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Calculation of Ionization Constants of Monoprotic Weak Acids in Aqueous Solutions

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Abstract

Motivation. The ionization constants are fundamental to explain the occurrence of numerous and varied processes of great importance in Chemistry and Biology. With the specific aim of contributing to the development of theoretical procedures to study the acidity constants in this work we show the feasibility of a DFT method that makes use of Tomasi's model to calculate the ionization constants of monoprotic weak acids in aqueous solutions.

Method. The B3LYP/6-311++G(d,p) and HF/6-311++G(d,p) methods were used for performing the calculations that permitted to describe the molecular conformations and solute-solvent interactions of the acids and their corresponding conjugate bases.

Results. Several ionization reactions and equilibria in protic solvents, which possess a high hydrogen-bond-donor capability, were proposed. It was considered that the solvation of the hydrogen and hydroxyl ions, as wells as of conjugate bases occurs by means of intermolecular hydrogen bonds that involve one molecule of the ion and one molecule of water. The calculated ionization constants show a good agreement with the experimental values reported in the literature.

Conclusions. The very good relationship that exists between the calculated pK_a values and those obtained experimentally constitutes a good support for the reactions and equilibria of ionization proposed in this paper.

Keywords. monoprotic weak acids, ionization constants, autoprotolysis of water, intermolecular hydrogen bonds, pK_a prediction, DFT calculations.

Abbreviations and notations

DFT, density functional method	K_a, ionization constant of monoprotic acids
K_i, ionization constant	*d*, distance between atoms
K_w, ionic product of water	*A*, H-bond angle
HBD, hydrogen-bond-donor capability	*D*, dihedral angle
IHB, intermolecular hydrogen bond	G^o_{sol}, total free energy in solution
K_C and K_N, equilibrium constants	*q*, total atomic charge (Mulliken)

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1 INTRODUCTION

It is well-known that the ionization constants are fundamental to explain the occurrence of numerous and varied processes of great importance in Chemistry and Biology. In particular, the knowledge of the ionization constants is indispensable for the development of new compounds with biological activity [1-3]. Different experimental procedures [4] are used for the determination of acidity constants. For example, capillary electrophoresis [5], potentiometry [6], and methods that involve spectrometric determinations in water or in mixtures of solvents [7,8]. On the other hand, it must be pointed out that important software has been developed for the calculation of pK_a values based on chemical structures [9]. The acidity-basicity behavior in gas phase of some substances has also been investigated by different theoretical methods [10,11]. However, there exist few studies dealing with the molecular structures and acid-base properties of compounds in aqueous solutions [12].

With the aim of contributing to the development of theoretical procedures for studying the acidity constants of compounds with biological and physicochemical significance, in this paper we show the feasibility of a DFT method that makes use of Tomasi's model to calculate the ionization constants of simple inorganic and organic acids in aqueous solutions.

2 METHODS

The following compounds were studied: (**1**) acetic acid; (**2**) fluoroacetic acid; (**3**) chloroacetic acid; (**4**) bromoacetic acid; (**5**) hypochlorous acid and (**6**) hypobromous acid. The initial molecular geometries of the acids and their corresponding conjugate bases were modeled by the semiempirical AM1 method included in the CS Chem3D program version 5.0 [13]. These geometries were optimized with the Gaussian 98 [14] program packages, using the B3LYP/6-311++G(d,p) method and the default convergence criteria. To analyze the solvent effects on all the species involved in the proposed ionization reactions, the Polarized Continuum model (PCM, SCF=Tight) of Tomasi *et al.* [15] was used.

3 RESULTS AND DISCUSSION

It is known that all aqueous solutions contain hydrogen (H^+) and hydroxyl (OH^-) ions. In pure water these ions derive completely from the ionization of the water molecules,

$$H_2O \rightleftharpoons H^+ + OH^- \qquad (1)$$

The above reaction represents the autoprotolysis of water, which is characterized by the equilibrium constant of ionization (K_i), defined as,

$$K_i = \frac{aH^+ aOH^-}{aH_2O} \qquad (2)$$

where aH^+, aOH^- and aH_2O are the activities of the species in equilibrium. Considering that water is very little dissociated, it is obtained from Eq. (2) that,

$$K_w = K_i\ aH_2O = (aH^+\ aOH^-) \qquad (3)$$

The K_w constant is the ionic product of water. Taking into account that the H^+ ion is hydrated, appearing predominantly as H_3O^+, the autoprotolysis of water is better represented by the following reaction,

$$2H_2O \rightleftharpoons H_3O^+ + OH^- \qquad (4)$$

To simplify the discussion we shall make the approximations of replacing the activities in acidity constants by the numerical values of the molar concentrations. Consequently,

$$K_w = [H_3O^+]\ [OH^-] \qquad (5)$$

At 298.15 K, $K_w = 1.008\ 10^{-14}$ [16], showing that only a few of the water molecules are ionized. Conventionally, Eqs. (4) and (5) are those more used in studies of acid-base equilibria in aqueous medium. However, we believe that both equations should be improved, considering the solvation of the hydroxyl ion. The solvation of anions is effective in protic solvents where hydrogen bonds may be formed between the proton of the solvent and the lone pairs of electrons of the anion [17].

The total energies of the alone and solvated OH^- ion were calculated in water at B3LYP/6-311++G(d,p), using Tomasi's model. To illustrate, Fig. 1 shows the structure of one hydroxyl ion solvated with four water molecules. It can be observed that the water molecules, exerting its high hydrogen-bond-donor (HBD) capability [18], form intermolecular hydrogen bonds (IHBs) with the OH^- ion. In our example, the distances (*d*) between the O_1^- atom of hydroxyl group and the H_5, H_7, H_{10} and H_{13} atoms of the four water molecules are equal to 1.749 Å. On the other hand, the distances between the oxygen atoms of the hydroxyl group and of the water molecules are equal to 2.715 Å. Furthermore, the bond angles (*A*) formed by the involved atoms ($O_3H_5O_1^-$, $O_6H_7\ O_1^-$,

$O_9H_{10}O_1^-$ and $O_{12}H_{13}O_1^-$) in the IHBs are similar to 163.2° in all cases. These data allow concluding that the IHBs between the OH^- ion and the water molecules of solvation belong to the class of moderate or strong H bonds [19].

Table 1 summarizes the variations of the total energy (kcal mol^{-1}) of the solvated OH^- ion per water molecule, as a function of the total number of solvation water molecules. It should be pointed out that $(H_2O)(OH^-)$, $2(H_2O)(OH^-)$, $3(H_2O)(OH^-)$ and $4(H_2O)(OH^-)$ are here used to stand for the solvated OH^- ions with 1, 2, 3 and 4 water molecules, respectively. Table 1 shows the striking decrease of the total energy of the OH^- ion when its solvation increases. For each solvation water molecule, the OH^- ion decreases its relative energy by 48,000 kcal mol^{-1} approximately. Considering these facts and in order to provide a more satisfactory representation of the protolysis of water, we propose the reaction that follows,

$$3H_2O \rightleftharpoons (H_2O)H^+ + (H_2O)OH^- \qquad (6)$$

In the above reaction, (H_2O) indicates the water molecules of solvation of the H^+ and OH^- ions. This is to say that the proposed reaction considers that both H^+ and OH^- ions are hydrated with one water molecule. It must be noted that H_3O^+ or $(H_2O)H^+$ will be used to represent the hydronium ion.

Moreover, indicating with K_N the equilibrium constant of the reaction of Eq. (6) and taking into account Eqs. (4) and (5), it is inferred that,

$$K_w = K_N\,[H_2O] \qquad (7)$$

where $[H_2O]$ is the molar concentration of water. Consequently, at 298.15 K, it was calculated that,

$$K_N = \frac{K_w}{[H_2O]} = 1.831\ \ 10^{-16} \qquad (8)$$

In alkaline solutions it was considered that monoprotic weak acids suffer a reaction of partial neutralization as follows,

$$AOH + (H_2O)(OH^-) \rightleftharpoons (H_2O)A(O^-) + (H_2O) \qquad (9)$$

In this reaction, AOH is the acid and $(H_2O)A(O^-)$ represents the conjugate base solvated with one water molecule. The previous reaction is characterized by an equilibrium constant, K_C, which was theoretically determined. In addition to the reaction described in Eq. (9), the ionization reaction of water described in Eq. (6) takes place as well. Combining Eqs. (6) and (9), we obtain the reaction of Eq. (10), which defines the ionization constant of monoprotic weak acids (K_a), and which considers the solvation of the $A(O^-)$ anion.

$$AOH + 2H_2O \rightleftharpoons (H_2O)A(O^-) + H_3O^+ \qquad (10)$$

It is evident that the constants K_C, K_N and K_a are related by the equation,

$$K_a = K_C\ K_N \tag{11}$$

The above equation was used to determine theoretically the value of the ionization constant of AOH in water. Tables 2-7 summarize the optimized values of molecular properties of all the species involved in the reaction described by Eq. (9) for acids 1-6, respectively. The experimental values of the corresponding ionization constants ($K_{a\ Exp}$) [20,21] are also given in these Tables.

It must be noted that the solvation of the conjugate bases with one water molecule implies the formation of IHBs between the O^- atom of the conjugate bases and the H atom of water molecules, which exert their high HBD ability [18]. The distances and angles that characterize these IHBs in compounds **1**-**4** (Tables 2-5) indicate that they belong to the class of moderate IHBs [19], while in compounds **5** and **6** (Tables 6 and 7) these IHBs are strong. On the other hand, it should be remarked that the $(H_2O)A(O^-)$ molecules practically maintain the same structure that characterizes the non-solvated AOH molecules. To illustrate, Fig. 2 shows the structures of non-solvated fluoroacetic acid and their corresponding solvated conjugate base. It was determined that the dihedral angles D-$O_3C_2O_4H_8$ (Fig. 2a) and D-$O_3C_2O_4H_9$ (Fig. 2b) are equal to 0°. Moreover, it is clear that the formation of an $A(O^-)$ anion implies that the electronic density of the carboxylate oxygen atom increases notably (in absolute value) with respect to the carboxyl oxygen atom of AOH.

The experimental pK_a values of the monoprotic acids analyzed [20,21], increase as,

$$pK_{a\ Exp}(\mathbf{2})=2.59 < pK_{a\ Exp}(\mathbf{3})=2.85 \approx pK_{a\ Exp}(\mathbf{4})=2.90 < pK_{a\ Exp}(\mathbf{1})= 4.76$$
$$< pK_{a\ Exp}(\mathbf{5})= 7.40 < pK_{a\ Exp}(\mathbf{6})=8.55 \tag{12}$$

On the other hand, the pK_a values calculated by us ($pK_{a\ Theo}$) increase in the following order,

$$pK_{a\ Theo}(\mathbf{2})=2.47 < pK_{a\ Theo}(\mathbf{3})=2.54 < pK_{a\ Theo}(\mathbf{4})=3.06 < pK_{a\ Theo}(\mathbf{1})= 4.82$$
$$< pK_{a\ Theo}(\mathbf{5})= 6.06 < pK_{a\ Theo}(\mathbf{6})=8.48 \tag{13}$$

Comparing Eqs. (12) and (13) it is inferred that the $pK_{a\ Theo}$ constants here obtained are in good agreement with the $pK_{a\ Exp}$ constants. The percentual deviations between the values of $pK_{a\ Theo}$ and $pK_{a\ Exp}$ for **1**, **2**, **3, 4, 5,** and **6**, are 1.26%; -4.63%, -10.9%, 5.52%, -18.1% and -0.82%, respectively. Moreover, from Tables 2-7 it is observed that the K_C constants increase when the total atomic charge (qO) of the carboxyl oxygen atom (compounds **1**-**4**) or of the oxygen atom bound to halogen atom (compounds **5** and **6**) decreases (in absolute value) in the AOH molecules. This fact indicates that the ionization of AOH is favored when its qO decreases.

The calculation of the ionization constants of **1**-**6** was also performed using the $CSpK_a$ predictor [9], which is based on topological structure descriptors and was developed by the use of artificial neural networks. Using this software, the following pK_a values were obtained,

$$pK_a\,(\mathbf{2})=3.12 < pK_a\,(\mathbf{3})=3.18 < pK_a\,(\mathbf{4})=3.74 < pK_a\,(\mathbf{1})= 4.33$$
$$< pK_a\,(\mathbf{5})= 6.05 < pK_a\,(\mathbf{6})=6.30 \qquad (14)$$

The above pK_a values are in reasonable agreement with the experimentally determined ones (Eq. (12)). However, the pK_a predicted with the $CSpK_a$ program are more distant from the experimental pK_a values than those calculated by us.

It is evident that in order to assure the reliability of a new method for the calculation of the ionization constants of monoprotic acids, it is necessary to consider a higher number of compounds than that considered in this work. Nevertheless, we conclude that the very good relationship between the calculated pK_a values and those obtained experimentally constitutes a good support for the reactions and equilibria of ionization proposed in this work.

4 CONCLUSIONS

We have calculated the ionization constants of monoprotic weak acids in aqueous solution, based on the proposal of new equations to describe the acid-base properties of the solvent and the solutes. Thus, a reaction for water autoprotolysis was put forward that considers the solvation of the hydrogen and hydroxyl ions; as well as other reactions and acid-base equilibria that take into account the solvation of the conjugate bases in protic solvents such as water, which possess a high hydrogen-bond-donor capability. Additionally, it was considered that the solvation of the ions occurs by means of intermolecular hydrogen bonds that involve one molecule of the ion and one molecule of water. The calculations were performed with the B3LYP/6-311++G(d,p) method and using Tomasi's model. The calculated ionization constants show good agreement with the experimental constants. It is concluded that this fact constitutes a good support for the reactions and equilibria of ionization in aqueous medium proposed in this work.

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Table 1. Calculated total energy using the Tomasi's method at B3LYP/6-311++G(d,p) for hydrated hydroxyl ion, at 298 K. (n = total number of solvation water molecules; G^o_{sol} = total free energy in solution; G^o_{sol}/ molecule = total energy of the solvated OH^- ion per water molecule).

n	Solvated hydroxyl ion	G^o_{sol} Hartree	G^o_{sol} kcal mol^{-1}	G^o_{sol}/molecule kcal mol^{-1}
0	(OH^-)	-75.982448	-47679.7	-47679.7
1	$(H_2O)(OH^-)$	-152.464452	-95673.0	-47836.5
2	$2(H_2O)(OH^-)$	-228.945367	-143665.5	-47888.5
3	$3(H_2O)(OH^-)$	-305.424030	-191656.6	-47914.2
4	$4(H_2O)(OH^-)$	-381.889946	-239639.8	-47928.0

Table 2. Calculated molecular parameters and properties whit the Tomasi's method at B3LYP/6-311++G(d,p) for acetic acid (AcOH), monohydrated hydroxyl ion ((H_2O)(OH^-)), monohydrated acetate anion ((H_2O)(AcO^-)) and water molecule (H_2O), in aqueous medium at 298 K. G^o_{sol}= total free energy in solution, kcal mol^{-1};. K_N= constant of Eq. (8); K_C= equilibrium constant of Eq. (9); $K_{a\ Theo}$= theoretical ionization constant of the acid in water, Eq. (11); $K_{a\ Exp}$= experimental ionization constant [20]; *q*= total atomic charge (Mulliken), a.u.; dH_{water}-O^-= distance of the IHB between the indicated atoms, Å; A-$O_wH_wO^-$= H-Bond angle (º).

Calculated magnitudes	AcOH	(H_2O)(OH^-)	(H_2O)(AcO^-)	H_2O
G^o_{sol}	-143809.8	-95673.0	-191509.6	-47988.1
K_N		$1.831\ 10^{-16}$		
K_C		$8.352\ 10^{10}$		
$K_{a\ Theo}$		$1.529\ 10^{-5}$		
$pK_{a\ Theo}$		4.82		
$K_{a\ Exp}$		$1.738\ 10^{-5}$		
$pK_{a\ Exp}$		4.76		
$qO_{Carbonyl}$	-0.409	---	-0.578	---
$qO_{Carboxyl}$	-0.224	---	-0.595	---
qH_{water}	---	---	0.353	---
dH_{water}-O^-	---	---	1.724	---
A-$O_wH_wO^-$	---	---	161.4	---

Table 3. Calculated molecular parameters and properties whit the Tomasi's method at B3LYP/6-311++G(d,p) for fluoroacetic acid (FAcOH), monohydrated hydroxyl ion ($(H_2O)(OH^-)$), monohydrated fluoroacetate anion ($(H_2O)(FAcO^-)$) and water molecule (H_2O), in aqueous medium at 298 K. G^o_{sol}= total free energy in solution, kcal mol^{-1};. K_N= constant of Eq. (8); K_C= equilibrium constant of Eq. (9); $K_{a\ Theo}$= theoretical ionization constant of the acid in water, Eq. (11); $K_{a\ Exp}$= experimental ionization constant [21]; *q*= total atomic charge (Mulliken), a.u.; dH_{water}-O^-= distance of the IHB between the indicated atoms, Å; A-$O_wH_wO^-$= H-Bond angle (º).

Calculated magnitudes	FAcOH	$(H_2O)(OH^-)$	$(H_2O)(FAcO^-)$	H_2O
G^o_{sol}	-206094.4	-95673.0	-253797.4	-47988.1
K_N		$1.831\ 10^{-16}$		
K_C		$1.851\ 10^{13}$		
$K_{a\ Theo}$		$3.389\ 10^{-3}$		
$pK_{a\ Theo}$		2.47		
$K_{a\ Exp}$		$2.570\ 10^{-3}$		
$pK_{a\ Exp}$		2.59		
$qO_{Carbonyl}$	-0.376	---	-0.555	---
$qO_{Carboxyl}$	-0.205	---	-0.533	---
qH_{water}	---	---	0.373	---
dH_{water}-O^-	---	---	1.761	---
A-$O_wH_wO^-$	---	---	161.0	---

Table 4. Calculated molecular parameters and properties whit the Tomasi's method at B3LYP/6-311++G(d,p) for chloroacetic acid (ClAcOH), monohydrated hydroxyl ion ((H_2O)(OH^-)), monohydrated chloroacetate anion ((H_2O)($ClAcO^-$)) and water molecule (H_2O), in aqueous medium at 298 K. G^o_{sol}= total free energy in solution, kcal mol^{-1};. K_N= constant of Eq. (8); K_C= equilibrium constant of Eq. (9); $K_{a\ Theo}$= theoretical ionization constant of the acid in water, Eq. (11); $K_{a\ Exp}$= experimental ionization constant [20]; *q*= total atomic charge (Mulliken), a.u.; dH_{water}-O^-= distance of the IHB between the indicated atoms, Å; A-$O_wH_wO^-$= H-Bond angle (º).

Calculated magnitudes	ClAcOH	(H_2O)(OH^-)	(H_2O)($ClAcO^-$)	H_2O
G^o_{sol}	-432220.4	-95673.0	-479923.3	-47988.1
K_N		$1.831\ 10^{-16}$		
K_C		$1.564\ 10^{13}$		
$K_{a\ Theo}$		$2.863\ 10^{-3}$		
$pK_{a\ Theo}$		2.54		
$K_{a\ Exp}$		$1.413\ 10^{-3}$		
$pK_{a\ Exp}$		2.85		
$qO_{Carbonyl}$	-0.352	---	-0.525	---
$qO_{Carboxyl}$	-0.183	---	-0.484	---
qH_{water}	---	---	0.367	---
dH_{water}-O^-	---	---	1.771	---
A-$O_wH_wO^-$	---	---	161.1	---

Table 5. Calculated molecular parameters and properties whit the Tomasi's method at B3LYP/6-311++G(d,p) for bromoacetic acid (BrAcOH), monohydrated hydroxyl ion ($(H_2O)(OH^-)$), monohydrated bromoacetate anion ($(H_2O)(BrAcO^-)$) and water molecule (H_2O), in aqueous medium at 298 K. G^o_{sol}= total free energy in solution, kcal mol^{-1};. K_N= constant of Eq. (8); K_C= equilibrium constant of Eq. (9); $K_{a\ Theo}$= theoretical ionization constant of the acid in water, Eq. (11); $K_{a\ Exp}$= experimental ionization constant [20]; *q*= total atomic charge (Mulliken), a.u.; dH_{water}-O^-= distance of the IHB between the indicated atoms, Å; A-$O_wH_wO^-$= H-Bond angle (º).

Calculated magnitudes	BrAcOH	$(H_2O)(OH^-)$	$(H_2O)(BrAcO^-)$	H_2O
G^o_{sol}	-1758729.8	-95673.0	-1806432.0	-47988.1
K_N	$1.831\ 10^{-16}$			
K_C	$4.798\ 10^{12}$			
$K_{a\ Theo}$	$8.784\ 10^{-4}$			
$pK_{a\ Theo}$	3.06			
$K_{a\ Exp}$	$1.259\ 10^{-3}$			
$pK_{a\ Exp}$	2.90			
$qO_{Carbonyl}$	-0.333	---	-0.483	---
$qO_{Carboxyl}$	-0.210	---	-0.554	---
qH_{water}	---	---	0.405	---
dH_{water}-O^-	---	---	1.777	---
A-$O_wH_wO^-$	---	---	161.3	---

Table 6. Calculated molecular parameters and properties whit the Tomasi's method at B3LYP/6-311++G(d,p) for hypochlorous acid (HClO), monohydrated hydroxyl ion ($(H_2O)(OH^-)$), monohydrated hypochlorite anion ($(H_2O)(ClO^-)$) and water molecule (H_2O), in aqueous medium at 298 K. G^o_{sol}= total free energy in solution, kcal mol^{-1};. K_N= constant of Eq. (8); K_C= equilibrium constant of Eq. (9); $K_{a\ Theo}$= theoretical ionization constant of the acid in water, Eq. (11); $K_{a\ Exp}$= experimental ionization constant [20]; *q*= total atomic charge (Mulliken), a.u.; dH_{water}-O^-= distance of the IHB between the indicated atoms, Å; A-$O_wH_wO^-$= H-Bond angle (°).

Calculated magnitudes	HClO	$(H_2O)(OH^-)$	$(H_2O)(ClO^-)$	H_2O
G^o_{sol}	-336356.5	-95673.0	-384054.6	-47988.1
K_N		$1.831\ 10^{-16}$		
K_C		$4.739\ 10^{9}$		
$K_{a\ Theo}$		$8.677\ 10^{-7}$		
$pK_{a\ Theo}$		6.06		
$K_{a\ Exp}$		$3.981\ 10^{-8}$		
$pK_{a\ Exp}$		7.40		
$qO_{\ Hypochlorous}$	-0.343	---	---	---
$qO_{\ Hypochlorite}$	---	---	-0.756	---
$qH_{\ water}$	---	---	0.379	---
dH_{water}-O^-	---	---	1.616	---
A-$O_wH_wO^-$	---	---	175.8	---

Table 7. Calculated molecular parameters and properties whit the Tomasi's method at B3LYP/6-311++G(d,p) for hypobromous acid (HBrO), monohydrated hydroxyl ion ($(H_2O)(OH^-)$), monohydrated hypobromite anion ($(H_2O)(BrO^-)$) and water molecule (H_2O), in aqueous medium at 298 K. G^o_{sol}= total free energy in solution, kcal mol^{-1};. K_N= constant of Eq. (8); K_C= equilibrium constant of Eq. (9); $K_{a\ Theo}$= theoretical ionization constant of the acid in water, Eq. (11); $K_{a\ Exp}$= experimental ionization constant [20]; *q*= total atomic charge (Mulliken), a.u.; dH_{water}-O^-= distance of the IHB between the indicated atoms, Å; A-$O_wH_wO^-$= H-Bond angle (º).

Calculated magnitudes	HBrO	$(H_2O)(OH^-)$	$(H_2O)(BrO^-)$	H_2O
G^o_{sol}	-1662871.8	-95673.0	-1710566.6	-47988.1
K_N	$1.831\ 10^{-16}$			
K_C	$1.806\ 10^{7}$			
$K_{a\ Theo}$	$3.307\ 10^{-9}$			
$pK_{a\ Theo}$	8.48			
$K_{a\ Exp}$	$2.818\ 10^{-9}$			
$pK_{a\ Exp}$	8.55			
$qO_{\ Hypobromous}$	-0.399	---	---	---
$qO_{\ Hypobromite}$	---	---	-0.791	---
$qH_{\ water}$	---	---	0.383	---
dH_{water}-O^-	---	---	1.631	---
A-$O_wH_wO^-$	---	---	175.7	---

Figure 1. Structure of the hydroxyl ion solvated with four water molecules.

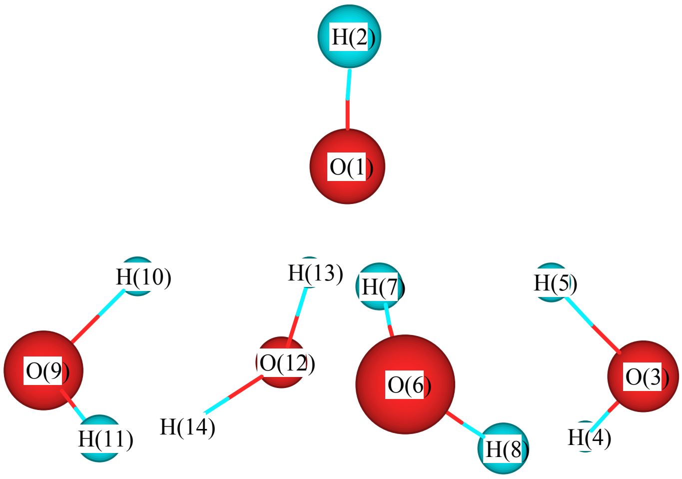

Figure 2. Calculated structures for fluoroacetic acid and their conjugate base solvated with one water molecule, at B3LYP/6-311++G(d,p) using the Tomasi's method, in water at 298 K.