Journal of the Iranian Chemical Society, Vol. 2, No. 1, March 2005, pp. 65-70.

JOURNAL OF THE
Iranian
Chemical Society

Calculations of pK_a Values of Carboxylic Acids in Aqueous Solution Using Möller-Plesset Perturbation Theory

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(Received 18 September 2004, Accepted 3 February 2005)

The acidity constants of some carboxylic acids in aqueous solution have been calculated. The calculations were carried out using Möller-Plesset (MP) perturbation theory. The Polarizable Continuum Model (PCM) is used to describe the solvent. This model furnishes pK_a values that agree more closely with experimental data than those obtained at the level of Hartree-Fock (HF) and Density Functional Theory (DFT-B3LYP). The root-mean-square of errors of the calculated pK_a values are less than 1.0 for the studied acids. The molecules analyzed consist of acids with pK_a values in the range of 1.30 to 5.05, and have been partitioned into three classes. Class I includes acids with pK_a values higher than 4.00. Class II includes strong acids with pK_a values between 3.00 to 4.00. Class III includes very strong acids with pK_a values less than 3.00. The calculated pK_a values for the acids in Class I and Class II agree more closely with experimental values. The root-mean-square of errors for the Class I and Class II compounds are 0.70 and 0.78 pK_a units, respectively.

Keywords: Möller-Plesset theory, MP2, Carboxylic acids, pK_a, PCM, Solvation

INTRODUCTION

Proton-transfer reactions, which constitute an important class of chemical reactions, play an important role in many areas of chemistry [1,2]. Determination of pK_a values is of special interest to chemists. It is useful for studying the role of ionizable groups in proton-transfer processes and studying the rate of the reactions, which depends on many factors, including the degree of dissociation of species involved [3,4]. Carboxylic acids are known to be strong organic acids and the pK_as of these substances usually fall in the range of 2-5. Carboxylic acids are important in many areas of organic chemistry such as synthesis, separation and identification of organic compounds.

Quantum chemical methods, which can provide reliable pK_a values, allow a better understanding of the different factors that influence pK_a values and are essential for interpretation of experimental values in various systems [5]. We recently reported the calculated pK_a of some carboxylic acids in aqueous solution [6,7]. The calculated pK_a values were obtained by employing *ab initio* calculations at the level of Hartree-Fock (HF) [6] and Density Functional Theory (DFT) at the level of B3LYP [7]. The solute-solvent interactions together with gas-phase energies were used to obtain pK_as and the results were compared with the experimental values. The root-mean-square errors were 1.41 and 1.04 pK_a units for HF and DFT methods of calculations, respectively [6,7].

In the present study, the pK_a values of the previously studied carboxylic acids in the aqueous phase have been calculated by employing Möller-Plesset (MP) perturbation theory at the level of MP2 [8]. Our results are better than those of previous reports.

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METHODS AND THEORETICAL CONSIDERATIONS

A Brӧnsted acid in aqueous solution dissociates as follows:

$$HA_{aq} + H_2O_{aq} \longrightarrow A^-_{aq} + H_3O^+_{aq} \quad (1)$$

The equilibrium constant is related to the change of standard Gibbs energy; therefore, there is a simple relationship between the change of standard Gibbs energy and pK_a:

$$\Delta G°_1 = -2.303\ RT \log(K_a/[H_2O]) \quad (2)$$

Meanwhile, by following Nascimento [3,4] and Goddard [9], a simpler form of Eq. (2) can be obtained:

$$\Delta G°_1\ (\text{kCal mol}^{-1}) = 1.36\ pK_a + 2.36 \quad (3)$$

where $\Delta G°_1$ is the standard change of the Gibbs energy in water at 298.15 K.

In order to calculate the $\Delta G°_1$, we have used an isodesmic reaction (4) and the dissociation of acetic acid (5) as a reference molecule:

$$HA_{aq} + CH_3COO^-_{aq} \longrightarrow A^-_{aq} + CH_3COOH_{aq} \quad (4)$$

$$CH_3COOH_{aq} + H_2O_{aq} \longrightarrow CH_3COO^-_{aq} + H_3O^+_{aq} \quad (5)$$

The standard of Gibbs energy of reaction (1), $\Delta G°_1$, can be written as the sum of the Gibbs energy of reaction (4), $\Delta G°_{rxn}$, and the Gibbs energy of reaction (5), $\Delta G°_2$.

$$\Delta G°1 = \Delta G°_{rxn} + \Delta G°_2 \quad (6)$$

$\Delta G°_2$ can be obtained by Eq. (3), with an experimental value of 4.76 for the pK_a of acetic acid [6]. In order to calculate $\Delta G°_{rxn}$, one should calculate the standard Gibbs energy of each component, $\Delta G°_i$, in reaction (4) and this is possible by the calculation of the gas-phase energy of each component, $\Delta G°_{i,gas}$, together with the solvation energy of the component, $\Delta G°_{i,solv}$ [3,4,7]:

$$\Delta G°_{rxn} = \sum \nu_i\ \Delta G°_i \quad (7)$$

$$\Delta G°_i = \Delta G°_{i,gas} + \Delta G°_{i,solv} \quad (8)$$

The gas-phase contribution to the Gibbs energy, $\Delta G°_{i,gas}$, can be determined from the Mӧller-Plesset perturbation theory [8].

Table 1. Carboxylic Acids Studied in this Work

Acids	Formula	pK_a (exp)[a]
	Class **I**	
1	$(CH_3)_3CCOOH$	5.05
2	CH_3CH_2COOH	4.87
3	$CH_3(CH_2)_2COOH$	4.82
4	CH_3COOH	4.76
5	$ClCH_2CH_2CH_2COOH$	4.52
6	p-$CH_3C_6H_4COOH$	4.36
7	$CH_2{=}CHCH_2COOH$	4.35
8	$C_6H_5CH_2COOH$	4.31
9	CH2=CHCOOH	4.26
10	C_6H_5COOH	4.20
11	CH_2ClCH_2COOH	4.10
	Class **II**	
12	p-ClC_6H_4COOH	3.99
13	$CH_3CHOHCOOH$	3.87
14	$HOCH_2COOH$	3.83
15	m-ClC_6H_4COOH	3.83
16	HCOOH	3.75
17	CH_3OCH_2COOH	3.54
18	p-$NO_2C_6H_4COOH$	3.41
19	$HC{\equiv}CCH_2COOH$	3.32
	Class **III**	
20	o-ClC_6H_4COOH	2.88
21	$BrCH_2COOH$	2.86
22	$ClCH_2COOH$	2.81
23	$CH_3CHClCOOH$	2.80
24	FCH_2COOH	2.66
25	$NCCH_2COOH$	2.44
26	O_2NCH_2COOH	1.32
27	$Cl_2CHCOOH$	1.30

[a] The experimental values are taken from Refs. [20,21].

Solvation energies, $\Delta G^{\circ}_{i,solv}$, have been calculated using Polarizable Continuum Model (PCM) [10-15]. The diffuse basis set of 6-31 + G (d,p) has been chosen since it is recommended for anions and molecules with lone pair electrons [16] and in consideration of the size of the studied molecules. A higher level of theory was not justified because of hardware limitations and the significant length of time for computations. Gaussian 98 has been employed for all MP2calculations [17].

RESULTS AND DISCUSSION

In this study, we analyzed the carboxylic acids studied in our previous work [6,7]. However, due to hardware

Table 2. Gas-phase and Solvation Energy of each Molecule and its Anion and the Change in Standard Gibbs Energy of Reaction (4), ΔG°_{rxn}

No.[a]	Gas-phase internal energies U[b] a.u.		$\Delta G^{\circ}_{i,sol}$ kCal mol^{-1}		ΔG°_{rxn} kCal mol^{-1}
	Acid	Anion	Acid	Anion	
1	-346.02530	-345.46774	-7.26	-73.95	1.86
2	-267.65253	-267.09118	-8.11	-77.92	1.12
3	-228.46999	-227.90690	-7.44	-76.58	2.88
4	-306.83665	-306.27517	-8.34	-79.35	0.00
5	-765.85857	-765.30701	-10.34	-74.30	0.83
6	-458.82054	-458.26804	-9.63	-76.13	-1.13
7	-305.61694	-305.06175	-8.69	-74.97	0.78
8	-458.81481	-458.26198	-12.53	-76.56	1.55
9	-266.43444	-265.87709	-7.02	-75.69	-0.25
10	-419.63213	-419.08123	-10.66	-76.55	-1.52
11	-726.67460	-726.12773	-9.54	-70.34	1.04
12	-878.65764	-878.11363	-9.90	-71.15	-1.20
13	-342.69305	-342.15323	-11.59	-71.26	-2.25
14	-878.65701	-878.11387	-10.10	-70.64	-1.04
15	-303.50274	-302.96321	-12.77	-71.77	-1.76
16	-189.27533	-188.71922	-9.00	-77.6	-0.96
17	-342.66477	-342.10907	-14.7	-82.96	-0.88
18	-623.64662	-623.11355	-12.75	-66.41	-0.48
19	-304.38148	-303.8313	-10.31	-75.15	-0.92
20	-878.65054	-878.10595	-10.69	-75.39	-4.29
21	-2797.88820	-2797.3444	-9.84	-72.56	-2.80
22	-687.48283	-686.93971	-10.51	-72.08	-2.08
23	-726.67301	-726.12802	-8.56	-71.66	-2.44
24	-327.47769	-326.93337	-11.11	-75.2	-3.85
25	-320.46583	-319.93201	-14.61	-70.87	-2.60
26	-432.47266	-431.94649	-17.17	-70.58	-4.56
27	-1146.49790	-1145.96630	-7.42	-66.17	-6.49

[a] See Table 1 for the list of compounds. [b,c] Energies are in atomic units, Hartree (1Hartree = 627.5095 kCal mol^{-1} [16]).

limitations, CF_3COOH was excluded in the present study. Table 1 shows a list of the studied acids in which a variety of substituted acids such as alkyl, alkenyl, halogen, cyano, nitro, *ortho* and *para* halogenated phenyl, can be seen. The list consists of a wide range of acids with pK_a values in the range of 1.30 to 5.05. The acids studied here can be partitioned into three classes. Class **I:** acids with pK_a values higher than 4.00, including acids with alkyl, alkenyl and phenyl substitutions. Class **II**: strong acids with pK_a values between 3.00 and 4.00, consisting of acids with hydroxyl, methoxy, *ortho* and *para* halogenated phenyl groups. Class **III**: very strong acids with pK_a values less than 3.00. One can see that the acids in this class have strong electron-withdrawing substitutions such as fluorine, chlorine, cyano and nitro.

Table 2 shows the calculated gas-phase energy and solvation energy of each acid and its corresponding anion. Comparison of the calculated solvation energies with the available experimental values shows that the PCM results are slightly overestimated. For instance, the experimental solvation energies of acetic acid, propanoic acid and butanoic acid are -6.70, -6.47, -6.35 kCal mol^{-1}, respectively [18]. The calculated solvation energies for these acids are -8.34, -8.11 and -7.44 kCal mol^{-1}, respectively. However, the trend of the calculated solvation energies is the same as the trend observed for the experimental values. The change in Gibbs energy of reaction (4), $\Delta G°_{rxn}$, obtained by Eqs. (7) and (8), are also included in Table 2.

The pK_a values calculated in this work using Eq. (3) are shown in Table 3 where they are compared with previously reported theoretical calculations and the experimental values. The calculated pK_a values for Class I acids agree relatively well with the experimental values. For instance, the calculated pK_a for propanoic acid is 4.84, whereas the experimental value is 4.87. The root-mean-square of errors for the Class I compounds is 0.70 pK_a units. The calculated pK_a values for the Class **II** acids also agree well with the experimental values. The root-mean-square of errors is only 0.78 pK_a units. In contrast, the calculated pK_a values for Class **III** acids deviate significantly from the experimental values, so that the root-mean-square of errors is 1.23. The Class **III** acids have strong withdrawing substitutions such as CN, NO_2 and F. These acids have very strong interactions with solvent, and some extra interactions such as hydrogen bonding, which were not considered in our calculations. Dimeric forms of acids, which affect the gas-phase energies, should be also considered. The spectroscopic and vapor-density measurements indicated that some carboxylic acids form hydrogen-bonded cyclic dimers in the gas phase [18].

The overall root-mean-square of errors for all twenty-seven acids is 0.92, which is a significant improvement over previous results.

CONCLUSIONS

This article extends our previous studies of the acidity of carboxylic acids in aqueous solution, which were carried out at HF and DFT levels of theory [6,7]. In the present work, the Möller-Plesset perturbation theory at the level of MP2 and a diffuse basis set have been employed, in order to calculate the Gibbs energies and pK_a values. The average discrepancy between theoretical MP2 calculations and experimental values is 0.90. For acids of moderate strength, the average error is even smaller (less than 0.78 pK_a units). The proposed method of calculation is likely to be useful in the prediction of pK_a values of other acids in aqueous solution. The inclusion of solvation energies, calculated by the PCM model of solvation, significantly improves the results and shows the prediction capability of the model for solute-solvent interactions.

ACKNOWLEDGEMENTS

The authors would like to thank Dr. Debra Bernhardt (Debra J. Searles) from Griffith University, Brisbane, Australia for the Gaussian calculation and her invaluable support.

REFERENCES

[1] D.H. Aue, M.T. Bovers, in: H.T. Bowers (Ed.), Gas Phase Ion Chemistry, Academic Press, New York, 1979, vol. 2.

[2] T. H. Lowry, K.S. Richardson, Mechanism and Theory in Organic Chemistry Third Edition, HarperCollinsPublishers Inc. New York, 1987.

[3] C.O. Silva, E.C. da Silva, M.A.C. Nascimento, J. Phys. Chem. A 104 (2000) 2402.

Table 3. Previously Reported Theoretical pK_a Calculations Compared to pK_a Values Calculated in this Work and Experimental Values

	Previous works		This work	
No.[a]	pK_a[b]	pK_a[c]	pK_a[d]	$pK_{a,exp}$[e]
Class **I**				
1	5.21	5.10	5.38	5.05
2	4.24	4.60	4.84	4.87
3	4.04	5.60	5.39	4.82
4	4.76	4.76	4.76	4.76
5	3.08	4.45	4.62	4.52
6	4.78	3.45	3.19	4.36
7	3.75	5.22	4.59	4.35
8	4.03	6.18	5.16	4.31
9	4.80	4.22	3.83	4.26
10	4.39	3.99	2.9	4.20
11	2.49	4.33	4.78	4.10
Class **II**				
12	3.57	3.06	3.13	3.99
13	4.18	3.65	2.36	3.87
14	3.06	4.20	3.25	3.83
15	1.74	3.72	2.72	3.83
16	4.11	2.87	3.31	3.75
17	2.84	3.79	3.37	3.54
18	2.10	3.38	3.67	3.41
19	1.61	4.25	3.33	3.32
Class **III**				
20	3.43	2.25	0.86	2.88
21	1.57	1.95	1.98	2.86
22	1.90	2.25	2.49	2.81
23	2.04	2.15	2.23	2.80
24	1.70	1.18	1.19	2.66
25	-0.63	-0.33	2.10	2.44
26	-1.24	0.32	0.66	1.32
27	-2.74	-1.44	-0.73	1.30
r.m.s.[f]	1.41	1.04	0.90	

[a] See Table 1 for the list of compounds. [b] Calculated at the level of HF, taken from Ref. [6]. [c] Calculated at the level of DFT-B3LYP, taken from Ref. [7]. [d] Calculated at the level of MP2. [e] The experimental values taken from Refs. [20,21]. [f] The root-mean-square error of deviations of calculated pK_a from experimental values.

[4] C.O. Silva, E.C. da Silva, M.A.C. Nascimento, J. Phys. Chem. A 103 (1999) 11194.

[5] I.A. Topol, S.K. Burt, A.A. Rashin, J.W. Erickson, J. Phys. Chem. A 104 (2000) 866.

[6] M. Namazian, H. Heidary, J. Mol. Struct. (Theochem) 620 (2003) 257.

[7] M. Namazian, S. Halvani, M.R. Noorbala, J. Mol. Struct. (Theochem) 711 (2004) 13.

[8] M.J. Frisch, M. Head-Gordon and J.A. Pople, Chem. Phys. Lett. 166 (1990) 275.

[9] Y.H. Jang, L.C. Sowers, T. Cagin, W.A. Goddard, J. Phys. Chem. A 105 (2001) 274.

[10] S. Miertus, E. Scrocco, J. Tomasi, Chem. Phys. 55 (1981) 117.

[11] M.T. Cances, V. Mennucci, J. Tomasi, J. Chem. Phys. 107 (1997) 3032.

[12] J.B. Foresman, T.A. Keith, K.B. Wiberg, J. Snoonian, M.J. Frisch, J. Phys. Chem. 100 (1996) 16098.

[13] V. Barone, M. Cossi, J. Phys. Chem. A 102 (1998) 1995.

[14] M. Cossi, V. Barone, J. Phys. Chem. A 104 (2000) 10614.

[15] M. Cossi, V. Barone, R. Cammi, J. Tomasi, Phys. Lett. 255 (1996) 327.

[16] J.B. Foresman, A.E. Frisch, Exploring Chemistry with Electronic Structure Methods, Gaussian, Inc. Pittsburgh, P.A., 1998.

[17] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, V.G. Zakrzewski, J.A. Montgomery, Jr., R.E. Stratmann, J.C. Burant, S. Dapprich, J.M. Millam, A.D. Daniels, K.N. Kudin, M.C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G.A. Petersson, P.Y. Ayala, Q. Cui, K. Morokuma, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J. Cioslowski, J.V. Ortiz, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, J.L. Andres, C. Gonzalez, M. Head-Gordon, E.S. Replogle, and J.A. Pople, Gaussian, Inc., Pittsburgh PA, 1998.

[18] C.J. Cramer, D.G. Truhlar, J. Computer-Aided Molecular Design 6 (1992) 629.

[19] L. Turi, J.J. Dannenberg, J. Phys. Chem. 97 (1993) 12197.

[20] M. Schrüümann, M. Cossi, V. Barone, J. Tomasi, J. Phys. Chem. A 102 (1998) 6706.

[21] J.F.J. Dippy, S.R.C. Hughes, A. Rozanski, J. Chem. Soc. (1959) 2492.