Ionization of Organic Acids in Dimethyl Sulfoxide Solution: A Theoretical Ab Initio Calculation of the pK_a Using a New Parametrization of the Polarizable Continuum Model

Gizelle I. Almerindo, Daniel W. Tondo, and Josefredo R. Pliego Jr.*

Departamento de Química−Universidade Federal de Santa Catarina,
CEP 88040-900 Florianópolis, SC, Brazil

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The pK_a values of over 41 organic acids in dimethyl sulfoxide (DMSO) solution were calculated using ab initio electronic structure methods at MP2 and MP4 levels of electron correlation and including basis set of 6-31+G(d) and 6-311+G(2df,2p) quality. The solvation was included through the polarizable continuum model (PCM), using the recent parametrization of Pliego and Riveros. The root-mean-square (RMS) error over this set of molecules having different functional groups is only 2.2 units. A linear fit on this data set decreases this error by only 0.2 units, indicating that this empirical correction is not necessary. The major error in the calculated pK_a value was −5.3 units for the CH_3SO_3H solute. Halogenated carboxylic acids have also presented a high deviation (∼4 units). An explanation for these high deviations is the possibility of strong hydrogen-bond formation involving the neutral acid molecule and DMSO. The pK_a values were also calculated using a combination of theoretical solvation data with experimental gas-phase data. In this case, the RMS error increased to 2.3 units for a set of 36 acids. Our results show that the performance of the PCM model with a fixed atomic radius in DMSO solution is very superior to its performance in aqueous solution, which is a behavior that can be attributed to the presence of strong and specific solute−solvent interactions of ionic solutes with water molecules. In addition, no extensive parametrization of the PCM model is needed to describe the solvation of anions in DMSO solution.

I. Introduction

Many chemical reactions are initiated by the ionization of a neutral organic molecule via proton abstraction. An important example is the ionization of a carbonyl compound, leading to an enolate, which has a central role in the aldol condensation reactions. Incidentally, a reliable theoretical calculation of the pK_a value in any solvent is critically important in the modeling of chemical reactions in the liquid phase.

In the past fifteen years, there has been a considerable increase in the theoretical works on the calculation of the pK_a value in aqueous solution.[1−34] In early reports by Jorgensen et al., the authors have made use of Monte Carlo (MC) simulations, coupled with free-energy perturbation.[33,34] The following works have concentrated mainly on the use of continuum solvation models, with the exception of some reports that used hybrid quantum mechanical/molecular mechanical methods[28] and integral equation theory.[29] The performance of continuum models in aqueous solution has been limited, and these methods are more adequate to predict differences in the pK_a values of molecules with the same functional group. In fact, a recent work by Pliego and Riveros has noted that the main deficiency of continuum models to predict pK_a is its inadequate treatment of the specific solute−solvent interactions in the first solvation shell.[5] These authors have proposed a hybrid method to describe the solvation of ions,[35] which is based on the introduction of two or three explicit water molecules to the bare ion and considers the resulting cluster as a chemical species solvated by a dielectric continuum. This cluster-continuum model predicts pK_a values in much better agreement with experimental data than pure continuum models. For comparison, the standard deviation of the pK_a value calculated by this hybrid method is just 2.2 units, versus 7.3 units for the PCM and 7.2 units for the SM5.42R method, using a set of 15 species. Pratt and coworkers have also obtained good results in the calculation of the hydrolysis reactions of hydrated metals such as $Fe(H_2O)_6{}^{3+}$ and the pK_a of $Be(H_2O)_4{}^{+}$, using a hybrid discrete/continuum model,[4,23] which the authors have named “quasi-chemical theory”. Other authors have also calculated the pK_a value of hydrated metal cations using hybrid approaches.[27]

Although the pK_a values in aqueous solution have received much attention, there are few reports on the calculation of pK_a in nonaqueous solvents.[8,36] An early work by Wiberg et al.[36] presented the calculation of the Gibbs free energy of proton transfer in a dimethyl sulfoxide (DMSO) solution but not the respective pK_a values. In the recent article by Chipman,[8] the author used an isodensity surface-based continuum solvation model to calculate the pK_a value of organic acids in water, DMSO, and acetonitrile. The correlation between the calculated and experimental pK_a was poor in water but much better in the organic solvents. This different performance can be attributed to the lack of strong and specific (hydrogen bond) solute−solvent interactions in the dipolar aprotic solvents. Indeed, the lack of ability of these solvents to solvate anions is long known,[37] and a recent work has provided quantitative solvation data of ions in water and DMSO solutions.[38]

Continuum models constitute a very simple representation of the solvent, and the introduction of some empiricism in the model is required to obtain good accuracy in the calculation of solvation free energies. The empirical parameter is usually the solute cavity, which is fitted to reproduce experimental solvation free energies[39−41] and is dependent on the solvent. Another

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* Author to whom correspondence should be addressed. E-mail: josef@qmc.ufsc.br.

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approach by Cramer and Truhlar[42−44] adds empirical terms to the dielectric continuum $\Delta G^*_{\mathrm{solv}}$ value to account for specific and nonelectrostatic contribution to the solvation free energy. However, their model uses the same atomic radius for the solute in any solvent. Considering that the electrostatic contribution to the $\Delta G^*_{\mathrm{solv}}$ value of anions is highly dependent on the cavity size, this approach does not work for comparing the solvation of anions in water and DMSO, because it predicts that these solvents will have the same solvation ability.[45]

Until recently, extensive solvation data of organic ions in organic solvent were unavailable, and, consequently, no continuum model was adequately parametrized to calculate the solvation free energy in these solvents. The usual procedure of only changing the dielectric constant but maintaining the cavities that are optimized for aqueous solutions is unreliable and can lead to serious errors in the calculated $\Delta G^*_{\mathrm{solv}}$ value. However, two recent papers by Pliego and Riveros have presented extensive solvation data of organic ions in DMSO solution[38] and made the first parametrization of the polarizable continuum model (PCM) to describe the solvation of anions in this important solvent.[45] A next step in establishing a reliable methodology to describe anions and neutral molecules in DMSO using the PCM is to test the parametrization. Thus, the present work is an extensive test of the performance of the Pliego and Riveros parametrization to predict pK_a values of organic acids in DMSO solution. We have studied the pK_a values of ~41 organic acids with diverse functional groups.

II. Calculation of pK_a

The calculation of the pK_a value in DMSO solution can be undertaken through the use of the following proton-transfer reaction:

$$HA + OH^- \rightarrow A^- + H_2O \tag{1}$$

This approach is more adequate than using the direct ionization of the HA acid, because it does not require the value of the experimental solvation free energy of the H^+ ion. Based on eq 1, we can write the general chemical equilibrium relationship:

$$\mu(A^-) + \mu(H_2O) - \mu(HA) - \mu(OH^-) = 0 \tag{2}$$

where $\mu_{\mathrm{sol}}(X)$ is the chemical potential of species X, namely

$$\mu_{\mathrm{sol}}(X) = \mu^*_g(X) + \Delta G^*_{\mathrm{solv}}(X) + RT\ln[X] \tag{3}$$

In eq 3, the first term on the right-hand side is the gas-phase chemical potential of X at a concentration of 1 mol L^{-1}, the second term is the solvation free energy, and the last term is related to the concentration of X in solution. Combining eqs 1 and 2 leads to the following relationship:

$$e^{-\Delta G^*_{\mathrm{sol}}/(RT)} = \frac{[A^-][H_2O]}{[HA][OH^-]} = \frac{K_a(HA)}{K_a(H_2O)} \tag{4}$$

where $\Delta G^*_{\mathrm{sol}}$ is given by

$$\Delta G^*_{\mathrm{sol}} = \Delta G^*_{\mathrm{g}} + \Delta\Delta G^*_{\mathrm{solv}} \tag{5}$$

$$\Delta G^*_{\mathrm{g}} = \mu^*_{\mathrm{g}}(A^-) + \mu^*_{\mathrm{g}}(H_2O) - \mu^*_{\mathrm{g}}(HA) - \mu^*_{\mathrm{g}}(OH^-) \tag{6}$$

$$\Delta\Delta G^*_{\mathrm{solv}} = \Delta G^*_{\mathrm{solv}}(A^-) + \Delta G^*_{\mathrm{solv}}(H_2O) - \Delta G^*_{\mathrm{solv}}(HA) - \Delta G^*_{\mathrm{solv}}(OH^-) \tag{7}$$

TABLE 1: Calculated Solvation Free Energy of Neutral and Anionic Species of Oxygen, Sulfur, and HF Acids in Dimethyl Sulfoxide Solution[a]

HA	$\Delta G^*_{\mathrm{solv}}$ (kcal mol^{-1})	A^-	$\Delta G^*_{\mathrm{solv}}$ (kcal mol^{-1})
H_2O	−5.04	OH^-	−82.30
CH_3SO_3H	−8.68	$CH_3SO_3^-$	−61.57
CF_3COOH	−4.55	CF_3COO^-	−55.99
$CHCl_2COOH$	−4.86	$CHCl_2COO^-$	−55.97
HONO	−4.04	ONO^-	−63.76
$(CF_3)_3COH$	−2.79	$(CF_3)_3CO^-$	−52.53
PhCOOH	−4.97	$PhCOO^-$	−60.22
CH_3COOH	−4.83	CH_3COO^-	−64.74
PhCONHOH	−6.44	$PhCONHO^-$	−67.92
PhOH	−4.37	PhO^-	−57.27
CF_3CH_2OH	−5.57	$CF_3CH_2O^-$	−61.45
CH_3OH	−3.62	CH_3O^-	−71.01
$(CH_3)_2CHOH$	−3.31	$(CH3)_2CHO^-$	−65.72
CH_3CH_2OH	−3.45	$CH_3CH_2O^-$	−68.15
$(CH_3)_3COH$	−3.23	$(CH3)_3CO^-$	−63.43
PhCOSH	−4.02	$PhCOS^-$	−55.78
PhSH	−2.56	PhS^-	−55.93
$PhCH_2SH$	−3.54	$PhCH_2S^-$	−59.45
HF	−4.20	F^-	−84.92

[a] Ab initio calculations made at the PCM/HF/6-31+G(d) level.

Taking the negative logarithm (−log) on each side of eq 4, we can obtain

$$pK_a(HA) = pK_a(H_2O) + \frac{\Delta G^*_{\mathrm{sol}}}{2.303RT} \tag{8}$$

Equations 5−8 were used in the present work to calculate the pK_a value of organic acids. We have also used the experimental pK_a value of 31.2 for water reported by Bordwell.[46]

III. Ab Initio Calculations

The structure of neutral and ionic species was obtained by full geometry optimization at the HF/6-31+G(d) level of theory, and the nature of the stationary points was determined by harmonic frequency calculations. To obtain accurate energies, we have performed single-point calculation on the optimized geometries at the MP2/6-311+G(2df,2p) and MP4/6-31+G(d) levels of theory. In addition, we have used the additivity approximation of the correlation energy to obtain effective MP4/6-311+G(2df,2p) energies. Cartesian Gaussian functions 10f and 6d was used instead of pure spherical 7f and 5d functions. The final gas-phase thermodynamic properties were calculated using standard statistical mechanics formulas.

The solvation free energy was calculated through the PCM,[47−49] including correction for the charges lying outside of the cavity surface. The BEM routine was used in conjunction with the HF/6-31+G(d) wave function, as well as a dielectric constant value of 46.7 for the DMSO solvent. Only electrostatic interactions were included in the solvation free-energy calculation. The cavity sizes were taken from the Pliego and Riveros work,[45] namely 1.20 (H), 1.50 (O), 1.60 (N), 1.70 (C), 1.40 (F), 1.81 (Cl), and 1.85 (S), with a scale factor of 1.35 for every atom. All theoretical calculations were performed using the PC Gamess[50] version of the Gamess (US) quantum chemistry package.[51]

IV. Results and Discussion

The molecules studied in the present work have very different functional groups, where the ionizable hydrogen is bonded to oxygen, nitrogen, carbon, and sulfur. The hydrofluoric acid (HF) was also included in the calculations. This large variety of

TABLE 2: Calculated Solvation Free Energy of Neutral and Anionic Species of Carbon and Nitrogen Acids in Dimethyl Sulfoxide Solution[a]

HA	ΔG^*_{solv} (kcal mol^{-1})	A^-	ΔG^*_{solv} (kcal mol^{-1})
$CH_2(CN)_2$	−8.05	$CH(CN)_2^-$	−51.84
HCN	−4.77	CN^-	−64.23
$(CH_3CO)_2CH_2$	−6.02	$(CH_3CO)_2CH^-$	−54.64
CH_3NO_2	−5.98	$CH_2NO_2^-$	−63.29
$PhCOCH_2F$	−4.99	$PhCOCHF^-$	−58.57
$PhCOCH_3$	−4.93	$PhCOCH_2^-$	−57.89
CH_3COCH_3	−4.50	$CH_3COCH_2^-$	−61.50
PhCCH	−3.03	$PhCC^-$	−59.97
CH_3CN	−5.13	CH_2CN^-	−59.12
CH_3SOCH_3	−8.53	$CH_3SOCH_2^-$	−60.33
$PhCH_3$	−1.96	$PhCH_2^-$	−51.91
HN_3	−3.51	N_3^-	−60.26
NH_2CN	−7.89	$NHCN^-$	−62.50
$PhCSNH_2$	−7.85	$PhCSNH^-$	−59.16
CF_3CONH_2	−6.39	CF_3CONH^-	−57.75
$CH_3SO_2NH_2$	−8.77	$CH_3SO_2NH^-$	−61.65
CH_3CSNH_2	−7.75	CH_3CSNH^-	−61.44
$PhCONH_2$	−7.29	$PhCONH^-$	−57.60
$HCONH_2$	−7.63	$HCONH^-$	−63.44
CH_3CONH_2	−7.33	CH_3CONH^-	−66.68
$(NH_2)_2CO$	−8.71	NH_2CONH^-	−68.14
$PhNH_2$	−4.38	$PhNH^-$	−55.98
NH_3	−3.54	NH_2^-	−77.39

[a] Ab initio calculations made at the PCM/HF/6-31+G(d) level.

functional groups is an important test of the present parametrization, because it evaluates the accuracy of the method for general situations. In fact, our intention is that this parametrization can be used for a reliable modeling of anion−molecule reactions in DMSO solution.

The solvation free energy for the studied acids and the respective anions are presented in Tables 1 and 2. The energy and free energy for the proton-transfer reaction between the HA acid and the hydroxide ion (eq 1) in gas phase and in DMSO solution are given in Tables 3 and 4. Finally, Tables 5 and 6 present the calculated pK_a values and the respective experimental values. A general overview of the performance of the present theoretical approach is shown in Figure 1, which shows the correlation between the theoretical and the experimental pK_a values. The $y = x$ curve is also included, to evaluate the quality of the correlation.

As can be observed, there is a good correlation between the theoretical and experimental pK_a values. The root-mean-square (RMS) error over all studied species is only 2.2 units. However, some species have an unexpected high error in their theoretical pK_a value. The major deviation occurs for the CH_3SO_3H acid (−5.3 units). Other oxygen acids also present a high deviation, such as the halogenated carboxylic acids. For example, the CF_3COOH and the $CHCl_2COOH$ species have a deviation of −4.7 and −4.1 units, respectively. On the other side, the theoretical pK_a value of the studied alcohols present a good agreement with the experimental data, with the exception of methanol, which has a deviation of 3.1 units. A high error is also observed for the only hydroxamic acid studied, PhCONHOH, which has a deviation of 3.6 units. Carbon acids have some species with high deviation; the major deviation occurs for the CH_3NO_2 acid (4.9 units). Ketones have deviations of >2 units, with exception of the $(CH_3CO)_2CH_2$ species, with an error of just 1.3 units. Interestingly, the trends in the deviations are positive in the case of carbon acids, which is a possible indication that the radius of the carbon is greater than the ideal value. A different situation is found for the nitrogen acids. In this case, there is an excellent correlation between the theoretical and experimental pK_a values; the major deviation is only −1.7 units, which is less than the overall standard deviation (RMS error). The results are yet better for the three sulfur acids, where excellent agreement is found between the theoretical and experimental pK_a values and the major error is 0.5 units.

To eliminate a possible error that originates from the ab initio method, the gas-phase contribution to the pK_a value must be analyzed. Although the MP4/6-311+G(2df,2p) level of theory used in this work is accurate to obtain electronic energies, it is possible that some molecules are more difficult to describe, which could lead to unexpected high error in the gas-phase reaction free energy. Thus, we have used the experimental gas-phase reaction ΔG^*_g, obtained from the NIST database,[52] in conjunction with our theoretical solvation free energy (see Tables 1 and 2) to calculate the pK_a value. This mixed theoretical−experimental pK_a value is shown in Table 7, as well as the experimental basicity, gas-phase reaction free energy, and the theoretical solvation contribution. Figure 2 shows the correlation between the calculated and the experimental pK_a value. Some species (PhCONHOH, PhCOSH, $PhCH_2SH$, $PhCOCH_2F$, $PhCSNH_2$) were not included, because of the lack of gas-phase data at NIST.

TABLE 3: Thermodynamic Properties for the $HA + OH^- \rightarrow A^- + H_2O$ Reaction Involving Oxygen, Sulfur, and HF Acids[a]

HA	HF/6-31+G(d)	MP2/6-31+G(d)	MP4/6-31+G(d)	MP2/ext[b]	MP4/ext[c]	ΔG^*_g	$\Delta\Delta G^*_{solv}$	ΔG^*_{sol}
CH_3SO_3H	−78.64	−72.29	−72.20	−73.24	−73.15	−72.01	24.34	−47.67
CF_3COOH	−71.82	−69.49	−69.64	−67.88	−68.04	−70.15	25.78	−44.37
$CHCl_2COOH$	−67.08	−63.08	−63.42	−63.63	−63.97	−65.51	26.11	−39.40
HONO	−57.21	−55.34	−54.86	−53.72	−53.25	−53.93	17.50	−36.43
$(CF_3)_3COH$	−57.07	−53.14	−53.67	−52.06	−52.58	−53.26	27.47	−25.79
PhCOOH	−52.60	−50.70	−51.13	−51.81	−52.24	−53.12	21.97	−31.15
CH_3COOH	−45.76	−43.10	−43.31	−43.82	−44.03	−46.10	17.31	−28.78
PhCONHOH	−31.65	−34.69	−33.05	−35.35	−33.72	−34.78	15.74	−19.04
PhOH	−42.87	−40.39	−41.52	−42.02	−43.14	−44.08	24.32	−19.76
CF_3CH_2OH	−31.93	−31.12	−31.79	−30.18	−30.84	−32.01	21.35	−10.66
CH_3OH	−7.19	−5.08	−5.38	−6.75	−7.04	−8.66	9.83	1.17
$(CH_3)_2CHOH$	−11.25	−11.55	−12.63	−13.15	−14.23	−16.31	14.81	−1.51
CH_3CH_2OH	−9.34	−8.86	−9.70	−10.44	−11.28	−13.43	12.52	−0.91
$(CH_3)_3COH$	−12.52	−13.12	−14.23	−14.85	−15.96	−17.34	17.03	−0.32
PhCOSH	−65.51	−59.30	−58.77	−62.18	−61.66	−60.27	25.46	−34.81
PhSH	−57.54	−51.24	−50.72	−55.07	−54.55	−52.29	23.85	−28.44
$PhCH_2SH$	−47.74	−40.05	−39.60	−43.65	−43.20	−42.31	21.31	−21.00
HF	−28.26	−26.79	−29.14	−20.51	−22.87	−19.79	−3.50	−23.28

[a] Units of kcal mol^{-1}. Standard state of 1 mol L^{-1}, $T = 298.15$ K. [b] Values correspond to MP2/6-311+G(2df,2p) calculations. [c] Values correspond to MP4/6-311+G(2df,2p) calculations obtained by additivity approximation.

TABLE 4: Thermodynamic Properties for the HA + OH^- → A^- + H_2O Reaction Involving Carbon and Nitrogen Acids[a]

HA	HF/6-31+G(d)	MP2/6-31+G(d)	MP4/6-31+G(d)	MP2/ext[b]	MP4/ext[c]	ΔG^*_g	$\Delta\Delta G^*_{solv}$	ΔG^*_{sol}
$CH_2(CN)_2$	−56.37	−52.39	−52.86	−58.67	−59.13	−60.45	33.43	−27.02
HCN	−48.67	−38.19	−39.20	−41.54	−42.55	−44.17	17.76	−26.41
$(CH_3CO)_2CH_2$	−47.06	−45.01	−44.13	−51.67	−50.79	−51.21	28.60	−22.61
CH_3NO_2	−34.66	−28.36	−28.09	−32.78	−32.51	−32.31	19.92	−12.39
$PhCOCH_2F$	−24.37	−26.82	−23.83	−33.77	−30.79	−32.46	23.64	−8.82
$PhCOCH_3$	−21.23	−21.94	−21.49	−29.16	−28.71	−29.95	24.26	−5.70
CH_3COCH_3	−16.69	−14.95	−14.37	−22.38	−21.81	−21.99	20.22	−1.77
PhCCH	−22.76	−16.54	−18.23	−20.89	−22.57	−23.36	20.28	−3.08
CH_3CN	−13.80	−8.46	−8.25	−16.33	−16.13	−18.66	23.23	4.57
CH_3SOCH_3	−9.74	−7.22	−7.11	−14.52	−14.41	−15.97	25.42	9.45
$PhCH_3$	0.24	3.17	2.56	−6.92	−7.54	−9.95	27.27	17.32
HN_3	−50.74	−56.53	−54.01	−57.19	−54.66	−52.32	20.47	−31.85
NH_2CN	−42.26	−37.77	−37.74	−43.10	−43.07	−44.13	22.61	−21.52
$PhCSNH_2$	−44.70	−37.94	−38.53	−43.19	−43.77	−44.83	25.92	−18.91
CF_3CONH_2	−43.75	−42.13	−42.69	−44.74	−45.29	−45.56	25.87	−19.70
$CH_3SO_2NH_2$	−43.95	−39.34	−39.34	−44.18	−44.18	−45.28	24.34	−20.94
CH_3CSNH_2	−41.65	−33.11	−33.55	−38.70	−39.14	−39.24	23.54	−15.70
$PhCONH_2$	−35.45	−33.69	−34.11	−37.26	−37.69	−38.64	26.91	−11.73
$HCONH_2$	−29.86	−27.66	−28.12	−30.44	−30.89	−31.30	21.41	−9.89
CH_3CONH_2	−21.42	−19.79	−20.33	−24.74	−25.28	−25.16	17.87	−7.29
$(NH_2)_2CO$	−20.82	−18.77	−19.40	−23.41	−24.03	−25.39	17.79	−7.60
$PhNH_2$	−19.21	−16.77	−17.86	−22.03	−23.12	−24.95	25.62	0.67
NH_3	18.89	21.11	21.08	14.80	14.77	12.07	3.37	15.44

[a] Units of kcal mol^{-1}. Standard state of 1 mol L^{-1}, $T = 298.15$ K. [b] Values correspond to MP2/6-311+G(2df,2p) calculations. [c] Values correspond to MP4/6-311+G(2df,2p) calculations obtained by additivity approximation.

TABLE 5: Theoretical and Experimental pK_a Values of Oxygen, Sulfur, and HF Acids in Dimethyl Sulfoxide Solution

HA	pK_a Value		ΔpK_a
	experimental[a]	theoretical	
CH_3SO_3H	1.6	−3.7	−5.3
CF_3COOH	3.4	−1.3	−4.7
$CHCl_2COOH$	6.4	2.3	−4.1
HONO	7.5	4.5	−3.0
$(CF_3)_3COH$	10.7	12.3	1.6
PhCOOH	11.0	8.4	−2.6
CH_3COOH	12.3	10.1	−2.2
PhCONHOH	13.6	17.2	3.6
PhOH	18.0	16.7	−1.3
CF_3CH_2OH	23.4	23.4	0.0
CH_3OH	29.0	32.1	3.1
$(CH_3)_2CHOH$	29.8	30.1	0.3
CH_3CH_2OH	30.2	30.5	0.3
$(CH_3)_3COH$	32.2	31.0	−1.2
PhCOSH	5.2	5.7	0.5
PhSH	10.3	10.4	0.1
$PhCH_2SH$	15.4	15.8	0.4
HF	15.0	14.1	−0.9

[a] Values taken from ref 46.

TABLE 6: Theoretical and Experimental pK_a Values of Carbon and Nitrogen Acids in Dimethyl Sulfoxide Solution

HA	pK_a Value		ΔpK_a
	experimental[a]	theoretical	
$CH_2(CN)_2$	11.0	11.4	0.4
HCN	12.9	11.8	−1.1
$(CH_3CO)_2CH_2$	13.3	14.6	1.3
CH_3NO_2	17.2	22.1	4.9
$PhCOCH_2F$	21.7	24.7	3.0
$PhCOCH_3$	24.7	27.0	2.3
CH_3COCH_3	26.5	29.9	3.4
PhCCH	28.7	29.0	0.3
CH_3CN	31.3	34.6	3.3
CH_3SOCH_3	35.1	38.1	3.0
$PhCH_3$	43.0	43.9	0.9
HN_3	7.9	7.9	0.0
NH_2CN	16.9	15.4	−1.5
$PhCSNH_2$	16.9	17.3	0.4
CF_3CONH_2	17.2	16.8	−0.4
$CH_3SO_2NH_2$	17.5	15.8	−1.7
CH_3CSNH_2	18.4	19.7	1.3
$PhCONH_2$	23.4	22.6	−0.8
$HCONH_2$	23.4	23.9	0.5
CH_3CONH_2	25.5	25.9	0.4
$(NH_2)_2CO$	26.9	25.6	−1.3
$PhNH_2$	30.6	31.7	1.1
NH_3	41.0	42.5	1.5

[a] Values taken from ref 46.

The overall performance of this mixed approach is similar to the full theoretical approach. Indeed, the RMS error (2.3 units for a set of 36 acids) is slightly greater than the error in our full theoretically calculated pK_a value (2.2 units for this same set of 36 acids). However, although the average deviations are similar, particular differences are originated from the gas-phase data. One notable observation is the decrease of the RMS error in the pK_a value for the carboxylic acids and the methanosulfonic acid. The error occurs in a systematic form, as a consequence of the theoretical ΔG^*_g data, to be ∼3−4 kcal mol^{-1} below of the experimental value. In the case of alcohols, excellent agreement is observed between the gas-phase data, with exception of the $(CF_3)_3COH$ species. In this case, the experimental value is 6.4 kcal mol^{-1} below the theoretical value. The calculated pK_a value is in error by −3.1 units, whereas for the full theoretical approach, the error is 1.6 units. In our opinion, there is considerable error in the experimental gas-phase data for this case. It is important to emphasize that many data from NIST are based on experiments that were conducted more than 20 years ago, and some values can be unreliable. More support to this argument is the calculated pK_a value of the nitrogen acids. The full theoretical values are similar to the experimental value, whereas the error in the pK_a values obtained by the mixed approach are greater and present some high deviations, the most notable of which is that for the HN_3 acid. For this species, the ab initio ΔG^*_g value is 6.5 kcal mol^{-1} more negative than the NIST value. Furthermore, the full theoretical pK_a value is in exact agreement with the experimental value, whereas the mixed calculated pK_a value has a deviation of 4.7 units. Thus, it seems

TABLE 7: Calculation of pK_a Using Combined Theoretical (Solvation Contribution) and Experimental (Gas-Phase Contribution) Data

HA	ΔG°_{bas} [a] (kcal mol^{-1})	ΔG^{*}_{g} [b] (kcal mol^{-1})	$\Delta\Delta G^{*}_{solv}$ (kcal mol^{-1})	ΔG^{*}_{sol} (kcal mol^{-1})	pK_a Value calculated[c]	pK_a Value experiment[d]	ΔpK_a
H_2O	383.7						
CH_3SO_3H	315.0	−68.7	24.3	−44.4	−1.3	1.6	−2.9
CF_3COOH	317.4	−66.3	25.8	−40.5	1.5	3.4	−1.9
$CHCl_2COOH$	321.9	−61.8	26.1	−35.7	5.0	6.4	−1.4
HONO	333.7	−50.0	17.5	−32.5	7.4	7.5	−0.1
$(CF_3)_3COH$	324.0	−59.7	27.5	−32.2	7.6	10.7	−3.1
PhCOOH	333.0	−50.7	22.0	−28.7	10.1	11.0	−0.9
CH_3COOH	341.1	−42.6	17.3	−25.3	12.7	12.3	0.4
PhOH	342.3	−41.4	24.3	−17.1	18.7	18.0	0.7
CF_3CH_2OH	354.1	−29.6	21.4	−8.2	25.2	23.4	1.8
CH_3OH	375.1	−8.6	9.8	1.2	32.1	29.0	3.1
$(CH_3)_2CHOH$	368.5	−15.2	14.8	−0.4	30.9	29.8	1.1
CH_3CH_2OH	371.7	−12.0	12.5	0.5	31.6	30.2	1.4
$(CH_3)_3COH$	368.1	−15.6	17.0	1.4	32.2	32.2	0.0
PhSH	333.8	−49.9	23.9	−26.1	12.1	10.3	1.8
HF	365.5	−18.2	−3.5	−21.7	15.3	15.0	0.3
$CH_2(CN)_2$	328.1	−55.6	33.4	−22.2	15.0	11.0	4.0
HCN	343.6	−40.1	17.8	−22.3	14.8	12.9	1.9
$(CH_3CO)_2CH_2$	336.7	−47.0	28.6	−18.4	17.7	13.3	4.4
CH_3NO_2	349.7	−34.0	19.9	−14.1	20.9	17.2	3.7
$PhCOCH_3$	354.5	−29.2	24.3	−4.9	27.6	24.7	2.9
CH_3COCH_3	361.9	−21.8	20.2	−1.6	30.0	26.5	3.5
PhCCH	362.9	−20.8	20.3	−0.5	30.8	28.7	2.1
CH_3CN	365.2	−18.5	23.2	4.7	34.7	31.3	3.4
CH_3SOCH_3	366.4	−17.3	25.4	8.1	37.2	35.1	2.1
$PhCH_3$	372.1	−11.6	27.3	15.7	42.7	43.0	−0.3
HN_3	337.9	−45.8	20.5	−25.3	12.6	7.9	4.7
NH_2CN	344.1	−39.6	22.6	−17.0	18.7	16.9	1.8
CF_3CONH_2	336.7	−47.0	25.9	−21.1	15.7	17.2	−1.5
$CH_3SO_2NH_2$	338.8	−44.9	24.3	−20.6	16.1	17.5	−1.4
CH_3CSNH_2	339.4	−44.3	23.5	−20.8	16.0	18.4	−2.4
$PhCONH_2$	347.0	−36.7	26.9	−9.8	24.0	23.4	0.6
$HCONH_2$	352.8	−30.9	21.4	−9.5	24.2	23.4	0.8
CH_3CONH_2	355.0	−28.7	17.9	−10.8	23.3	25.5	−2.2
$(NH_2)_2CO$	355.7	−28.0	17.8	−10.2	23.7	26.9	−3.2
$PhNH_2$	359.1	−24.6	25.6	1.0	31.9	30.6	1.3
NH_3	396.0	12.3	3.4	15.7	42.7	41.0	1.7

[a] Gas-phase basicity obtained from the NIST tables (ref 52). [b] Experimental reaction free energy for the gas-phase $HA + OH^- \rightarrow A^- + H_2O$ process. Based on data obtained from the NIST tables (ref 52). [c] pK_a calculated using the experimental gas-phase reaction free energy and the theoretical solvation contribution from data in Tables 1 and 2. [d] Experimental data taken from ref 46.

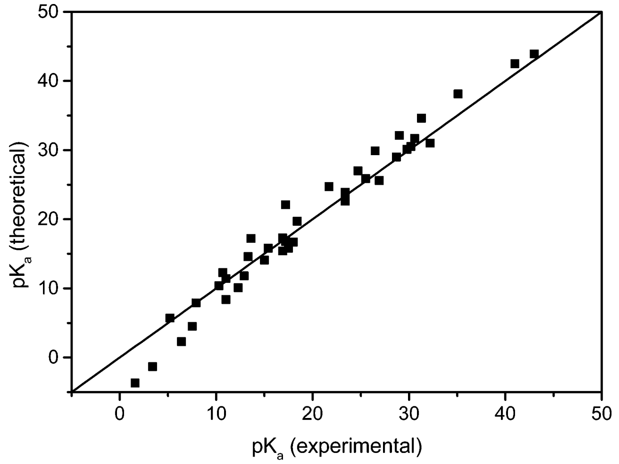

Figure 1. Theoretical versus experimental pK_a values. Straight line corresponds to the $y = x$ function. Data taken from Tables 5 and 6.

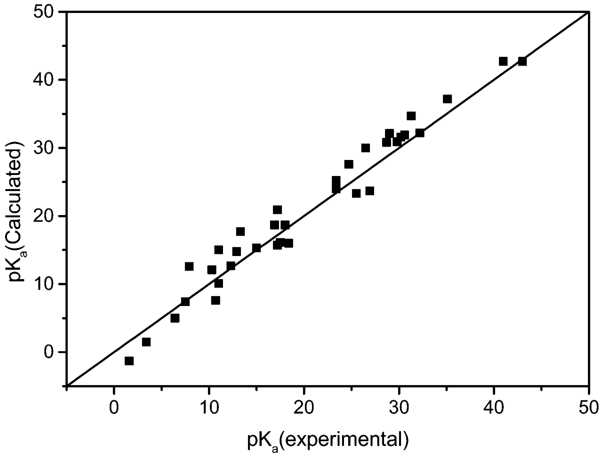

Figure 2. Calculated versus experimental pK_a values. Straight line corresponds to the $y = x$ function. Data taken from Table 7.

evident that some NIST values are in considerable error and we believe that our full theoretically calculated gas phase ΔG^{*}_{g} value is more reliable on the average. Incidentally, more work using the higher-level CCSD(T) method would be needed to provide more-accurate gas-phase data. In addition, it is possible that, for strong acids such as CH_3SO_3H, specific solute−solvent (hydrogen bond) interactions that involve the neutral acid and the DMSO molecule could occur, leading to error in the solvation free energy. Not considering such strong hydrogen bonding would lead to negative deviations in the pK_a value, as was observed in our theoretical calculations.

In a recent report by Chipman,[8] the author determined that the SSC(V)PE continuum model works very well in the prediction of the pK_a value of some species in DMSO solution.

However, he has performed a linear fit of the theoretical versus experimental pK_a values, to reproduce the experimental data, and used a small set of molecules. The present work uses a much more extended set of molecules without including a linear fit. Our objective is to establish a method with a minimum of empirism. Nevertheless, we have tested a linear fit and we have found that it does not lead to a great improvement in the standard deviation, which reduces to 2.0 units. In our opinion, it is a further indication that the Pliego and Riveros[45] parametrization of the PCM model is very adequate to describe anion−molecule reactions in DMSO solution, and the use of an empiricism such as linear fit is not necessary.

An important conclusion that emerges of the present study is that continuum models work adequately in solvents that do not have strong and specific interactions with the solute. On the other hand, solvents such as water, which can make strong hydrogen bonds with the solutes, is not accurately described by continuum models. This claim is also supported by a recent study[5] of the pK_a values of 15 species in water solution, which used continuum models as well as an hybrid discrete/continuum solvation model. In that study, the RMS error in the calculated pK_a value by the continuum models PCM and SM5.42R were ∼7 units, versus 2 units in the present study for DMSO as the solvent. Thus, it seems reasonable to suggest that continuum models should not be used to describe solvation in solvents that present specific interaction with the solute, because it would require the use of extensive parametrization of the atomic radius to calculate reliable solvation free energies. This procedure is not physically sound and should be of questionable performance in more-general situations. Rather, in these solvents where specific solvation occur, the use of a hybrid discrete/continuum model would be the physically correct approach and should lead to more-reliable results.

V. Conclusion

The present study supports the reliability of the Pliego and Riveros parametrization of the PCM model to describe the solvation of anions in dimethyl sulfoxide (DMSO) solution and to predict the pK_a values of neutral acids. In addition, note that this parametrization can be used for a quantitative study of anion−molecule reactions in DMSO solution. Another point that deserves attention is the fact that no extensive parametrization of the atomic cavities was needed to obtain good results. A linear fit of the theoretical pK_a value versus the experimental pK_a value does not lead to high improvement of the RMS error, which decreases by only 0.2 units. Future directions in the research to obtain further improvements in the theoretical calculation of the pK_a value in DMSO should make use of the more-accurate CCSD(T) method, decrease the cavity size of the C atom, and include specific solute−solvent interactions in the case of strong acids.

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