

# A microsolvation approach to the prediction of the relative enthalpies and free energies of hydration for ammonium ions

G. N. Merrill · G. D. Fletcher

Received: 13 November 2006 / Accepted: 12 February 2007 / Published online: 5 May 2007  
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**Abstract** Hartree–Fock (HF) and second-order Møller–Plesset (MP2) calculations were used to investigate the structures and thermochemistry of methylammonium–water clusters ( $\text{Me}_{4-m}\text{NH}_m^+(\text{H}_2\text{O})_n$ ,  $m=1-4$ ,  $n=1-4$ ). Water molecules were treated ab initio and with effective fragment potentials (EFP). In addition to a thorough phase-space search, the importance of basis set, electron correlation, and thermodynamic effects was systematically examined. Cluster structures resulted from hydrogen bond formation between the ammonium group and water molecules; upon saturation of the hydrogen bonding sites of the ammonium group, water molecules entered the second hydration shell. With only four water molecules, the experimental relative enthalpies of hydration were well reproduced at the HF level, while the MP2 relative free energies were in best agreement with experiment. Absolute energies of hydration were calculated using an empirical correction. These results strongly suggest that a HF-based microsolvation approach employing a small number of water molecules can be used to compute relative enthalpies of hydration.

**Keywords** Microsolvation · Ab initio · Methylammonium ions

## 1 Introduction

Ab initio chemistry has achieved a remarkable degree of success in reproducing experimental, gas-phase thermochemistry [1]. It is now routinely possible to calculate ionization potentials, electron and proton affinities, and heats of formation for small molecules within 2–3 kcal/mol (0.1–0.2 eV/mol) of experiment. Such accuracy is often within experimental error. While these gas-phase results are impressive, most chemistry occurs in condensed phases, where solvation, aggregation, and counterion effects can be significant. The accurate prediction of solution thermochemistry has yet to be achieved, and the development of quantitative solvation models continues to be a paramount goal of computational chemistry.

In modeling solvation phenomena, computational chemists possess two major paradigms: continuum and microsolvation. Continuum methods treat the solvent in bulk as an amorphous, polarizable medium [2]. Continuum approaches are usually the methods of first choice for computational chemists because of their simplicity and low cost. Continuum methods, however, demand a number of tradeoffs. For example, they offer at best an ad hoc description of specific solute–solvent and solvent–solvent interactions (e.g., hydrogen bonding). They also have difficulty in describing an asymmetric solvent environment (e.g., the hydration of halides) [3,4].

It is this lack of *molecularity* that has engendered microsolvation methods. The spirit of these approaches is clearly embodied by the following quote of Christian Reichardt,

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Contribution to the Mark S. Gordon 65th Birthday Festschrift Issue.

**Electronic supplementary material** The online version of this article (doi:10.1007/s00214-007-0307-5) contains supplementary material, which is available to authorized users.

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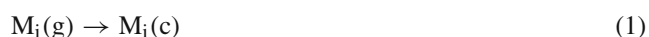
G. N. Merrill (✉)  
Department of Chemistry, The University of Texas at San Antonio,  
One UTSA Circle,  
San Antonio, TX 78249-0698, USA  
e-mail: grant.merrill@utsa.edu

G. D. Fletcher  
Computational Science and Engineering Department,  
CCLRC, Daresbury Laboratory, Warrington,  
Cheshire WA4 4AD, UK

A solvent should not be considered a macroscopic continuum characterized only by physical constants such as density, dielectric constant, index of refraction, etc., but as a discontinuum which consists of individual, mutually interacting solvent molecules [5].

In the microsolvation approach, solvent molecules are included explicitly in the calculation [6].<sup>1</sup> These methods permit individual solute–solvent and solvent–solvent interactions to be considered, and the solvent may array itself in an asymmetric fashion. A significant increase in computational expense is, however, incurred when the solvent is considered explicitly. In addition, a number of questions (e.g., long-range interactions, minimum number of solvent molecules, adequate sampling of the phase space) plague this method.

At first thought, it would appear unlikely that the inclusion of a small number of solvent molecules could afford an accurate treatment of bulk solvation. This is almost certainly true for the description of *absolute* enthalpies ( $\Delta_s H$ ) and free energies ( $\Delta_s G$ ) of solvation (Eq. 1),



where  $M_i(g)$  corresponds to the species in the gas phase and  $M_i(c)$  to that in the condensed phase. If one eschews absolute values and is content with the prediction of *relative* enthalpies ( $\Delta\Delta_s H$ ) and free energies ( $\Delta\Delta_s G$ ) of solvation (Eq. 2),



one might be able to achieve this more limited goal through a cancellation of errors. This is the very idea behind the use of isodesmic reactions to predict gas-phase thermochemistry [7]. The use of isodesmic-type reactions to describe solution thermochemistry is predicated upon the hypothesis that, for a given class of compounds, bulk solvation behavior is quantitatively similar. If accurate relative values can be computed, absolute values may be obtained via an empirical correction.

The work outlined in this article was undertaken to investigate the following hypothesis: can relative enthalpies and free energies of solvation be predicted via a microsolvation approach? Toward this end, the aqueous thermochemistry of methylammonium ions ( $\text{NH}_4^+$ ,  $\text{MeNH}_3^+$ ,  $\text{Me}_2\text{NH}_2^+$ , and  $\text{Me}_3\text{NH}^+$ ) was investigated. This system was selected for a number of reasons: the availability of high-quality experimental data [8–12]; as charged species, electrostatic effects should dominate, which should prove theoretically more tractable [13]; and these acids and their conjugate bases are of considerable interest in and of themselves; for example, the reordering of the gas-phase basicities ( $\text{NH}_3 < \text{MeNH}_2 <$

$\text{Me}_2\text{NH} < \text{Me}_3\text{N}$ ) upon aqueous solvation ( $\text{NH}_3 < \text{Me}_3\text{N} < \text{MeNH}_2 < \text{Me}_2\text{NH}$ ) [14–22].

To test the above hypothesis, four water molecules were sequentially added to each methylammonium ion. With the addition of each water molecule, the conformational and configurational spaces for each cluster were systematically searched. (It should be noted that the first hydration shell, aka coordination sphere, would correspond to four, three, two, and one water molecule(s) for the  $\text{NH}_4^+$ ,  $\text{MeNH}_3^+$ ,  $\text{Me}_2\text{NH}_2^+$ , and  $\text{Me}_3\text{NH}^+$  ions, respectively.) Water molecules beyond that needed to complete the first hydration shell were added to the second hydration shell.

Given the inherent expense of microsolvation methods and our desire to develop models that are applicable to *real* chemical systems, only modest levels of ab initio theory were employed. Optimizations and Hessian were, therefore, carried out only at the Hartree–Fock (HF) and second-order Møller–Plesset (MP2) levels of theory. Furthermore, a second set of calculations was performed in which the water molecules were modeled with effective fragment potentials (EFP) [23–25]. In the EFP approach, interactions between water molecules and the methylammonium ions and between water molecules themselves are described by three, one-electron terms added to the Hamiltonian. These three terms account for electrostatic, polarization, and charge transfer/exchange repulsion interactions. Because most of the expense of an ab initio computation involves four-center, two-electron integrals, the inclusion of one-electron terms results in little additional cost. EFPs were only employed at the HF level of theory, and this aspect of the present work follows up in a systematic fashion on that of Caskey et al. [22].

## 2 Materials and methods

All structures were fully optimized at the Hartree–Fock (HF) level of theory [26,27]. Structures were deemed converged when the root-mean-square and maximum component of the gradients fell below 0.004 and 0.012 kcal/molÅ, respectively. To verify that all optimized structures corresponded to minima, Hessians were computed at the same level of theory. The force constant matrices permitted zero-point energy (ZPE), finite-temperature (FT), and entropic (S) corrections to be computed. All HF ZPEs and vibrational frequencies were scaled by empirical factors of 0.9135 and 0.8953, respectively, regardless of basis set, to compensate for the known overestimation of harmonic frequencies at the HF level of theory [28,29].

To assess the importance of dynamic electron correlation, two additional sets of calculations were carried out with second-order Møller–Plesset (MP2) perturbation theory [30–32]. First, MP2 single-point energy calculations were performed upon the HF optimized structures. These single-

<sup>1</sup> We know of no general review of the microsolvation approach. The results of this method are scattered over dozens of articles.

point energy calculations employed the same basis set used in the HF optimizations. Second, all structures were fully reoptimized and their associated Hessians computed at the MP2 level. Here, MP2 ZPEs and vibrational frequencies were scaled by empirical factors of 0.9661 and 0.9427, respectively, regardless of basis set [28,29]. In both sets of calculations, only the valence electrons were subjected to the perturbation; i.e., the frozen-core (fc) approximation was used.

Basis set effects were investigated by carrying out calculations with the 6-31G double split-valence basis set of Pople and co-workers to which sets of polarization and diffuse functions were added [33–35]. Five basis sets were employed in the present calculations: 6-31G; 6-31G(d)  $\equiv$  6-31G\*; 6-31G(d,p)  $\equiv$  6-31G\*\*; 6-31+G(d)  $\equiv$  6-31+G\*; and 6-31++G(d,p)  $\equiv$  6-31++G\*\*.

Water molecules were treated all ab initio at the HF and MP2 levels of theory. Additionally at the HF level, water molecules were modeled with effective fragment potentials (EFP), implemented for use with a HF Hamiltonian [23–25].

Electrostatic/exchange (ESEX), polarization (POL), charge transfer (CT), and basis set superposition error (BSSE) energies for the HF/6-31++G\*\* optimized methylammonium monohydrates were determined using the reduced variational space (RVS) energy decomposition scheme [40–42].

The calculations were carried out on a small cluster of personal computers with the GAMESS program [43], which is freely available from the Gordon group website at Iowa State University (<http://www.msg.ameslab.gov>).

### 3 Results

#### 3.1 Cluster structures

Figure 1 shows the structures of the lowest energy methylammonium–water clusters. All structures possess  $C_1$  symmetry unless otherwise noted. Given the absence of experimental data regarding the structures of methylammonium–water clusters, only a cursory comparison of the structures obtained from the three levels of theory is warranted. Complete hydrogen bond data as a function of level of theory and basis set can be found in Tables S1–S4 of the Supplementary Information.

All three levels of theory (HF, MP2, HF–EFP) produced qualitatively similar structures. As the cations can act only as hydrogen-bond donors, interactions between the cations and water molecules in the first hydration shell are governed primarily by the formation of hydrogen bonds between the ammonium hydrogen atoms and the oxygen atoms of the water molecules. The hydrogen bond sites of the cations are sequentially filled with the addition of water molecules, and only upon saturation of the first hydration shell are water molecules added to the second shell of hydration. This process

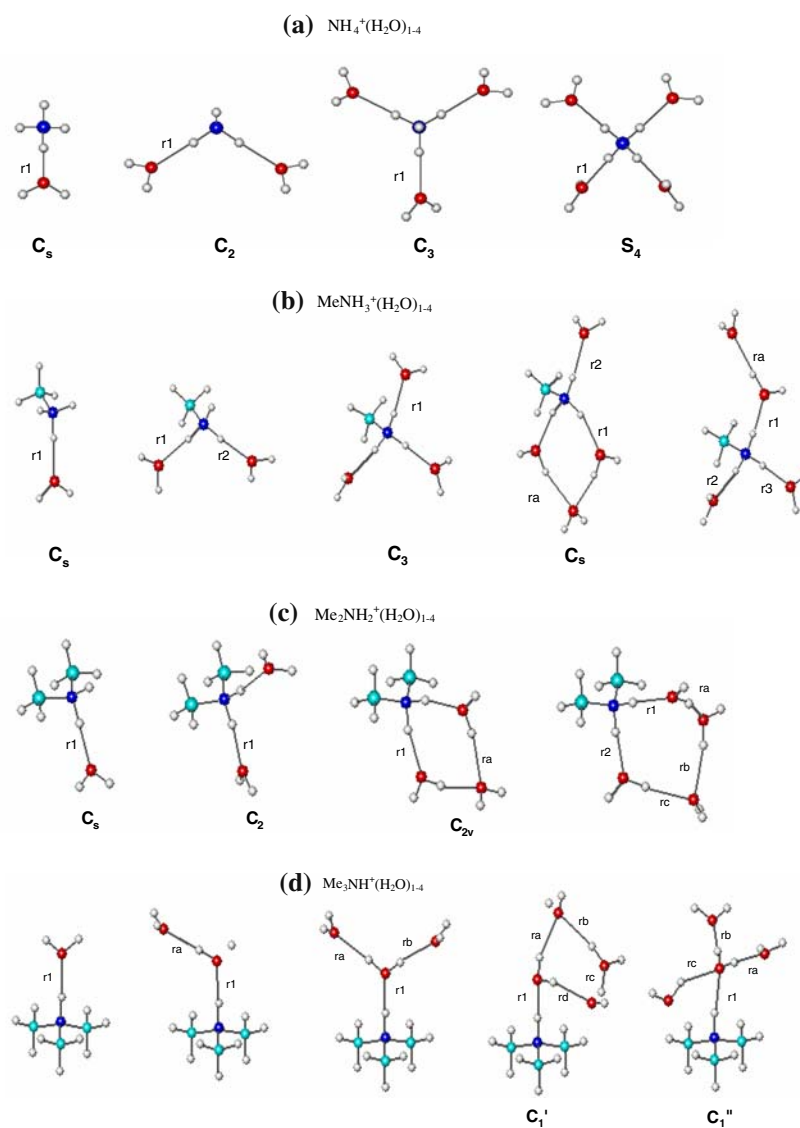
is always enthalpically and (generally) entropically favored. These structures result, therefore, from the attempt of the water molecules to quench the positive charge on the ammonium group through hydrogen bond formation.

Hydrogen bonding between water molecules only becomes important upon completion of the first hydration shell. The filling of the second shell of hydration is a function of a subtle balance between enthalpic and entropic factors; i.e., a reduction in enthalpy through hydrogen bond formation versus an increase in entropy by maximizing the cluster's degrees of freedom. In this regard, two clusters are particularly noteworthy:  $\text{MeNH}_3^+(\text{H}_2\text{O})_4$  and  $\text{Me}_3\text{NH}^+(\text{H}_2\text{O})_4$ . Given only enthalpic considerations, the  $C_s$  structure of  $\text{MeNH}_3^+(\text{H}_2\text{O})_4$  is preferred over the  $C_1$  structure; if entropy is also considered, then the  $C_1$  structure is favored over the  $C_s$  one. A similar situation exists for the  $\text{Me}_3\text{NH}^+(\text{H}_2\text{O})_4$  clusters, where the *ringed* structure ( $C_1'$  in Fig. 1) is enthalpically favored, while the *nonringed* structure ( $C_1''$  in Fig. 1) is entropically preferred. (In the thermochemical discussion that follows, only those structures with the lowest free energies will be considered; e.g., the  $C_1$  and  $C_1''$  structures for the  $\text{MeNH}_3^+(\text{H}_2\text{O})_4$  and  $\text{Me}_3\text{NH}^+(\text{H}_2\text{O})_4$  clusters, respectively. Under constant temperature and pressure conditions, experimental measurements are only made on the lowest free energy species).

The HF structures show a general lack of sensitivity with respect to basis set effects. If the smallest basis (6-31G) is excluded, the remaining four bases differ by no more than 0.07 Å in their hydrogen bonds distances. The  $\text{Me}_{4-n}\text{NH}_n^+ \cdots \text{OH}_2$  bonds range from 1.70 to 1.93 Å, while the  $\text{HOH} \cdots \text{OH}_2$  bonds cover a range from 1.86 to 2.15 Å. The bond lengths obtained with the 6-31G basis are appreciably shorter by 0.08 to 0.18 Å for the  $\text{Me}_{4-n}\text{NH}_n^+ \cdots \text{OH}_2$  bonds and by 0.03 to 0.25 Å for the  $\text{HOH} \cdots \text{OH}_2$  bonds. Regardless of which basis set is used, four general trends are seen: (1) the  $\text{Me}_{4-n}\text{NH}_n^+ \cdots \text{OH}_2$  distances increase as the number of hydrogen bond sites on the cations are filled; (2) the  $\text{Me}_{4-n}\text{NH}_n^+ \cdots \text{OH}_2$  distances decrease as the second hydration shell is filled; (3) hydrogen bonding between water molecules in the second hydration shell is shorter than in the first hydration shell; and (4) multiply hydrogen-bonded water molecules in the second hydration shell evince longer hydrogen bonds than those that are singly hydrogen-bonded.

Upon inclusion of electron correlation at the MP2 level, the length of all hydrogen bonds decrease regardless of basis set. Again excluding the 6-31G basis, an average decrease of about 0.09 Å is seen for all hydrogen bonds. This decrease is more modest for structures obtained with the 6-31G basis (0.03 Å on average). The same qualitative trends in hydrogen bonding seen at the HF level are found at the MP2 level. It is also important to note that the MP2 structures show a general insensitivity to basis set after the first set of (d-type) polarization functions is added.

**Fig. 1** Methylammonium-water cluster structures. All structures have  $C_1$  symmetry unless noted otherwise. See Tables S1–S4 in Supplementary Information for hydrogen bond distances ( $r_1, r_2, \dots, r_a, r_b, \dots$ )

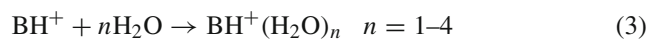


The HF–EFP structures are in fair agreement with their HF counterparts. For all the structures, save those determined with the largest basis (6-31++ $G^{**}$ ), the hydrogen bonds are on average longer. A monotonic decrease in this average *overestimation* is seen as the basis set size increases: 6-31 $G$  = 0.17; 6-31 $G^*$  = 0.05; 6-31 $G^{**}$  = 0.03; 6-31+ $G^*$  = 0.02; and 6-31++ $G^{**}$  =  $-0.01 \text{ \AA}$ . As was the case for the HF and MP2 structures, an insensitivity toward basis set is seen in the HF–EFP structures, the largest difference in hydrogen bond distances is only  $0.07 \text{ \AA}$  for all bases.

### 3.2 Cluster thermochemistry

Two sets of benchmark calculations, which compared computational results with experimental data, were carried out in an attempt to determine the appropriate level of theory to predict the relative enthalpies and free energies for the hydra-

tion of the methylammonium ions. In the first set, the total energies for the sequential addition of water molecules to the cations were computed,



where  $\text{BH}^+ = \text{NH}_4^+, \text{MeNH}_3^+, \text{Me}_2\text{NH}_2^+, \text{and } \text{Me}_3\text{NH}^+$ . In the second set, the differential energies for the addition of water molecules to the cation–water clusters were calculated.



The importance of basis set effects was assessed by carrying out the benchmark calculations at the Hartree–Fock (HF) level of theory with five basis sets of increasing completeness: 6-31 $G$ ; 6-31 $G^*$ ; 6-31 $G^{**}$ ; 6-31+ $G^*$ ; and 6-31++ $G^{**}$ . While the largest basis is clearly far from the Hartree–Fock limit, it does offer a good tradeoff between completeness and practicality. The necessity of electron correlation was eval-

uated by also performing the benchmark calculations with second-order Møller–Plesset (MP2) perturbation theory. While the MP2 level does not represent the state-of-the-art in electron correlation treatments, it is in widespread use given its cost effectiveness<sup>2</sup>.

As the experimental data correspond to enthalpies and free energies at 298 K and 1 atm, calculations were undertaken to determine the importance of enthalpic (zero-point energy, ZPE, and finite-temperature, FT) and entropic (S) corrections in reproducing the experimental values.<sup>3</sup> It should be stated that, given the rather flat nature of the potential energy surfaces for the methylammonium–water clusters, the use of the harmonic and rigid rotor approximations to compute the enthalpic and entropic corrections might be suspect. As mentioned in the introduction, the present objective was the calculation of relative energies of hydration. It was hoped, therefore, that the errors associated with these thermodynamic corrections would cancel one another. To the extent that such cancellations were not achieved, more sophisticated approaches would need to be employed; e.g., ones that explicitly consider anharmonicities and mode coupling [44–46]. It should also be noted that, for a given level of theory, the computed frequencies were not particularly sensitive to the choice of basis set.

Water molecules were also approximated by effective fragment potentials (EFP) in an attempt to further reduce the cost of the computations. These calculations were carried out at the HF level (HF–EFP), and they were compared to the HF results obtained with an all ab initio description of the water molecules.

In what follows, results obtained with the largest basis set, 6-31++G\*\*, will be discussed at all four levels of theory. This will permit a direct comparison of the results. The best results obtained at a given level will also be given in order to provide an idea as to the best accuracy that can be achieved.

Experimental and selected theoretical total internal energies ( $\Delta U$ ), enthalpies ( $\Delta H$ ), and free energies ( $\Delta G$ ) for the hydration of the methylammonium ions (Eq. 3) are given in Table 1. A comparison of the experimental enthalpies with those computed at the HF level of theory with the 6-31++G\*\* basis set reveals the internal energies to be in best agreement with experiment (mean error,  $\mu = -1.3$ , standard deviation,

$\sigma = 1.4$ , and absolute maximum error,  $|\max| = 3.4$  kcal/mol). With the inclusion of ZPE and FT corrections, which yield the respective enthalpies at 0 and 298 K, all the above measures of error increase. The per water errors mirror these results, where again the best agreement with the experimental enthalpies is found for the internal energies ( $\mu = -0.5$ ,  $\sigma = 0.6$ ,  $|\max| = 1.2$  kcal/mol), and the inclusion of enthalpic corrections led to an increase in the per water errors.

The best overall agreement between the experimental enthalpies was found for the HF enthalpies at 0 K with the 6-31G\*\* basis ( $\mu = -0.4$ ,  $\sigma = 1.3$ ,  $|\max| = 2.2$  kcal/mol), while the per water errors also dropped ( $\mu = -0.2$ ,  $\sigma = 0.6$ ,  $|\max| = 1.2$  kcal/mol). This mean error and standard deviation are within experimental error ( $\pm 1.1$  kcal/mol), and the absolute maximum error is nearly so. This is a remarkable accomplishment given the rather modest level of theory employed. If the smaller 6-31G\* basis is used to compute the HF enthalpies at 0 K, the errors are essentially the same ( $\mu = -0.5$ ,  $\sigma = 1.3$ ,  $|\max| = 2.3$  kcal/mol) as are the per water errors ( $\mu = -0.2$ ,  $\sigma = 0.7$ ,  $|\max| = 1.3$  kcal/mol). These results suggest that small bases at the HF level can be quite effective in reproducing experimental total enthalpies of hydration for ammonium ions.

At the HF–EFP level with the 6-31++G\*\* basis set, the best agreement with the experimental enthalpies was obtained for the enthalpies at 0 K:  $\mu = 2.2$ ,  $\sigma = 1.7$ , and  $|\max| = 4.8$  kcal/mol. The per-water (i.e., EFP) errors were also quite low:  $\mu = 0.9$ ,  $\sigma = 0.8$ , and  $|\max| = 2.6$  kcal/mol. When these HF–EFP enthalpies at 0 K were corrected to 298 K, all measures of error increased dramatically. This is not too surprising given the rigid-body approximation inherent in the EFP model, and as such, all degrees of freedom internal to the *water molecules* are ignored. The best agreement between the experimental enthalpies and the HF–EFP level of theory is seen for the internal energies computed with the smallest basis set (6-31G):  $\mu = -1.5$ ,  $\sigma = 1.9$ , and  $|\max| = 4.2$  kcal/mol; the associated per water errors are also quite good:  $\mu = -0.5$ ,  $\sigma = 0.8$ , and  $|\max| = 1.4$  kcal/mol.

Using MP2 theory, the best agreement with the experimental enthalpies was found for the theoretical results determined with the largest basis set (6-31++G\*\*). This observation is consistent with the demands of perturbation theory for polarization and diffuse functions in the recovery of correlation energy [7]. While the best agreement is obtained when the internal energies are ZPE corrected ( $\mu = -2.7$ ,  $\sigma = 2.2$ ,  $|\max| = 5.7$  kcal/mol), the MP2 results do not compare as favorably with those found at the HF level, especially given their inherent expense and need for larger bases. The cost of the fully correlated computations can be offset by performing MP2 single-point energy calculations at the HF optimized geometries (MP2//HF). Like the all-MP2 results, the best agreement between the experimental enthalpies and the MP2//HF level is found for the computations with the

<sup>2</sup> Density functional theory calculations have also been performed upon the present system. These calculations have been carried out with the B3LYP functional and the current five bases. These results will be reported in a future paper in this journal.

<sup>3</sup> Caution must be exercised in this regard. While many comparisons between internal energies and enthalpies are valid, free energies should be compared within the context of supermolecular calculations, which encompasses microsolvation. To the extent that theory does a poor job in calculating entropies, comparisons between free energies become more dubious.

**Table 1** Total internal energies,  $\Delta U$ , enthalpies  $\Delta H$ , and free energies  $\Delta G$  for the addition of water molecules to ammonium ions:  $\text{BH}^+ + n\text{H}_2\text{O} \rightarrow \text{BH}^+(\text{H}_2\text{O})_n$ ,  $\text{BH}^+ = \text{NH}_4^+$ ,  $\text{MeNH}_3^+$ ,  $\text{Me}_2\text{NH}_2^+$ ,  $\text{Me}_3\text{NH}^+$  and  $n = 1-4$ 

$n$	Experiment <sup>a</sup>	HF	MP2	MP2//HF	HF-EFP
$\Delta U(\text{NH}_4^+)$					
1	-20.6	-19.7	-21.7	-21.6	-19.9 (-19.3) <sup>d</sup>
2	-38.0	-36.6	-40.2	-40.0	-37.1 (-36.1) <sup>d</sup>
3	-51.7	-51.3	-56.4	-56.1	-52.2 (-50.9) <sup>d</sup>
4	-62.5	-64.0	-70.5	-70.2	-65.2 (-63.8) <sup>d</sup>
$\Delta U(\text{MeNH}_3^+)$					
1	-16.8	-17.6	-19.9	-19.8	-18.0 (-17.4) <sup>d</sup>
2	-31.4	-33.0	-37.3	-37.0	-33.8 (-32.9) <sup>d</sup>
3	-43.7	-46.5	-52.7	-52.3	-47.7 (-46.6) <sup>d</sup>
4	-54.0	-57.3 <sup>b</sup>	-65.7 <sup>b</sup>	-65.0 <sup>b</sup>	-58.7 <sup>b</sup> (-57.4) <sup>b,d</sup>
$\Delta U(\text{Me}_2\text{NH}_2^+)$					
1	-15.0	-16.2	-18.8	-18.6	-16.7 (-16.1) <sup>d</sup>
2	-28.5	-30.5	-35.5	-35.1	-31.5 (-30.6) <sup>d</sup>
3	-39.8	-43.2	-51.4	-50.7	-45.2 (-44.0) <sup>d</sup>
4	-50.3	-53.3	-64.4	-63.2	-55.8 (-54.5) <sup>d</sup>
$\Delta U(\text{Me}_3\text{NH}^+)$					
1	-14.5	-15.2	-18.1	-17.8	-15.8 (-15.2) <sup>d</sup>
2	-25.9	-26.9	-32.6	-31.9	-27.8 (-27.0) <sup>d</sup>
3	-35.9	-37.0	-45.1	-44.2	-38.8 (-37.5) <sup>d</sup>
4	-44.3	-45.3 <sup>c</sup>	-56.5 <sup>c</sup>	-55.2 <sup>c</sup>	-49.0 <sup>c</sup> (-48.0) <sup>c,d</sup>
Statistics					
		HF	MP2	MP2//HF	HF-EFP
Overall	$\mu$	-1.3	-7.1	-6.6	-2.5 (-1.5) <sup>d</sup>
	$\sigma$	1.4	3.9	3.6	2.0 (1.9) <sup>d</sup>
	max	3.4	14.1	12.9	5.5 (4.2) <sup>d</sup>
Per water	$\mu$	-0.5	-2.8	-2.6	-1.0 (-0.5) <sup>d</sup>
	$\sigma$	0.6	0.9	0.8	0.7 (0.8) <sup>d</sup>
	max	1.2	3.9	3.6	1.8 (1.4) <sup>d</sup>
$n$	Experiment <sup>a</sup>	HF	MP2	MP2//HF	HF-EFP
$\Delta H_{0\text{K}}(\text{NH}_4^+)$					
1	-20.6	-17.9 (-19.7) <sup>e</sup>	-19.9	-19.8	-18.0
2	-38.0	-33.0 (-36.3) <sup>e</sup>	-36.5	-36.4	-33.5
3	-51.7	-46.1 (-50.4) <sup>e</sup>	-51.2	-50.9	-46.9
4	-62.5	-57.5 (-62.6) <sup>e</sup>	-63.8	-63.6	-58.5
$\Delta H_{0\text{K}}(\text{MeNH}_3^+)$					
1	-16.8	-16.0 (-17.6) <sup>e</sup>	-18.3	-18.1	-16.2
2	-31.4	-29.8 (-32.8) <sup>e</sup>	-34.1	-33.8	-30.5
3	-43.7	-41.9 (-45.9) <sup>e</sup>	-48.0	-47.6	-42.9
4	-54.0	-50.8 <sup>b</sup> (-55.7) <sup>b,e</sup>	-58.9 <sup>b</sup>	-58.5 <sup>b</sup>	-51.6 <sup>b</sup>
$\Delta H_{0\text{K}}(\text{Me}_2\text{NH}_2^+)$					
1	-15.0	-14.7 (-16.2) <sup>e</sup>	-17.3	-17.0	-15.1
2	-28.5	-27.5 (-30.3) <sup>e</sup>	-32.5	-32.1	-28.4
3	-39.8	-37.2 (-41.7) <sup>e</sup>	-45.2	-44.8	-38.7
4	-50.3	-45.4 (-51.0) <sup>e</sup>	-56.0	-55.3	-46.8

**Table 1** continued

<i>n</i>	Experiment <sup>a</sup>	HF	MP2	MP2//HF	HF-EFP
$\Delta H_{0K}(\text{Me}_3\text{NH}^+)$					
1	−14.5	−13.7 (−15.2) <sup>e</sup>	−16.7	−16.4	−14.3
2	−25.9	−23.4 (−26.0) <sup>e</sup>	−29.0	−28.5	−23.9
3	−35.9	−31.8 (−35.3) <sup>e</sup>	−39.8	−39.1	−32.5
4	−44.3	−38.1 <sup>c</sup> (−43.0) <sup>c,e</sup>	−48.8 <sup>c</sup>	−48.0 <sup>c</sup>	−40.5 <sup>c</sup>
Statistics					
		HF	MP2	MP2//HF	HF-EFP
Overall	$\mu$	3.0 (−0.4) <sup>e</sup>	−2.7	−2.3	2.2
	$\sigma$	1.9 (1.3) <sup>e</sup>	2.2	2.1	1.7
	max	6.2 (2.2) <sup>e</sup>	5.7	5.0	4.8
Per water	$\mu$	1.2 (−0.2) <sup>e</sup>	−1.1	−1.0	0.9
	$\sigma$	0.7 (0.6) <sup>e</sup>	0.9	0.9	0.8
	max	2.7 (1.2) <sup>e</sup>	2.3	2.0	2.6
$\Delta H_{298K}(\text{NH}_4^+)$					
<i>n</i>	Experiment <sup>a</sup>	HF	MP2	MP2//HF	HF-EFP
1	−20.6	−18.3 (−20.2) <sup>e</sup>	−20.5	−20.2	−15.9
2	−38.0	−33.8 (−37.0) <sup>e</sup>	−37.5	−37.1	−29.2
3	−51.7	−46.9 (−51.2) <sup>e</sup>	−52.1	−51.7	−40.3
4	−62.5	−58.1 (−63.2) <sup>e</sup>	−64.6	−64.2	−49.3
$\Delta H_{298K}(\text{MeNH}_3^+)$					
1	−16.8	−16.2 (−17.9) <sup>e</sup>	−18.6	−18.3	−14.0
2	−31.4	−30.0 (−33.0) <sup>e</sup>	−34.4	−34.0	−25.8
3	−43.7	−42.0 (−46.0) <sup>e</sup>	−48.3	−47.8	−35.8
4	−54.0	−51.2 <sup>b</sup> (−56.0) <sup>b,e</sup>	−59.6 <sup>b</sup>	−58.9 <sup>b</sup>	−42.5 <sup>b</sup>
$\Delta H_{298K}(\text{Me}_2\text{NH}_2^+)$					
1	−15.0	−14.7 (−16.3) <sup>e</sup>	−17.4	−17.1	−12.7
2	−28.5	−27.5 (−30.3) <sup>e</sup>	−32.6	−32.1	−23.6
3	−39.8	−38.2 (−42.6) <sup>e</sup>	−46.5	−45.8	−32.6
4	−50.3	−46.7 (−52.3) <sup>e</sup>	−57.8	−56.6	−38.8
$\Delta H_{298K}(\text{Me}_3\text{NH}^+)$					
1	−14.5	−13.7 (−15.1) <sup>e</sup>	−16.7	−16.3	−11.8
2	−25.9	−23.8 (−26.3) <sup>e</sup>	−29.6	−28.8	−19.5
3	−35.9	−32.3 (−35.6) <sup>e</sup>	−41.2	−39.5	−26.1
4	−44.3	−38.9 <sup>c</sup> (−43.7) <sup>c,e</sup>	−50.1 <sup>c</sup>	−48.8 <sup>c</sup>	−32.1 <sup>c</sup>
Statistics					
		HF	MP2	MP2//HF	HF-EFP
Overall	$\mu$	2.5 (−0.9) <sup>e</sup>	−3.4	−2.8	7.7
	$\sigma$	1.6 (1.2) <sup>e</sup>	2.4	2.1	3.7
	max	5.4 (2.8) <sup>e</sup>	7.5	6.3	13.2
Per water	$\mu$	1.0 (−0.4) <sup>e</sup>	−1.4	−1.1	3.1
	$\sigma$	0.6 (0.5) <sup>e</sup>	0.9	0.8	0.7
	max	2.3 (1.3) <sup>e</sup>	2.4	2.1	4.7

**Table 1** continued

<i>n</i>	Experiment <sup>a</sup>	HF	MP2	MP2//HF	HF-EFP
$\Delta G(\text{NH}_4^+)$					
1	-13.3	-14.3 (-14.7) <sup>f</sup>	-15.4	-16.2	-24.9
2	-22.2	-21.4 (-22.0) <sup>f</sup>	-25.0	-24.7	-45.2
3	-28.5	-27.2 (-28.1) <sup>f</sup>	-32.0	-31.9	-62.7
4	-32.4	-32.5 (-33.7) <sup>f</sup>	-38.1	-38.6	-78.9
$\Delta G(\text{MeNH}_3^+)$					
1	-10.3	-10.3 (-10.8) <sup>f</sup>	-13.9	-12.5	-21.5
2	-17.7	-17.7 (-18.4) <sup>f</sup>	-21.5	-21.7	-40.8
3	-22.8	-22.0 (-22.9) <sup>f</sup>	-27.9	-27.7	-57.5
4	-26.5	-24.8 (-26.2) <sup>f</sup>	-32.1	-32.5	-70.4
$\Delta G(\text{Me}_2\text{NH}_2^+)$					
1	-8.2	-8.7 (-9.1) <sup>f</sup>	-11.2	-11.1	-20.3
2	-14.3	-14.5 (-15.2) <sup>f</sup>	-19.5	-19.1	-38.3
3	-18.3	-14.2 (-15.4) <sup>f</sup>	-21.5	-21.7	-49.5
4	-21.3	-15.5 (-17.1) <sup>f</sup>	-24.5	-25.4	-60.5
$\Delta G(\text{Me}_3\text{NH}^+)$					
1	-7.3	-8.0 (-8.5) <sup>f</sup>	-10.9	-10.7	-21.9
2	-11.3	-10.7 (-11.6) <sup>f</sup>	-15.9	-15.7	-33.1
3	-13.9	-12.3 (-13.5) <sup>f</sup>	-17.4	-19.5	-45.8
4	-15.9	-9.9 (-11.5) <sup>f</sup>	-18.9	-19.8	-55.6
Statistics					
		HF	MP2	MP2//HF	HF-EFP
Overall	$\mu$	1.3 (0.2) <sup>f</sup>	-3.8	-4.0	-27.7
	$\sigma$	2.2 (1.7) <sup>f</sup>	1.1	1.2	11.7
	max	6.0 (4.2) <sup>f</sup>	5.7	6.2	46.5
Per water	$\mu$	0.3 (-0.1) <sup>f</sup>	-1.9	-1.9	-11.4
	$\sigma$	0.7 (0.7) <sup>f</sup>	0.9	0.7	1.1
	max	1.5 (1.4) <sup>f</sup>	3.6	3.4	14.6

Basis set is 6-31++G\*\* unless parenthetically noted. All values in kcal/mol

<sup>a</sup> Experimental error =  $\pm 1.1$  kcal/mol [10, 11]

<sup>b</sup>  $\text{MeNH}_3^+(\text{H}_2\text{O})_4 = \text{C}_1$  structure

<sup>c</sup>  $\text{Me}_3\text{NH}^+(\text{H}_2\text{O})_4 = \text{C}'_1$  structure

<sup>d</sup> 6-31G

<sup>e</sup> 6-31G\*\*

<sup>f</sup> 6-31+G\*

6-31++G\*\* basis set, specifically the ZPE-corrected internal energies ( $\mu = -2.3$ ,  $\sigma = 2.1$ ,  $|\text{max}| = 5.0$  kcal/mol). These results are, nevertheless, still in poorer agreement with the experimental enthalpies than those obtained at the HF level with the smaller 6-31G\* and 6-31G\*\* bases. It is important to note that the largest discrepancy between the MP2 and MP2//HF calculations is quite small ( $\Delta U = 1.3$ ,  $\Delta H_{0\text{K}} = 0.8$ ,  $\Delta H_{298\text{K}} = 1.7$  kcal/mol), and the differences between the mean errors, standard deviations, and absolute maximum errors are actually smaller still. This suggests that MP2 opti-

mized structures and Hessians offer little benefit in reproducing the experimental total enthalpies.

The agreement between the experimental and theoretical total free energies is worse than that found for the total enthalpies. At the HF level of theory with the 6-31++G\*\* basis set, the mean error ( $\mu = 1.3$  kcal/mol) and standard deviation ( $\sigma = 2.2$  kcal/mol) are nearly as good as the values for the analogous enthalpies, but the absolute maximum deviation ( $|\text{max}| = 6.0$  kcal/mol) is appreciably larger. The best agreement between experiment and the HF level of theory



was found for the 6-31+ $G^*$  basis:  $\mu = 0.2$ ,  $\sigma = 1.7$ , and  $|\max| = 4.2$  kcal/mol. For both bases, the per-water errors are quite low (6-31++ $G^{**}$ :  $\mu = 0.3$ ,  $\sigma = 0.7$ ,  $|\max| = 1.5$ ; 6-31+ $G^*$ :  $\mu = -0.1$ ,  $\sigma = 0.7$ ,  $|\max| = 1.4$  kcal/mol).

The agreement between the experimental total free energies and those determined at the HF–EFP level with the 6-31++ $G^{**}$  basis is far worse ( $\mu = -27.7$ ,  $\sigma = 11.7$ ,  $|\max| = 46.5$  kcal/mol) than the comparable total enthalpies. Even the per-water errors ( $\mu = -11.4$ ,  $\sigma = 1.1$ ,  $|\max| = 14.6$  kcal/mol) are unacceptably large. The HF–EFP level of theory is clearly inadequate in reproducing experimental total free energies; this is once again the result of the rigid-body approximation (*vide supra*).

The inclusion of electron correlation does not improve the theoretical agreement with the experimental free energies. As was seen for the total enthalpies, the best results are obtained with the 6-31++ $G^{**}$  basis (MP2:  $\mu = -3.8$ ,  $\sigma = 1.1$ ,  $|\max| = 5.7$ ; MP2//HF:  $\mu = -4.0$ ,  $\sigma = 1.2$ ,  $|\max| = 6.2$  kcal/mol). The agreement between the MP2 and MP2//HF calculations is again very good, where with one exception, all of the differences are within one kilocalorie per mole of one another. As was also observed for the total enthalpies, MP2 optimized geometries and Hessians do not improve the theoretical agreement with the experimental total free energies.

The rather poor agreement between theory and experiment for the total free energies appears to derive largely from the entropic corrections. As was previously pointed out, this is likely due to the inadequate nature of the thermodynamic approximations used.

Table 2 contains experimental and selected theoretical differential energies of hydration for the methylammonium ions (Eq. 4). The HF internal energies computed with the 6-31++ $G^{**}$  basis set are in excellent agreement with the experimental enthalpies ( $\mu = -0.6$ ,  $\sigma = 0.8$ ,  $|\max| = 1.9$  kcal/mol). The inclusion of ZPE and FT corrections does not lead to improved results. If the smaller 6-31 $G^{**}$  basis is used, the best agreement between experiment and HF theory is achieved if the internal energies are enthalpically corrected at the HF level ( $\Delta\Delta H_{0K}$ :  $\mu = -0.1$ ,  $\sigma = 0.8$ ,  $|\max| = 1.4$  kcal/mol;  $\Delta\Delta H_{298K}$ :  $\mu = -0.3$ ,  $\sigma = 0.7$ ,  $|\max| = 1.3$  kcal/mol). Virtually identical results are obtained for the enthalpies computed with the 6-31 $G^*$  basis.

When EFPs are substituted for all ab initio water molecules at the HF level, the internal energies ( $\mu = -1.1$ ,  $\sigma = 0.8$ ,  $|\max| = 2.4$  kcal/mol) and enthalpies at 0 K ( $\mu = 0.9$ ,  $\sigma = 1.0$ ,  $|\max| = 2.6$  kcal/mol) computed with the 6-31++ $G^{**}$  basis reproduce their HF counterparts. As is to be expected, the HF–EFP enthalpies corrected to 298 K are in poorer agreement. Much the same results were found for the other four bases. The HF–EFP level once again demonstrates an insensitivity to basis set effects. It is, therefore, possible to substitute EFPs for all ab initio water molecules

in the description of experimental differential enthalpies of hydration for methylammonium ions.

As was the case for the total enthalpies of hydration, the best results at the MP2 and MP2//HF levels were obtained with the 6-31++ $G^{**}$  basis for the differential values. All of the differential values are, moreover, in better agreement with experiment than their total counterparts. While the average errors for the internal energies are outside the range of experimental error ( $\pm 1.4$  kcal/mol), those found for the enthalpies at 0 K (MP2:  $\mu = -1.0$ ; MP2//HF:  $\mu = -0.9$  kcal/mol) and 298 K (MP2:  $\mu = -1.3$ ; MP2//HF:  $\mu = -1.1$  kcal/mol) are within this range. The standard deviations are also within experimental error for the MP2 and MP2//HF internal energies and enthalpies. The agreement between the MP2 and MP2//HF differential energies is even better than that found for the total energies; maximum differences of 0.5, 0.3, and 0.9 kcal/mol are seen for the respective  $\Delta\Delta U$ ,  $\Delta\Delta H_{0K}$ , and  $\Delta\Delta H_{298K}$  values. There would appear to be no reason for MP2 optimizations and Hessians in the prediction of differential enthalpies.

The experimental differential free energies of hydration are fairly well reproduced at the HF level with the 6-31++ $G^{**}$  basis, although the absolute maximum error is too large ( $\mu = 0.8$ ,  $\sigma = 1.7$ ,  $|\max| = 4.4$  kcal/mol). These statistics are improved somewhat if the 6-31 $G^{**}$  basis is used:  $\mu = -0.5$ ,  $\sigma = 1.7$ , and  $|\max| = 3.0$  kcal/mol. Nearly identical results, save a larger absolute maximum error, are found at the HF/6-31 $G^*$  level. The HF–EFP free energies are, once again, in very poor agreement with experiment ( $\mu = -10.6$ ,  $\sigma = 2.1$ ,  $|\max| = 14.6$  kcal/mol). The use of a basis other than 6-31++ $G^{**}$  fails to improve the agreement with experiment. The MP2 free energies offer a level of agreement with experiment similar to that found at the HF level of theory. With the 6-31++ $G^{**}$  basis, errors at the MP2 ( $\mu = -1.1$ ,  $\sigma = 1.6$ ,  $|\max| = 3.6$  kcal/mol) and MP2//HF ( $\mu = -1.3$ ,  $\sigma = 1.5$ ,  $|\max| = 3.4$  kcal/mol) levels are found to rival those calculated at the HF level. The agreement between the MP2 and MP2//HF levels of theory is slightly worse for the differential free energies ( $|\max| = 2.3$  kcal/mol). Given the additional expense incurred for the MP2 calculations, however, this level of theory does not seem to be warranted.

On the basis of the foregoing benchmark calculations, a number of conclusions can be drawn with regard to the selection of an appropriate level of theory required to reproduce experimental enthalpies and free energies of hydration for the methylammonium ions. (1) The inclusion of electron correlation is not required, especially in light of the added expense. If such a treatment is desired, MP2 single point energies based upon HF optimized geometries is more than adequate. (2) At the HF level, one can obtain good results with small bases (e.g., 6-31 $G^{**}$ ). This stands in stark contrast to calculations at the MP2 level, where large bases (e.g., 6-31++ $G^{**}$ ) are required. (3) While ZPE corrections improve

**Table 2** Differential internal energies,  $\Delta\Delta U$ , enthalpies  $\Delta\Delta H$ , and free energies  $\Delta\Delta G$  for the addition of water molecules to ammonium ion–water clusters:  $(\text{BH}^+)_{n-1} + \text{H}_2\text{O} \rightarrow \text{BH}^+(\text{H}_2\text{O})_n$ ,  $\text{BH}^+ = \text{NH}_4^+$ ,  $\text{MeNH}_3^+$ ,  $\text{Me}_2\text{NH}_2^+$ ,  $\text{Me}_3\text{NH}^+$  and  $n = 1-4$ 

$n$	Experiment <sup>a</sup>	HF	MP2	MP2//HF	HF-EFP
$\Delta\Delta U(\text{NH}_4^+)$					
1	-20.6	-19.7	-21.7	-21.6	-19.9
2	-17.4	-16.9	-18.5	-18.4	-17.2
3	-13.7	-14.7	-16.1	-16.1	-15.0
4	-10.8	-12.7	-14.1	-14.1	-13.0
$\Delta\Delta U(\text{MeNH}_3^+)$					
1	-16.8	-17.6	-19.9	-19.8	-18.0
2	-14.6	-15.4	-17.4	-17.3	-15.8
3	-12.3	-13.5	-15.4	-15.3	-13.9
4	-10.3	-10.8 <sup>b</sup>	-13.0 <sup>b</sup>	-12.7 <sup>b</sup>	-11.0 <sup>b</sup>
$\Delta\Delta U(\text{Me}_2\text{NH}_2^+)$					
1	-15.0	-16.2	-18.8	-18.6	-16.7
2	-13.5	-14.3	-16.7	-16.5	-14.8
3	-11.3	-12.7	-15.9	-15.6	-13.7
4	-10.5	-10.1	-13.0	-12.5	-10.6
$\Delta\Delta U(\text{Me}_3\text{NH}^+)$					
1	-14.5	-15.2	-18.1	-17.8	-15.8
2	-11.4	-11.8	-14.5	-14.1	-12.0
3	-10.0	-10.0	-12.5	-12.3	-10.9
4	-8.4	-8.4 <sup>c</sup>	-11.5 <sup>c</sup>	-11.0 <sup>c</sup>	-10.2 <sup>c</sup>
Statistics					
		HF	MP2	MP2//HF	HF-EFP
Overall	$\mu$	-0.6	-2.9	-2.7	-1.1
	$\sigma$	0.8	0.9	0.9	0.8
	max	1.9	4.6	4.3	2.4
$n$	Experiment <sup>a</sup>	HF	MP2	MP2//HF	HF-EFP
$\Delta\Delta H_{0K}(\text{NH}_4^+)$					
1	-20.6	-17.9 (-19.7) <sup>d</sup>	-19.9	-19.8	-18.0
2	-17.4	-15.1 (-16.5) <sup>d</sup>	-16.7	-16.7	-15.6
3	-13.7	-13.1 (-14.2) <sup>d</sup>	-14.6	-14.5	-13.4
4	-10.8	-11.4 (-12.2) <sup>d</sup>	-12.6	-12.7	-11.6
$\Delta\Delta H_{0K}(\text{MeNH}_3^+)$					
1	-16.8	-16.0 (-17.6) <sup>d</sup>	-18.3	-18.1	-16.2
2	-14.6	-13.8 (-15.1) <sup>d</sup>	-15.8	-15.7	-14.3
3	-12.3	-12.1 (-13.1) <sup>d</sup>	-13.9	-13.8	-12.5
4	-10.3	-8.9 <sup>b</sup> (-9.8) <sup>b,d</sup>	-10.9 <sup>b</sup>	-10.8 <sup>b</sup>	-8.7 <sup>b</sup>
$\Delta\Delta H_{0K}(\text{Me}_2\text{NH}_2^+)$					
1	-15.0	-14.7 (-16.2) <sup>d</sup>	-17.3	-17.0	-15.1
2	-13.5	-12.9 (-14.1) <sup>d</sup>	-15.2	-15.1	-13.3
3	-11.3	-9.7 (-11.3) <sup>d</sup>	-12.7	-12.7	-10.2
4	-10.5	-8.2 (-9.4) <sup>d</sup>	-10.8	-10.6	-8.1

**Table 2** continued

<i>n</i>	Experiment <sup>a</sup>	HF	MP2	MP2//HF	HF-EFP
$\Delta\Delta H_{0K}(\text{Me}_3\text{NH}^+)$					
1	-14.5	-13.7 (-15.2) <sup>d</sup>	-16.7	-16.4	-14.3
2	-11.4	-9.7 (-10.8) <sup>d</sup>	-12.3	-12.1	-9.6
3	-10.0	-8.4 (-9.2) <sup>d</sup>	-10.8	-10.6	-8.6
4	-8.4	-6.3 <sup>c</sup> (-7.7) <sup>c,d</sup>	-9.0 <sup>c</sup>	-9.0 <sup>c</sup>	-8.0 <sup>c</sup>
Statistics					
		HF	MP2	MP2//HF	HF-EFP
Overall	$\mu$	1.2 (-0.1) <sup>d</sup>	-1.0	-0.9	0.9
	$\sigma$	0.9 (0.8) <sup>d</sup>	0.9	0.9	1.0
	max	2.7 (1.4) <sup>d</sup>	2.3	2.0	2.6
<i>n</i>	Experiment <sup>a</sup>	HF	MP2	MP2//HF	HF-EFP
$\Delta\Delta H_{298K}(\text{NH}_4^+)$					
1	-20.6	-18.3 (-20.2) <sup>d</sup>	-20.5	-20.2	-15.9
2	-17.4	-15.4 (-16.8) <sup>d</sup>	-17.0	-16.9	-13.3
3	-13.7	-13.2 (-14.2) <sup>d</sup>	-14.6	-14.5	-11.1
4	-10.8	-11.2 (-12.0) <sup>d</sup>	-12.5	-12.5	-9.1
$\Delta\Delta H_{298K}(\text{MeNH}_3^+)$					
1	-16.8	-16.2 (-17.9) <sup>d</sup>	-18.6	-18.3	-14.0
2	-14.6	-13.9 (-15.1) <sup>d</sup>	-15.9	-15.7	-11.8
3	-12.3	-12.0 (-13.0) <sup>d</sup>	-13.8	-13.8	-10.0
4	-10.3	-9.1 <sup>b</sup> (-10.0) <sup>b,d</sup>	-11.3 <sup>b</sup>	-11.1 <sup>b</sup>	-6.7 <sup>b</sup>
$\Delta\Delta H_{298K}(\text{Me}_2\text{NH}_2^+)$					
1	-15.0	-14.7 (-16.3) <sup>d</sup>	-17.4	-17.1	-12.7
2	-13.5	-12.8 (-14.0) <sup>d</sup>	-15.2	-15.0	-10.9
3	-11.3	-10.7 (-12.3) <sup>d</sup>	-14.0	-13.7	-9.0
4	-10.5	-8.5 (-9.7) <sup>d</sup>	-11.3	-10.8	-6.2
$\Delta\Delta H_{298K}(\text{Me}_3\text{NH}^+)$					
1	-14.5	-13.7 (-15.1) <sup>d</sup>	-16.7	-16.3	-11.8
2	-11.4	-10.1 (-11.2) <sup>d</sup>	-12.9	-12.5	-7.7
3	-10.0	-8.5 (-9.3) <sup>d</sup>	-11.6	-10.7	-6.6
4	-8.4	-6.6 <sup>c</sup> (-8.1) <sup>c,d</sup>	-9.0 <sup>c</sup>	-9.3 <sup>c</sup>	-6.0 <sup>c</sup>
Statistics					
		HF	MP2	MP2//HF	HF-EFP
Overall	$\mu$	1.0 (-0.3) <sup>d</sup>	-1.3	-1.1	3.0
	$\sigma$	0.7 (0.7) <sup>d</sup>	0.8	0.8	0.8
	max	2.3 (1.3) <sup>d</sup>	2.7	2.4	4.7
<i>n</i>	Experiment <sup>a</sup>	HF	MP2	MP2//HF	HF-EFP
$\Delta\Delta G(\text{NH}_4^+)$					
1	-13.3	-14.3 (-16.3) <sup>d</sup>	-15.4	-16.2	-24.9
2	-8.9	-7.1 (-8.4) <sup>d</sup>	-9.6	-8.6	-20.3
3	-6.3	-5.8 (-6.8) <sup>d</sup>	-7.1	-7.2	-17.5
4	-3.9	-5.3 (-6.1) <sup>d</sup>	-6.0	-6.6	-16.2

**Table 2** continued

<i>n</i>	Experiment <sup>a</sup>	HF	MP2	MP2//HF	HF-EFP
$\Delta\Delta G(\text{MeNH}_3^+)$					
1	-10.3	-10.3 (-11.7) <sup>d</sup>	-13.9	-12.5	-21.5
2	-7.4	-7.4 (-8.7) <sup>d</sup>	-7.7	-9.2	-19.3
3	-5.1	-4.3 (-5.7) <sup>d</sup>	-6.4	-6.0	-16.7
4	-3.7	-2.9 (-4.0) <sup>d</sup>	-4.2	-4.8	-12.9
Statistics					
		HF	MP2	MP2//HF	HF-EFP
$\Delta\Delta G(\text{Me}_2\text{NH}_2^+)$					
1	-8.2	-8.7 (-10.1) <sup>d</sup>	-11.2	-11.1	-20.2
2	-6.1	-5.8 (-7.1) <sup>d</sup>	-8.3	-8.0	-18.0
3	-4.0	0.3 (-1.7) <sup>d</sup>	-2.0	-2.7	-11.1
4	-3.0	-1.3 (-1.7) <sup>d</sup>	-3.0	-3.7	-11.0
$\Delta\Delta G(\text{Me}_3\text{NH}^+)$					
1	-7.3	-8.0 (-10.0) <sup>d</sup>	-10.9	-10.7	-21.9
2	-4.0	-2.7 (-3.3) <sup>d</sup>	-4.9	-5.0	-11.3
3	-2.6	-1.6 (-2.8) <sup>d</sup>	-1.5	-3.8	-12.6
4	-2.0	2.4 (0.8) <sup>d</sup>	-1.6	-0.2	-9.8
Statistics					
		HF	MP2	MP2//HF	HF-EFP
Overall	$\mu$	0.8 (-0.5) <sup>d</sup>	-1.1	-1.3	-10.6
	$\sigma$	1.7 (1.7) <sup>d</sup>	1.6	1.5	2.1
	max	4.4 (3.0) <sup>d</sup>	3.6	3.4	14.6

Basis set is 6-31++G\*\* unless parenthetically noted. All values in kcal/mol

<sup>a</sup> Experimental error =  $\pm 1.4$  kcal/mol [11, 12]

<sup>b</sup>  $\text{MeNH}_3^+(\text{H}_2\text{O})_4 = C_1$  structure

<sup>c</sup>  $\text{Me}_3\text{NH}^+(\text{H}_2\text{O})_4 = C_1'$  structure

<sup>d</sup> 6-31G\*\*

agreement with the experimental enthalpies, FT corrections do not improve said agreement. (4) Internal energies and enthalpies at 0 K computed at the HF level with EFPs substituted for all ab initio water molecules are cost-effective alternatives in the reproduction of experimental enthalpies, especially differential ones. The HF-EFP level of theory is completely inadequate in the reproduction of experimental free energies. (5) Differential experimental quantities are more easily reproduced by theory than are their total counterparts. This is likely due to a cancellation of errors. Similarly, experimental enthalpies are better duplicated by theory than free energies. The relatively poor performance at all levels of theory in reproducing experimental free energies is probably the result of the thermodynamic approximations used to compute the entropic corrections.

It is important to acknowledge two recent studies related to the hydration of methylammonium ions, the most note-

worthy being that of Caskey et al. [22]. In addition to providing a thorough overview of the phenomenon known as the anomalous ordering of amine basicities, the authors report on calculations carried out at the HF/6-31+G\*\* level on  $\text{NH}_4^+$ ,  $\text{MeNH}_3^+$ ,  $\text{Me}_2\text{NH}_2^+$ , and  $\text{Me}_3\text{NH}^+$  clustered with 0–6, 10, and 14 water molecules modeled by EFPs. Specifically, total ZPE-corrected internal energies ( $\Delta H_0$  K) are given. Our analogous values (Table 1) generally correspond to those of the authors with minor differences attributable to their use of unscaled zero-point energies. Two notable exceptions are the  $\text{MeNH}_3^+(\text{H}_2\text{O})_4$  and  $\text{Me}_3\text{NH}^+(\text{H}_2\text{O})_4$  clusters, where our values are more exothermic by 3.6 and 1.6 kcal/mol, respectively. This discrepancy is due to our use of the lowest free energy species, while they employed the structures with the lowest enthalpies (vide supra). One potentially troubling result present by Caskey and co-workers is the apparent lack of convergence of the

relative enthalpies of hydration with increasing numbers of water molecules. A number of possible reasons may exist for this lack of convergence: the inadequacy of the HF–EFP/6-31++G\*\* level of theory; the failure to locate the global minima for the larger clusters or perform Boltzmann averaging; or the general failure of the microsolvation method in the current context (*vide infra*). Finally, two articles by Wang et al. [47, 48] strongly suggest that the pattern of hydration of the  $\text{NH}_4^+$  ion involves the sequential addition of water molecules to the four hydrogen-bonding sites of the ion with additional water molecules entering the second hydration shell. Calculations they carried out at the MP2/6-31+G\* and B3LYP/6-31+G\* levels of theory are generally consistent with our results. Our work stands in distinction to that of the above authors in that it offers a comprehensive microsolvation study of the methylammonium ion system, in which the importance of basis set, electron correlation, and thermodynamic corrections has been established. It can, therefore, serve as the point of departure for more complex descriptions of hydration of ammonium ions; e.g., embedding the above clusters in a continuum.

### 3.3 Hydration energies

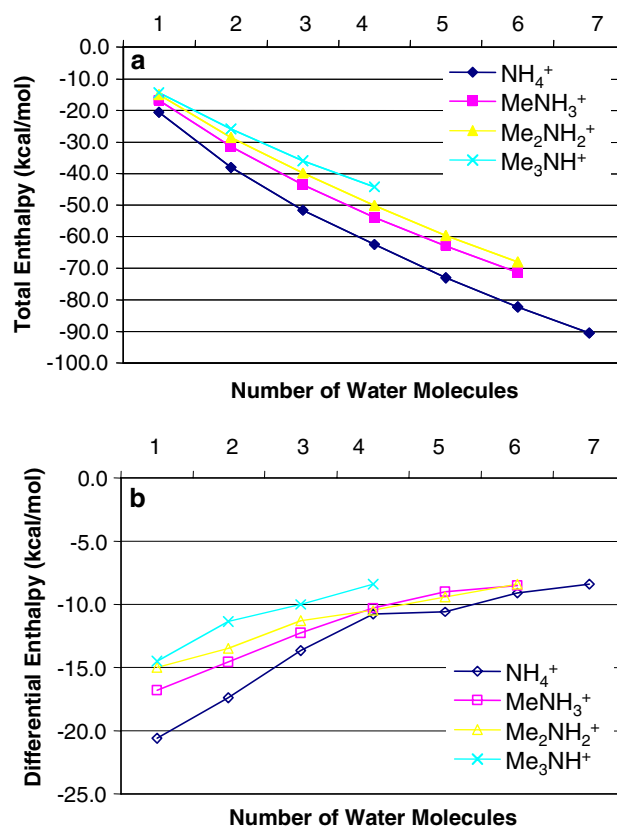
The absolute enthalpies ( $\Delta_{\text{aq}}H$ ) and free energies ( $\Delta_{\text{aq}}G$ ) of hydration for the methylammonium ions correspond to the respective changes in enthalpy and free energy upon transfer of the ion from the gas phase to an infinite volume of water,



where  $\text{BH}^+ = \text{NH}_4^+, \text{MeNH}_3^+, \text{Me}_2\text{NH}_2^+, \text{and } \text{Me}_3\text{NH}^+$ . While the prescription for calculating the enthalpy and free energy of the gas-phase ion is straightforward, it is not for the aqueous ion within the context of the microsolvation model. The most important question that needs to be answered is: How many water molecules are required to approximate an infinite volume?

Some idea of the difficulty in answering this seminal question can be gained from an examination of the experimental gas-phase data [10, 11]. As water molecules are sequentially added to the methylammonium ions, the total enthalpies decrease monotonically without limit (Fig. 2). It is, therefore, impossible to obtain absolute energies of hydration from total energies of hydration. Considering that the experimental absolute enthalpy of hydration for the ammonium ion,  $\Delta_{\text{H}_{\text{aq}}}(\text{NH}_4^+)$ , is equal to  $-76.5 \text{ kcal/mol}$ , [49, 50]<sup>4</sup> between five and six water molecules are required to reproduce this

<sup>4</sup> The absolute enthalpies and free energies of hydration for the  $\text{NH}_4^+$  ion are derived from the respective energies for the  $\text{H}^+$  ion. Different absolute enthalpies and free energies of hydration for the  $\text{H}^+$  ion will obviously lead to different respective energies for the  $\text{NH}_4^+$  ion. For example,  $\Delta_{\text{aq}}H(\text{NH}_4^+) = -83.8 \text{ kcal/mol}$  and  $\Delta_{\text{aq}}G(\text{NH}_4^+) = -77.1 \text{ kcal/mol}$ .



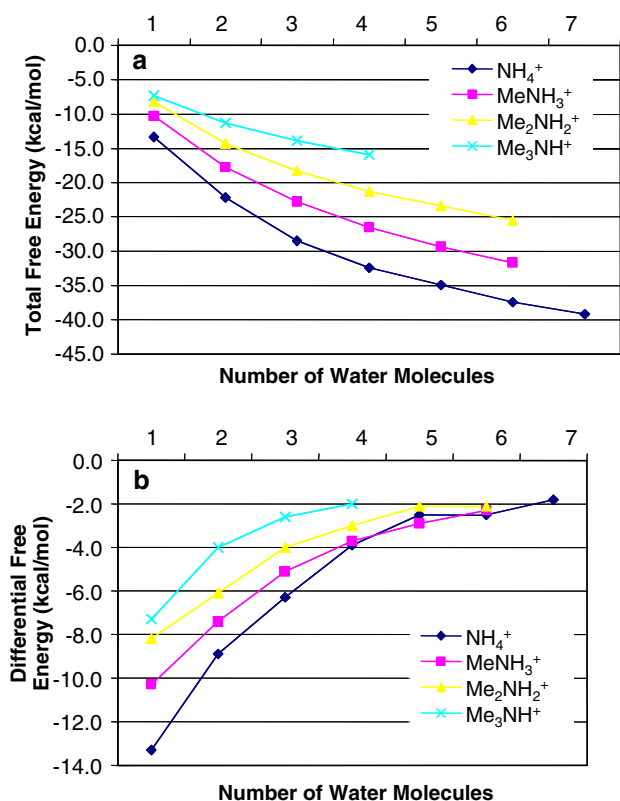
**Fig. 2** Experimental gas-phase total (a) and differential (b) enthalpies. Derived from [10, 11]

experimental value. Similarly, for the  $\text{MeNH}_3^+$  and  $\text{Me}_2\text{NH}_2^+$  ions, one also sees that between five and six water molecules are required to reproduce the experimental enthalpies of hydration of  $-70.8$  and  $-65.1 \text{ kcal/mol}$ , respectively. The number of water molecules necessary to duplicate the experimental enthalpy of hydration for the  $\text{Me}_3\text{NH}^+$  ion ( $-57.7 \text{ kcal/mol}$ ) cannot be estimated given the limited experimental gas-phase data.

An appeal to the experimental free energies of hydration is even less useful (Fig. 3a). In this case, the experimental data would appear to indicate that many more water molecules are required to reproduce the experimental free energies of hydration for the ammonium ion ( $\Delta_{\text{aq}}G(\text{NH}_4^+) = -69.8 \text{ kcal/mol}$ ) [49, 50]. It would appear, therefore, that a microsolvation approach to predicting absolute free energies of hydration is a formidable task. It should also be noted that the calculation of absolute enthalpies and free energies of hydration would require consideration of water clusters,  $(\text{H}_2\text{O})_n$ , via Eq. 6.



Both of these issues, greater numbers of water molecules and explicit consideration of water clusters, as they pertain to methylammonium ions are currently under investigation in



**Fig. 3** Experimental gas-phase total (a) and differential (b) free energies. Derived from [10, 11]

our laboratories. Finally, it is worth reiterating that a necessary first step along this path is the accurate reproduction of experimental total enthalpies and free energies of hydration for the ammonium ions.

While the calculation of absolute values of any type is generally a challenge to computational chemistry, relative values are often far easier to compute. In the case of micro-solvation calculations, the ability to compute relative solvation energies is predicated upon a cancellation of bulk solvation effects (i.e., perhaps outside the first few solvation shells). Justification for this hypothesis can again be found in the experimental gas-phase data, specifically the differential enthalpies and free energies of hydration for the methylammonium ions. With the possible exception of the Me<sub>3</sub>NH<sup>+</sup> ion, the other three ions appear to yield the same differential enthalpies upon addition of four or more water molecules (Fig. 2b). A similar result is seen for the differential free energies (Fig. 3b). It is possible to conjecture, therefore, that the uniqueness of the ions with respect to hydration disappears with completion of the first hydration shell.

The relative enthalpies ( $\Delta\Delta_{\text{aq}}H$ ) and free energies ( $\Delta\Delta_{\text{aq}}G$ ) of hydration were computed by taking the differences in absolute enthalpies and free energies of hydration

for the methylammonium ions,



where  $\text{BH}^+ = \text{MeNH}_3^+, \text{Me}_2\text{NH}_2^+, \text{and Me}_3\text{NH}^+$ . Given the apparent convergence of the gas-phase differential enthalpies and free energies with four (or perhaps five) water molecules,  $n$  was set to four in Eq. 7. The experimental and selected theoretical relative values are listed in Table 3.

The experimental enthalpies are very well reproduced at the HF level with the 6-31++G\*\* basis; specifically, the computed internal energies and enthalpies are within experimental error ( $\pm 1.0$  kcal/mol)! With the exception of the 6-31G basis, these results are nearly duplicated by the smaller bases, the largest discrepancy being 1.3 kcal/mol for the  $\Delta\Delta_{\text{aq}}U(\text{Me}_2\text{NH}_2^+)$  values calculated with the 6-31G\* and 6-31G\*\* bases.

The HF calculations that make use of EFPs in lieu of explicit water molecules also do a very good job in reproducing the experimental enthalpies. While the internal energies and enthalpies at 298 K are not quite within experimental error, the enthalpies at 0 K are. When the smaller bases are used, the agreement with experiment is essentially unchanged. In fact, the HF–EFP relative internal energies and enthalpies of hydration are all within 0.8 kcal/mol of one another regardless of basis set.

For the correlated relative energies, the best agreement with the experimental relative enthalpies was found for the enthalpies at 0 K computed with the 6-31++G\*\* basis (MP2:  $\mu = -2.7$ ,  $\sigma = 1.7$ ,  $|\text{max}| = 3.8$  kcal/mol; MP2//HF:  $\mu = -2.3$ ,  $\sigma = 1.5$ ,  $|\text{max}| = 3.2$  kcal/mol). As was seen for the benchmark calculations (vide supra), the two sets of MP2 data are in fairly good agreement with one another.

The HF and HF–EFP relative free energies are unfortunately not in as good agreement with experiment as their enthalpic counterparts. With the 6-31++G\*\* basis, the HF values for the MeNH<sub>3</sub><sup>+</sup> and Me<sub>3</sub>NH<sup>+</sup> ions are in good and fair agreement with experiment, respectively, while the error associated with the Me<sub>2</sub>NH<sub>2</sub><sup>+</sup> ion (3.1 kcal/mol) is too large. It is interesting that the smallest basis set (6-31G) leads to an improvement of the results, with errors of  $-0.1$ ,  $0.4$ , and  $1.6$  kcal/mol for the MeNH<sub>3</sub><sup>+</sup>, Me<sub>2</sub>NH<sub>2</sub><sup>+</sup>, and Me<sub>3</sub>NH<sup>+</sup> ions, respectively. The HF–EFP results are in equally poor agreement with experiment. While the errors associated with the MeNH<sub>3</sub><sup>+</sup> and Me<sub>3</sub>NH<sup>+</sup> ions are only slightly out of the range of experimental error, that for the Me<sub>2</sub>NH<sub>2</sub><sup>+</sup> ion (4.5 kcal/mol) is unacceptably large. It should also be noted that use of the other bases does not substantially improve agreement with experiment at the HF or HF–EFP levels of theory.

The MP2 relative free energies computed with the 6-31++G\*\* basis are, however, in very good agreement with experiment, clearly outperforming the values obtained at the comparable HF levels. The nominally best results were found

**Table 3** Relative internal energies,  $\Delta\Delta_{\text{aq}}U$ , enthalpies,  $\Delta\Delta_{\text{aq}}H$ , and free energies,  $\Delta\Delta_{\text{aq}}G$  for the hydration of ammonium ions:  $\text{BH}^+(\text{H}_2\text{O})_4 + \text{NH}_4^+ \rightarrow \text{NH}_4^+(\text{H}_2\text{O})_4 + \text{BH}^+$ 

$\text{BH}^+$	Experiment <sup>a</sup>	HF	MP2	MP2//HF	HF-EFP
$\Delta\Delta_{\text{aq}}U$					
$\text{MeNH}_3^+$	5.7	6.7	4.8	5.2	6.5 (6.6) <sup>b</sup>
$\text{Me}_2\text{NH}_2^+$	11.4	10.7	6.1	7.0	9.4 (9.6) <sup>b</sup>
$\text{Me}_3\text{NH}^+$	18.8	18.7	14.0	15.0	16.2 (16.5) <sup>b</sup>
$\Delta\Delta_{\text{aq}}H_{0\text{K}}$					
$\text{MeNH}_3^+$	5.7	6.7	4.9 (3.4) <sup>b</sup>	5.1 (5.7) <sup>b</sup>	6.9 (6.8) <sup>c</sup>
$\text{Me}_2\text{NH}_2^+$	11.4	12.1	7.8 (7.7) <sup>b</sup>	8.3 (8.0) <sup>b</sup>	11.7 (11.5) <sup>c</sup>
$\text{Me}_3\text{NH}^+$	18.8	19.4	15.0 (13.1) <sup>b</sup>	15.6 (16.6) <sup>b</sup>	18.0 (17.5) <sup>c</sup>
$\Delta\Delta_{\text{aq}}H_{298\text{K}}$					
$\text{MeNH}_3^+$	5.7 (8.5) <sup>f</sup>	6.9	5.0	5.3 (5.9) <sup>b</sup>	6.8 (7.0) <sup>b</sup>
$\text{Me}_2\text{NH}_2^+$	11.4 (12.2) <sup>f</sup>	11.4	6.8	7.6 (7.2) <sup>b</sup>	10.5 (10.8) <sup>b</sup>
$\text{Me}_3\text{NH}^+$	18.8 (18.2) <sup>f</sup>	19.2	14.5	15.4 (16.3) <sup>b</sup>	17.2 (17.6) <sup>b</sup>
$\Delta\Delta_{\text{aq}}G$					
$\text{MeNH}_3^+$	7.0 (5.9) <sup>f</sup>	7.7 (6.9) <sup>d</sup>	6.0 (8.2) <sup>b</sup>	6.1 (6.4) <sup>e</sup>	8.5 (8.0) <sup>c</sup>
$\text{Me}_2\text{NH}_2^+$	13.9 (11.1) <sup>f</sup>	17.0 (14.3) <sup>d</sup>	13.6 (15.0) <sup>b</sup>	13.2 (13.4) <sup>e</sup>	18.4 (18.1) <sup>c</sup>
$\text{Me}_3\text{NH}^+$	20.9 (16.5) <sup>f</sup>	22.6 (22.5) <sup>d</sup>	19.2 (21.3) <sup>b</sup>	18.8 (19.5) <sup>e</sup>	23.3 (22.6) <sup>c</sup>

Basis set is 6-31++G\*\* unless parenthetically noted. All values in kcal/mol

<sup>a</sup> Experimental error =  $\pm 1.0$  kcal/mol [9]

<sup>b</sup> 6-31G\*\*

<sup>c</sup> 6-31+G\*

<sup>d</sup> 6-31G

<sup>e</sup> 6-31G\*

<sup>f</sup> Gas-phase data [10, 11]

**Table 4** Reduced variational space (RVS) energy decomposition performed at the HF/6-31++G\*\* level of theory for the methyl ammonium monohydrate clusters

Compound	ESEX	POL	CT	BSSE	Total
$\text{NH}_4^+$	-13.2	-3.7	-2.2	-0.5	-19.7
$\text{CH}_3\text{NH}_3^+$	-12.4	-3.1	-1.5	-0.6	-17.6
$(\text{CH}_3)_2\text{NH}_2^+$	-11.6	-2.7	-1.1	-0.6	-16.0
$(\text{CH}_3)_3\text{NH}^+$	-11.0	-2.5	-0.9	-0.7	-15.1

Total = electrostatic/exchange (ESEX) + polarization (POL) + charge transfer (CT) + basis set superposition error (BSSE). All values in kcal/mol

at the MP2 level with the 6-31G\*\* basis ( $\mu = 0.9$ ,  $\sigma = 0.4$ ,  $|\text{max}| = 1.2$  kcal/mol) and at the MP2//HF level with the 6-31G\* basis ( $\mu = -0.9$ ,  $\sigma = 0.4$ ,  $|\text{max}| = 1.4$  kcal/mol). Regardless of the basis set employed, the MP2 and MP2//HF standard deviations are all less than a kilocalorie per mole.

Given the quality of the theoretical relative enthalpies of hydration, it is possible to combine them with the experimental, absolute enthalpy of hydration for the  $\text{NH}_4^+$  ion ( $\Delta_{\text{aq}}H = -76.5$  kcal/mol) to obtain semiempirical absolute values that are in better agreement with experiment. For example, using the relative HF enthalpies at 0 K computed with the 6-31++G\*\* basis, the following enthalpies of hydration were found:  $\text{MeNH}_3^+ = -70.0$ ,  $\text{Me}_2\text{NH}_2^+ = -67.1$ , and  $\text{Me}_3\text{NH}^+ = -60.3$  kcal/mol. These semiempirical val-

ues are now in much better agreement with experiment. Carrying out the analogous calculations at the HF-EFP level with the 6-31++G\*\* basis also produces values in better agreement with experiment:  $\text{MeNH}_3^+ = -69.6$ ;  $\text{Me}_2\text{NH}_2^+ = -64.8$ ; and  $\text{Me}_3\text{NH}^+ = -58.5$  kcal/mol. Corrections to the MP2 and MP2//HF enthalpies at 0 K calculated with the 6-31++G\*\* basis lead to results comparable to those found at the HF level (MP2:  $\text{MeNH}_3^+ = -71.6$ ,  $\text{Me}_2\text{NH}_2^+ = -68.7$ ,  $\text{Me}_3\text{NH}^+ = -61.5$ ; MP2//HF:  $\text{MeNH}_3^+ = -71.4$ ,  $\text{Me}_2\text{NH}_2^+ = -68.2$ ,  $\text{Me}_3\text{NH}^+ = -60.9$  kcal/mol).

If one uses the experimental free energy of hydration for the  $\text{NH}_4^+$  ion ( $\Delta_{\text{aq}}G = -69.8$  kcal/mol), it is also possible to correct the theoretical relative free energies to yield absolute values. Using the 6-31++G\*\* basis at the HF level,

one obtains the following absolute free energies:  $\text{MeNH}_3^+ = -62.1$ ,  $\text{Me}_2\text{NH}_2^+ = -52.8$ , and  $\text{Me}_3\text{NH}^+ = -47.2$  kcal/mol. These values compare favorably to the experimental ones:  $\text{MeNH}_3^+ = -62.8$ ,  $\text{Me}_2\text{NH}_2^+ = -55.9$ , and  $\text{Me}_3\text{NH}^+ = -48.9$  kcal/mol. Correcting the HF-EFP/6-31++G\*\* calculations produces the following absolute free energies:  $\text{MeNH}_3^+ = -61.3$ ,  $\text{Me}_2\text{NH}_2^+ = -51.4$ , and  $\text{Me}_3\text{NH}^+ = -46.5$  kcal/mol. While the average agreement is not as good as one would hope, this is due solely to the values for the  $\text{Me}_2\text{NH}_2^+$  ion, the other two ions being in very good agreement with experiment.<sup>5</sup> The correlated relative free energies can also be adjusted to good effect. Using the 6-31++G\*\* basis at the MP2 ( $\text{MeNH}_3^+ = -63.8$ ,  $\text{Me}_2\text{NH}_2^+ = -56.2$ , and  $\text{Me}_3\text{NH}^+ = -50.6$  kcal/mol) and the MP2//HF ( $\text{MeNH}_3^+ = -63.7$ ,  $\text{Me}_2\text{NH}_2^+ = -56.6$ , and  $\text{Me}_3\text{NH}^+ = -51.0$  kcal/mol) levels, absolute free energies are produced that are in good agreement with experiment.

These results are particularly encouraging. If a level of theory yields relative energies in good agreement with experiment, either a statistical correlation can be derived or an empirical offset can be used to reproduce experimental absolute energies. This is all the more impressive given the very modest levels of theory employed.

### 3.4 Reduced variational space analysis

A reduced variational space (RVS) analysis [40–42] was performed upon the monohydrate methylammonium clusters at the HF/6-31++G\*\* level of theory. These calculations allowed the intermolecular interaction energy to be decomposed into electrostatic/exchange repulsion (ESEX), polarization (POL), and charge transfer (CT) components. In addition, the basis set superposition error (BSSE) was computed [51,52]. The results of these calculations are given in Table 4. The bulk of the interaction is electrostatic in nature. The polarization energies are approximately a quarter of the electrostatic energies, and the charge transfer energies are smaller still, contributing no more than 2.2 kcal/mol. It is worth noting that the basis set superposition error averages only 0.6 kcal/mol per water molecule regardless of which ammonium ion is considered. Basis set superposition errors should not, therefore, contribute in a significant way to any of the relative energy calculations, and they should, moreover, mostly cancel in the relative energy calculations.

## 4 Conclusions

The structures and thermochemistry of methylammonium–water clusters were investigated at the HF and MP2 levels of

theory. Water molecules were treated all ab initio at the HF and MP2 levels, while an additional series of calculations was performed at the HF level with water molecules replaced by EFPs. The importance of basis set effects and thermodynamic corrections was examined.

Qualitatively similar cluster structures were found at all levels of theory. Hydrogen bonds were formed between the hydrogen atoms of the ammonium groups and the oxygen atoms of the water molecules. Only upon saturation of the hydrogen bonding sites of the ammonium group did water molecules begin to fill the second hydration shell. The structures reflect a balance between enthalpic and entropic considerations. The structures exhibited a general lack of sensitivity with respect to basis set at all levels. MP2 optimizations resulted in shorter hydrogen bonds on average than those found at the HF level, while the HF-EFP structures evinced longer hydrogen bonds on average.

Total energies for the addition of one to four water molecules to the methylammonium ions were calculated and compared to experiment. At the HF/6-31G\*\* level, ZPE-corrected internal energies were found to have a mean error within the experimental uncertainty for the total enthalpies of hydration. The HF/6-31+G\* total free energies also led to a mean error within experimental uncertainty.

HF/6-31G\* ZPE-corrected internal energies resulted in differential enthalpies with a mean error, standard deviation, and maximum absolute error within experimental uncertainty. The agreement between the experimental differential free energies and the HF/6-31G\*\* values also produced a mean error within experimental error.

Results obtained at the other levels of theory were evaluated in light of the values obtained at the HF level. The best agreement between the experimental total enthalpies and those determined at the MP2 level were also for the ZPE corrected internal energies calculated with the 6-31++G\*\* basis. The statistical agreement with experiment was poorer than that found at the HF level and was obtained at significantly higher cost. Similar results were found for the MP2 total free energies, the best agreement with experiment found with the 6-31++G\*\* basis. The ZPE-corrected differential internal energies computed at the MP2/6-31++G\*\* level were found to be in much better agreement with experiment, yielding a mean error and standard deviation within experimental error. The MP2/6-31++G\*\* differential free energies were also found to be in better agreement with experiment, again offering a mean error and standard deviation within the range of experimental uncertainty. Given the overall poor performance of the MP2 level relative to that HF, the inclusion of electron correlation does not appear to be warranted, especially given the added computational expense. This increased expense can be somewhat mitigated by calculating MP2 single-point energies at HF optimized geometries, as this level leads to virtually identical results.

<sup>5</sup> These results possibly suggest that the absolute values for the enthalpy and free energy of hydration for the  $\text{Me}_2\text{NH}_2^+$  should be re-examined.



The use of EFPs in lieu of ab initio water molecules drops the cost of the HF calculations precipitously. The experimental total enthalpies are best reproduced at the HF–EFP level with the smallest basis (6-31G) without ZPE or FT corrections. The experimental differential enthalpies are also reproduced by the HF–EFP internal energies, but with the largest basis (6-31++G\*\*). The HF–EFP level is incapable of duplicating either the total or differential free energies. The potential value of the HF–EFP method appears to lie in its ability to accurately calculate differential enthalpies of large hydrated systems, without the need of costly bases or thermodynamic corrections.

A simple chemical model was employed to reproduce experimental absolute and relative enthalpies and free energies of hydration for the methylammonium ions: water molecules were added to each cation until the first hydration shell was saturated, with a total of four water molecules added to each cluster to ensure that each cluster was treated equally. While all levels of theory underestimated the absolute enthalpies and free energies of hydration, strong linear correlations were found to exist between the theoretical and experimental values. It was, therefore, possible to employ an empirical correction to the theoretical values to obtain a better fit with experiment.

By taking the difference between the theoretical total energies for the  $\text{BH}^+(\text{H}_2\text{O})_4$  clusters, the relative experimental energies of hydration were estimated. Internal energies and enthalpies at 0 K computed at the HF/6-31++G\*\* level led to relative enthalpies all within experimental error. It is rather remarkable that such a modest level of theory can duplicate such a complex thermodynamic quantity. The HF/6-31G relative free energies are within experimental error for the  $\text{MeNH}_3^+$  and  $\text{Me}_2\text{NH}_2^+$  ions, while that for  $\text{Me}_3\text{NH}^+$  lies just above this range of error. This impressive result appears to arise from a fortuitous cancellation of errors associated with basis set and entropic corrections.

The MP2 and MP2//HF relative internal energies and enthalpies are in poorer agreement with the experimental relative enthalpies of hydration. The relative free energies are in much better agreement with experiment, with both the  $\text{MeNH}_3^+$  and  $\text{Me}_2\text{NH}_2^+$  ions falling within experimental uncertainty and the  $\text{Me}_3\text{NH}^+$  ion just outside this range. At the HF–EFP level, the ZPE-corrected internal energies generally produced values that were within experimental error for the relative enthalpies regardless of which basis set was employed. If these results prove to be general, the HF–EFP method would be applicable to chemical systems, which are outside the purview of most ab initio methods owing to their size. Once again, the HF–EFP method is not up to the task of reproducing experimental relative free energies of hydration.

The present results are on balance very encouraging. HF calculations that employ rather modest basis sets can be used

to reproduce experimental relative enthalpies and free energies of hydration. The chemical model developed here is straightforward in its application: water molecules are added until the first hydration shell is filled, and additional water molecules are added to permit comparisons between clusters with unequal numbers of water molecules in their first hydration shells. This promise is currently being explored in our laboratories, and the following questions are being addressed. (1) Are the results for the relative hydration energies truly converged at four water molecules? (2) Is it possible to calculate absolute hydration energies through explicit consideration of water clusters? (3) Can absolute hydration energies be computed by embedding the methylammonium–water clusters in a continuum? (4) Can the above models be used with amines? And if so, can the two sets of results be combined to predict  $\text{p}K_{\text{b}}$  values? And (5), do the models have applicability to systems other than methylammonium ions? The results from these investigations will be reported in due course.

**Acknowledgements** The authors would like to express their thanks to Dr. Waldemar Gorski (Department of Chemistry, University of Texas at San Antonio, San Antonio, TX, USA) and Dr. Jamie M. Rintelman (Daresbury Laboratory, Warrington, Cheshire, UK) for commenting on an earlier draft of this paper.

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