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pK_a predictions of some aniline derivatives by ab initio calculations

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Abstract

In this work, different levels of theory containing HF, B3LYP, and MP2 with different basis sets such as 6-31G, 6-31G*, 6-311G, 6-311+G, 6-31+G*, 6-31+G are used to predict relative acidity constants of some aniline derivatives. Three different kinds of radii containing UAHF, Bondi, and Pauling are used to study how cavity forms change acidity constants. In all cases, DPCM model is used to simulate solvation Gibbs free energy. Furthermore, one similar level and basis set has been linked to IEFPCM and DPCM models to compare the results.To relate gas-phase Gibbs free energy to the solution Gibbs free energy, a simple thermodynamic cycle is used. Results show that quantum chemical calculations are robust techniques for estimating acidity constants.

Keywords: Ab initio, aniline, acidity constant, pK_a, DFT

Introduction

Estimating acidity constants in aqueous solution is an exciting subject in computational quantum chemistry. Methods consist of quantitative structure-property relationship (QSPR) modeling, statistical mechanical models, or microscopic quantum chemical calculations by which gas and solvation phase Gibbs free energies are estimated [1]. The first approach is straightforward, but needs more experimental data. On the other hand, the second approach requires more CPU time based on ab initio calculations. The main error of quantum mechanical method is due to the continuum model used to simulate solvent role.

Different factors control continuum model behavior. Choice of cavity size, values of es-

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caped charges, discreteness of surface charges, and smoothness of reaction field are some factors that change free energy of solvation. Escaped charges have close relationship with cavity sizes of solutes. Cossi et al. have stated that the UAHF model gives the best results for different levels and basis sets [2]. On the other hand, they have not compared the results of different cavity models for different levels and basis sets. In this work, we have developed our previous study on the subject of cavity form effects on the accuracy of relative acidity constant predictions [3-5]. Previous results showed that, for small amines (as bases), low levels of theory predict acidity constants better than high levels of theory in all cavity models. In this work, calculations are repeated for aniline derivatives (as acids) at different forms of cavities, levels and basis sets to study role of these factors on the accuracy of relative acidity constant predictions.

Computational method

Deprotonation of a Brönsted acid in aqueous solution can be written as:

$$AH \rightleftharpoons A^- + H^+ \qquad (1)$$

Standard free energy change of above reaction in the gas phase (ΔG_{gas}) is written as:

$$\Delta G^0_{gas} = G^0_{gas}\left(A^-\right) + G^0_{gas}\left(H^+\right) - G^0_{gas}\left(AH\right) \quad (2)$$

In aqueous solution, standard free energy change of reaction (1) is calculated as follows:

$$\Delta G^0_{aq} = G^0_{aq}\left(A^-\right) + G^0_{aq}\left(H^+\right) - G^0_{aq}\left(AH\right) \qquad (3)$$

The standard free energy change in solution (ΔG^0_{aq}) can be calculated by considering thermodynamic cycle shown in Figure 1.

$$\begin{array}{ccccc} AH_{gas} & \xrightarrow{\Delta G_{gas}} & A^-_{gas} & + & H^+_{gas} \\ \downarrow \Delta G_S(AH) & & \downarrow \Delta G_S(A^-) & & \downarrow \Delta G_S(H^+) \\ AH_{aq} & \xrightarrow{\Delta G_{aq}} & A^-_{aq} & + & H^+_{aq} \end{array}$$

Figure 1. Thermodynamic cycle used to calculate standard Gibbs free energy change of reaction (1).

ΔG^0_{aq} is equal to the sum of the solvation standard free energy change ($\Delta\Delta G^0_s$) and the gas standard free energy change (ΔG^0_{gas}) [6]:

$$\Delta G^0_{aq} = \Delta G^0_{gas} + \Delta\Delta G^0_s \qquad (4)$$

Where, $\Delta\Delta G^0_s$ is calculated as follows:

$$\Delta\Delta G^0_s = \Delta G^0_s\left(A^-\right) - \Delta G^0_s\left(AH\right) + \Delta G^0_s\left(H^+\right) \quad (5)$$

Equilibrium constant (K_a) for the reaction (1) is defined as:

$$K_a = \frac{\left[A^-_{aq}\right]\left[H^+_{aq}\right]}{\left[AH_{aq}\right]} \qquad (6)$$

Where K_a is acidity constant for AH_{aq}, K_a can be associated with the change of the standard Gibbs free energy by

$$\Delta G^0_{aq} = -2.303RT\log\left(K_a\right). \qquad (7)$$

By following da Silva et al. [7-8] and Jang et al. [9], we can write:

$$\Delta G^0_{aq}\left(\text{kcalmol}^{-1}\right) = 1.36\,\text{p}K_a \qquad (8)$$

Where ΔG^0_{aq} is the standard Gibbs free energy change of reaction (1) in water at 298.15 K, to avoid calculation of $\Delta G_s\left(H^+_{aq}\right)$, following method has been used. Reaction (1) is divided to the sum of two below reactions:

$$AH_{aq} + Ph-NH^-_{aq} \rightleftarrows A^- + Ph-NH_{2,aq} \quad \Delta G^o_{1,aq} \qquad (9)$$

$$Ph-NH_{2,aq} \rightleftarrows Ph-NH^-_{aq} + H^+_{aq} \quad \Delta G^0_{2,aq} \qquad (10)$$

It is clear that $\Delta G^0_{aq} = \Delta G^0_{1,aq} + \Delta G^0_{2,aq}$. Experimental p$K_a$ of aniline is used to calculate $\Delta G^0_{2,aq}$ for the reaction (10). $\Delta G^0_{1,aq}$ can be obtained by calculation of gas-phase energy change of each component in equation (9) together with its solvation free energy. This kind of approach for calculation of acidity constants has been used earlier in the literature [10].

The gas-phase and solvation contribution to the Gibbs free energy has been calculated at the levels of MP2, density functional theory (B3LYP), and HF; and the solvation energies have been determined using polarizable continuum model (DPCM and IEFPCM) of Tomasi and coworkers [2,11-12]. Different basis sets containing 6-31G, 6-31G*, 6-311G, 6-311+G, 6-31+G*, 6-31+G have been chosen to study effects of basis sets on the acidity constants. Gaussian 98 (G98W) has been used for all calculations [13]. All zero-point energy corrections, in all levels and basis sets, have been scaled by NIST scaling factors [14].

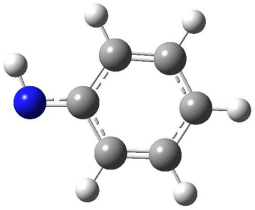
Results and discussion

List of anilines considering in this work has been shown in the Table 1. Figure 2 shows optimized geometries of neutral and anions in the best level and basis set (IEFPCM/B3LYP/6-31G). Table 2 and 3 show gas phase and solution Gibbs free energy chenge (ΔG^0_{aq}) for all of the species of reaction (9) for PCM and IEFPCM models, respectively. Table 4 shows MADs of three cavity models (UAHF, Bondi and Pauling) for different levels and basis sets (MAD is the mean absolute deviation between calculation and experimental values of pK_a). Although UAHF is original form that has been used for optimization of DPCM at HF/6-31G*, data show that

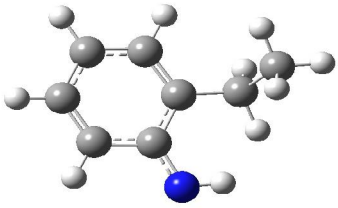
for HF/6-31G*, B3LYP/6-31+G*, MP2/6-31G and MP2/6-31G*, in the case of aniline derivatives, Bondi and Pauling models are the best cavity models. Table 4 shows that the best result belongs to Pauling cavity model at IEFPCM/B3LYP/6-31G level of theory with 0.09 for MAD).

Table 1. List of aniline derivatives and their experimental acidity constants

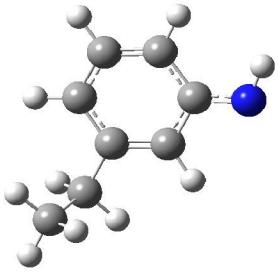
No.	Name	pK_a (Exp.)
1 (Ref.)	Aniline	4.62
2	2-Ethyl aniline	4.42
3	3-Ethyl aniline	4.70
4	4-Ethyl aniline	5.00
5	4-Ethoxyaniline	5.25
6	3-Ethoxyaniline	4.17



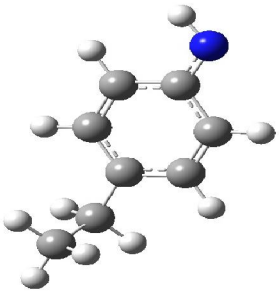
A1 (Anion Aniline)



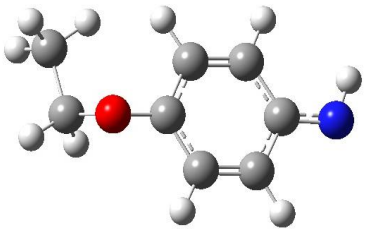
A2 (Anion 2-Ethyl aniline)



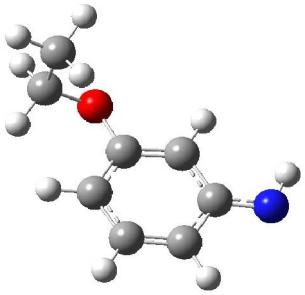
A3 (Anion 3-Ethyl aniline)



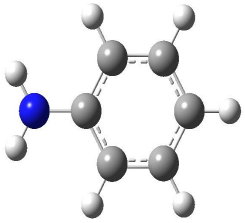
A4 (Anion 4-Ethyl aniline)



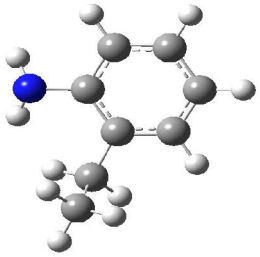
A5 (Anion 4-Ethyl aniline)



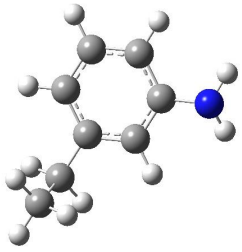
A6 (Anion 3-Ethoxy aniline)



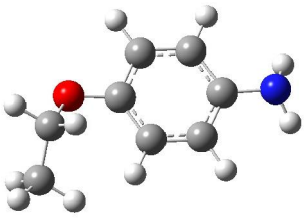
M1 (Aniline)



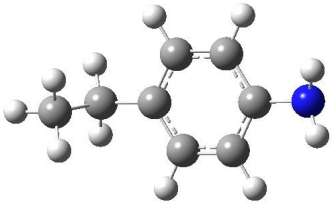
M2 (2-Ethyl aniline)



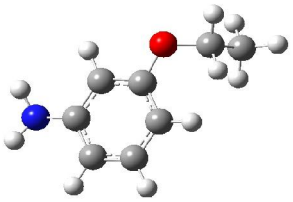
M3 (3-Ethyl aniline)



M4 (4-Ethyl aniline)



M5 (4-Ethoxy aniline)



M6 (3-Ethoxy aniline)

Figure 2. Optimized geometries of anions (A1-A6) and neutral forms (M1-M6) of aniline derivatives

Table 2. Gas-phase ($G^0_{1,gas}$), solvation ($\Delta G^0_{1,s}$), and solution ($\Delta G^0_{1,aq}$) standard Gibbs free energy, and predicted pK_a using PCM/B3LYP/6-31G//B3LYP/6-31G method.

Compound	$G^0_{1,gas}$	UAHF			Bondi			Pauling		
		$\Delta G^0_{1,s}$	$\Delta G^0_{1,aq}$	pK_a	$\Delta G^0_{1,s}$	$\Delta G^0_{1,aq}$	pK_a	$\Delta G^0_{1,s}$	$\Delta G^0_{1,aq}$	pK_a
1(AH) Ref.	-287.44	-6.83	0	4.62	-3.2	0	4.62	-3.63	0	4.62
1(A-) Ref.	-286.83	-58.78			-58.74			-61.77		
2(AH)	-365.99	-5.49	-0.96	3.91	-0.22	-0.53	4.23	-0.13	-0.57	4.20
2(A-)	-365.39	-56.87			-54.76			-57.31		
3(AH)	-365.99	-5.74	0.36	4.88	-0.39	0.28	4.82	-0.46	0.09	4.68
3(A-)	-365.39	-56.9			-55.22			-58.08		
4(AH)	-365.99	-6.03	1.11	5.43	-0.6	0.98	5.34	-0.39	0.42	4.93
4(A-)	-365.39	-56.13			-54.42			-57.37		
5(AH)	-441.17	-7.73	-1.62	3.42	-2.78	0.88	5.27	-3.48	1.16	5.48
5(A-)	-440.56	-59.33			-55.46			-58.48		
6(AH)	-441.17	-7.59	-2.09	3.08	-2.64	-0.57	4.20	-3.27	-0.71	4.09
6(A-)	-440.56	-59.98			-57.1			-60.47		

Units: Energies in the gas phase are in atomic unit and Solvation Energies are in kcal/mol.

Table 3. Gas-phase ($G^0_{1,gas}$), solvation ($\Delta G^0_{1,s}$), and solution ($\Delta G^0_{1,aq}$) standard Gibbs free energy, and predicted pK_a using IEFPCM/B3LYP/6-31G//B3LYP/6-31G method.

Compound		UAHF			Bondi			Pauling		
	$G^0_{1,gas}$	$\Delta G^0_{1,s}$	$\Delta G^0_{1,aq}$	pK_a	$\Delta G^0_{1,s}$	$\Delta G^0_{1,aq}$	pK_a	$\Delta G^0_{1,s}$	$\Delta G^0_{1,aq}$	pK_a
1(AH) Ref.	-287.44	-6.86	0	4.62	-3.1	0	4.62	-3.43	0	4.62
1(A-) Ref.	-286.83	-57.60			-57.40			-59.71		
2(AH)	-365.99	-5.69	-0.73	4.08	-0.16	-0.19-	4.48	0.29	-0.46	4.28
2(A-)	-365.39	-55.63			-53.12			-54.92		
3(AH)	-365.99	-5.75	0.15	4.73	-0.40	0.47	4.97	0.12	0.14	4.73
3(A-)	-365.39	-55.9			-53.79			-55.58		
4(AH)	-365.99	-5.90	1.15	5.46	-0.35	0.82	5.22	0.23	0.42	4.93
4(A-)	-365.39	-54.75			-53.09			-54.89		
5(AH)	-441.17	-7.66	-1.73	3.35	-2.46	0.88	5.27	-2.54	0.86	5.25
5(A-)	-440.56	-58.15			-53.90			-55.98		
6(AH)	-441.17	-7.64	-1.95	3.19	-2.45	-0.74	4.08	-2.64	-0.90	3.96
6(A-)	-440.56	-58.68			-55.84			-58.17		

Units: Energies in the gas phase are in atomic unit and Solvation Energies are in kcal/mol.

Table 4. MADs of UAHF, Bondi and Pauling cavity models at different levels and basis sets

Level/basis set	UAHF	Bondi	Pauling
PCM/HF/6-31G//HF/6-31G	0.73	0.32	0.24
PCM/HF/6-31G*//HF/6-31G*	0.59	0.34	0.35
PCM/HF/6-311G//HF/6-311G	0.66	0.29	0.62
PCM/HF/6-311+G//HF/6-311+G	0.87	0.48	0.48
PCM/HF/6-31+G*//HF/6-31+G*	0.99	0.81	0.94
PCM/HF/6-31+G*//B3LYP/6-31+G*	0.52	1.19	0.94
PCM/B3LYP/6-31G//B3LYP/6-31G	0.67	0.12	0.10
PCM/MP2/6-31G//MP2/6-31G	0.40	2.49	0.66
PCM/B3LYP/6-31G*//B3LYP/6-31G*	0.72	0.66	0.60
PCM/MP2/6-31G*//MP2/6-31G*	0.72	1.51	0.90
PCM/B3LYP/6-31+G*//B3LYP/6-31+G*	0.71	1.41	1.09
PCM/B3LYP/6-31+G*// MP2/6-31G*	0.54	0.74	1.07
IEFPCM/B3LYP/6-31G //B3LYP/6-31G	0.74	0.13	0.09

ΔG_{solv} is sum of electrostatic and non-electrostatic energies. The non-electrostatic energy is sum of the three contributions containing cavitation, dispersion and repulsion energies. Table 5 shows cavitation, dispersion, repulsion, and total non-electrostatic energies for (Pauling model in the level PCM/B3LYP/6-31G//B3LYP/6-31G). From

Table 5, it is clear that the cavitation energies of neutrals are somewhat greater than anions-because of the greater volumes of neutral species due to the presence of hydrogen atoms. On the other hand, Table 6 shows that electrostatic term is greater for anions than neutrals, since charges on anions are more diffused than neutrals by which more interaction between anions and solvent molecules are occurred. Comparing calculated pK_a with experimental ones shows that the quantum chemical methods are good techniques for predicting acidity constants.

Table 5. Cavitation, Dispersion, Repulsion, and total non electrostatic energy, all in kcal/mol, for neutrals and anions by PCM/B3LYP/6-31G//B3LYP/6-31G level using Pauling cavity.

No.	Cavitation energy		Dispersion energy		Repulsion energy		Total non-elec.	
	neutral	anion	neutral	anion	neutral	anion	neutral	anion
1	17.57	17.31	-17.26	-16.68	3.12	3.12	3.43	3.75
2	24.18	23.33	-20.96	-20.48	3.43	3.44	6.64	6.30
3	24.61	23.97	-21.20	-20.63	3.47	3.47	6.88	6.81
4	24.62	23.93	-21.22	-20.65	3.48	3.48	6.88	6.77
5	25.85	25.56	-22.85	-21.92	3.79	3.70	6.78	7.34
6	25.74	25.07	-22.84	-22.21	3.81	3.79	6.71	6.65
Mean	23.76	23.19	-21.06	-20.43	3.52	3.50	6.22	6.27

Table 6. Electrostatic energy term, in kcal/mol, for neutrals and anions by PCM/B3LYP/6-31G//B3LYP/6-31G level using Pauling cavity.

No.	Total electrostatic energy	
	neutral	**anion**
1	-7.06	-65.52
2	-6.77	-63.61
3	-7.34	-64.89
4	-7.27	-64.14
5	-10.26	-65.82
6	-9.98	-67.12
Mean	-8.11	-65.18

Conclusion

Some levels and basis sets of theory accompanied with polarizable continuum model (DPCM) of solvation have been used to estimate pK_a values of some aniline derivatives. Very good results have been obtained with ab initio calculations. Data show that quantum chemical calculations are robust techniques for estimating acidity constants. Comparing the results with the experimental data shows that Bondi and Pauling cavities are the best choices for moderate or low levels of theory; and for high levels, UAHF is the best method. Present data for anilines (as acids) are in good line with our previous results for amines (as bases).

Acknowledgments

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