	0.0	*1*	0.0	*1*
25	41.0	*15*	42.2	*16*	41.1	*16*	42.6	*16*	40.6	*18*	41.2	*17*
26	33.8	*12*	35.0	*12*	34.3	*13*	36.7	*13*	32.6	*12*	34.5	*13*
27	21.7	*8*	22.8	*9*	22.5	*6*	22.0	*6*	20.6	*5*	21.0	*4*
28	41.7	*17*	42.8	*17*	41.5	*17*	42.6	*17*	40.4	*17*	39.8	*16*
29	87.7	*38*	88.8	*38*	77.6	*37*	84.1	*38*	76.2	*37*	77.5	*38*
30	51.3	*23*	52.4	*25*	43.8	*19*	45.5	*20*	42.0	*19*	43.6	*18*
31	58.7	*30*	59.9	*30*	52.8	*28*	52.0	*28*	51.1	*26*	49.6	*27*
32	82.5	*37*	83.6	*37*	74.3	*35*	77.6	*36*	71.1	*34*	74.2	*36*
33	32.7	*11*	33.8	*11*	23.6	*9*	24.6	*9*	22.8	*9*	21.1	*6*
34	20.2	*7*	21.3	*8*	14.1	*2*	17.3	*2*	13.6	*2*	18.2	*2*
35	51.7	*24*	52.8	*26*	43.3	*18*	47.3	*23*	39.0	*15*	46.9	*22*
36	56.7	*27*	57.9	*27*	47.2	*23*	49.3	*25*	44.3	*21*	48.0	*25*
37	59.5	*31*	60.6	*31*	47.6	*24*	50.1	*27*	43.0	*20*	47.4	*24*
38	48.1	*21*	49.2	*23*	35.3	*14*	37.1	*14*	33.0	*13*	37.3	*14*
39	45.4	*20*	46.5	*21*	32.1	*11*	34.8	*12*	27.5	*11*	31.0	*11*

[a] Species that decarboxylates at this level of theory; the reported value was estimated using the gas-octanol correlation equation (see Table 4.S5); [b] Since PFOA **24** is the 0.0 value, all gas values are estimated relative to it.

Table 4.S3c. Relative G values (in kJ/mol at 298.15 K) and stability order of the 39 anionic PFOA isomers calculated at the B97D /6-31++G(d,p) level of theory in the gas phase, octanol and water.

PFOA **n**	**Gas phase**		**n-Octanol**		**Water**	
n	**ΔG**	***Order***	**ΔG**	***Order***	**ΔG**	***Order***
1	53.5 [a]	*21*	43.5	*17*	43.5	*17*
2	53.8 [a]	*22*	43.6	*19*	43.6	*19*
3	18.7	*3*	24.2	*5*	24.2	*5*
4	39.5	*14*	46.1	*21*	46.1	*21*
5	37.2 [a]	*12*	31.7	*12*	31.7	*13*
6	19.8 [a]	*5*	14.1	*3*	14.1	*3*
7	41.5	*16*	44.1	*20*	44.1	*20*
8	35.5	*11*	37.0	*14*	37.0	*14*
9	61.4	*27*	60.9	*30*	60.9	*30*
10	76.9	*33*	71.8	*34*	71.8	*34*
11	113.3	*39*	103.5	*39*	103.5	*39*
12	35.2 [a]	*10*	31.8 [c]	*13*	27.9	*8*
13	15.3 [a]	*2*	10.8	*2*	10.8	*2*
14	40.1	*15*	43.6	*18*	43.6	*18*
15	60.0	*24*	59.5	*29*	59.5	*29*
16	18.9	*4*	20.8	*4*	20.8	*4*
17	79.1	*35*	74.9	*35*	74.9	*35*
18	74.7	*32*	67.0	*31*	67.0	*31*
19	49.2	*19*	67.0	*32*	67.0	*32*
20	28.8	*8*	31.2	*11*	31.2	*12*
21	26.8	*6*	30.5	*9*	30.5	*10*
22	78.0	*34*	70.1	*33*	70.1	*33*
23	90.0	*36*	82.0	*37*	82.0	*37*
24	0.0 [a,b]	*1*	0.0	*1*	0.0	*1*
25	49.6	*20*	46.9	*22*	46.9	*22*
26	41.7	*17*	41.5	*16*	41.5	*16*
27	28.6	*7*	25.5	*6*	25.5	*6*
28	44.6	*18*	41.0	*15*	41.0	*15*
29	92.8	*38*	86.9	*38*	86.9	*38*
30	58.7	*23*	30.5	*10*	30.5	*11*
31	60.9	*26*	50.9	*25*	50.9	*25*
32	90.1	*37*	80.6	*36*	80.6	*36*
33	37.7	*13*	26.0	*7*	26.0	*7*
34	32.4	*9*	28.4	*8*	28.4	*9*
35	63.0	*29*	52.0	*26*	52.0	*26*
36	69.6	*30*	55.8	*27*	55.8	*27*
37	70.8	*31*	57.0	*28*	57.0	*28*
38	60.4	*25*	48.1	*23*	48.1	*23*
39	62.2	*28*	48.1	*24*	48.1	*24*

[a] Species that decarboxylates at this level of theory; the reported value was estimated using the gas-water correlation equation (see Table 4.S5; [b] Since PFOA **24** is the 0.0 value, all gas values are estimated relative to it; [c] This anion could only be optimized in water; the octanol-water correlation was used to estimate this value.

Table 4.S3d. Relative G values (in kJ/mol at 298.15 K) and stability order of the 39 anionic PFOA isomers calculated at the PM6 level of theory in the gas phase, octanol and water.

PFOA **n**	**Gas phase**		**n-Octanol**		**Water**	
n	**ΔG**	***Order***	**ΔG**	***Order***	**ΔG**	***Order***
1	65.6 [a]	*10*	57.6	*10*	58.4	*11*
2	45.2 [a]	*6*	39.7	*6*	38.5	*7*
3	40.4	*4*	37.8	*4*	32.1	*5*
4	65.4	*9*	68.1	*14*	68.2	*17*
5	0.0 [a,b]	*1*	0.0	*1*	0.0	*1*
6	47.1 [a]	*7*	41.4	*7*	40.9	*8*
7	95.8	*22*	93.1	*26*	91.8	*31*
8	89.4	*19*	80.8	*20*	69.4	*19*
9	88.1	*16*	88.6	*23*	86.7	*27*
10	106.1	*28*	98.4	*30*	90.6	*30*
11	114.4	*30*	109.3	*35*	103.4	*37*
12	43.4 [a]	*5*	38.1	*5*	37.7	*6*
13	25.0 [a]	*2*	22.0	*2*	21.6	*2*
14	66.7	*11*	55.2	*9*	50.9	*9*
15	106.2	*29*	98.0	*29*	81.3	*25*
16	47.4	*8*	41.7	*8*	30.7	*4*
17	82.2	*14*	76.4	*16*	73.9	*20*
18	89.2	*18*	75.7	*15*	67.3	*15*
19	96.7	*25*	95.6	*28*	88.3	*28*
20	95.9	*23*	88.8	*24*	80.1	*24*
21	96.6	*24*	92.4	*25*	76.7	*23*
22	120.5	*33*	113.0	*37*	105.9	*38*
23	140.5	*39*	113.9	*39*	111.0	*39*
24	29.6 [a]	*3*	26.0	*3*	21.7	*3*
25	90.2	*20*	81.1	*21*	69.2	*18*
26	88.3	*17*	78.6	*18*	67.4	*16*
27	81.0	*13*	67.3	*13*	61.5	*13*
28	75.8	*12*	66.4	*12*	58.8	*12*
29	129.3	*36*	113.5	*38*	103.4	*36*
30	102.0	*27*	82.9	*22*	75.0	*22*
31	97.4	*26*	77.8	*17*	66.6	*14*
32	133.8	*38*	112.8	*36*	100.0	*35*
33	85.3	*15*	63.3	*11*	51.3	*10*
34	95.4	*21*	80.3	*19*	74.3	*21*
35	114.8	*31*	99.3	*31*	89.0	*29*
36	127.0	*34*	102.6	*32*	94.6	*32*
37	129.1	*35*	106.1	*33*	95.0	*33*
38	119.2	*32*	94.1	*27*	86.0	*26*
39	132.1	*37*	107.5	*34*	99.4	*34*

[a] Species that decarboxylates at this level of theory; the reported value was estimated using the gas-octanol correlation equation (see Table 4.S5); [b] Since PFOA **5** is the 0.0 value, all the gas values are estimated relative to it.

Table 4.S3e. Relative G values (in kJ/mol at 298.15 K) and stability order of the 39 anionic PFOA isomers calculated at the LC-ωPBE/6-31++G(d,p) level of theory in the gas phase, octanol and water.

PFOA **n**	**Gas phase**		**n-Octanol**		**Water**	
n	**ΔG**	***Order***	**ΔG**	***Order***	**ΔG**	***Order***
1	41.2 [a]	*16*	42.9	*16*	39.0	*14*
2	50.3 [a]	*21*	49.9	*24*	47.7	*19*
3	13.8	*3*	22.9	*5*	23.3	*5*
4	39.1	*15*	47.9	*20*	47.4	*18*
5	30.4 [a]	*7*	32.1	*9*	28.8	*7*
6	27.3 [a]	*5*	29.0	*7*	25.9	*6*
7	46.0	*19*	49.5	*23*	50.7	*24*
8	37.3	*12*	38.1	*13*	34.6	*11*
9	63.4	*28*	64.6	*31*	66.3	*31*
10	78.4	*33*	71.7	*33*	73.6	*33*
11	111.9	*39*	106.3	*39*	109.1	*39*
12	37.8 [a]	*13*	36.9	*12*	35.8	*13*
13	11.9 [a]	*2*	14.9	*2*	11.2	*2*
14	37.9	*14*	45.7	*18*	45.3	*17*
15	61.5	*26*	60.9	*30*	61.8	*30*
16	18.1	*4*	15.7	*3*	15.5	*3*
17	78.5	*34*	75.7	*35*	77.8	*35*
18	76.4	*32*	66.2	*32*	68.3	*32*
19	53.4	*22*	56.3	*26*	55.4	*26*
20	33.1	*10*	36.8	*11*	34.9	*12*
21	31.2	*8*	33.3	*10*	31.9	*10*
22	83.8	*35*	75.6	*34*	77.3	*34*
23	91.2	*37*	82.1	*37*	83.4	*36*
24	0.0 [a,b]	*1*	0.0	*1*	0.0	*1*
25	48.2	*20*	47.0	*19*	47.9	*20*
26	42.1	*17*	40.8	*14*	39.8	*15*
27	30.2	*6*	28.4	*6*	29.4	*8*
28	43.7	*18*	42.5	*15*	40.0	*16*
29	96.9	*38*	91.0	*38*	94.1	*38*
30	56.5	*23*	47.9	*21*	48.1	*22*
31	61.9	*27*	51.0	*25*	52.3	*25*
32	90.6	*36*	82.0	*36*	83.6	*37*
33	33.1	*11*	19.7	*4*	22.5	*4*
34	33.0	*9*	31.9	*8*	30.3	*9*
35	63.4	*29*	57.6	*27*	58.0	*27*
36	67.5	*30*	59.6	*29*	58.4	*28*
37	71.2	*31*	58.9	*28*	59.4	*29*
38	58.9	*24*	45.4	*17*	49.1	*23*
39	60.6	*25*	48.8	*22*	48.0	*21*

[a] The reported value was estimated using the gas-octanol correlation equation (see Table 4.S5); [b] Since PFOA **24** is the 0.0 value, all gas values are estimated relative to it.

Table 4.S4. Differences in G values (in kJ/mol) for the neutral and anionic PFOA isomers between the three environments calculated at the M06-2X/6-311++(3df,3p) level of theory.

PFOA **n**	**Neutrals**			**Anions**		
n	**Gas-Octanol**	**Gas-Water**	**Octanol-Water**	**Gas-Octanol**	**Gas-Water**	**Octanol-Water**
1	17.7	-2.0	-19.7	182.3	186.7	4.4
2	14.6	-4.0	-18.6	182.5	187.5	5.0
3	15.4	-3.4	-18.8	173.0	179.5	6.5
4	15.0	-4.2	-19.1	173.9	181.6	7.7
5	14.0	-3.3	-17.3	178.9	185.9	7.0
6	15.8	-3.3	-19.1	181.4	186.5	5.0
7	14.5	-3.3	-17.8	179.0	186.9	7.9
8	14.7	-4.4	-19.1	179.9	186.7	6.8
9	14.7	-3.1	-17.8	178.6	188.0	9.4
10	15.2	-2.3	-17.5	186.1	196.5	10.3
11	14.0	-3.1	-17.0	189.7	200.7	11.0
12	16.3	-3.5	-19.7	181.3	187.6	6.3
13	14.6	-4.1	-18.7	179.5	185.5	6.0
14	12.7	-6.7	-19.4	179.3	188.1	8.8
15	16.7	-0.2	-16.9	182.6	191.7	9.1
16	14.9	-3.0	-18.0	183.9	193.4	9.5
17	14.1	-2.4	-16.5	183.5	193.9	10.4
18	16.1	-1.9	-17.9	190.6	201.0	10.4
19	14.6	-3.9	-18.5	181.1	188.7	7.5
20	15.4	-5.2	-20.6	180.0	184.2	4.3
21	16.2	-4.0	-20.2	179.6	187.5	7.8
22	16.7	-2.1	-18.8	186.8	197.4	10.6
23	15.6	-3.4	-18.9	187.6	197.0	9.4
24	15.9	-3.8	-19.7	178.9	185.8	6.9
25	15.8	-2.3	-18.1	182.6	191.4	8.9
26	15.9	-3.7	-19.6	182.9	190.9	8.0
27	15.6	-3.4	-19.0	184.0	192.4	8.3
28	14.4	-3.2	-17.6	187.2	197.2	10.0
29	15.6	-1.7	-17.2	186.5	197.2	10.7
30	15.8	-1.4	-17.2	192.2	201.4	9.2
31	15.2	-2.6	-17.9	191.5	201.1	9.6
32	13.5	-4.0	-17.6	191.3	199.8	8.5
33	16.3	0.6	-15.7	190.3	200.4	10.1
34	20.2	1.2	-19.0	184.8	189.8	5.0
35	15.8	-3.2	-19.0	191.7	200.0	8.2
36	14.8	-3.1	-18.0	188.0	195.6	7.6
37	14.9	-3.7	-18.6	194.2	203.8	9.6
38	15.3	-2.8	-18.1	193.5	200.9	7.4
39	14.4	-3.1	-17.5	192.7	200.8	8.1
MAD[a]	15.4	3.1	18.4	184.4	192.6	8.1

[a] Mean absolute differences.

Table 4.S4a. Differences in G values (in kJ/mol) for the neutral and anionic PFOA isomers between the three environments calculated at the M06-2X/6-31++(d,p) level of theory.

PFOA **n**	**Neutrals**			**Anions**		
n	**Gas-Octanol**	**Gas-Water**	**Octanol-Water**	**Gas-Octanol**	**Gas-Water**	**Octanol-Water**
1	19.3	0.5	-18.8	183.0	186.8	3.8
2	18.9	-2.7	-21.6	183.6	188.9	5.3
3	16.3	-1.1	-17.4	174.0	181.9	7.9
4	17.1	-2.1	-19.2	174.8	182.7	7.9
5	15.8	-1.0	-16.8	180.1	187.3	7.2
6	16.9	-1.4	-18.4	182.2	187.8	5.6
7	16.6	-1.7	-18.3	179.6	187.9	8.3
8	17.1	-1.4	-18.5	181.0	188.4	7.4
9	16.7	0.5	-16.2	179.3	189.3	9.9
10	17.5	1.0	-16.6	187.3	198.1	10.9
11	16.5	0.0	-16.5	190.4	202.1	11.7
12	16.7	-0.8	-17.5	182.3	189.0	6.7
13	16.3	-1.9	-18.2	180.5	187.3	6.8
14	16.2	-2.1	-18.3	178.1	185.5	7.4
15	19.0	2.7	-16.3	183.0	192.2	9.2
16	17.0	-0.7	-17.7	184.9	194.2	9.4
17	16.1	0.3	-15.8	183.8	195.4	11.6
18	18.1	1.1	-17.0	192.6	203.5	11.0
19	15.9	-2.6	-18.4	181.4	189.3	7.8
20	16.9	-2.7	-19.5	180.4	185.3	4.9
21	18.9	-1.1	-20.0	180.5	187.7	7.3
22	19.9	1.8	-18.1	184.7	196.1	11.4
23	18.1	-0.7	-18.8	189.0	198.6	9.6
24	17.3	-2.2	-19.4	179.8	188.8	9.0
25	18.5	0.6	-17.9	183.7	192.6	8.9
26	18.9	-0.6	-19.5	184.4	192.1	7.7
27	18.3	-0.2	-18.5	184.3	194.1	9.8
28	15.9	-1.8	-17.7	188.2	197.5	9.3
29	17.6	0.6	-17.1	187.9	198.8	10.9
30	18.0	1.8	-16.2	192.9	203.6	10.8
31	16.8	-0.7	-17.4	193.8	203.3	9.5
32	15.9	-1.0	-16.9	191.0	200.8	9.8
33	19.0	1.9	-17.1	191.9	201.7	9.8
34	20.3	-1.6	-21.9	186.0	193.8	7.9
35	17.9	0.3	-17.6	192.3	200.8	8.5
36	17.8	0.7	-17.1	192.9	201.1	8.3
37	16.8	-1.5	-18.3	194.7	205.2	10.5
38	19.0	1.5	-17.5	194.3	204.0	9.7
39	17.2	0.2	-17.0	197.0	203.9	6.9
MAD[a]	17.5	1.3	18.0	185.4	194.0	8.6

[a] Mean absolute differences.

Table 4.S4b. Differences in G values (in kJ/mol) for the neutral and anionic PFOA isomers between the three environments calculated at the B3LYP/6-31++G(d,p) (PCM/SMD) level of theory.

PFOA **n**	**Neutrals**						**Anions**					
	Gas-Octanol		**Gas-Water**		**Octanol-Water**		**Gas-Octanol**		**Gas-Water**		**Octanol-Water**	
	PCM	**SMD**	**PCM**	**SMD**	**PCM**	**SMD**	**PCM**	**SMD**	**PCM**	**SMD**	**PCM**	**SMD**
1	64.6	17.0	80.4	-3.4	15.7	-20.3	214.9	181.4	240.0	183.3	25.1	1.9
2	64.3	14.0	79.3	-5.4	15.0	-19.4	215.0	181.6	240.0	185.3	24.9	3.7
3	62.0	15.8	77.5	-2.8	15.5	-18.7	199.9	170.8	226.0	176.6	26.2	5.8
4	64.7	17.1	82.5	-1.1	17.8	-18.3	200.7	172.6	228.0	176.8	27.3	4.2
5	61.1	15.7	75.9	-1.6	14.8	-17.3	215.0	181.5	240.1	186.1	25.0	4.6
6	65.2	16.2	80.4	-3.0	15.3	-19.2	213.8	180.7	239.9	185.3	26.2	4.7
7	65.4	15.7	80.5	-1.3	15.1	-17.1	205.6	175.0	233.9	182.2	28.2	7.2
8	72.9	16.2	95.4	-2.3	22.5	-18.5	217.4	177.0	245.7	182.5	28.3	5.5
9	67.1	16.5	82.9	0.4	15.8	-16.1	213.3	177.0	239.0	186.2	25.7	9.2
10	64.3	18.3	80.0	0.6	15.7	-17.8	214.4	183.9	242.2	192.2	27.8	8.2
11	68.2	21.5	86.4	1.3	18.2	-20.3	218.3	181.2	250.2	191.8	31.9	10.6
12	63.8	13.5	79.2	-4.0	15.4	-17.5	214.6	181.2	240.6	186.8	26.0	5.6
13	64.9	16.2	82.6	-1.4	17.7	-17.6	213.5	180.7	241.1	185.3	27.6	4.7
14	61.4	14.0	76.1	-4.1	14.7	-18.1	202.5	171.7	228.4	179.5	25.9	7.9
15	70.0	16.9	86.2	-0.6	16.1	-17.5	209.6	178.8	236.9	186.5	27.3	7.7
16	64.0	16.7	79.3	-0.7	15.3	-17.3	209.4	178.6	235.8	185.8	26.4	7.2
17	64.7	16.2	79.9	1.7	15.3	-14.5	211.1	179.4	239.4	192.2	28.3	12.7
18	65.0	17.5	79.8	0.3	14.8	-17.2	216.8	185.2	245.1	195.4	28.3	10.2
19	67.8	17.2	84.3	-1.2	16.5	-18.3	209.5	175.0	236.6	181.9	27.1	6.9
20	68.2	19.4	84.9	-0.4	16.7	-19.9	208.6	175.4	236.5	179.8	27.9	4.4
21	69.5	18.7	86.5	2.1	17.0	-16.6	208.6	177.6	237.4	184.9	28.9	7.3
22	66.9	15.5	84.9	-2.5	18.1	-18.0	218.4	184.5	246.7	191.4	28.3	6.8
23	73.8	18.6	92.6	0.7	18.8	-17.9	220.4	182.5	250.9	192.1	30.4	9.6
24	69.1	17.1	85.3	0.1	16.2	-17.0	212.8	180.0	239.6	185.7	26.8	5.7
25	65.8	20.0	83.6	-2.6	17.9	-22.6	212.7	179.5	240.0	186.7	27.3	7.1
26	69.1	17.3	86.0	0.9	16.9	-16.4	212.4	178.2	240.8	186.2	28.5	8.0
27	68.4	17.2	85.0	-2.0	16.5	-19.2	212.0	180.8	240.6	187.6	28.7	6.8
28	65.1	18.2	80.9	-0.2	15.8	-18.3	212.9	180.2	240.8	188.7	27.9	8.6
29	73.3	18.2	87.8	1.8	14.4	-16.4	222.9	184.7	251.1	197.0	28.2	12.3
30	67.8	18.2	83.6	-0.4	15.8	-18.6	220.3	186.9	248.8	194.5	28.5	7.7
31	65.1	16.7	81.5	0.8	16.4	-15.9	218.7	187.9	247.2	195.9	28.5	8.1
32	69.8	17.1	87.5	0.4	17.7	-16.7	221.0	186.0	251.0	195.1	29.9	9.1
33	70.3	17.0	83.0	-1.0	12.6	-18.1	221.9	189.2	249.4	198.4	27.5	9.2
34	69.7	16.2	86.0	-5.1	16.3	-21.3	218.8	184.0	246.1	188.7	27.3	4.8
35	70.4	20.0	89.0	-4.1	18.6	-24.1	221.2	185.4	252.2	191.6	31.1	6.1
36	69.0	17.7	85.9	0.7	16.9	-17.0	222.3	188.6	251.9	195.6	29.7	7.0
37	71.4	17.8	87.7	-0.4	16.3	-18.2	224.7	190.5	256.1	198.9	31.4	8.4
38	72.4	18.1	89.7	1.5	17.3	-16.6	225.6	192.1	254.6	197.7	29.0	5.6
39	72.9	20.8	90.4	0.3	17.5	-20.5	226.1	191.7	257.4	201.2	31.4	9.6
MAD[a]	67.4	17.2	83.9	1.7	16.4	18.2	214.8	181.5	242.8	188.7	28.0	7.2

[a] Mean absolute differences.

Table 4.S4c. Differences in G values (in kJ/mol) for the neutral and anionic PFOA isomers between the three environments calculated at the B97D/6-31++G(d,p) level of theory.

PFOA **n**	**Neutrals**			**Anions**		
n	**Gas-Octanol**	**Gas-Water**	**Octanol-Water**	**Gas-Octanol**	**Gas-Water**	**Octanol-Water**
1	14.7	-4.7	-19.4	181.1	181.5	0.3
2	13.3	-6.7	-20.0	181.4	181.5	0.1
3	13.0	-5.4	-18.5	165.7	170.3	4.6
4	14.9	-3.0	-17.8	164.6	169.9	5.3
5	14.6	-2.7	-17.3	176.7	179.3	2.6
6	14.8	-4.5	-19.4	176.9	177.0	0.1
7	13.9	-3.5	-17.4	168.6	174.0	5.5
8	17.0	-1.9	-18.9	169.6	177.2	7.6
9	15.3	-3.3	-18.6	171.7	177.5	5.8
10	15.9	-2.0	-17.9	176.3	184.6	8.3
11	14.5	-1.8	-16.3	181.0	188.9	7.9
12	13.0	-4.7	-17.8	174.6	179.1	4.4
13	14.3	-4.1	-18.4	175.7	176.4	0.7
14	11.8	-6.5	-18.3	167.8	176.0	8.3
15	15.8	-1.0	-16.8	171.6	179.8	8.2
16	14.5	-3.8	-18.3	169.3	175.3	6.0
17	15.4	-2.9	-18.3	175.4	183.4	8.0
18	16.5	-1.8	-18.3	178.9	188.4	9.5
19	13.9	-3.7	-17.6	153.4	162.8	9.5
20	15.5	-6.5	-22.0	168.8	173.0	4.3
21	15.6	-4.8	-20.4	167.5	173.2	5.7
22	12.5	-6.7	-19.1	179.1	186.1	6.9
23	16.8	0.0	-16.8	179.2	187.4	8.2
24	13.6	-4.1	-17.7	171.2	174.4	3.2
25	16.3	-0.6	-16.9	173.9	179.4	5.5
26	14.7	-3.6	-18.3	171.3	177.5	6.2
27	16.9	-3.4	-20.3	174.3	179.4	5.1
28	14.5	-4.6	-19.1	174.8	181.5	6.7
29	16.1	-0.3	-16.4	177.1	187.5	10.3
30	16.5	-3.5	-20.0	199.4	187.5	7.3
31	14.4	-3.0	-17.4	181.1	188.6	7.5
32	16.4	-1.8	-18.2	180.7	187.0	6.3
33	14.4	-3.3	-17.7	182.9	191.8	8.9
34	15.3	-6.7	-22.0	175.2	178.6	3.3
35	15.8	-2.8	-18.5	182.2	188.4	6.2
36	15.2	-3.8	-19.1	185.0	190.6	5.6
37	15.5	-2.3	-17.8	185.1	191.3	6.2
38	14.8	-5.1	-19.9	183.5	189.4	5.9
39	17.7	-3.8	-21.5	185.3	191.6	6.2
MAD[a]	15.0	3.6	18.6	175.4	181.2	5.8

[a] Mean absolute differences.

Table 4.S4d. Differences in G values (in kJ/mol) for the neutral and anionic PFOA isomers between the three environments calculated at the PM6 level of theory.

PFOA **n**	**Neutrals**			**Anions**		
n	**Gas-Octanol**	**Gas-Water**	**Octanol-Water**	**Gas-Octanol**	**Gas-Water**	**Octanol-Water**
1	10.6	-7.2	-17.8	187.9	199.5	11.6
2	11.5	-7.0	-18.6	185.4	198.9	13.5
3	7.4	-8.7	-16.1	182.4	200.5	18.1
4	8.2	-10.2	-18.4	177.2	189.4	12.2
5	13.2	-6.7	-19.9	179.9	192.2	12.3
6	12.7	-4.5	-17.1	185.6	198.5	12.9
7	11.3	-4.8	-16.1	182.6	196.3	13.7
8	8.2	-9.0	-17.2	188.5	212.3	23.8
9	11.1	-5.8	-16.9	179.4	193.7	14.2
10	13.7	-1.2	-14.9	187.5	207.7	20.2
11	9.4	-8.2	-17.6	185.0	203.2	18.2
12	13.4	-3.9	-17.3	185.2	197.9	12.7
13	14.0	-3.2	-17.2	182.9	195.7	12.8
14	12.1	-6.9	-19.0	191.4	208.0	16.6
15	11.1	-6.6	-17.6	188.2	217.2	29.0
16	11.8	-2.3	-14.1	185.7	208.9	23.3
17	9.5	-7.9	-17.4	185.7	200.5	14.8
18	13.7	-7.3	-21.0	193.4	214.1	20.8
19	8.3	-9.5	-17.8	181.0	200.6	19.6
20	8.0	-10.4	-18.4	187.0	208.0	21.0
21	7.2	-11.7	-18.9	184.1	212.2	28.0
22	10.8	-10.0	-20.8	187.3	206.8	19.5
23	7.6	-5.7	-13.4	206.5	221.7	15.2
24	10.8	-7.9	-18.8	183.5	200.1	16.6
25	11.0	-9.1	-20.0	189.0	213.2	24.2
26	9.1	-6.4	-15.5	189.5	213.1	23.6
27	11.2	-7.8	-19.0	193.6	211.8	18.2
28	9.7	-8.2	-18.0	189.3	209.2	19.9
29	10.1	-7.3	-17.4	195.7	218.1	22.4
30	17.9	-2.0	-19.9	199.0	219.2	20.2
31	12.9	-3.3	-16.1	199.6	223.1	23.5
32	8.4	-10.0	-18.5	200.9	226.0	25.1
33	13.0	-7.0	-20.0	201.9	226.1	24.3
34	8.1	-8.5	-16.7	195.0	213.4	18.4
35	6.8	-11.8	-18.7	195.5	218.0	22.6
36	9.2	-8.9	-18.1	204.2	224.6	20.4
37	7.1	-11.1	-18.2	202.9	226.3	23.4
38	7.0	-9.8	-16.8	205.0	225.4	20.4
39	6.7	-13.7	-20.3	204.5	224.9	20.4
MAD[a]	10.4	7.5	17.8	190.5	209.6	19.2

[a] Mean absolute differences.

Table 4.S4e. Differences in G values (in kJ/mol) for the neutral and anionic PFOA isomers in the three environments calculated at the LC-ωPBE/6-31++G(d,p) level of theory.

PFOA **n**	**Neutrals**			**Anions**		
n	**Gas-Octanol**	**Gas-Water**	**Octanol-Water**	**Gas-Octanol**	**Gas-Water**	**Octanol-Water**
1	18.7	-1.0	-19.7	187.2	191.7	4.5
2	14.9	-4.4	-19.3	187.7	193.9	6.2
3	15.8	-2.6	-18.4	175.5	184.2	8.7
4	17.7	-0.1	-17.8	176.8	184.6	7.8
5	15.5	-1.6	-17.1	186.6	191.6	5.0
6	16.6	-2.0	-18.6	186.5	191.6	5.2
7	15.5	-1.0	-16.5	180.4	189.9	9.5
8	17.7	-1.1	-18.9	187.8	192.6	4.8
9	16.1	-1.1	-17.1	182.1	192.2	10.1
10	17.3	-0.3	-17.6	189.8	200.0	10.3
11	19.6	3.0	-16.6	187.8	199.0	11.2
12	13.4	-4.5	-17.9	187.0	194.3	7.3
13	15.3	-3.5	-18.8	185.6	190.3	4.7
14	15.3	-1.5	-16.8	177.6	185.5	8.0
15	17.8	1.4	-16.5	184.7	193.9	9.2
16	16.9	-0.7	-17.6	187.6	195.7	8.1
17	14.2	-2.1	-16.4	185.8	196.2	10.4
18	17.2	-0.3	-17.5	193.2	203.6	10.4
19	17.2	0.3	-16.9	183.1	190.5	7.5
20	19.3	-2.8	-22.1	183.2	189.7	6.5
21	19.4	-1.8	-21.2	184.3	191.3	6.9
22	19.0	0.2	-18.8	191.5	201.5	10.0
23	17.3	0.0	-17.3	192.9	202.5	9.6
24	17.2	-1.7	-18.9	185.0	193.4	8.4
25	18.7	-0.6	-19.3	185.3	194.6	9.3
26	16.8	-1.9	-18.7	187.3	194.7	7.4
27	16.9	-1.3	-18.2	185.9	195.2	9.3
28	15.6	-0.8	-16.3	188.8	199.0	10.2
29	17.1	-0.3	-17.4	187.9	199.3	11.4
30	17.9	2.2	-15.7	193.4	201.9	8.5
31	16.1	-0.9	-17.1	194.6	204.3	9.7
32	15.8	-0.9	-16.7	192.0	201.9	9.9
33	18.2	-2.2	-20.4	195.6	206.8	11.2
34	18.9	-1.1	-20.0	187.8	194.5	6.8
35	18.6	-0.6	-19.2	190.4	199.2	8.8
36	15.8	-1.1	-16.9	194.1	201.3	7.2
37	17.6	1.7	-15.9	196.9	205.7	8.8
38	16.6	-0.7	-17.3	194.9	206.9	12.0
39	16.6	1.4	-15.2	197.7	205.2	7.5
MAD[a]	17.0	1.5	17.9	187.7	196.2	8.4

[a] Mean absolute differences.

Table 4.S5. Various correlations between the calculated G values of neutral and anionic PFOA isomers at different levels of theory.[a]

		Neutrals-Anions [b]			Neutrals [c]			Anions [c]		
		Gas phase	Octanol	Water	Gas-Octanol	Gas-Water	Octanol-Water	Gas-Octanol	Gas-Water	Octanol-Water
M06-2X	R^2	0.908	0.961	0.961	0.997	0.996	0.998	0.975	0.966	0.996
	A	0.769	0.902	0.926	0.993	1.003	1.009	1.120	1.156	1.035
	B	4.255	2.806	1.631	-0.126	0.587	0.753	0.000	-0.323	-0.409
M06-2X[d]	R^2	0.892	0.957	0.963	0.997	0.996	0.996	0.968	0.959	0.995
	A	0.758	0.893	0.917	1.004	1.020	1.015	1.125	1.166	1.039
	B	4.498	2.334	-0.477	0.170	0.857	0.753	0.000	-2.288	-2.152
B3LYP (PCM)	R^2	0.883	0.963	0.976	0.973	0.955	0.994	0.924	0.896	0.993
	A	0.821	0.941	0.971	0.976	0.962	0.991	1.044	1.048	1.016
	B	3.937	1.864	1.468	-0.634	0.192	0.583	0.000	1.103	0.510
B3LYP (SMD)	R^2	0.881	0.947	0.961	0.993	0.991	0.992	0.949	0.934	0.992
	A	0.818	0.892	0.943	1.005	1.022	1.014	1.033	1.094	1.064
	B	3.573	1.301	1.519	-0.105	-2.010	-1.751	0.000	-1.211	-1.365
B97D	R^2	0.883	0.943	0.956	0.996	0.994	0.995	0.929	0.935	0.990
	A	0.755	0.854	0.895	1.013	1.043	1.028	1.071	1.152	1.068
	B	3.244	0.284	1.551	0.890	-1.214	-2.022	0.827	0.000	-0.377
PM6	R^2	0.851	0.933	0.965	0.989	0.985	0.994	0.956	0.922	0.978
	A	0.592	0.759	0.824	0.946	0.952	1.004	1.138	1.203	1.064
	B	0.136	-3.547	-4.920	0.152	1.772	1.777	0.000	3.290	2.368
LC-wPBE	R^2	0.924	0.982	0.988	0.995	0.996	0.996	0.958	0.950	0.995
	A	0.817	0.905	0.921	1.003	1.038	1.033	1.056	1.104	1.048
	B	4.823	2.936	1.228	-0.269	-1.029	-0.636	0.000	-2.417	-2.376

[a] R^2 is the correlation coefficient, A and B are the curve fitting parameters; [b] $G_{neutral} = A \times G_{anion} + B$; [c] $G_{environment1} = A \times G_{environment2} + B$;

[d] Using the 6-31++G(d,p) basis set.

Table 4.S6. Relative G differences (M06-2X and PM6, in kJ/mol) for neutral and anionic PFOAs in different environments.

PFOA **n**	**Neutral PFOAs**			**Anionic PFOAs**		
n	**gas**	**octanol**	**Water**	**gas**	**octanol**	**water**
1	-14.0	-18.4	-16.2	-34.2	-29.5	-27.7
2	-4.1	-4.5	-4.1	-11.2	-9.4	-6.2
3	-10.5	-15.8	-12.8	-40.3	-31.9	-25.7
4	-7.5	-11.6	-10.5	-32.7	-30.3	-31.1
5	0.4	2.3	0.0	0.0	0.0	0.0
6	-11.1	-11.5	-9.3	-23.4	-20.2	-17.7
7	-23.7	-24.2	-22.2	-50.0	-47.4	-47.0
8	-10.7	-14.5	-12.3	-46.7	-39.1	-27.5
9	-18.3	-19.2	-18.1	-24.2	-24.3	-24.8
10	-14.3	-13.1	-10.2	-37.0	-36.6	-32.1
11	11.6	9.7	9.5	0.4	-5.2	-3.4
12	-6.1	-6.3	-3.5	-21.0	-18.1	-17.0
13	-8.5	-6.4	-4.6	-19.1	-16.7	-15.3
14	2.7	4.7	5.5	-39.9	-28.7	-26.3
15	6.0	3.0	2.6	-48.5	-43.9	-29.3
16	-15.1	-15.5	-11.3	-35.7	-34.9	-26.5
17	0.7	-1.3	-1.9	-21.2	-19.9	-20.9
18	-8.3	-7.9	-10.7	-29.6	-27.8	-22.8
19	-4.1	-7.6	-6.6	-38.6	-39.7	-33.0
20	-10.7	-15.4	-12.9	-49.0	-43.0	-31.6
21	-9.4	-15.8	-14.2	-47.9	-44.4	-29.5
22	-0.5	-3.7	-5.4	-29.8	-30.3	-26.7
23	-3.4	-8.7	-2.8	-42.3	-24.4	-24.0
24	-12.3	-14.7	-13.5	-29.5	-26.0	-21.6
25	-9.8	-12.0	-13.5	-37.2	-31.7	-21.7
26	-10.3	-14.4	-9.9	-39.6	-33.9	-23.7
27	-9.7	-11.5	-11.1	-40.3	-31.7	-27.2
28	-7.2	-9.4	-9.2	-32.7	-31.5	-27.0
29	-6.7	-9.5	-9.3	-35.6	-27.4	-21.1
30	-14.2	-9.4	-11.7	-39.5	-33.7	-28.0
31	-11.9	-11.6	-9.6	-39.6	-32.5	-23.9
32	-4.9	-7.4	-7.9	-41.5	-32.8	-21.6
33	-15.9	-16.6	-20.6	-50.8	-40.2	-31.4
34	-7.1	-16.4	-13.8	-46.2	-37.0	-29.0
35	-2.8	-9.1	-8.4	-36.7	-34.0	-25.0
36	-9.2	-12.1	-11.9	-48.8	-33.5	-26.1
37	-7.1	-12.3	-11.5	-45.0	-37.3	-28.8
38	-6.1	-11.8	-10.1	-46.0	-35.4	-27.8
39	-6.0	-11.1	-13.6	-49.4	-38.6	-31.6
MAD [a]	8.8	11.0	10.1	35.4	30.3	24.7

[a] Mean absolute differences.

Table 4.S6a. Relative G differences (M06-2X and LC-ωPBE, in kJ/mol) for neutral and anionic PFOAs in different environments.

PFOA **n**	**Neutral PFOAs**			**Anionic PFOAs**		
n	**gas**	**octanol**	**Water**	**gas**	**octanol**	**water**
1	-9.1	-9.4	-10.1	-9.8	-11.0	-12.2
2	-13.3	-14.3	-15.8	-16.4	-17.4	-17.5
3	-15.7	-16.6	-17.0	-13.7	-17.4	-16.5
4	-10.9	-9.5	-8.9	-6.4	-9.6	-10.9
5	-31.0	-30.8	-31.3	-30.4	-28.8	-32.1
6	-3.9	-4.5	-4.7	-3.6	-4.7	-5.9
7	-5.3	-5.6	-5.0	-0.3	-5.0	-4.8
8	3.7	5.4	5.0	5.4	7.2	3.8
9	-3.2	-3.2	-3.3	0.6	-2.0	-2.7
10	-13.2	-12.4	-13.3	-9.3	-11.8	-13.2
11	-6.5	-2.2	-2.4	2.9	-5.1	-6.3
12	-12.3	-16.5	-15.3	-15.4	-15.8	-16.2
13	-7.7	-8.3	-9.1	-6.0	-6.0	-8.7
14	-6.8	-5.5	-3.6	-11.0	-18.9	-21.1
15	3.4	3.2	2.9	-3.8	-7.7	-9.0
16	-10.8	-10.2	-10.6	-6.4	-8.7	-11.5
17	-20.4	-21.6	-22.2	-17.5	-21.3	-22.7
18	-22.0	-22.2	-22.5	-16.8	-20.4	-21.7
19	-0.2	1.1	2.0	4.7	0.5	-0.9
20	11.1	13.6	11.4	13.8	10.9	11.8
21	14.6	16.4	14.7	17.6	16.1	13.9
22	4.2	5.2	4.4	6.9	5.5	3.6
23	3.2	3.6	4.5	6.9	6.1	4.9
24	0.0	0.0	0.1	0.0	0.0	0.1
25	1.9	3.4	1.5	4.8	1.5	0.5
26	2.6	2.2	2.4	6.6	4.9	2.9
27	4.3	4.3	4.4	10.5	6.3	5.9
28	-7.1	-10.8	-6.7	-0.6	-5.2	-10.7
29	-8.6	-8.5	-9.3	-3.3	-8.0	-8.7
30	-0.1	0.7	1.5	6.1	1.2	-0.9
31	-8.5	-8.9	-8.8	-4.0	-7.0	-8.3
32	-5.9	-5.0	-4.9	1.8	-3.6	-3.6
33	-3.3	-2.7	-8.1	1.4	0.6	0.3
34	17.3	14.8	13.0	16.1	13.0	13.4
35	8.1	9.5	8.7	14.7	7.3	6.5
36	6.0	5.6	5.9	10.7	10.7	8.9
37	6.2	7.6	9.6	12.9	9.4	7.3
38	7.4	7.4	7.5	14.3	9.6	12.8
39	16.9	17.8	19.3	22.1	21.0	19.0
MAD [a]	8.6	9.0	9.0	9.1	9.4	9.8

[a] Mean absolute differences.

Table 4.S6b. Relative G differences (M06-2X and B3LYP, in kJ/mol) for neutral and anionic PFOAs in different environments.

PFOA **n**	**Neutral PFOAs**			**Anionic PFOAs**		
n	**gas**	**octanol**	**Water**	**gas**	**octanol**	**water**
1	-11.2	-13.2	-16.3	-13.4	-15.3	-16.6
2	-15.7	-17.6	-21.0	-15.4	-17.4	-17.4
3	-21.2	-22.0	-24.4	-20.7	-24.1	-23.5
4	-8.8	-7.8	-9.5	-5.3	-7.6	-9.8
5	-45.2	-44.7	-47.2	-47.2	-45.7	-46.8
6	3.7	2.9	0.3	2.6	0.8	1.7
7	-0.5	-0.5	-2.3	4.6	-0.4	0.2
8	11.5	11.7	9.8	13.1	9.2	9.1
9	3.3	3.9	3.0	5.6	3.0	4.1
10	-12.3	-10.3	-13.2	-8.7	-12.0	-12.8
11	2.9	9.2	3.5	10.1	0.6	1.4
12	-15.0	-19.0	-19.3	-16.8	-17.9	-17.4
13	-11.2	-10.8	-12.2	-15.1	-15.0	-15.1
14	-8.3	-8.2	-9.4	-16.9	-25.6	-25.2
15	-5.5	-6.5	-9.6	-0.8	-5.7	-5.8
16	-14.6	-14.1	-16.0	-9.5	-15.8	-16.9
17	-23.5	-22.7	-23.2	-21.5	-26.6	-23.0
18	-24.4	-24.2	-26.0	-19.3	-25.9	-24.8
19	6.5	7.9	5.5	13.1	5.9	6.6
20	24.9	27.7	25.8	27.0	21.3	22.7
21	25.8	27.0	28.1	29.5	26.4	27.1
22	18.6	16.1	14.3	21.2	17.8	15.4
23	16.0	17.8	16.3	19.1	12.9	14.4
24	0.0	0.0	0.1	0.0	0.0	0.1
25	7.4	10.3	3.3	10.9	6.8	6.3
26	10.0	10.1	10.7	13.7	8.0	9.2
27	12.2	12.6	9.9	17.9	13.6	13.3
28	-6.7	-7.7	-7.5	0.3	-7.8	-8.0
29	1.2	2.6	0.9	4.8	1.9	4.7
30	5.5	6.7	2.8	10.1	3.7	3.5
31	-5.5	-5.3	-5.9	-2.0	-6.7	-7.0
32	2.3	4.6	3.0	8.7	2.3	4.2
33	-3.3	-3.8	-8.7	0.7	-1.5	-1.1
34	28.7	23.6	18.7	27.9	26.0	27.1
35	20.2	23.2	15.6	25.3	18.0	17.1
36	17.3	18.9	17.3	20.4	19.8	20.5
37	18.3	20.0	17.9	23.5	18.7	18.7
38	19.3	20.8	19.8	24.0	21.5	20.9
39	33.0	38.1	32.6	36.2	34.1	36.8
MAD [a]	13.4	14.2	13.6	14.9	13.9	14.3

[a] Mean absolute differences.

Table 4.S6c. Relative G differences (M06-2X and B97D, in kJ/mol) for neutral and anionic PFOAs in different environments.

PFOA **n**	**Neutral PFOAs**			**Anionic PFOAs**		
n	**gas**	**octanol**	**Water**	**gas**	**octanol**	**water**
1	-10.7	-11.4	-12.9	-22.0	-15.5	-15.8
2	-9.9	-8.9	-12.2	-19.9	-13.3	-14.4
3	-13.1	-13.2	-14.8	-18.7	-18.3	-16.4
4	-4.2	-2.0	-2.6	-6.8	-8.3	-7.0
5	-30.6	-27.7	-29.6	-37.2	-31.7	-32.3
6	4.7	6.1	3.9	4.0	7.1	6.0
7	3.9	5.6	4.1	4.3	1.6	2.9
8	7.7	12.3	10.6	7.3	4.7	9.3
9	3.7	6.7	3.9	2.5	3.4	3.6
10	-7.3	-4.3	-6.6	-7.8	-10.0	-8.2
11	1.4	4.3	3.1	1.5	0.5	1.1
12	-9.3	-10.3	-10.2	-12.8	-11.8	-9.9
13	-9.7	-7.7	-9.2	-9.4	-5.5	-7.0
14	-0.5	0.8	0.1	-13.3	-17.1	-13.9
15	-4.5	-3.1	-4.9	-2.3	-5.5	-2.6
16	-11.0	-9.1	-11.3	-7.2	-14.1	-13.8
17	-14.2	-10.6	-14.3	-18.0	-18.4	-17.0
18	-15.0	-12.3	-14.6	-15.1	-19.1	-16.2
19	5.5	7.1	6.1	9.0	-11.1	-5.4
20	19.7	22.1	18.8	18.1	14.6	18.4
21	21.3	23.0	21.0	21.9	17.5	19.2
22	17.7	15.7	13.4	12.7	12.7	12.9
23	9.6	13.1	13.3	8.2	7.5	10.0
24	0.0	0.0	0.1	0.0	0.0	0.1
25	4.9	7.7	7.0	3.4	2.5	2.9
26	7.1	8.2	7.6	7.0	3.2	5.1
27	10.2	13.8	10.6	12.1	10.2	10.7
28	-2.2	-3.3	-3.2	-1.5	-6.2	-5.7
29	1.5	4.3	3.3	0.8	-0.8	2.6
30	4.6	7.6	2.9	3.8	-0.3	1.5
31	-2.6	-1.1	-2.5	-3.0	-5.6	-4.0
32	1.6	6.8	4.3	2.2	-0.6	0.9
33	-1.9	-1.5	-5.4	-3.2	-2.9	-0.3
34	20.0	17.4	12.6	16.8	15.0	17.1
35	16.0	18.3	16.9	15.1	13.3	15.0
36	11.0	13.7	10.7	8.6	13.4	15.1
37	13.1	15.9	14.9	13.3	11.8	12.2
38	13.3	15.1	11.4	12.8	10.6	12.9
39	22.0	27.5	21.6	20.5	20.8	22.7
MAD [a]	9.4	10.2	9.7	10.4	9.9	10.0

[a] Mean absolute differences.

Table 4.S7. Comparison of relative G values (in kJ/mol) of neutral and anionic PFOAs in the gas phase using the M06-2X method with two basis sets.

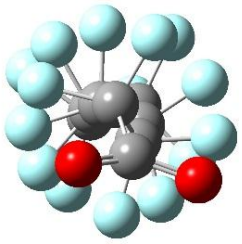
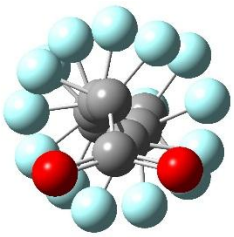
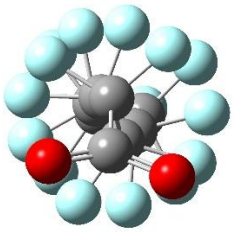
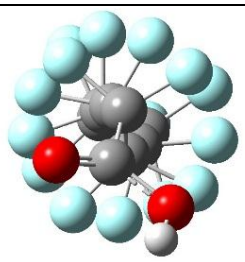
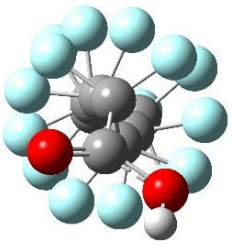
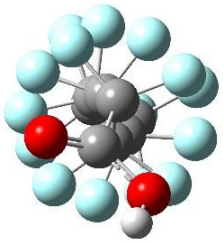
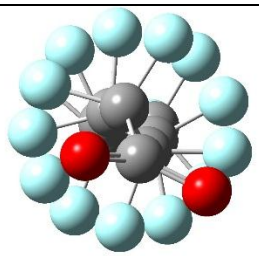
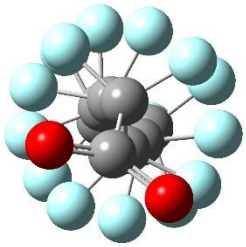
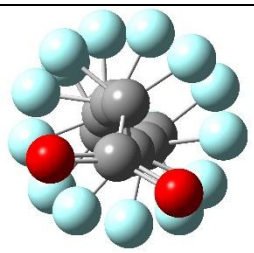
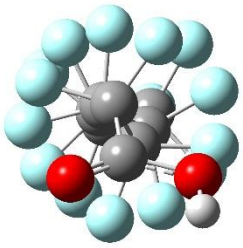
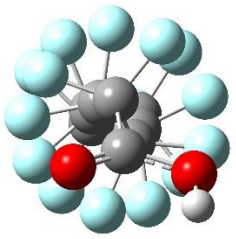
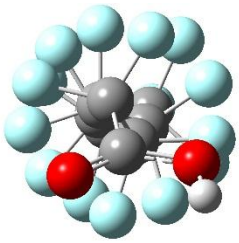
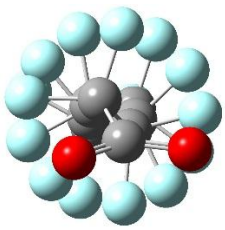
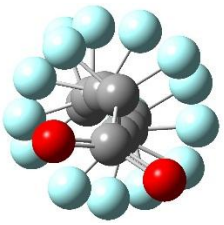
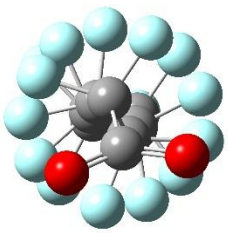
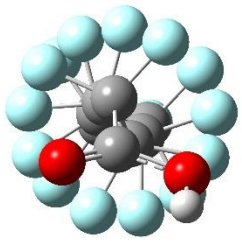
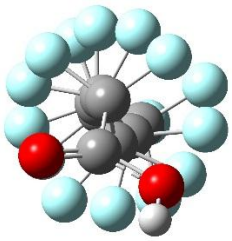
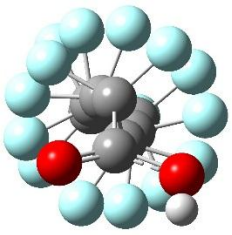
PFOA n	Neutrals			Anions		
n	**6-311++G(3df,3p)**	**6-31++G(d,p)**	**AD[a]**	**6-311++G(3df,3p)**	**6-31++G(d,p)**	**AD[a]**
1	*35.8*	*32.8*	3.0	*31.4*	*28.8*	2.6
2	*28.6*	*26.9*	1.7	*33.9*	*34.4*	0.5
3	*7.1*	*8.6*	1.5	*0.0*	*1.7*	1.7
4	*38.2*	*37.5*	0.7	*32.7*	*31.9*	0.8
5	*0.4*	*3.1*	2.7	*0.0*	*3.0*	3.0
6	*23.0*	*20.6*	2.4	*23.7*	*22.0*	1.7
7	*45.0*	*44.5*	0.5	*45.8*	*45.4*	0.4
8	*43.9*	*42.8*	1.1	*42.7*	*42.3*	0.4
9	*59.6*	*57.7*	1.9	*64.0*	*61.9*	2.1
10	*55.4*	*54.2*	1.2	*69.1*	*67.4*	1.7
11	*95.8*	*94.5*	1.3	*114.8*	*112.7*	2.1
12	*22.3*	*22.7*	0.4	*22.4*	*22.7*	0.3
13	*4.8*	*4.5*	0.3	*5.9*	*6.6*	0.7
14	*38.5*	*40.6*	2.1	*26.8*	*26.2*	0.6
15	*67.6*	*67.0*	0.6	*57.7*	*56.6*	1.1
16	*4.9*	*6.2*	1.3	*11.7*	*13.4*	1.7
17	*51.4*	*52.3*	0.9	*61.0*	*62.3*	1.3
18	*40.2*	*42.2*	2.0	*59.6*	*62.3*	2.7
19	*54.8*	*52.8*	2.0	*58.1*	*56.6*	1.5
20	*47.2*	*44.8*	2.4	*46.9*	*44.8*	2.1
21	*48.8*	*46.6*	2.2	*48.7*	*45.2*	3.5
22	*78.8*	*76.6*	2.2	*90.7*	*85.7*	5.0
23	*82.9*	*79.6*	3.3	*98.2*	*94.5*	3.7
24	*0.0*	*0.0*	0.0	*0.0*	*0.0*	0.0
25	*47.1*	*46.0*	1.1	*53.1*	*51.6*	1.5
26	*42.9*	*41.8*	1.1	*48.7*	*47.4*	1.3
27	*32.8*	*32.1*	0.7	*40.7*	*39.3*	1.4
28	*28.8*	*28.9*	0.1	*43.1*	*41.9*	1.2
29	*77.6*	*75.4*	2.2	*93.6*	*92.2*	1.4
30	*44.9*	*43.7*	1.2	*62.5*	*61.3*	1.2
31	*38.7*	*38.0*	0.7	*57.9*	*58.6*	0.7
32	*72.2*	*71.4*	0.8	*92.3*	*90.8*	1.5
33	*15.0*	*16.3*	1.3	*34.5*	*36.5*	2.0
34	*45.8*	*43.2*	2.6	*49.2*	*49.0*	0.2
35	*60.1*	*56.7*	3.4	*78.1*	*77.0*	1.1
36	*60.6*	*58.6*	2.0	*78.2*	*78.4*	0.2
37	*62.2*	*59.6*	2.6	*84.1*	*82.0*	2.1
38	*52.0*	*50.0*	2.0	*73.2*	*70.9*	2.3
39	*62.5*	*59.5*	3.0	*82.7*	*80.5*	2.2
MAD[b]			1.6		**MAD**	1.6

[a] Absolute differences; [b] Mean absolute differences.

Table 4.S8. Stability order and substitution pattern of the 39 anionic PFOA isomers in the gas phase (M06-2X).[a]

				Type of substitution (*Position of the substitution*)									
n	**Stability order**	**Chain length**[b]	ACL[c]	CH_3 (α)	CH_3 (β)	CH_3 (γ)	CH_3 (δ)	CH_3 (ε)	CH_3CH_2 (α)	CH_3CH_2 (β)	CH_3CH_2 (γ)	$(CH_3)_2CH_2$ (α)	$CH_3CH_2CH_2$ (α)
5	*1*	3		2	2								
24	*2*	5		2									
3	*3*	3			2				1				
13	*4*	4		2		1							
16	*5*	4		1		2							
12	*6*	4		2	**1**								
6	*7*	4	3.8	1					1				
14	*8*	4		1	**2**								
1	*9*	3							2				
4	*10*	3			1							1	
2	*11*	3		1	1				1				
33	*12*	5					2						
27	*13*	5		1			1						
8	*14*	4				1			1				
28	*15*	5			**2**								
7	*16*	4			1				1				
20	*17*	4											1
26	*18*	5		1		**1**							
21	*19*	5							1				
34	*20*	6	4.5	1									
25	*21*	5		1	**1**								
15	*22*	4		1	**1**	1							
31	*23*	5				**2**							
19	*24*	4										1	
18	*25*	4			**1**	2							
17	*26*	4			**2**	1							
30	*27*	5			**1**		1						
9	*28*	4		1						**1**			
10	*29*	4			**1**					**1**			
38	*30*	6						1					
35	*31*	6			**1**								
36	*32*	6				**1**							
39	*33*	7	5.2										
37	*34*	6					**1**						
22	*35*	5								**1**			
32	*36*	5				**1**	1						
29	*37*	5			**1**	**1**							
23	*38*	5									**1**		
11	*39*	4				1				**1**			

[a] The position of the substitution is represented by α (carbon next to the -COOH group, position one), β, γ, δ and ε (positions 2, 3, 4 and 5 after the -COOH group, respectively); coloured numbers represent the number of substitutions (yellow and clear background represents a substitution either in position α or at the tail, and blue represents a substitution elsewhere); [b] Length of the unsubstituted backbone; [c] Average chain length.

Method	Species	Gas	Octanol	Water
LC-ωPBE	Anion			
	Neutral			
M06-2X	Anion			
	Neutral			
B3LYP (PCM)	Anion			
	Neutral			

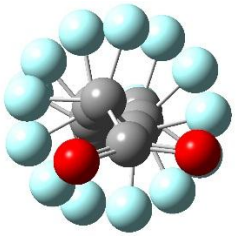
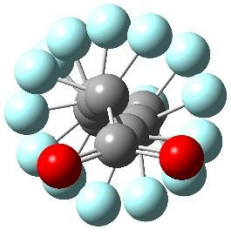
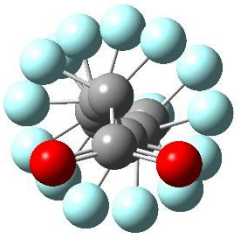
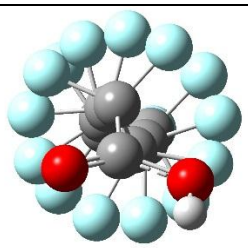
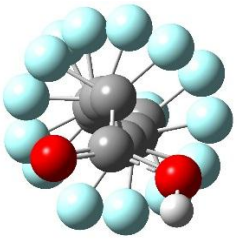
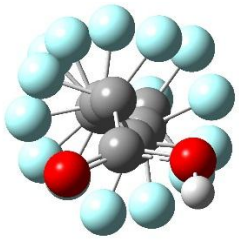
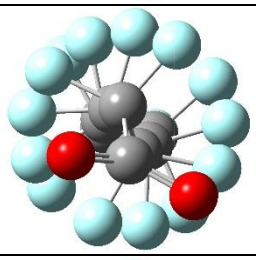
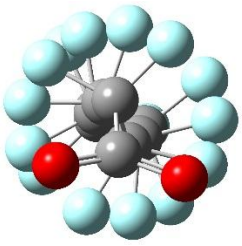
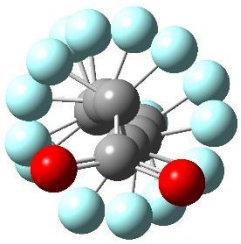
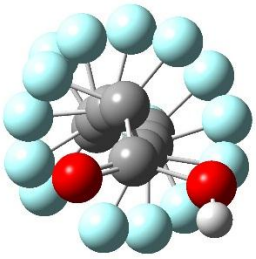
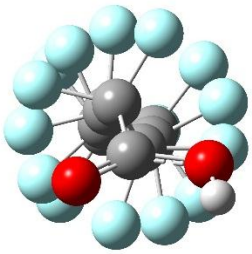
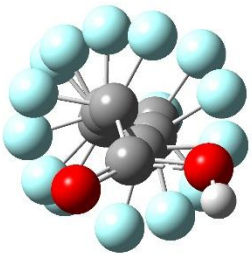
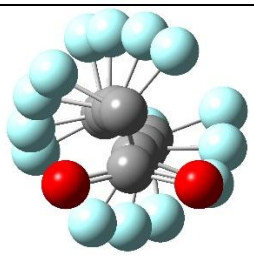
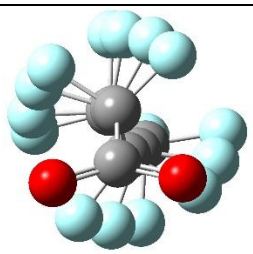
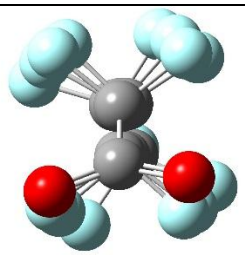
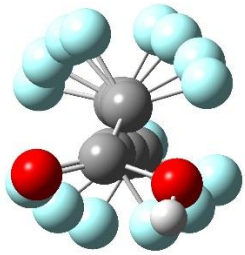
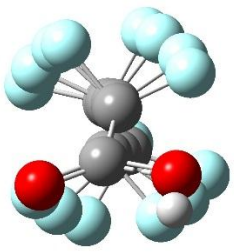
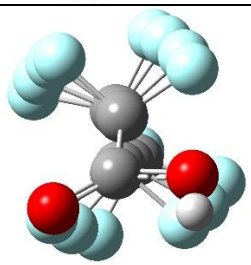
Method	Species	Gas	Octanol	Water
B3LYP (SMD)	Anion			
	Neutral			
B97D	Anion			
	Neutral			
PM6	Anion			
	Neutral			

Figure 4.S1. Frontal view of the optimized structure of PFOA **39** calculated at different levels of theory.

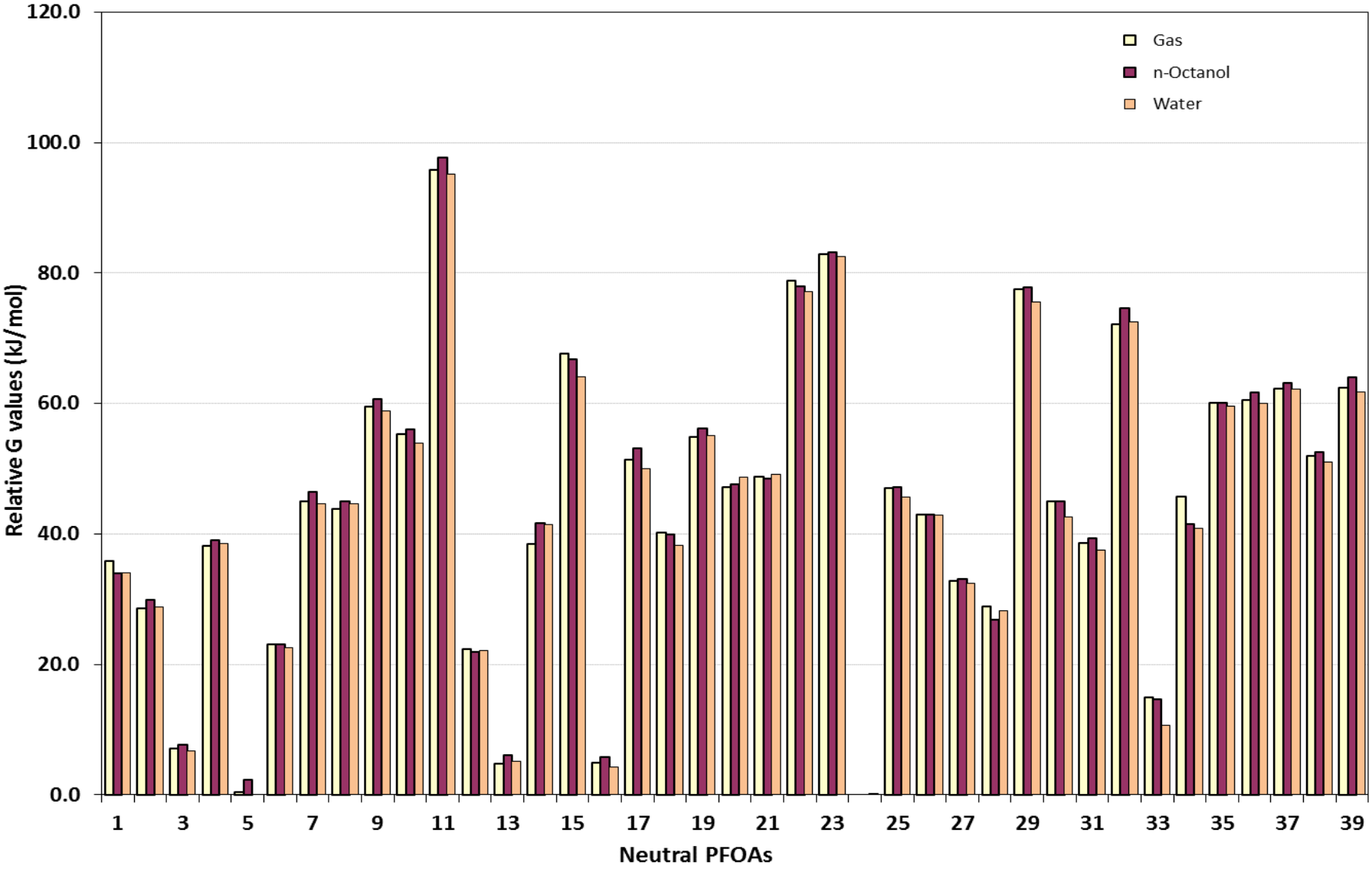


Figure 4.S2. Comparison of M06-2X relative G values of neutral PFOA isomers in the gas phase, octanol and water.

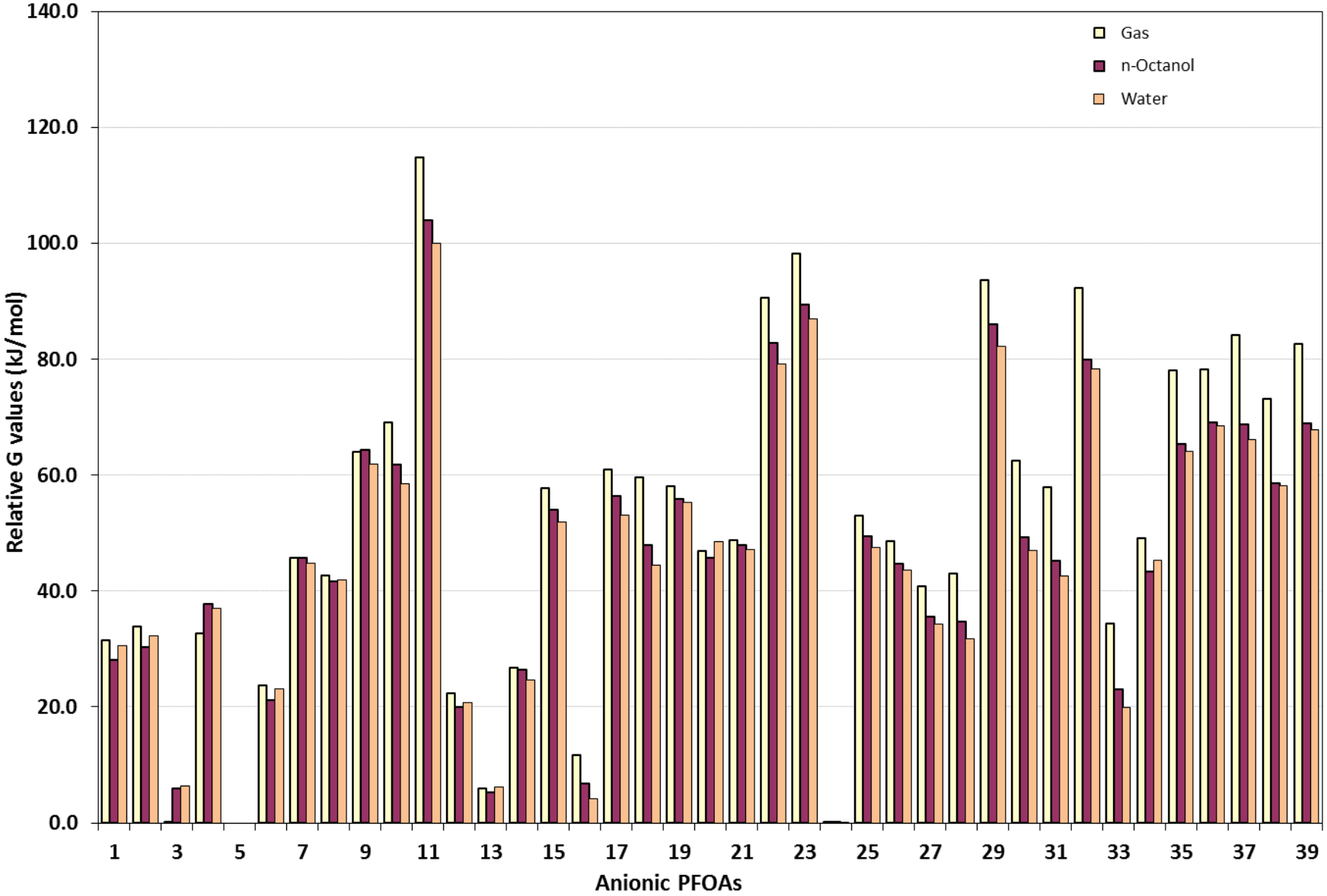


Figure 4.S3. Comparison of M06-2X relative G values of anionic PFOA isomers in the gas phase, octanol and water.

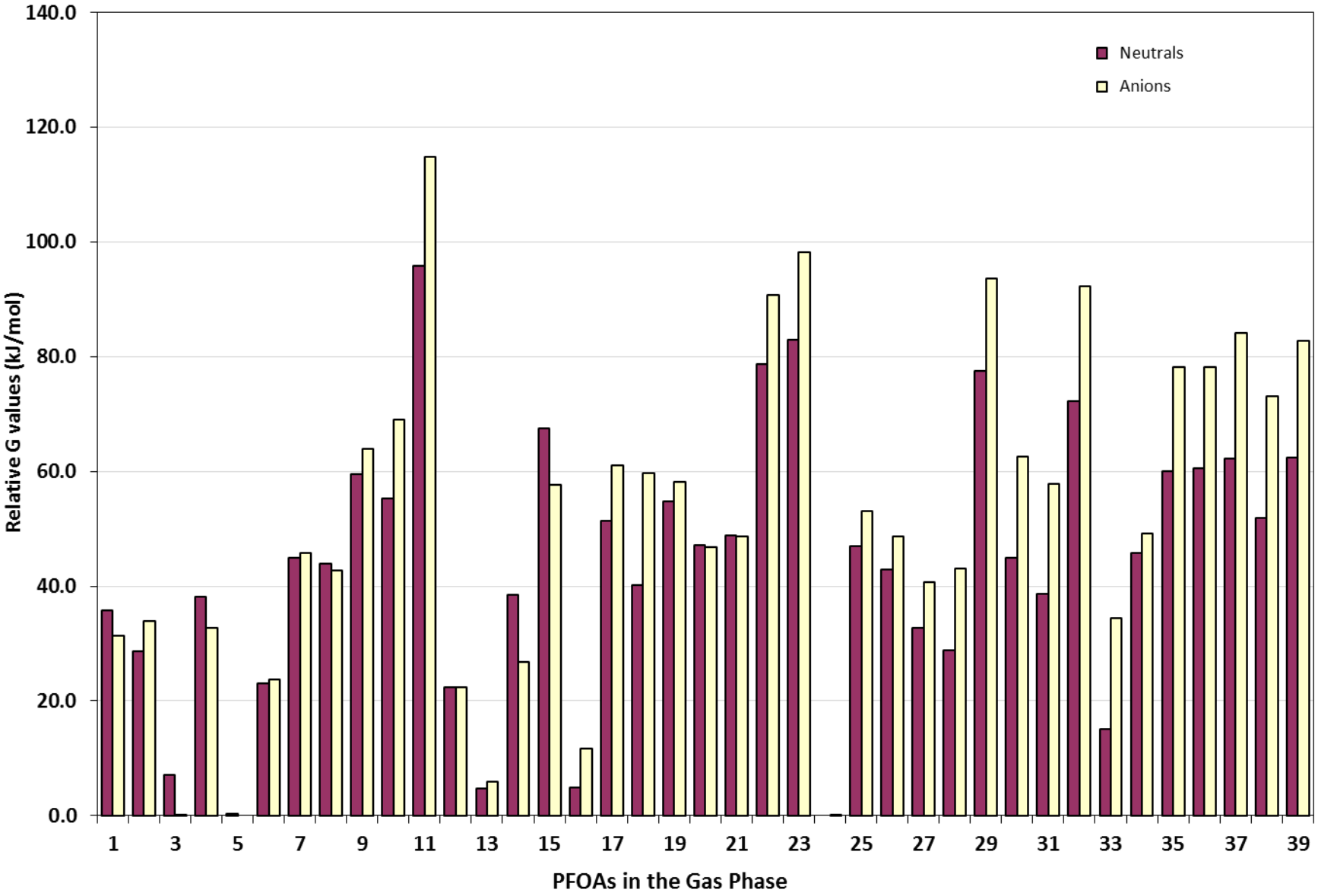


Figure 4.S4. Comparison of M06-2X relative G values of neutral and anionic PFOA isomers in the gas phase.

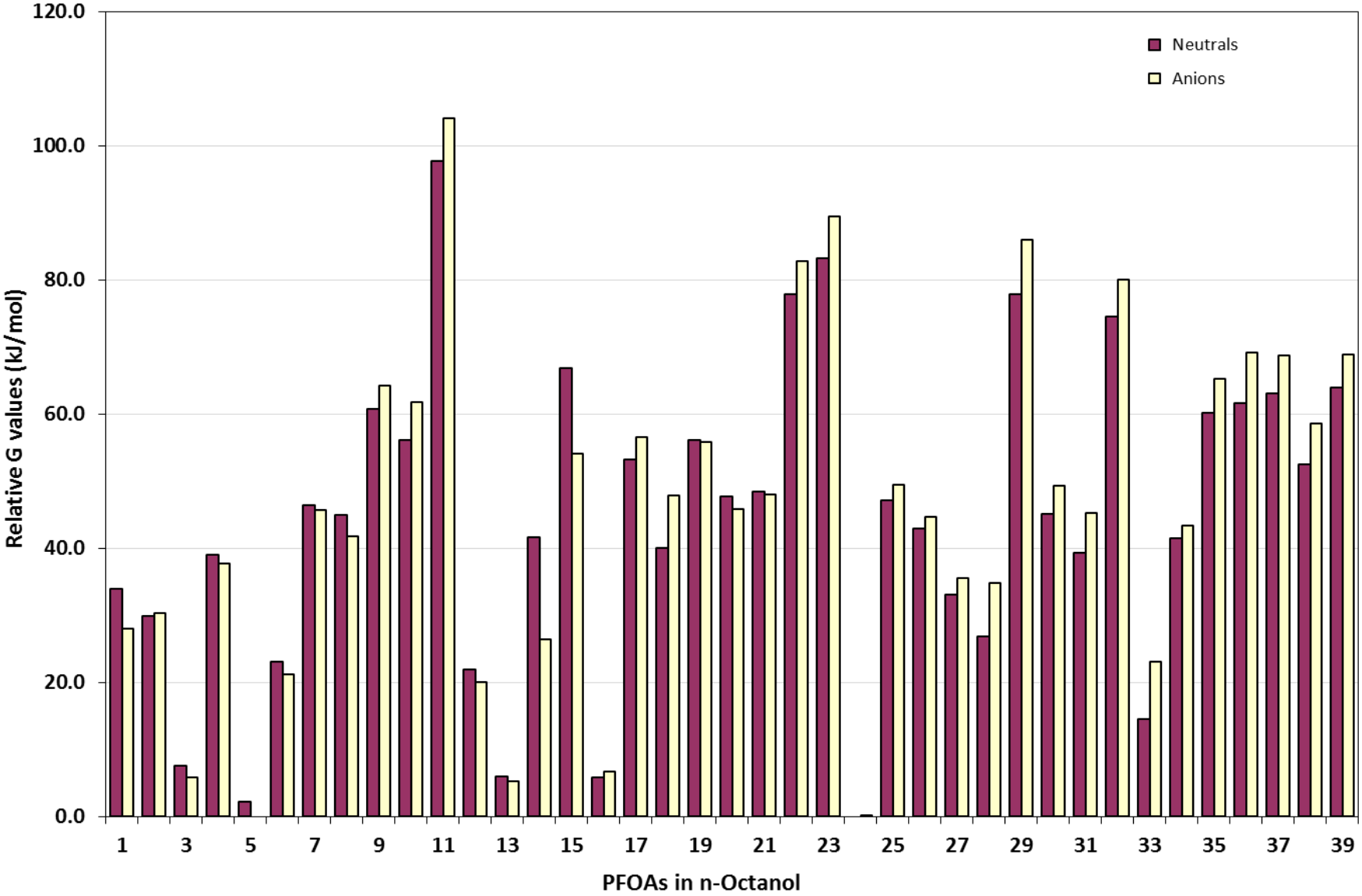


Figure 4.S5. Comparison of M06-2X relative G values of neutral and anionic PFOA isomers in octanol.

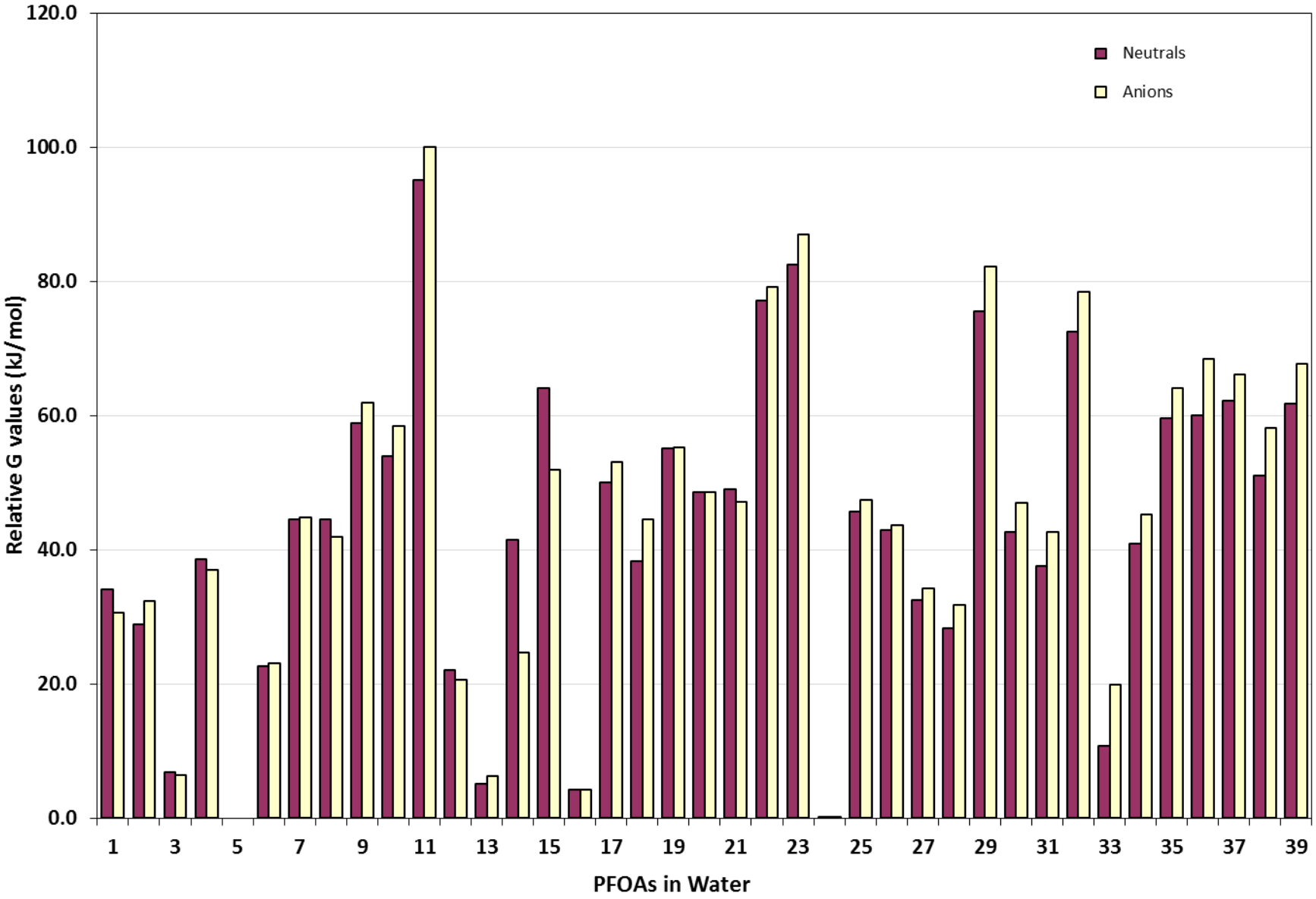


Figure 4.S6. Comparison of M06-2X relative G values of neutral and anionic PFOA isomers in water.

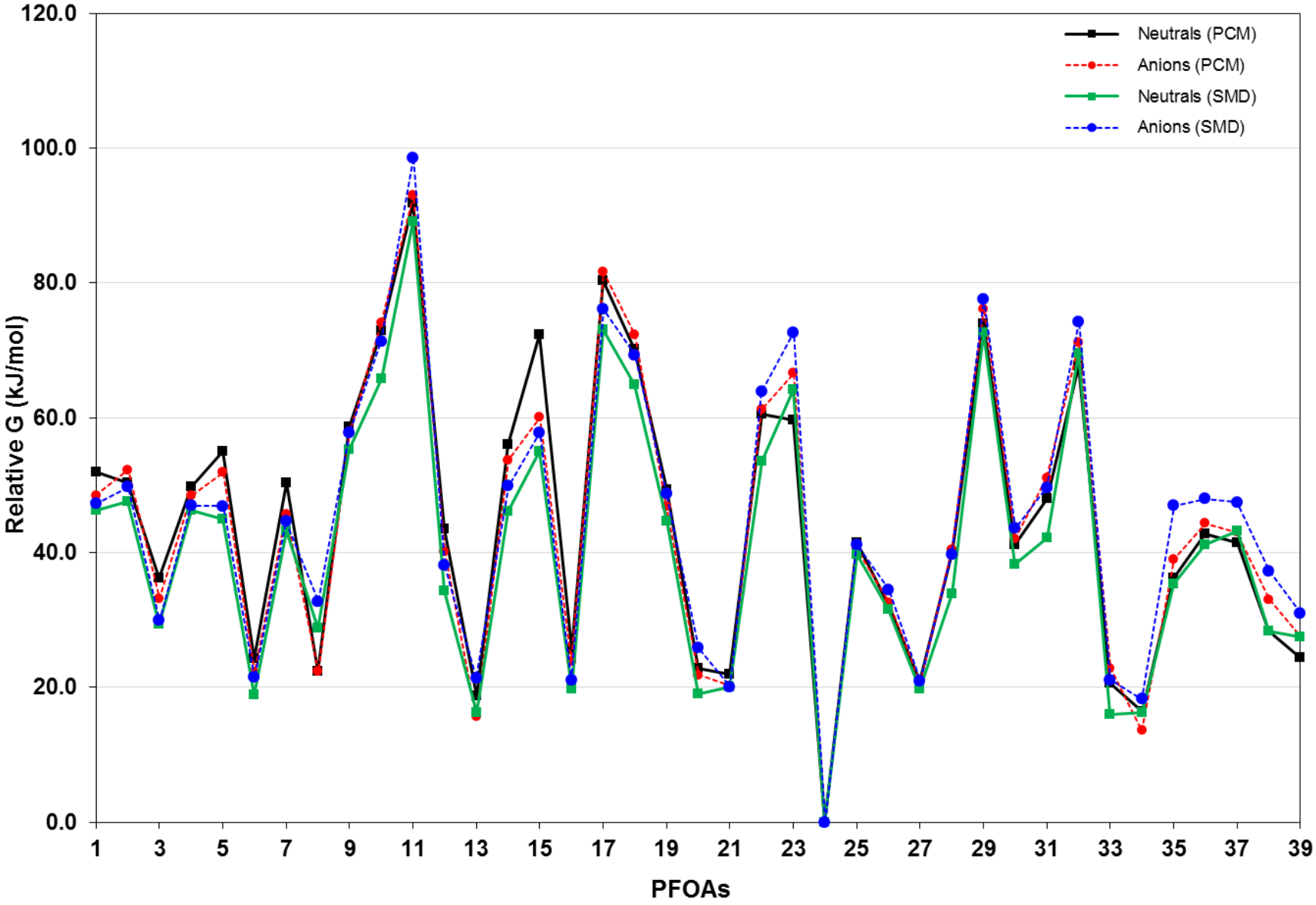


Figure 4.S7. B3LYP relative G values for neutral and anionic PFOAs using two solvation methods.

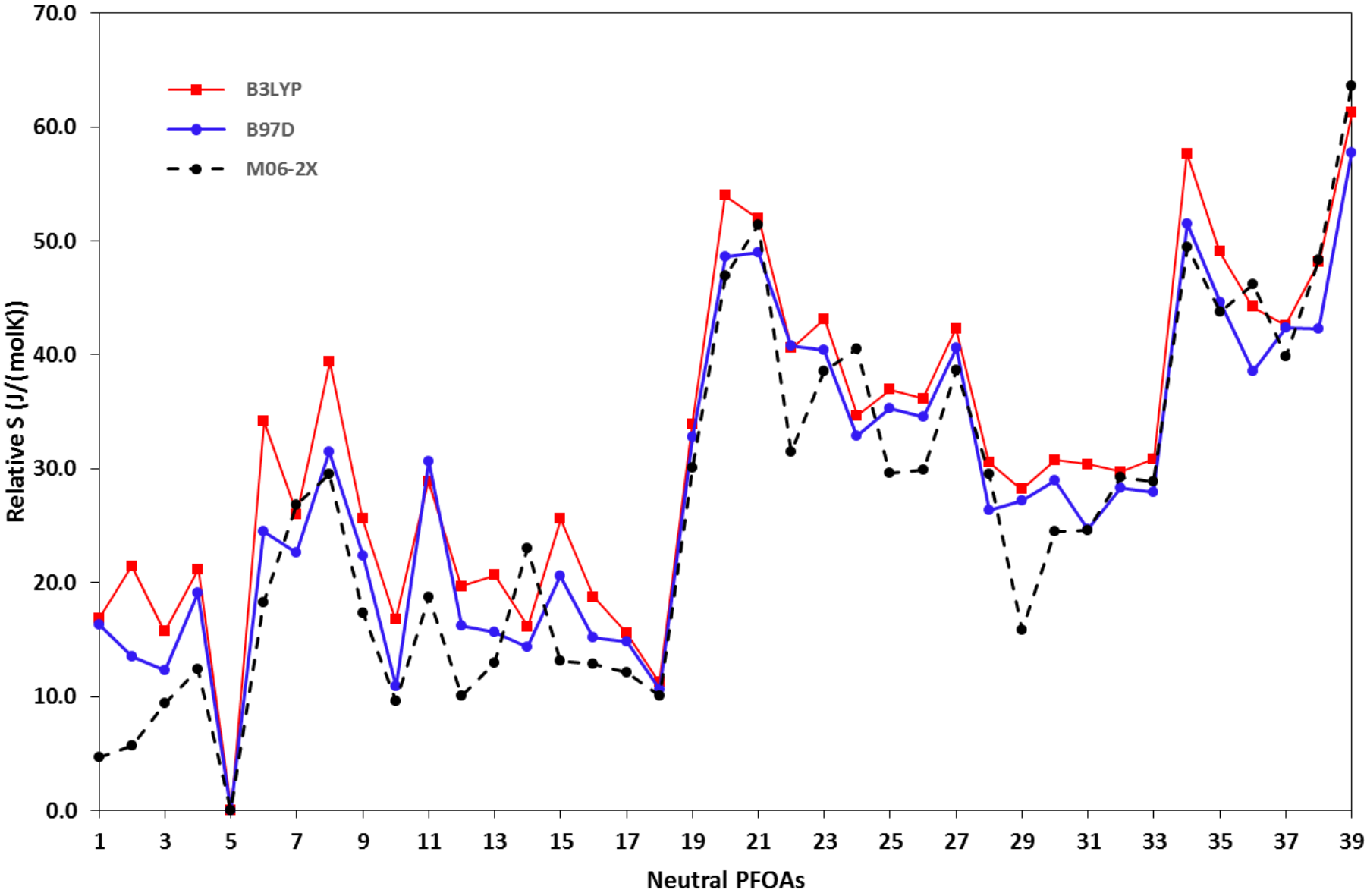


Figure 4.S8. M06-2X, B97D and B3LYP relative standard entropies of the neutral PFOAs in the gas phase.

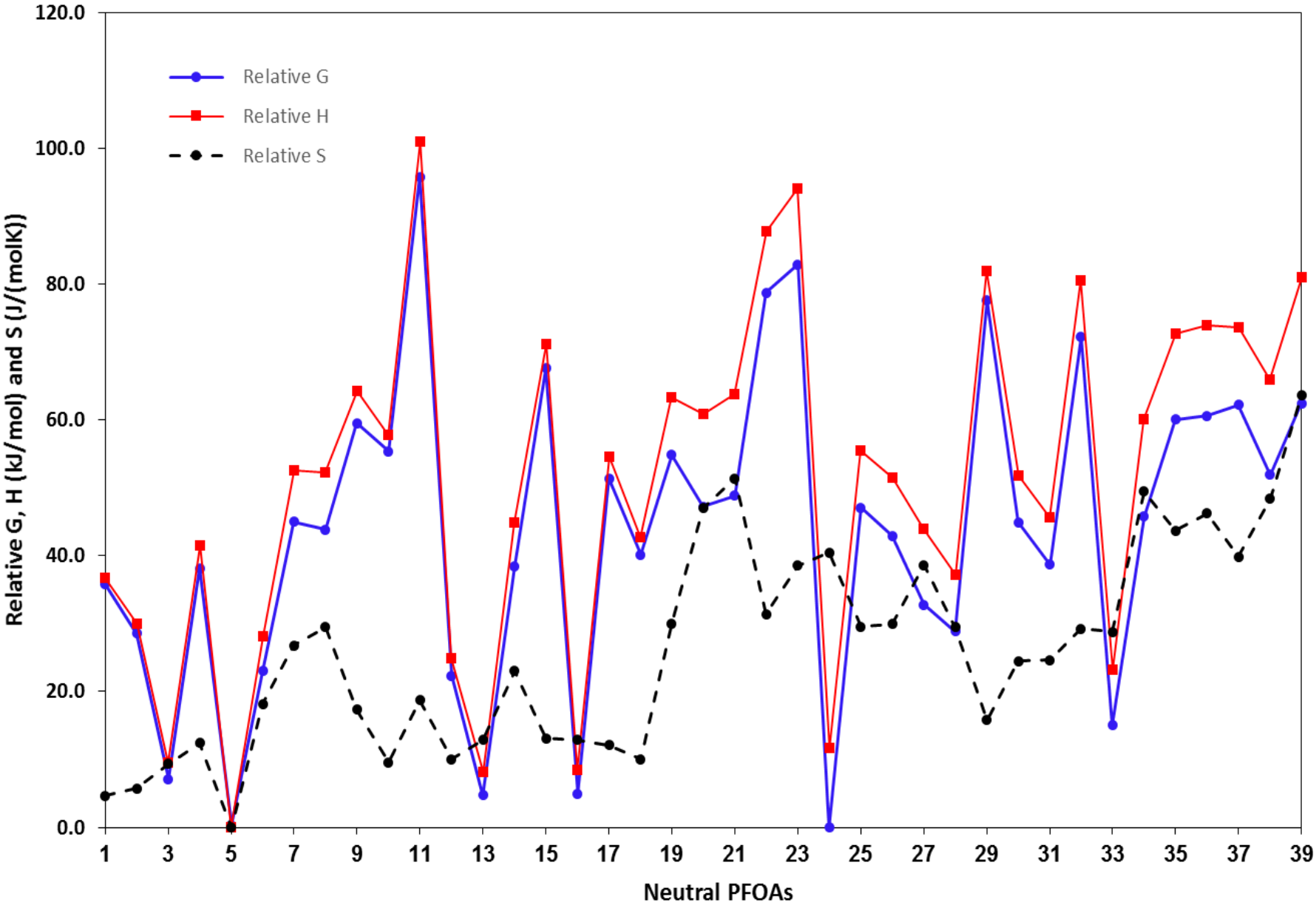


Figure 4.S9. Comparison of M06-2X relative G, H and S values of neutral PFOAs in the gas phase.

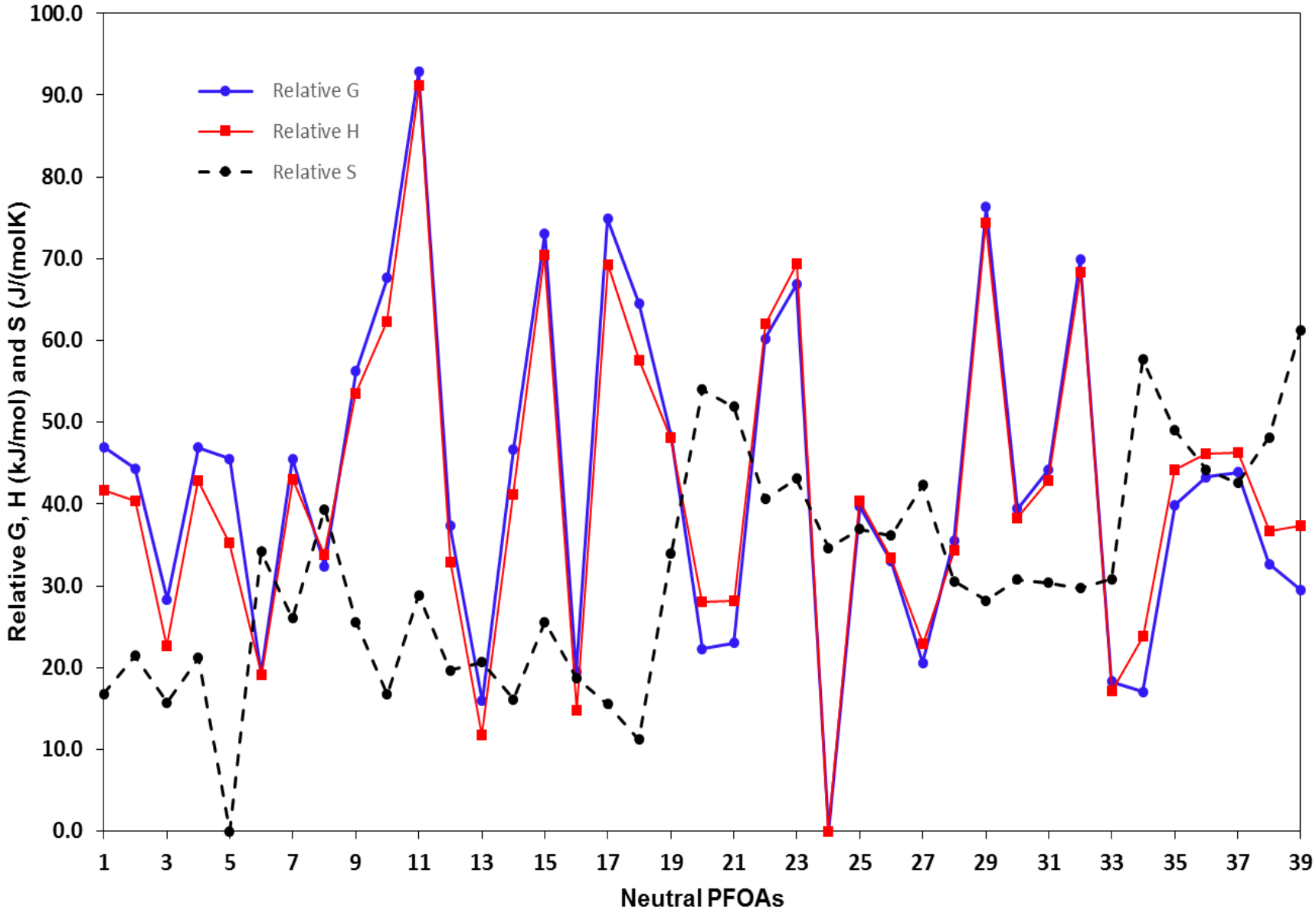


Figure 4.S10. Comparison of B3LYP relative G, H and S values of neutral PFOAs in the gas phase.

Chapter 5. Concluding Remarks and Future Directions

5.1. Determination of physico-chemical properties of perfluorinated compounds

This work represents the first application of density functional theory methods to the calculation of octanol-water partition coefficients, the Log P values of perfluorinated compounds, particularly perfluorinated alkyl acids (PFAAs). The missing Log P values of some families of linear organic acids (perfluorinated or not) and their corresponding conjugate bases were predicted. Of particular interest was the determination of partition coefficients for the linear isomers of perfluoalkyl carboxylic acids and perfluoroalkyl sulfonic acids with structures containing 2-11 carbon atoms.

The curves of experimental and calculated Log P values with the number of carbon atoms exhibit a similar pattern, with a parallel relationship found for the curves of Log P for anionic and neutral species of alkyl and perfluoroalkyl acids (either carboxylic or sulphonic). Such a relationship between the curves of neutral and anions was used to estimate Log P values of neutral alkyl perfluorinated carboxylic acids using the slope of the curve for their corresponding alkyl perfluorinated carboxylates. A similar methodology, using a sole experimental Log P value for the anion of perfluorooctane sulfonic acid with eight carbon atoms, was used to determine the partition coefficients for the rest of the anions and the neutrals.

The lack of experimental values for some of these families of compounds impeded a more detailed analysis of the results obtained. In addition, the broad spectrum of calculated Log P values used in the literature for environmental fate studies raises questions about whether the previously used data should be revised. The values obtained for Log P in this study demonstrate a potential need for environmental researchers to re-evaluate their estimations.

5.1.1. Future work

Other partition coefficients, such as air-water or soil organic carbon-water, have been proposed for use in environmental studies with linear PFAAs. Very little information about these compounds is available in the literature and some of the limited data is contradictory or incomplete. We believe

that a revised approach based on our current work would allow an updated estimation of some of these coefficients.

Traditional studies of the environmental fate of perfluorinated acids involve the use of partition compounds, with their implementation usually requiring input of acid constants, pKa. However, the lack of sufficient experimental data for these families of compounds and contradictory pKa values reported for some of the species most studied, means that researchers mainly use estimated values or else find themselves trying to predict which value better fits their data. Several attempts to calculate the pKa of perfluorinated acids have been made, but there is still no consensus on which value should be accepted. The Minnesota family of functionals and the implementations of an adequate solvation method must be explored for the determination of pKa values of these group of molecules.

5.2. Relative stability of structural isomers of perfluorooctanoic acid

The relative stability of the 39 isomers of perfluorooctanoic acid (PFOA) was theoretically determined using M06-2X, LC-ωPBE, B97D, B3LYP and PM6 methods. Similar to what has been observed with other families of alkyl compounds, there is a predominance of more branched isomers among the groups that exhibit higher stability when the M06-2X functional was used. On the contrary, the most linear compounds rank among the least stable. PM6 performance is in close agreement with M06-2X for the neutrals, but not so for the anions. The relative stability observed with M06-2X contradicts the experimentally observed relative abundance for these isomers, as the most linear group generally is present at higher concentration, which reinforces the previously published idea of a kinetically-driven relative proportion mediated by specific mechanisms of synthesis that favour the more linear isomers.

The calculated relative stability, which was found to be mostly enthalpic, seems dependant not only on the level of branching, but on the position such branches occupy along the carbonated backbone. Some types of branches seem to destabilize the molecule when they occur in the middle of the chain.

5.2.1. Future work

Some researchers suggest that partition among the different environmental compartments is unequal for the more linear isomers in relation to the branched ones. Discrepancies have also been reported in terms of biological retention among isomers. Others suggest that very little differences in terms of pKa values must exist among the 39 PFOA isomers, which would make their separation and identification much harder. In that regard, the determination of partition coefficients and pKa values for the 39 isomers of PFOA could pave the way to a better understanding of the relative distribution of these compounds and would shed light on the mechanisms involved in establishing observed differences.