Irregular Order in Basicities of Methylamines in Aqueous Solution: A RISM-SCF Study

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Abstract: The irregular order in basicities of a series of methylamines in aqueous solution is studied by means of an ab initio quantum chemical calculation combined with the extended reference interaction site method in statistical mechanics of molecular liquids (RISM-SCF method). By using the restricted Hartree−Fock level approximation in the theoretical treatment for solute electronic structure, the irregular order in basicities is reproduced in qualitative agreement with well-established experimental results. The method does not require a priori cavity assumption in solution, which introduces ambiguous parameters into the theories and enables us to explain the physical origin of the basicity entirely from a microscopic point of view. Solvation structures around methylamines are also examined in terms of radial distribution functions. The result is an encouraging indication of the potential usefulness of the RISM-SCF approach to investigate a variety of quantum processes in solution.

I. Introduction

It is well-known that acidity and basicity are seriously affected by the environment: the relative order of strength among a series of compounds is drastically altered by solvent effects. The irregular order in basicities of a series of methylamines[1] in aqueous solution has been a typical problem in the fundamental acid−base concept in solution. While the basicity increases monotonically with methyl substitution in the gas phase,[2−6] the order reverses with trimethylamine in aqueous solution.[7−10] Theoretical studies[11−16] have been carried out to clarify the origin of this phenomenon with particular interest in the solvent effect on chemical processes in which the electronic structure of the solute plays an essential role. One of the successful approaches for calculating the electronic structure of a solvated molecule is based on the continuum solvent model, but this leaves several conceptual ambiguities unresolved. A cavity artificially introduced to represent a solute molecule and parameters associated with boundary conditions for the continuum model seriously affect the results of free energy of the system as well as the solute electronic structure.

In this article, we report results of a theoretical investigation concerningthe irregular order in basicities of a series of methylamines in aqueous solution compared with those in the gas phase on the basis of the recently developed RISM-SCF method.[17,18] The RISM-SCF method is an ab initio self-consistent field method in quantum chemistry combined with an extended version of the reference interaction site method (RISM)[19] in statistical mechanics of molecular liquids. Unlike the quantum chemical calculations based on the continuum solvent models, the present method employs a microscopic model for the solvent as well as the solute, thereby, it does not introduce any ambiguous parameters such as the dielectric constant of the solvent and the cavity size. This method provides information concerning the microscopic structure of the solvent around a solute molecule, such as hydrogen bonds, in terms of the correlation functions for solute−solvent and solvent−solvent pairs of molecules. The electrostatic field produced on the solute molecule, which is considered as one of the major contributions to the basicity, can be calculated on the basis of pair correlation functions. With this method, we can calculate the electronic structure of solute molecules in solution along with the microscopic solvation structure around solute molecules in a self-consistent manner without introducing a priori such an ambiguous concept as *cavity*.

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(1) NH_3, $(CH_3)NH_2$, $(CH_3)_2NH$, and $(CH_3)_3N$.

(2) Munson, M. S. B. *J. Am. Chem. Soc.* **1965**, *87*, 2332−2336.

(3) Brauman, J. I.; Blair, L. K. *J. Am. Chem. Soc.* **1969**, *91*, 2126−2127.

(4) Brauman, J. I.; Riveros, J. M.; Blair, L. K. *J. Am. Chem. Soc.* **1971**, *93*, 3914−3916.

(5) Arnett, E. M.; Jones, F. M.; Taagepera, M.; Henderson, W. G.; Beauchamp, J. L.; Holtz, D.; Traft, R. W. *J. Am. Chem. Soc.* **1972**, *94*, 4724−4726.

(6) Aue, D. H.; Webb, H. M.; Bowers, M. T. *J. Am. Chem. Soc.* **1972**, *94*, 4726−4728.

(7) Aue, D. H.; Webb, H. M.; Bowers, M. T. *J. Am. Chem. Soc.* **1976**, *98*, 311−317.

(8) Aue, D. H.; Webb, H. M.; Bowers, M. T. *J. Am. Chem. Soc.* **1976**, *98*, 318−329.

(9) Taft, R. N.; Wolf, J. F.; Beauchamp, J. L.; Scorrano, G.; Arnett, E. M. *J. Am. Chem. Soc.* **1978**, *100*, 1240−1249.

(10) King, E. J. *Acid Base Equilibra*; Pergamon Press: New York, 1965; p 141.

(11) Eades, R. A.; Scanlon, K.; Ellenberger, M. R.; Dixon, D. A.; Marynick, D.S. *J. Phys. Chem.* **1980**, *84*, 2840−2842.

(12) Eades, R. A.; Well, D. A.; Dixon, D. A.; Douglass, C. H. *J. Phys. Chem.* **1981**, *85*, 981−986.

(13) Galera, S.; Oliva, A.; Lluch, J. M.; Bertran, J. *J. Mol. Struct. (THEOCHEM)* **1984**, *110*, 15−21.

(14) Drago, R. S.; Cundari, T. R.; Ferris, D. C. *J. Org. Chem.* **1989**, *54*, 1042−1047.

(15) Pascual-Ahuir, J. L.; Andres, J.; Silla, E. *Chem. Phys. Lett.* **1990**, *169*, 297−300.

(16) Tunon, I.; Silla, E.; Tomasi, J. *J. Phys. Chem.* **1992**, *96*, 9043−9048.

(17) Ten-no, S.; Hirata, F.; Kato, S. *Chem. Phys. Lett.* **1993**, *214*, 391−396.

(18) Ten-no, S.; Hirata, F.; Kato, S. *J. Chem. Phys.* **1994**, *100*, 7443−7453.

(19) (a) Chandler, D.; Andersen, H. C. *J. Chem. Phys.* **1972**, *57*, 1930−1937. (b) Hirata, F.; Rossky, P. J. *Chem. Phys. Lett.* **1981**, *83*, 329−334. (c) Hirata, F.; Pettitt, B. M.; Rossky, P. J. *J. Chem. Phys.* **1982**, *77*, 509−520. (d) Pettitt, B. M.; Rossky, P. J. *J. Chem. Phys.* **1982**, *77*, 1451−1457. (e) Hirata, F.; Rossky, P. J.; Pettitt, B. M. *J. Chem. Phys.* **1983**, *78*, 4133−4144. (f) Pettitt, B. M.; Rossky, P. J. *J. Chem. Phys.* **1986**, *84*, 5836−5844.

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Table 1. Dipole Moments of Methylamines and Protonated Methylamines (in Debye)[a]

	gas phase			aqueous solution	
molecule	DMI[b]	DPC[b]	exp.[c]	DMI	DPC
NH_3	1.82	1.86	1.47	2.57	2.60
$(CH_3)NH_2$	1.47	1.37	1.24 or 1.35	2.02	1.92
$(CH_3)_2NH$	1.11	1.22	1.03	1.96	2.08
$(CH_3)_3N$	0.74	0.88	0.67	1.60	1.78
NH_4^+	0.00	0.00		0.00	0.01
$(CH_3)NH3^+$	2.23	2.18		2.65	2.59
$(CH_3)_2NH_2^+$	1.50	1.48		1.95	1.92
$(CH_3)_3NH^+$	0.87	0.90		1.27	1.30

[a] Dipole moments of protonated methylamines are calculated with respect to the center of mass. [b] See text. [c] Experimental data in the gas phase (ref 23).

An important aspect of this article is to present the results of the calculation by means of the recently developed RISM-SCF method. The detailed explanations of the theoretical methods and the related methodological issues for the problems are therefore omitted. In the following section, brief explanations of the important points of the theoretical methods for the problems are only presented. We refer readers who are interested in the methodology to our previous articles.[17,18] Results and discussions are provided in Section III, in which the irregular order in basicities is analyzed in terms of components of the free energy.

II. Methods

Prior to the RISM-SCF calculation, the geometries of methylamines and the corresponding ammonium ions (protonated methylamines) are optimized in vacuum at the restricted Hartree–Fock level approximation. The 6-31G basis set,[20] augmented by d polarization functions on carbon and nitrogen atoms and p polarization functions on hydrogen atoms directly attached to nitrogen atoms, is employed throughout this investigation. A normal mode analysis is also performed to evaluate the zero-point energy for each solute molecule in vacuum and then the total free energy change on the protonation of each methylamine in the gas phase is calculated. In the RISM-SCF calculation, the solute electronic structures are calculated from solvated Fock operators that include the microscopic mean field generated by charge distributions of classical solvent molecules. On the other hand, the statistical solvent structures are determined by RISM integral equations in which the solute-induced potential field is incorporated via partial charges[21] distributed on each interaction site of the solute molecule. Both the electronic structure of the solute molecule and the solvent distribution are derived simultaneously in a self-consistent manner. In the ab initio calculation, we use the Hartree–Fock level approximation and the RISM equations are solved with a hyper-netted chain (HNC)-like approximation that is regarded superior to other approximations for polar solvent.

Concerning the determination of partial charges of solute molecules, those obtained from the Mulliken population analysis[22] are notorious in depending on the basis set. In order to minimize the error associated with the determination of partial charges, we employ the least-squares fitting procedures in order to reproduce the electrostatic field around a solute molecule.[17,18] The first moment of the charge distribution, or the dipole moment, is the primary measure for the accuracy of the fitting procedure. In Table 1, the dipole moments calculated from the molecular integrals (DMI) and from the partial charges (DPC) are compared for the methylamines as well as the protonated methylamines.

In aqueous solution, the DPC agrees well with the corresponding DMI. The agreement is satisfactory, demonstrating the reliability of the fitting procedure. In the gas phase, though the comparison between DMI and DPC is not directly concerned with the RISM-SCF calculation, the results are in good agreement for each molecule. The theoretical results are also in fair agreement with experimental data, demonstrating the reliability of our calculations.

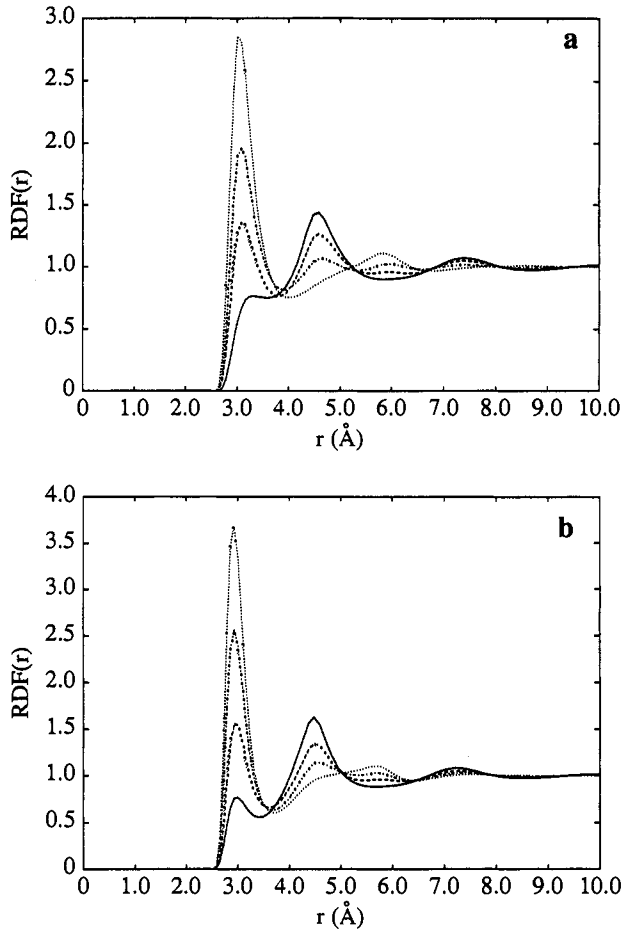

Figure 1. (a) Radial distribution functions of water oxygen around nitrogen atoms of methylamines: dotted line, NH_3; dash-dot line, $(CH_3)NH_2$; dashed line, $(CH_3)_2NH$; solid line, $(CH_3)_3N$. (b) Radial distribution functions of water oxygen around nitrogen atoms of protonated methylamines: dotted line, NH_4^+; dash-dot line, $(CH_3)NH_3^+$; dashed line, $(CH_3)_2NH_2^+$; solid line, $(CH_3)_3NH^+$.

Among several choices of models for solvent molecules, we employ a SPC-like water model[24,25] which has been successfully used in liquid simulations. Further, in order to describe the van der Waals interactions between solute and solvent molecules, the Lennard-Jones parameters for solute molecules are taken from the OPLS.[26] We fix the Lennard-Jones parameters because the van der Waals interaction does not change too much compared to the electrostatic interaction during the RISM-SCF procedure.

III. Results and Discussions

The radial distribution functions (RDF) of water oxygen around nitrogen atoms of methylamines and of the corresponding ammonium ions are plotted in Figure 1, parts a and b, respectively, as typical examples to show the solvation structure.

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(20) (a) Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys.* **1971**, *56*, 2257–2261. (b) Binkley, J. S.; Pople, J. A.; Hehre, W. J. *J. Am. Chem. Soc.* **1980**, *102*, 939–947.

(21) Bash, P. A.; Singh, U. C.; Langridge, R.; Kollman, P. A. *Science* **1987**, *236*, 564–568.

(22) Mulliken, R. S.; Ermler, W. C. *Diatomic Molecules: Results of Ab Initio Calculations*; Academic: New York, 1977.

(23) Weast, R. C.; Astle, M. J.; Beyer, W. H. *CRC Handbook of Chemistry and Physics*; CRC Press, Inc.: Boca Raton, FL, 1989.

(24) (a) Berendsen, H. J. C.; Postma, J. P. M.; van Gunstern, W. F.; Hermas, J. In *Intermolecular Forces* Pullman, B., Ed.; Reidel: Dordrecht, 1981; p 331. (b) Berendsen, H. J. C.; Grigera, J. R.; Straatsma, T. P. *J. Phys. Chem.* **1987**, *91*, 6269–6271.

(25) Van der Waals parameters of $\sigma = 1.0$Å and $\epsilon = 0.0545$ kcal/mol are assigned to the H site.

(26) (a) Weiner, S. J.; Kollman, P. A.; Case, D. A.; Singh, U. C.; Ghio, C.; Alagona, G.; Profeta, S., Jr.; Weiner, P. *J. Am. Chem. Soc.* **1984**, *106*, 765–784. (b) Weiner, S. J.; Kollman, P. A.; Nguyen, D. T.; Case, D. A. *J. Comput. Chem.* **1986**, *7*, 230–252.

Table 2. Free Energy Changes of Methylamines upon Protonation in Aqueous Solution (in kcal/mol)

molecule	ΔG(solute)[a]	ΔG(solvent)[a]	ΔG[a]
NH_3	0.0	0.0	0.0
$(CH_3)NH_2$	−7.9	4.8	−3.0
$(CH_3)_2NH$	−15.4	10.0	−5.3
$(CH_3)_3N$	−18.5	14.3	−4.3

[a] Free energy changes relative to those of ammonia. See text.

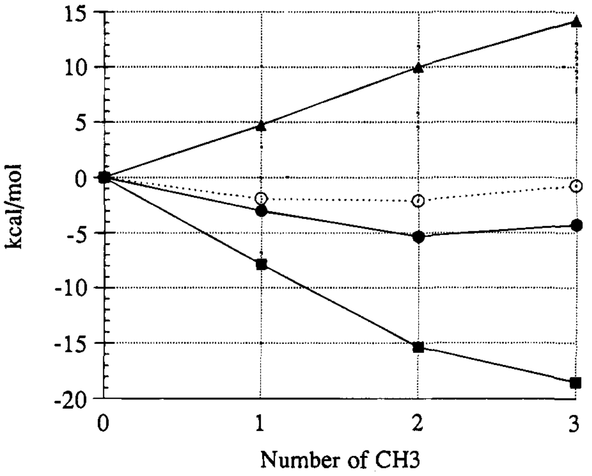

Figure 2. Free energy changes upon protonation referred to NH_3: (▲) ΔG(solvent); (■) ΔG(solute); (●) ΔG in solution; (○) experimental values.

The first and second peaks of the curve for NH_3 (Figure 1a) located at ca. 3.2 and 5.8 Å correspond to the positions of oxygen atoms in the first and second solvation shells. Both of them decrease with successive methyl substitutions due essentially to the volume exclusion effect of the methyl groups. The new peaks appearing at ca. 4.7 Å with successive methyl substitutions are assigned to oxygen atoms next to the methyl groups and grow with a cost to the peaks at ca. 3.1 and 5.8 Å. Such alteration in the water distribution or solvation structure causes significant changes in the potential field on the solute molecule and consequently in its electronic structure. The curves for the protonated form (Figure 1b) show essentially the same behavior with the unprotonated form. It is important to notice that the present method is capable of reproducing such complicated behavior in solvation structure associated with methyl substitutions.

The free energy changes, ΔG, upon protonation[27] of methylamines in aqueous solution relative to ammonia, $\Delta G[NH_3]$, are tabulated in Table 2 and shown in Figure 2.

ΔG can be expressed as a sum of contributions from the solute itself, ΔG(solute), and from solute−solvent interaction as well as solvent reorganization, ΔG(solvent). It should be noted that the former includes the solvent-induced change in the electronic structure, although the changes in the small contributions from other degrees of freedom such as vibration are neglected. As is expected from experiments and theoretical calculations in the gas phase,[28] the free energy changes ΔG(solute) from solute electronic structure decrease with the number of methyl substituents due to the inductive effect or the polarization effect in both the gas phase and aqueous solution, whereas ΔG(solvent) from solute−solvent interactions increases with successive methyl substitutions. The total free energy change concerned with basicities, viz. a sum of the above two terms, decreases up to dimethyl substitution. However, tertiary substitution destabilizes by 1.0 kcal/mol, and this increase in the free energy, namely the decrease in basicity, corresponds to the irregular order in basicity experimentally observed in aqueous solution.[8]

The solvation free energy ΔG(solvent) can be conceptually divided into two major contributions: the work required to form a cavity to accommodate a solute, or the free energy of cavity formation, and the interaction between solute and solvent molecules. The cavity so defined is a physically sensible concept unlike the *cavity* used in the continuum model. The two cavity concepts should not be confused. The free energy of cavity formation is positive in general and it increases on each methyl substitution. The first peak position in the RDF of water oxygen around nitrogen atoms roughly corresponds to the cavity size. In unprotonated forms, as can be seen in Figure 1a, the first peaks are at 3.07, 3.10, 3.15, and 3.25 Å for NH_3, $(CH_3)NH_2$, $(CH_3)_2NH$, and $(CH_3)_3N$, respectively. In the protonated forms, as can be seen in Figure 1b, the corresponding values are at 2.92, 2.93, 2.97, and 3.01 Å, respectively. The deviations of the position due to protonation are nearly constant, thereby the differences of these deviations with methyl substitutions are negligible. In the methylamines, the dominant contribution to increase G(solvent) upon methyl substitutions referred to NH_3 comes from the cavity formation, whereas in the portonated from, viz. positive ions, the Born-like free energy makes as significant contribution as that of cavity formation to increase G(solvent). Since the contributions from the cavity formation cancel each other in the protonated and unprotonated forms, the difference in G(solvent) can be largely due to the Born-like free energy. This part is sensitive to the size and shape of the solute molecules, so that it is important to evaluate such quantities entirely from a microscopic point of view without any artificial presumptions.

To summarize, the methyl substitution gives essentially two competing effects on the basicity: the inductive effect, which makes the basicity higher, and the steric effect on the electrostatic solute−solvent interaction, which makes basicity lower in solution. With trimethylamine, the latter effect becomes dominant. The conclusion is apparently in accord with the intuitive pictures given by using less sophisticated theories.[11−16] However, it should be indicated that the present approach does not depend on any ad hoc assumptions concerning the solvent structure as well as the solute electronic structure. It is an advantage of the method employed here to be able to explore the detailed structure of solvent around the solute molecule. Further analyses of the solvation structure and free energy in terms of the solute−solvent RDF are under investigation for the forthcoming publication.

Tunon and co-workers[16] could reproduce the irregular order in basicities with continuum solvent models but with more sophisticated treatment for electron correlations in the quantum chemical calculation. The present calculation based on the microscopic solvent model also attains qualitatively similar results with Tunon et al. without including electron correlations. It remains an open question for further investigation which gives more significant effect on the cause of the irregularity.

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[27] Denoting the free energy change associated with the protonation ($A + H^+ \rightarrow AH^+$) by ΔG, and we define the basicity by $-\Delta G$.

[28] Umeyama, H.; Morokuma, K. *J. Am. Chem. Soc.* **1976**, *98*, 4400−4404.