Computation of pK_a Values of Substituted Aniline Radical Cations in Dimethylsulfoxide Solution

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A newly developed computation strategy was used to calculate the absolute pK_a values of 18 substituted aniline radical cations in dimethylsulfoxide (DMSO) solution with the error origin elucidated and deviation minimized. The B3LYP/6-311++G(2df,2p) method was applied and was found to be capable of reproducing the gas-phase proton-transfer free energies of substituted anilines with a precision of 0.83 kcal/mol. The IEF-PCM solvation model with gas-phase optimized structures was adopted in calculating the pK_a values of the substituted neutral anilines in DMSO, regenerating the experimental results within a standard deviation of 0.4 pK_a unit. When the IEF-PCM solvation model was applied to calculate the standard redox potentials of anilide anions, it showed that the computed values agreed well with experiment, but the redox potentials of substituted anilines were systematically overestimated by 0.304 eV. The cause of this deviation was found to be related to the inaccuracy of the calculated solvation free energies of aniline radical cations. By adjusting the size of the cavity in the IEF-PCM method, we derived a reliable procedure that can reproduce the experimental pK_a values of aniline radical cations within 1.2 pK_a units to those from experiment.

1. Introduction

Radical cations formed by removal of an electron from neutral protonic species (HA) (eq 1) are known to be important transient intermediates in the oxidation of both organic and inorganic compounds.

$$\mathrm{HA} \xrightarrow{-\mathrm{e}} \mathrm{HA}^{\bullet +} \qquad (1)$$

The cation that bears a properly situated hydrogen atom may lose a proton to form a radical:

$$\mathrm{HA}^{\bullet +} \overset{K_a}{\rightleftharpoons} \mathrm{H}^{+} + \mathrm{A}^{\bullet} \qquad (2)$$

The fundamental importance of radical cations as transient intermediates in both chemical and biological processes has long been recognized, and their thermodynamic tendency to undergo acidic dissociation has attracted quite intensive research activities in the past.[1−3] However, most of the thermodynamic acidity data reported earlier were derived from a thermochemical cycle and the accuracy of these estimates on acidities has not been dedicatedly confirmed from outside sources. On the other hand, the direct detection of equilibrium concentrations of the transient radicals and radical cations requires complicated instrumentation. Even the less complicated indirect thermochemical method still involves accurate experimental determination of the pK_a and reversible electrode potentials of the corresponding species in the equilibrium that again often encounters substantial experimental difficulties.

The rapid development of computation methodologies now allows the acidity/basicity of small molecules in the gas phase to be calculated with equivalent or greater accuracy than that obtained from experiment.[4] A number of approaches to deal with the solvation effects have been developed at meanwhile for the evaluation of acidity/basicity in solution.[5−8] Among various solvation models applied, the dielectric continuum methods[8] become more popular in recent years.

A good representative of the dielectric continuum method is the polarized continuum model (PCM) developed by Tomasi and co-workers.[9] The mean errors of this model with respect to the experimental absolute solvation energies in water can be as low as 0.2 and 1.0 kcal/mol for neutral molecules and ions, respectively, and the errors in predicting pK_a values of various acids in aqueous solution can reach to as small as 0.5−2.2 pK_a units.[10] Fu and Guo et al., on the other hand, have used the PCM to calculate pK_a values for 105 neutral organic acids in DMSO with a precision of 1.7−1.8 pK_a units.[11] They also used this model to predict the pK_a values of neutral acids in acetonitrile with a precision of 1.0 pK_a unit. At the same time, they calculated the standard redox potentials of 270 structurally unrelated organic molecules in acetonitrile with the standard deviation of 0.17 eV.[12]

Despite the great success in predicting pK_a values and other physicochemical properties of the closed-shell organic molecules and ions in both aqueous and organic solutions, little work has been done to calculate the pK_a values of open-shell radical cations in organic solution. Thus it remains to be an important and challenging objective of computational chemistry. If the acidity of radical cations in solution can be accurately and readily predicted especially for those that are experimentally difficult or even impossible to measure, it will benefit not only a better understanding of the radical cation-related reaction mechanisms, but also the synthetic designs of many reactions.

Stimulated by such a demand and with the experimental pK_a values in our own hand,[2] we have in this work developed a procedure that is able to reproduce the experimental pK_a values

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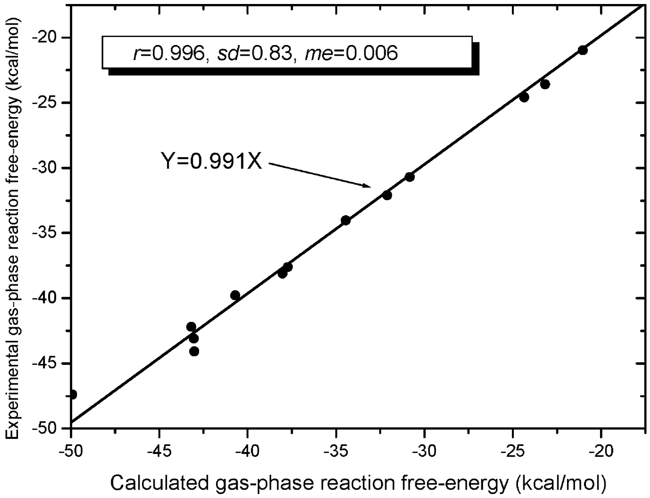


Figure 1. Correlation between the experimental and theoretical gas-phase reaction free-energy changes.

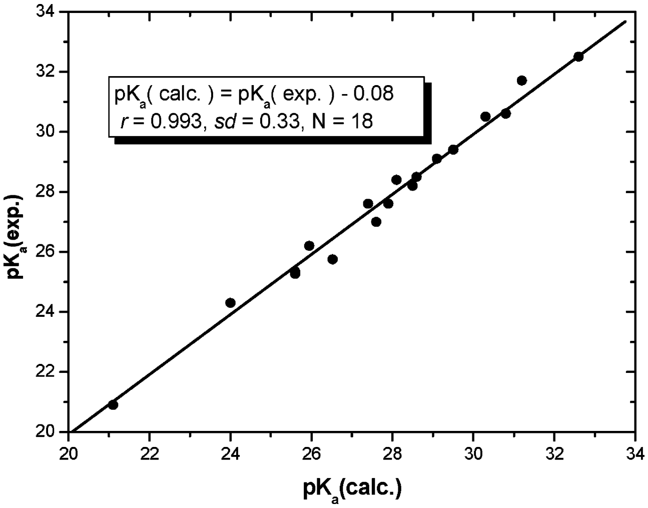


Figure 2. Correlation between the experimental and theoretical pK_a values for neutral anilines in DMSO.

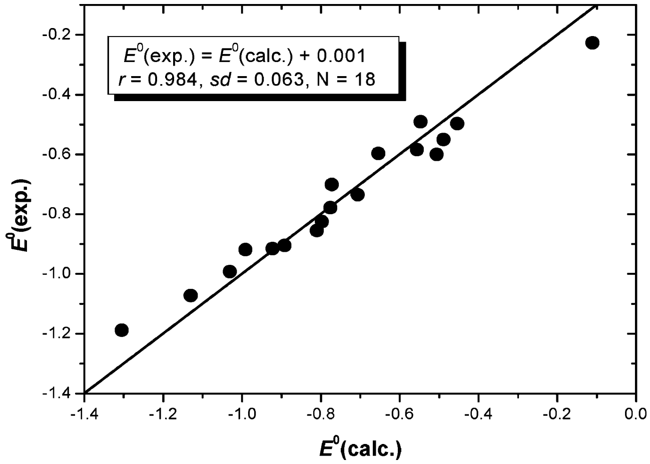


Figure 3. Correlation between the experimental and theoretical standard redox potentials for anilide anions in DMSO.

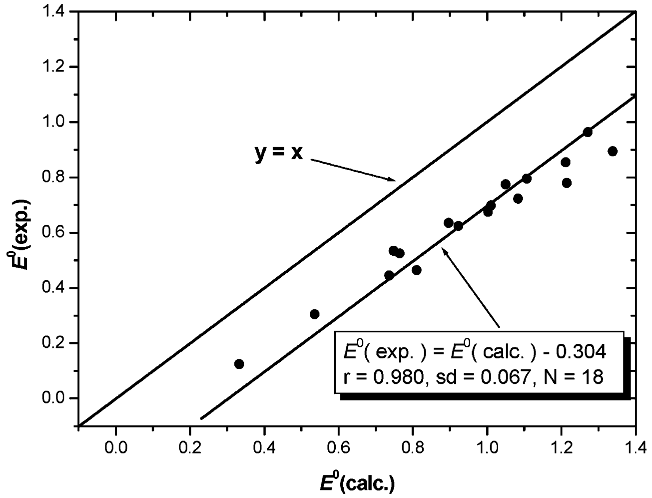


Figure 4. Correlation between the experimental and theoretical standard redox potentials for neutral anilines in DMSO.

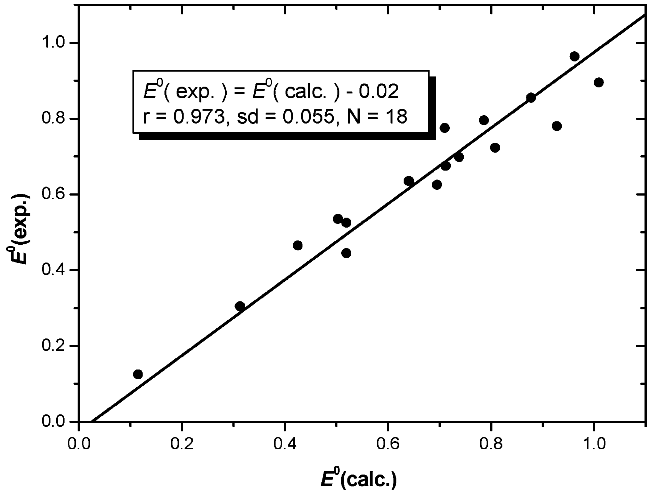


Figure 5. Correlation between the experimental and theoretical standard redox potentials for neutral anilines using the IEF-PCM (f = 1.025) solvation free energies of aniline radical cations in DMSO.

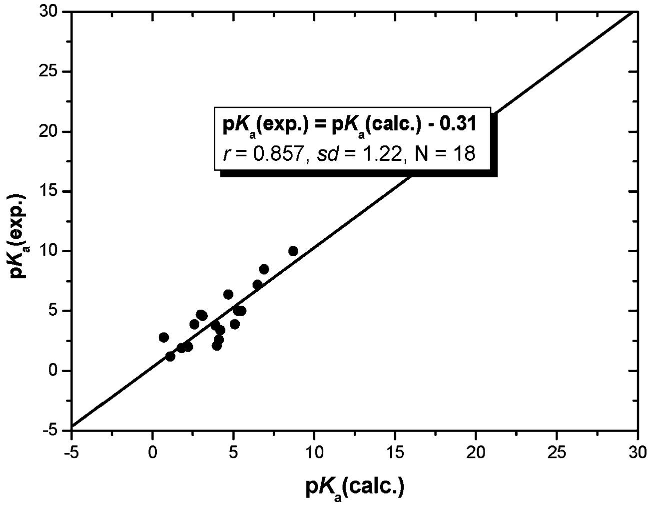


Figure 6. Correlation between the experimental and theoretical pK_a values for aniline radical cations in DMSO.

of substituted aniline radical cations in DMSO solution. This work involves two aspects: (1) development of an applicable theoretical method that can readily calculate the absolute pK_a values of substituted aniline radical cations in organic solution, and (2) analysis of the possible origin of the discrepancies in the pK_a calculation for radical cations, a remaining problem that has not been successfully modeled using other presently available ab initio theoretical computations.

2. Direct Calculation of pK_a Values of Substituted Aniline Radical Cations in DMSO

Similar to that for neutral molecules, the pK_a calculation of the substituted aniline radical cations in DMSO can be undertaken on the basis of the proton-transfer reaction in[13,14]

$$HA^{\bullet +} + OH^- \leftrightarrow A^{\bullet} + H_2O \qquad (3)$$

If the free-energy change of the above reaction in DMSO is defined as ΔG^*_{sol}, the pK_a of the corresponding radical cation can be calculated from eq 4, where ΔG^*_{sol} is given by

$$pK_a(HA^{\bullet +}) = pK_a(H_2O) + \frac{\Delta G^*_{sol}}{2.303RT} \qquad (4)$$

$$\Delta G^*_{sol} = \Delta G^*_g + \Delta G^*_{solv}(A^{\bullet}) + \Delta G^*_{solv}(H_2O) - \Delta G^*_{solv}(HA^{\bullet +}) - \Delta G^*_{solv}(OH^-) \qquad (5)$$

Here ΔG^*_g is the gas-phase reaction free energy (1 mol/L standard state) relative to eq 3, and $\Delta G^*_{solv}(X)$ is the solvation free energy of species X in DMSO. When eq 4 was used to calculate the pK_a values of aniline radical cations, the experimental pK_a of 31.4 for water was adopted.[15]

It was reported that the pK_a values of organic compounds in DMSO can be accurately computed using the IEF-PCM model (radii = UA0).[14] In the present work, the radii scale factor (alpha (f)) of 1.10 was initially chosen for the IEF-PCM model in calculating the pK_a values of aniline radical cations in DMSO. A comparison of the computational results with experimental data showed that the calculated pK_a values are in average 4 pK_a units lower than experimental (see Table 1). Though the results were not satisfactory, the fairly constant negative deviations for all those calculated pK_a values implied that there must be a systematic error in the predicted values.

While the origins of the disagreement in pK_a values were initially not known, it is thought that the accuracy of the calculated pK_a values should rely primarily on the quality of the calculated free energies of every species involved in the gas phase and in solution. To the best of our knowledge, there are no systematic experimental determinations of the solvation energies for organic radical cations available in the literature. This makes it difficult to understand where the systematic errors occur in our calculations. This may also explain why there are few predictions of pK_a values for radical cations in organic solvent.

SCHEME 1: Thermodynamic Cycle for Calculating pK_a Values of Radical Cations

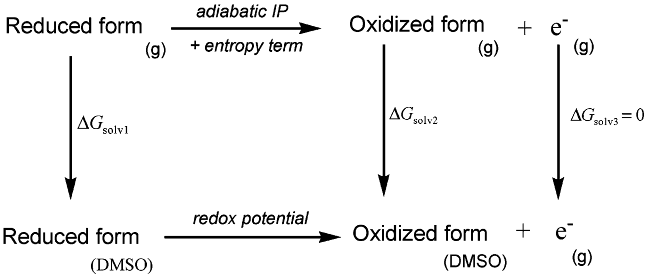
$$HA + OH^- \rightleftharpoons A^- + H_2O \qquad pK_a(HA) \qquad (6)$$

$$A^- \rightleftharpoons A^{\bullet} + e^- \qquad E^0(A^-) \qquad (7)$$

$$HA^{\bullet +} + e^- \rightleftharpoons HA \qquad -E^0(HA) \qquad (8)$$

$$HA^{\bullet +} + OH^- \rightleftharpoons A^{\bullet} + H_2O \qquad pK_a(HA^{\bullet +}) \qquad (9)$$

SCHEME 2: Free-Energy Cycle for Calculating Redox Potential in DMSO



3. Indirect Calculation of pK_a Values of Substituted Aniline Radical Cations in DMSO

To find out the possible sources of the discrepancies between experiment and computation by the direct procedure, we also calculated the pK_a values of the substituted aniline radical cations by an indirect procedure following the strategy of Bordwell et al.[2] who successfully estimated many pK_a values of organic radical cations in DMSO using a thermodynamic cycle (Scheme 1).

On the basis of the cycle, the acidity of a radical cation can be evaluated using

$$pK(HA^{\bullet +}) = pK_a(HA) + [E^0(A^-) - E^0(HA)] \times 23.06/1.37 \qquad (10)$$

where pK_a(HA) denotes the free energy of deprotonation of neutral parent molecule in DMSO and the terms $E^0(A^-)$ and $E^0(HA)$ are the standard redox potentials of the anion and neutral molecule, respectively. The last term, 23.06/1.37, stands for the converting factor between volt and pK_a unit.

3.1. Calculation of pK_a Values of Neutral Anilines in DMSO. The pK_a values of neutral anilines in DMSO were calculated using eq 6. The B3LYP/6-311++G(2df,2p)//B3LYP/6-31+G(d) method was applied to derive the free-energy changes of the gas-phase reaction, and the IEF-PCM model was used for the solvation energy in DMSO.

The calculated free-energy changes of the gas-phase reaction, the pK_a values of the corresponding neutral parent molecules, along with the experimentally available data are presented in Table 2. Figure 1 presents the correlation between the theoretical and experimental gas-phase reaction free-energy changes of 13 substituted anilines. As demonstrated in the figure, the calculated free-energy changes are in excellent agreement with experimental results with a standard deviation (sd) of 0.83 kcal/mol and a mean error (me) of 0.01 kcal/mol. It indicates that theoretical predictions for the gas-phase deprotonation free-energy changes are sufficiently accurate for neutral anilines at the B3LYP/6-311++G(2df,2p)//B3LYP/6-31+G(d) level.

To our satisfaction, the predicted pK_a values in DMSO are also found to agree very well with the experimental values of 18 neutral substituted anilines (Figure 2) with a correlation coefficient of 0.993, a standard deviation of 0.33 pK_a unit, and a mean error of 0.08 pK_a unit. The largest absolute error is only 0.75 pK_a. Therefore, it is safe to conclude that the method used in the present work for calculating the pK_a values of neutral compounds in DMSO is reliable.

3.2. Calculation of Standard Redox Potentials of Neutral Anilines and Corresponding Anions in DMSO. By convention, standard redox potentials of neutral acid (HA) and anion (A^-) are defined by the following half reactions:

$$E^0(HA): \qquad HA \rightarrow HA^{\bullet +} + e^-(g) \qquad (11)$$

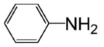
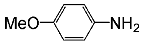
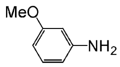
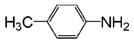
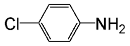
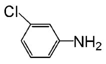
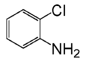
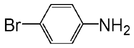
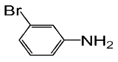
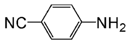
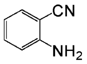
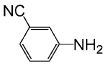
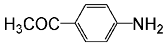
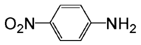
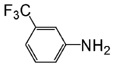
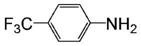
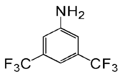
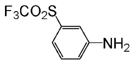
$$E^0(A^-): \qquad A^- \rightarrow A^{\bullet} + e^-(g) \qquad (12)$$

where the E^0 value is usually measured relative to a reference electrode, for instance, the normal hydrogen electrode (NHE). So E_0 is related to the free-energy change of eqs 13 and 14:

$$\Delta G^0: \qquad HA + H^+_{(aq)} \rightarrow HA^{\bullet +} + 1/2H_{2(g)} \qquad (13)$$

$$\Delta G^0: \qquad A^- + H^+_{(aq)} \rightarrow A^{\bullet} + 1/2H_{2(g)} \qquad (14)$$

TABLE 1: Thermodynamic Properties[a] for the HA + OH^- → A^- + H_2O Reaction and Comparison between Calculated and Experimental pK_a Values for Substituted Aniline Radical Cations

Compounds	$(\Delta G^*_g)^b$	$(\Delta\Delta G^*_{\mathrm{solv}})^c$	$\Delta G^{*\,d}_{\mathrm{sol}}$	$pK_{a(\mathrm{calc.})}$	$pK_{a(\mathrm{exp.})}^{\;e}$	ΔpK_a
	-161.78	120.20	-41.58	0.93	6.4	-5.5
	-150.43	114.37	-36.06	4.97	10	-5.0
	-154.81	115.85	-38.96	2.85	7.2	-4.4
	-155.98	117.35	-38.63	3.09	8.5	-5.4
	-161.85	120.67	-41.18	1.22	5	-3.8
	-165.31	122.04	-43.27	-0.30	3.4	-3.7
	-164.33	119.79	-44.54	-1.20	3.9	-5.1
	-161.01	119.87	-41.14	1.25	5	-3.8
	-164.70	121.22	-43.48	-0.50	3.8	-4.3
	-171.25	126.44	-44.81	-1.40	2.6	-4.0
	-171.79	123.21	-48.58	-4.20	2.8	-7.0
	-172.82	127.63	-45.19	-1.70	2.1	-3.8
	-163.99	121.45	-42.54	0.22	3.9	-3.7
	-175.27	127.91	-47.36	-3.30	2	-5.3
	-169.83	124.81	-45.02	-1.60	4.6	-6.2
	-170.22	125.02	-45.20	-1.70	4.7	-6.4
	--176.82	128.31	-48.51	-5.40	1.2	-6.6
	-174.32	126.03	-48.29	-5.90	1.9	-7.8

[a] In units of kcal/mol. Standard state of 1 mol/L, $T = 298.15$ K. [b] Gas-phase reaction free-energy change. [c] Solvation free-energy contribution calculated by the IEF-PCM model. [d] Solution-phase reaction free-energy change. [e] Experimental data are taken from ref 2f.

In the above equations, $E^0 = \triangle G^0/F$, where F is the Faraday constant equal to 23.06 kcal/(mol•V). In this work, the standard redox potentials were calculated according to eqs 15 and 16, which are related to the adiabatic IPs, gas-phase entropy changes, and solvation free energies (Scheme 2).[17,18]

$$E_0(\mathrm{HA})_{(\mathrm{vs,NHE})} = \mathrm{IP} + \frac{1}{23.06}(-T\Delta S + \Delta G^*_{\mathrm{solv}}(\mathrm{HA}^{\bullet+}) - \Delta G^*_{\mathrm{solv}}(\mathrm{HA})) - 4.44 \quad (15)$$

$$E_0(\mathrm{A}^-)_{(\mathrm{vs,NHE})} = \mathrm{IP} + \frac{1}{23.06}(-T\Delta S + \Delta G^*_{\mathrm{solv}}(\mathrm{A}^{\bullet}) - \Delta G^*_{\mathrm{solv}}(\mathrm{A}^-)) - 4.44 \quad (16)$$

Because the electrode potentials of molecules and anions in DMSO were referenced to the ferrocenium/ferrocene (Fc^+/Fc) redox couple in the literature,[19] eq 17 is used to convert the $E^0{}_{(\mathrm{vs,NHE})}$ to $E^0{}_{(\mathrm{vs,Fc/Fc^+})}$.

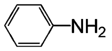
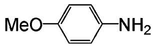
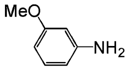
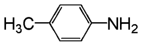
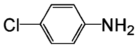
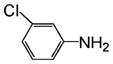
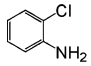
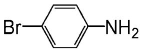
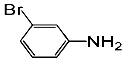
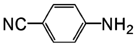
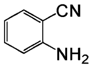
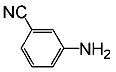
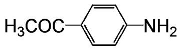
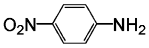
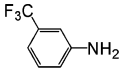
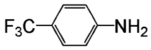
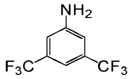
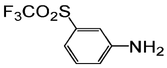
$$E^0{}_{(\mathrm{vs,Fc/Fc+})} = E^0{}_{(\mathrm{vs,NHE})} - 0.537 \quad (17)$$

3.2.1. Calculation of the Gas-Phase Ionization Potentials (IPs). The gas-phase adiabatic ionization potential (IP) is defined as the enthalpy change of the following reaction in the gas phase at 298.15 K, 1 atm:

$$\text{reduced form (g)} \rightarrow \text{oxidized form (g)} + \mathrm{e}^-(\mathrm{g}) \quad (18)$$

Though high-level theoretical methods such as G3 and CBS-Q can provide accurate IPs, these methods are too demanding for general applications. On the other hand, early studies showed that the HF and MP2 methods are inappropriate for IP

TABLE 2: Theoretical and Experimental Gas-Phase Free-Energy Changes[a] for HA + OH^- → A^- + H_2O Reaction and the pK_a Values of Neutral Anilines in DMSO

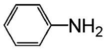
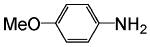
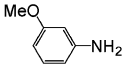
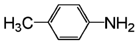
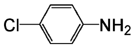
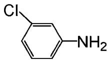
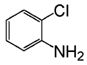
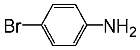
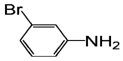
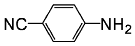
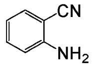
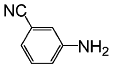
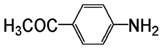
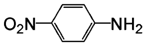
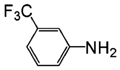
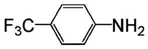
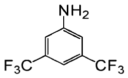
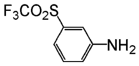
Compounds	(ΔG_g^*)		$pK_a(HA)$		
	$\Delta G_g^*(calc.)$	$\Delta G_g^*(\text{exp.})^b$	$pK_a(calc.)$	$pK_a(\text{exp.})^c$	ΔpK_a
	-24.34	-24.6	30.8	30.6	0.2
	-21.03	-20.99	32.6	32.5	0.1
	-25.41	--	30.3	30.5	-0.2
	-23.17	-23.6	31.2	31.7	-0.5
	-30.82	-30.7	29.5	29.4	0.1
	-32.10	-32.1	28.6	28.5	0.1
	-31.43	--	27.4	27.6	-0.2
	-31.81	--	29.1	29.1	0.0
	-32.76	--	28.1	28.4	-0.3
	-43.18	-42.2	25.6	25.26	0.34
	-40.56	--	24.0	24.3	-0.3
	-38.02	-38.1	27.9	27.6	0.3
	-40.70	-39.8	25.6	25.35	0.25
	-49.92	-47.4	21.1	20.9	0.2
	-34.44	-34.03	28.5	28.2	0.3
	-37.73	-37.6	27.6	27	0.6
	-43.04	-43.1	26.5	25.75	0.75
	-43.01	-44.1	26.0	26.2	-0.2

[a] In units of kcal/mol. Standard state of 1 mol/L, T = 298.15 K. [b] Experimental data are taken from the NIST tables (ref 16). [c] Experimental data are taken from ref 2f.

calculation.[20] Therefore, the B3LYP/6-311++G(2df,2p)// B3LYP/6-31+G(d) method was used in the present work to calculate the adiabatic IP values of 18 substituted anilines and their corresponding anions. According to the extensive calculations of Guo et al. on 160 structurally unrelated molecules,[12,14] the IPs were systematically underestimated by 0.28 eV with the B3LYP/6-311++G(2df,2p)//B3LYP/6-31+G(d) method. Thus, the computed IP values of the present work were accordingly calibrated. The derived theoretical results and the available experimental data are presented in Table 3. Table 3 shows that the theoretical and experimental gas-phase ionization potentials are in good agreement. The mean error is 0.082 eV and the maximal absolute error is 0.18 eV, indicating that the B3LYP/6-311++G(2df,2p)//B3LYP/6-31+G(d) method should be reliable to predict gas-phase adiabatic ionization potentials.

3.2.2. Calculation of Standard Redox Potentials of Anilines and Anilide Anions in DMSO. With the reliable theoretical gas-phase adiabatic IPs available, standard redox potentials of neutral anilines and corresponding anions were then computed. The

TABLE 3: Theoretical and Experimental Adiabatic Ionization Potentials, Standard Redox Potentials for 18 Anilines, and the Corresponding Anions (eV)

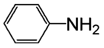
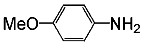
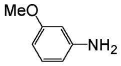
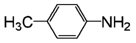
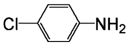
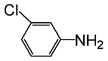
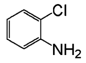
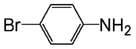
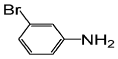
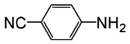
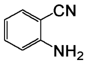
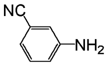
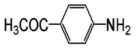
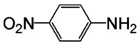
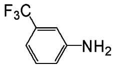
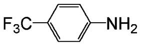
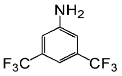
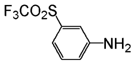
Compound	$IP(A^-)$		$IP(HA)$		$E^0(A^-)$		$E^0(HA)$	
	$IP_{calc.}$ [a]	$IP_{exp.}$ [b]	$IP_{calc.}$ [a]	IP_{exp} [b]	E^0_{calc}	$E^0_{exp.}$ [c]	E^0_{calc}	$E^0_{exp.}$ [c]
	1.86	--	7.82	7.72	-1.031	-0.992	0.736	0.445
	1.60	--	7.16	7.08	-1.305	-1.188	0.332	0.125
	1.88	--	7.68	7.76	-0.991	-0.919	0.810	0.465
	1.75	--	7.52	--	-1.130	-1.072	0.535	0.305
	2.11	--	7.80	7.8	-0.923	-0.915	0.748	0.535
	2.24	--	8.02	--	-0.810	-0.855	0.896	0.635
	2.19	--	7.96	7.9	-0.776	-0.779	0.922	0.625
	2.17	--	7.78	--	-0.892	-0.905	0.764	0.525
	2.27	--	8.00	--	-0.797	-0.825	0.896	0.635
	2.79	--	8.34	8.17	-0.489	-0.55	1.106	0.795
	2.70	--	8.39	--	-0.454	-0.497	1.214	0.78
	2.55	2.37	8.40	--	-0.707	-0.735	1.049	0.775
	2.66	--	8.06	--	-0.506	-0.6	1.002	0.675
	3.16	--	8.60	8.43	-0.111	-0.227	1.338	0.895
	2.37	--	8.24	--	-0.772	-0.701	1.010	0.698
	2.56	--	8.30	--	-0.654	-0.597	1.083	0.723
	2.84	2.73	8.62	8.59	-0.547	-0.491	1.271	0.964
	2.82	--	8.52	--	-0.556	-0.584	1.211	0.855

[a] Calculated by the B3LYP/6-311++G(2df,2p)//B3LYP/6-31+G(d) method and calibrated by adding 0.28 eV (see text). [b] Experimental data are taken from the NIST tables (ref 16). [c] Experimental data are taken from ref 2f.

predicted redox potentials are also listed in Table 3. Figures 3 and 4 reveal the correlations between the experimental and theoretical data of anilide ions and neutral anilines, respectively. For anilide ions, the computation is quite good. The correlation coefficient is 0.984, and the standard deviation is 0.063 eV, suggesting that the calculation for anilide ions is reliable. Though the present standard deviation seems to be a little too high, it should be reminded that all the experimental redox potentials compared within this work are not reversible values and for most of the redox data the experimental errors were around 0.1 eV. Therefore, the IEF-PCM model (radii = UA0, f = 1.10) is reasonably successful for predicting the standard redox potentials of anilide ions.

As seen from Figure 4, the correlation between experiment and theory for neutral anilines is quite satisfactory with regression coefficient of 0.980 and standard deviation of 0.067 eV. The intercept of the correlation equation is slightly larger, however. Nevertheless, these calculations demonstrate that both the reaction free energies and ionization potentials of anilines and their anions in the gas phase can be quite confidently

TABLE 4: Experimental and Theoretical Standard Redox Potentials (eV) for 18 Neutral Anilines[a]

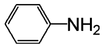
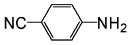
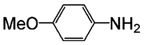
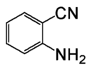
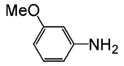
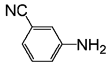
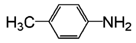
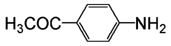
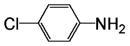
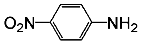
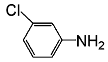
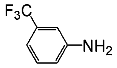
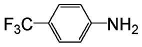
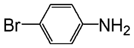
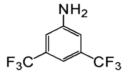
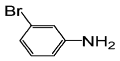
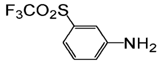
Compounds	$E^\circ(HA)$ exp.	$f = 0.950$	$f = 0.975$	$f = 1.000$	$f = 1.025$	$f = 1.050$	$f = 1.075$	$f = 1.100$	$f = 1.125$
	0.445	0.133	0.277	0.398	0.519	0.590	0.666	0.736	0.796
	0.125	-0.230	-0.100	0.125	0.115	0.197	0.268	0.332	0.388
	0.465	0.225	0.363	0.482	0.425	0.670	0.744	0.810	0.865
	0.305	-0.030	0.106	0.217	0.313	0.397	0.469	0.535	0.592
	0.535	0.129	0.273	0.397	0.503	0.595	0.674	0.748	0.812
	0.635	0.247	0.398	0.528	0.640	0.737	0.820	0.896	0.963
	0.625	0.345	0.481	0.595	0.695	0.78	0.855	0.922	0.979
	0.525	0.145	0.289	0.413	0.519	0.611	0.691	0.764	0.828
	0.635	0.248	0.400	0.529	0.641	0.738	0.820	0.896	0.965
	0.795	0.312	0.492	0.650	0.786	0.904	1.008	1.106	1.192
	0.780	0.491	0.657	0.801	0.928	1.035	1.128	1.214	1.290
	0.775	0.246	0.428	0.588	0.710	0.847	0.951	1.049	1.136
	0.675	0.281	0.448	0.588	0.712	0.821	0.916	1.002	1.078
	0.895	0.527	0.711	0.869	1.009	1.132	1.239	1.338	1.426
	0.698	0.323	0.482	0.619	0.738	0.839	0.928	1.010	1.082
	0.723	0.399	0.558	0.690	0.808	0.910	1.000	1.083	1.155
	0.964	0.508	0.684	0.832	0.962	1.077	1.182	1.271	1.355
	0.855	0.383	0.572	0.736	0.878	1.004	1.113	1.211	1.300
me[b]	--	0.376	0.219	0.078	-0.025	-0.135	-0.223	-0.304	-0.375
sd[c]	--	0.075	0.064	0.064	0.055	0.057	0.061	0.067	0.074

[a] Experimental data are taken from ref 2f. [b] Mean error between the experimental and theoretical data. [c] Standard deviation between the experimental and theoretical data.

predicted at the B3LYP/6-311++G(2df,2p)//B3LYP/6-31+G-(d) level of theory, and the pK_a values of neutral anilines and the standard redox potentials of anilide anions in DMSO can also be reproduced using the IEF-PCM model. The only notable disagreement from the experimental data is the calculated standard redox potentials of neutral anilines. This immediately implies that the underestimation of the pK_a values of aniline radical cations from the above direct computational procedure may have primarily come from the calculation of the standard redox potentials of neutral anilines in DMSO solution.

The deviation of the IEF-PCM model in predicting standard redox potentials for neutral anilines may be traced to the calculation of solvation free energy in DMSO. It is known that when PCM model is employed to calculate solvation energies in high accuracy, it requires parametrization of the shape and size of the dielectric cavity of a molecule.[21] Unfortunately, computational works reported to date rarely involved extensive parametrization for radical cations. In the present study, the observed agreement between theory and experiment for anilines pK_a values and anilides redox potentials suggests that there

TABLE 5: Theoretical and Experimental pK_a values of Substituted Aniline Radical Cations in DMSO[a]

Compounds	pK_a(*calc.*)	pK_a(exp.)	ΔpK_a	*Compounds*	pK_a(*calc.*)	pK_a(exp.)	ΔpK_a
	4.7	6.4	-1.7		4.1	2.6	1.5
	8.7	10	-1.3		0.7	2.8	-2.1
	6.5	7.2	-0.7		4.0	2.1	1.9
	6.9	8.5	-1.6		5.1	3.9	1.2
	5.5	5	0.5		2.2	2	0.2
	4.2	3.4	0.8		3.1	4.6	-1.5
	2.6	3.9	-1.3		3.0	4.7	-1.7
	5.3	5	0.3		1.1	1.2	-0.1
	3.9	3.8	0.1		1.8	1.9	-0.1

[a] Experimental data are taken from ref 2f, theoretical values are calculated by using solvation energies of substituted aniline radical cations with IEF-PCM model (f =1.025).

should be no considerable deviation in the calculations of the free energies of solvation of anilines, anilides, and even the neutral radicals. For aniline radical cations, however, the originally used IEF-PCM (f = 1.10) model may have yielded an untrue cavity size and resulted in a deviation in the dielectric continuum contribution to free energy of solvation. Therefore, the solvation related scale factor f in the IEF-PCM model has been adjusted to a value that can regenerate the experimental redox potentials of anilines (so as to the pK_a values of aniline radical cations). This strategy has also been used by Guo et al. in their recent calculations of standard redox potentials in acetonitrile (CH_3CN) and showed to be successful in reproducing experimental values.[14]

Various f values were examined for calculating solvation free energies of substituted aniline radical cations using the UA0 radii, and f =1.025 was found to give the best fit in calculation to regeneration of experimental redox potentials of anilines. The computed results derived with different f values are listed in Table 4. The standard deviation and mean error between theoretical and experimental redox potentials with the scale factor f of 1.025 are improved to be 0.055 and 0.025 eV, respectively. The correlation plot of the standard redox potentials of the neutral anilines thus calculated with those from experiment is demonstrated in Figure 5.

3.3. Calculation of pK_a Values of Aniline Radical Cations in DMSO Using the Computed pK_a Values and Redox Potentials. On the basis of the convinced calculation of pK_a values and standard redox potentials of neutral anilines and corresponding anions, we were able to calculate the pK_a values for aniline radical cations in DMSO (Table 5) using eq 10. The confidence of the computed pK_a values of aniline radical cations can be established by comparison of the computed data with those of Bordwell et al.[2f] from experimental measurements. The maximal absolute error is 2.1 pK_a units, and the standard deviation is 1.22 pK_a units (see also Figure 6), both are substantially smaller than those calculated from the direct procedure (Table 1) and are well within the experimental uncertainty of ± 3 pK_a units as estimated in the literature.[2]

It is now understood that the large discrepancies found before in the direct calculation of the pK_a($HA^{\bullet +}$) values (see Table 1) should have mainly come from the deviation in the calculated solvation free energies of aniline radical cations in DMSO solution. This has been further confirmed by recalculation of the pK_a values of 18 substituted aniline radical cations in DMSO using the IEF-PCM (f = 1.025) model for solvation free energies. To our satisfaction, the results are indeed greatly improved. The standard deviation between theory and experiment drops to 1.2 pK_a units, which is consistent with the calculated result by the indirect method (see Supporting Information).

4. Conclusion

In the present work, we developed a computational scheme to obtain reliable pK_a values for organic radical cations in DMSO. The B3LYP/6-311++G(2df,2p) method was used to calculate the gas-phase deprotonation free energies and the integral equation formalism version of polarizable continuum model (IEF-PCM) was adopted to compute the solvation energies in DMSO. By optimizing the scale factor f of the radical cation, the pK_a values of aniline radical cations in DMSO have been calculated with good accuracy (sd of 1.2 pK_a units).

An indirect method that combines the pK_a of neutral molecule and the standard redox potentials of molecule and anion was applied to calculate the absolute pK_a values for all the 18 aniline radical cations. Comparisons of the computational results from the indirect method with those from the direct method using an uncorrected scale factor f allowed us to figure out that the discrepancies found between theory and experiment by the original direct procedure must have come from the unjustified scale factor f that overestimated the solvation free energies of radical cations in DMSO. The results are greatly improved with the calibrated parameter to a comparable level of accuracy as reported in the literature.

5. Computational Methodology

All theoretical calculations were carried out using the Gaussian 03 packages[22] mounted on NKStar supercomputer. The geometry of each species was fully optimized at the B3LYP/6-31+G(d) level with no symmetry constraints. For the molecules that have more than one possible conformation, the one with the lowest electronic energy was singled out and used in the ensuing calculations. Frequency calculations were computed on these geometries at the same level to verify that they are real minima on the potential-energy surface without any imaginary frequency.

To obtain accurate energies, single-point electronic energy calculations on the optimized geometries have been performed at the B3LYP/6-311++G(2df,2p) level of theory. The free energy was obtained by combining the B3LYP/6-311++G(2df,2p) single-point electronic energies with ZPE, thermal corrections (298 K), and the entropy terms obtained at the B3LYP/6-31+G(d) level (unscaled).

The solvation free energies were calculated using the integral equation formalism version of PCM (IEF-PCM),[23] as implemented in Gaussian 03. The cavity was built with the United Atom model (UA0).[22] All the IEF-PCM calculations were performed at the B3LYP/6-31+G(d, p) level with the geometries optimized in gas phase. Both the electrostatic and nonelectrostatic contributions were included for the total solvation energies.

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Supporting Information Available: Calculated gas-phase thermodynamic data; calculated solvation free energies; experimental and theoretical pK_a values. This material is available free of charge via the Internet at http://pubs.acs.org.

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