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Theoretical studies on the pK_a values of perfluoroalkyl carboxylic acids

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ABSTRACT

Computational studies were conducted using the major levels of semiempirical, ab initio, density functional theory (DFT), and the CBS-Q//B3 method and various solvation models on a homologous series of straight chain perfluoroalkyl carboxylic acids (PFCAs) ranging in chain length from C_1(trifluoroacetic acid) to C_9(*n*-perfluorodecanoic acid) as well as the monomethyl branched C_7(*n*-perfluorooctanoic acid; *n*-PFOA) isomers. Regardless of perfluoroalkyl chain length and theoretical method employed, application of a computational thermodynamic cycle indicated no significant change in the estimated aqueous monomeric pK_a values between C_1 and C_9, all having a relatively constant pK_a of about 0 that is in agreement with earlier predictions and recent experimental evidence. Perfluoroalkyl chain helicity does not appear to result in increased monomeric PFCA pK_a values at chain lengths greater than 5. Increasing chain length does not substantially influence the structural or electronic character of the carboxylic acid head group. A MMFF94 conformational search yielded 2915 separate low- through high-energy conformers of *n*-PFOA. Ranking of these structures gave the 94 lowest MMFF94 energy conformations that were subjected to DFT investigations. Application of a thermodynamic cycle approach, coupled with aqueous and gas phase DFT calculations on the molecular and anionic forms for each of the conformers, gave conformationally averaged pK_a values for *n*-PFOA equal to the global minimum helical conformer pK_a. The conformational populations under study occupy ~100% of the global *n*-PFOA conformational space, indicating no higher energy/low acidity conformations remain unexamined that could influence the predicted composite aqueous monomeric pK_a of zero for this compound.

1. Introduction

Perfluoroalkyl carboxylic acids (PFCAs; Fig. 1) are widespread environmental contaminants that are persistent to natural degradation processes, can undergo long-range transport by both aquatic and atmospheric pathways, and are of toxicological concern [1–3]. The pK_a values of these compounds are of interest given the primary role this property plays in various environmental transport and partitioning processes and biological activities. Waste treatment methods for PFCAs are also likely to display different mechanisms, product profiles, and kinetics from the molecular versus dissociated forms [2]. Although the aqueous monomeric pK_a of the C_1 PFCA (trifluoroacetic acid [TFA]) is well established at about 0.3–0.5 [4–6], there has been substantial debate in the literature regarding the aqueous monomeric acidity constants for longer chain PFCAs such as *n*-perfluorooctanoic acid (*n*-PFOA) [1,7–17].

At present, there are three competing estimates for the aqueous monomeric pK_a of *n*-PFOA in the literature. Goss has argued that based on analogy considerations using other highly fluorinated carboxylic acids, as well as computational data obtained from the COSMOtherm and SPARC software programs, the monomeric pK_a of *n*-PFOA should be about 0 [11,12]. Recent experimental evidence by Cheng et al. [10] using electrospray ionization mass spectrometry has provided an upper limit boundary for a monomeric *n*-PFOA pK_a at $\leqslant 1$, consistent with the prediction of Goss [11,12]. As part of their studies into the air–water partitioning constant of *n*-PFOA, Kutsuna and Hori proposed a pK_a of 1.3 from the best fit of their experimental data [14]. In contrast, Burns et al. [8] used a potentiometric titration method and recently reported a monomeric *n*-PFOA pK_a of 3.8 ± 0.1. This result has caused controversy [9,13] not only due to its intrinsically high value (i.e., in the range of non-fluorinated carboxylic acid pK_a values, and 3.5 units above that of TFA), but also because Burns et al. [8] indicated that the pK_a of monomeric *n*-PFOA was higher than that of its aggregated forms, in contrast to general expectations for various oxyacids [18–20].

Together, this information suggested that previous reports on the pK_a values of other aggregated PFCAs may accurately represent, or even underestimate, the pK_a values of the corresponding monomeric forms. Consequently, the results of Burns et al. [8] caused a re-evaluation of the current and historical composite experimental dataset on PFCA pK_a values [8,17], suggesting that the computa-

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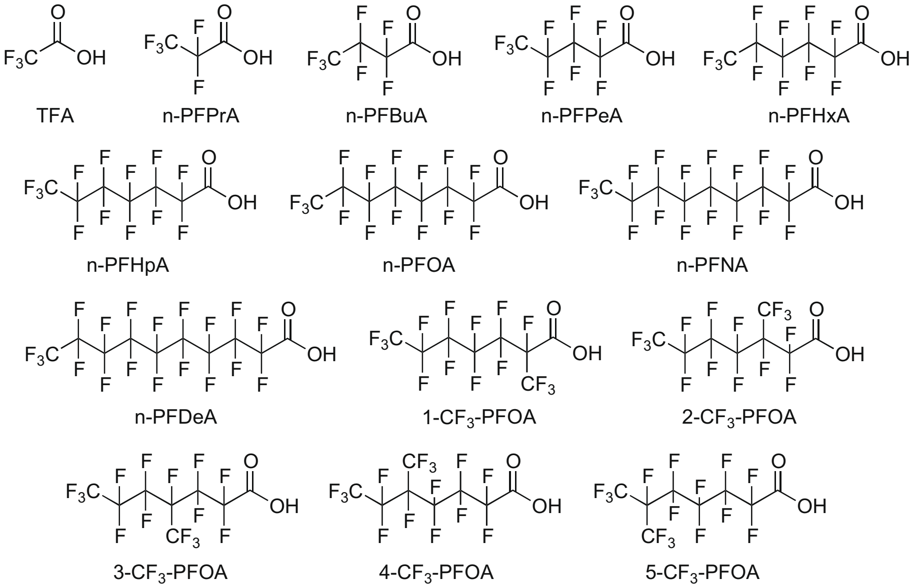

Fig. 1. Structures of the perfluoroalkyl carboxylic acids under consideration.

tional estimates provided in the literature may be underestimating pK_a values of longer chain PFCAs, and that – starting at about C_4 – the monomeric pK_a values of PFCAs may increase with increasing chain length to an upper limit near 3.8 for C_7 and longer homologs.

The rationale put forward by Burns et al. [8] to explain this apparent increase in PFCA monomeric pK_a by more than 3 units between the short- and long-chain isomers was based on the relative conformations of the perfluoroalkyl chain, and the effects such conformations would have on the acidity of the carboxylate head group. These authors claimed that "[i]t is clear, however, that the rigid perfluoroalkyl helical twist conformation exhibited by long-chain PFCAs mitigates their acidity, causing an increase in pK_a for the monomeric species, and that a fundamental conformational change, brought about by electronic factors, requires the pK_a to be different for the short chain PFCAs and their longer chain homologues" [8]. It was also stated in this work that ab initio (Hartree–Fock) and density functional theory (DFT) computational evidence existed to support a significant change in the electronic character of the carboxylate group, but to date, no further details have been provided. In order to help resolve the current controversy in this field, and to shed light on the likely true pK_a values of monomeric long-chain PFCAs, we have undertaken comprehensive theoretical studies at all major levels of computational theory on a homologous series of straight chain PFCAs and the monomethyl branched *n*-PFOA isomers in order to better understand what role, if any, that perfluoroalkyl chain conformations may play in the acidity constants of these important environmental contaminants.

2. Materials and methods

Theoretical monomeric aqueous pK_a values were calculated using the following approach. In aqueous solution, monomeric carboxylic acids dissociate according to the following general reaction:

$$\mathrm{RCOOH}_{aq} \rightarrow \mathrm{RCOO}^-_{aq} + \mathrm{H}^+_{aq} \ldots \qquad (1)$$

The pK_a value of RCOOH_{aq} is defined as the $-\log K$ of Eq. (1) (i.e., the K_a), and can be related to the total Gibbs free energy ($\Delta G^\circ_{D,aq}$) of reaction (1) via Eq. (2):

$$\mathrm{p}K_a = \Delta G^\circ_{D,aq}/2.303\mathrm{RT} \ldots \qquad (2)$$

$\Delta G^\circ_{D,aq}$ can be obtained via a thermodynamic cycle comprised of Eqs. (3)–(5),

$$\Delta G^\circ_{D,aq} = \Delta G^\circ_{D,g} + \delta\Delta G^\circ_{solv} \ldots \qquad (3)$$

$$\Delta G^\circ_{D,g} = G^\circ_{g,\mathrm{RCOO}^-} + G^\circ_{g,\mathrm{H}^+} - G^\circ_{g,\mathrm{RCOOH}} \ldots \qquad (4)$$

$$\delta\Delta G^\circ_{solv} = \Delta G^\circ_{solv,\mathrm{RCOO}^-} + \Delta G^\circ_{solv,\mathrm{H}^+} - \Delta G^\circ_{solv,\mathrm{RCOOH}} \ldots \qquad (5)$$

where $\Delta G^\circ_{D,g}$ is the gas phase Gibbs free energy change of reaction (1) and $\delta\Delta G^\circ_{solv}$ is the sum of the solvation energies for each species, where G°_{g,H^+} is -6.32 kcal/mol and $\Delta G^\circ_{solv,\mathrm{H}^+}$ is -265.9 kcal/mol, and a value of 1.89 kcal/mol has been added to calculated gas phase energies to convert from standard state of 1 atm to 1 mol/L [4,21–24].

Calculations were conducted using Gaussian 09 [25]. All calculations used the same gas phase starting geometries obtained with the PM6 semiempirical method [26] as employed in MOPAC 2009 (http://www.openmopac.net/; v. 9.099). Semiempirical calculations used the AM1 [27,28], PM3 [29,30], PM6 [26], and PDDG [31–34] methods as reimplemented [35,36] in Gaussian 09. Hartree–Fock (HF) ab initio calculations were conducted using the 6-31G(d,p), 6-31++G(d,p), and 6-311++G(d,p) Pople-type basis sets [37–40]. Density functional theory (DFT) calculations were conducted using the B3LYP [41–43] and M062X [44] hybrid functionals and the dispersion corrected B97D [45] pure functional. B3LYP calculations employed the 6-31G(d,p), 6-31++G(d,p), 6-311++G(d,p), and 6-311++G(3df,2p) Pople-type basis sets [37–40] and the aug-cc-pVDZ Dunning-type basis set [46,47]. M062X and B97D calculations used the 6-311++G(d,p) basis set [37–40]. High accuracy energy calculations used the Complete Basis Set (CBS) methods CBS-4M [48,49], CBS-Q//B3 [48,50], and CBS-APNO [49], as well as the Gaussian methods Gaussian-4 (G4) and G4MP2 [51,52]. Aqueous phase calculations in Gaussian 09 employed the polarizable continuum solvation model with the integral equation formalism variant using UFF radii (IEFPCM-UFF) [53], the polarizable conductor calculation solvation model using UFF, UAHF, and UAKS radii (CPCM-UFF, CPCM-UAHF, and CPCM-UAKS, respectively) [54,55], and the SMD solvation model [56] for both geometry optimizations and frequency calculations. All gas and aqueous phase optimized structures were confirmed as true minima by vibrational analysis at the same level.