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An ab Initio Study of Proton Transfers from Gas-Phase Dications: Complications in Kinetic Methods for Determining Acidities

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Electrospray ionization provides a general method for the formation of poly-ions in the gas phase and is allowing chemists to explore the reactivity of these unusual species;[1−3] however, interpretation of kinetic data from the reactions of poly-ions requires a solid understanding of the subtle features of the potential energy surface. Unfortunately, even for a simple process such as proton transfer from a dication, there has been little theoretical work to support recent experimental studies.[4,5] In the present contribution, we will demonstrate that the relationship between kinetic and thermodynamic acidities is more complicated than has been previously assumed.[6] Moreover, we will show that in a recent study of doubly protonated diamines,[7,8] the analysis of the gas-phase acidities is flawed.

For our computational study (MP2/6-31(+)G*//HF/6-31G*),[9,10] we have used one of Williams' systems (doubly protonated 1,7-diaminoheptane, **I**) and analyzed its acidity as well as the potential energy surface for its reaction with NH_3. Given the strong Coulomb repulsion in the dication, a fully extended conformation is expected. Building from the work of Williams,[7] we have assumed that the singly protonated diamine, **II**, is initially formed in an extended conformation (*i.e.* kinetic measurements address this conformation). With these assumptions, a ΔH_{acid} of 181.6 kcal/mol is predicted at 298 K (eq 1). It should be stressed that this value corresponds to the extended dication to the extended monocation.[11,12]

$$\underset{\mathbf{I}}{{}^{+}H_3N(CH_2)_7NH_3{}^{+}} \xrightarrow[\Delta H_{\mathrm{acid}}(\mathbf{I})]{} \underset{\mathbf{II}}{{}^{+}H_3N(CH_2)_7NH_2} + H^{+} \quad (1)$$

For comparison, primary alkyl ammoniums generally have ΔH_{acid} values in the range of 215−220 kcal/mol.[13−16] Therefore Coulomb repulsion (CR) in the dication increases the thermodynamic acidity (*i.e.* reduces ΔH_{acid}) by 34−38 kcal/mol. Not surprisingly, the acidifying effect of the second charge is similar to the CR (∼33 kcal/mol) calculated for two charges 10 Å apart (the N−N distance in **I**).[17]

A number of workers have suggested that the reactions of dications should have large reverse activation barriers (RAB) because at the transition state there has been little charge separation and therefore much of the Coulomb repulsion remains.[7,18−21] For example, Petrie *et al.* estimated the acidity of a protonated fullerene cation ($C_{60}H^{2+}$) by determining its kinetic (apparent) acidity with a bracketing technique and then correcting the value for the estimated Coulomb repulsion in the transition state.[19] Williams and coworkers have attempted to apply the same approach to doubly protonated diamines; however, their analysis leads to remarkably low ΔH_{acid} values for the dications.[7] For example, Williams assigns a ΔH_{acid} value of 160 kcal/mol to **I**,[22] a value over 20 kcal/mol below our theoretical estimate. We will show that the difference is the result of three factors.

Gill and Radom[20] have shown that in the charge separation reactions of dications, the transition states may exhibit exceptionally long bond lengths as a result of the competition between bonding interactions and Coulomb repulsions.[4] Hydrogen bonding between ammonium ions and Lewis bases (such as amines) is strong over relatively long distances so one might expect elongated bonds in the transition states of proton transfers from dications. This can be seen in a plot of the potential energy surface for the reaction of **I** with ammonia (Figure 1). Moving from left to right in the graph, the first feature is an ion−dipole attraction leading to a complex of **I** and NH_3. Within this cluster, proton transfer[23] can occur to give a hydrogen-bonded complex of **II** and $NH_4{}^{+}$. As this complex separates, the energy initially rises as the hydrogen bond is weakened, but eventually, the advantage of increasing the charge separation dominates and the energy begins to drop. This leads to a transition state which corresponds to a charge separation ($N^{+}\cdots N^{+}$) of ∼16.5 Å. This transition state is ∼4.5 kcal/mol more stable than the separated reactants (**I** and NH_3); however, the proton transfer ($\mathbf{I} + NH_3 \Rightarrow \mathbf{II}$ and $NH_4{}^{+}$) is calculated to be exothermic by 22.6 kcal/mol. This implies a RAB of ∼ 18 kcal/mol (Figure 1) and suggests that in bracketing experiments, the proton transfer onset

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[1] Blade, A. T.; Kebarle, P. *J. Am. Chem. Soc.* **1994**, *116*, 10761.

[2] Kelly, M. A.; Vestling, M. M.; Fenselau, C. C.; Smith, P. B. *Org. Mass Spectrom.* **1992**, *27*, 1143.

[3] Van Berkel, G. J.; Glish, G. L.; McLuckey, S. A. *Anal. Chem.* **1990**, *62*, 1284.

[4] Bursey, M. M.; Pedersen, L. G. *Org. Mass Spectrom.* **1992**, *27*, 974.

[5] Williams has explored the potential energy surface with a simple model based on charges, dipoles, and polarizabilities. Schnier, P. D.; Gross, D. S.; Williams, E. R. *J. Am. Chem. Soc.* **1995**, *117*, 6747.

[6] Gas-phase chemists generally have not used the term kinetic acidity. When thermoneutral proton transfers have effectively no barrier, kinetic techniques, such as bracketing, yield values that approximate the thermodynamic acidity. However in systems where a thermoneutral proton transfer has a significant barrier (such as these), kinetic measurements no longer approximate thermodynamic acidities. The term kinetic acidity is appropriate in these situations.

[7] Gross, D. S.; Rodriguez-Cruz, S. E.; Bock, S.; Williams, E. R. *J. Phys. Chem.* **1995**, *99*, 4034.

[8] Gross, D. S.; Williams, E. R. *J. Am. Chem. Soc.* **1995**, *117*, 883.

[9] For the MP2 calculations, a standard set of diffuse sp functions were placed on the nitrogens. They are required for accurate acidity calculations. The values are converted to 298 K by standard methods involving the ab initio frequencies.

[10] GAUSSIAN92: Frisch, M. J.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. H.; Foresman, J. B.; Johnson, B. D.; Schlegel, H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, R.; Anfres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; DeFrees, D. J.; Baker, J. J. P.; Pople, J. A.; Gaussian, Inc.: Pittsburgh, PA, 1992.

[11] The proton affinity of the cyclic form is ∼14 kcal/mol lower than the extended form. Yamdagni, R.; Kebarle, P. *J. Am. Chem. Soc.* **1973**, *95*, 3504.

[12] The ΔH_{acid} of **I** is equivalent to the proton affinity of **II** in an extended conformation.

[13] For consistency, all values are based on McMahon's recent proton affinity scale. Additional values are taken from refs 14 and 15, but the absolute values are adjusted to match reference points in McMahon's scale. Szulejko, J. E.; McMahon, T. B. *J. Am. Chem. Soc.* **1993**, *115*, 7839.

[14] Lias, S. G.; Bartmess, J. E.; Liebman, J. F.; Holmes, J. L.; Levin, R. D.; Mallard, W. G. *J. Phys. Chem. Ref. Data, Suppl. 1* **1988**, *17*, 1.

[15] Meot-Ner, M.; Sieck, W. L. *J. Am. Chem. Soc.* **1991**, *113*, 4448.

[16] The present level of theory should be capable of reasonably accurate acidity estimates. For example, we calculate 215.3 for $CH_3NH_3{}^{+}$ (exp = 215.4, see ref 13).

[17] An effective dielectric of 1 is used in these calculations. Other studies in our lab suggest that this is not an unreasonable choice. Details of this work will be published elsewhere. Although his thermochemical analysis is incorrect, Williams also reports a value near unity (see ref 7)

[18] In the reactions of dications, the need to consider kinetic barriers and the possibility of loose transition states has been appreciated for many years. For example, see: Spears, K. G.; Fehsenfeld, F. C.; McFarland, M.; Ferguson, E. E. *J. Chem. Phys.* **1972**, *56*, 2562.

[19] Petrie, S.; Javahery, G.; Wincel, H.; Bohme, D. K. *J. Am. Chem. Soc.* **1993**, *115*, 6290.

[20] Gill, P. W.; Radom, L. *Chem. Phys. Lett.* **1987**, *136*, 294.

[21] Tonkyn, R.; Weisshaar, J. C. *J. Am. Chem. Soc.* **1986**, *108*, 7128.

[22] Williams reports his value in terms of ΔG. We have converted to ΔH using entropy estimates based on the values in ref 15. In the absence of solid entropy information for **I**, we will report values only to the nearest kcal/mol.

[23] There is a tight transition state separating the two hydrogen-bonded complexes. The associated barrier is small.

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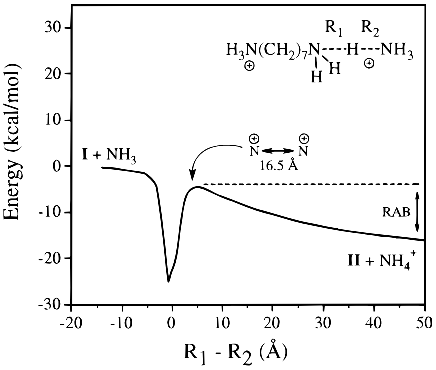

Figure 1. Potential energy surface for the reaction of **I** with NH_3. Calculations at the MP2/6-31(+)G*//HF/6-31G* level. The reverse activation barrier (RAB) is indicated as the extrapolation to infinite $R_1 - R_2$.

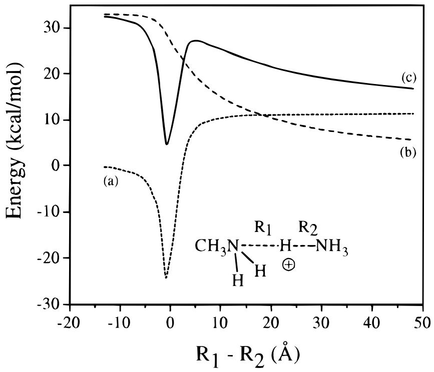

Figure 2. Potential energy surfaces for model systems. (a) The reaction of $CH_3NH_3^+$ with NH_3. (···). (b) The Coulomb energy of two point charges separated by a distance appropriate for **I** (- - -). (c) The sum of the two plots (——). Values for (a) are from calculations at the MP2/6-31(+)G*//HF/6-31G* level.

measurement will require a reference base whose proton affinity is ~18 kcal/mol greater than the thermodynamic acidity of the dication. It is important to note that because of the long intercharge distance in the transition state, the RAB is much smaller than the CR calculated from the reactant $N^+ \cdots N^+$ distance (~33 kcal/mol) or Williams' estimate from a model for the reactant complex (~30 kcal/mol). *Therefore, the Coulomb repulsion in the reactant is a poor model for the RAB.*

There is nothing particularly unusual about the potential energy surface of this reaction and it can be approximated with a very simple model (Figure 2). The reaction of $CH_3NH_3^+$ can be used to model the bonding interactions on the surface (Figure 2a). The effect of the second charge can be modeled with a pair of point charges separated by distances appropriate for the reaction of **I** and NH_3 (Figure 2b).[24] The sum of these two surfaces (Figure 2c) is very similar to the actual potential energy surface for the reaction of **I** with NH_3 (Figure 1) and also predicts a transition state charge separation of ~16.5 Å. It should be noted that Williams has presented a similar model for the process.[5] It involves cruder approximations, but yields the same qualitative picture.

Aside from the estimation of the RAB, another factor played a role in the underestimation of the ΔH_{acid} of **I**.[7] In Williams' experiment, a kinetic acidity (the observed onset of proton transfer from the dication to a reference base) was measured; however, it was treated as if it were a kinetic basicity (the observed onset of proton transfer from a reference acid to the monoprotonated diamine). *Kinetic acidities and basicities are not equivalent in exothermic reactions.* Since the reference state for the kinetic (apparent) acidity is **I** + base (B) whereas the reference state for the kinetic (apparent) basicity is **II** + BH^+, these two terms will differ by the exothermicity of the reaction. For these systems, the exothermicity is approximately the RAB; therefore the previous analysis introduces an error of ~18 kcal/mol. *Moreover these bracketing experiments fundamentally do not yield enough information to determine the Coulomb repulsion of the dication, the RAB, or* ΔH_{acid}(dication). The proper equations for analyzing the acidities of doubly protonated systems are given below:

$$\mathrm{CR(dication)} = \underline{\Delta H_{\mathrm{acid}}\mathrm{(model)}} - \Delta H_{\mathrm{acid}}\mathrm{(dication)} \quad (2)$$

$$\mathrm{RAB} = \underline{\mathrm{kinetic}\ \ \Delta H_{\mathrm{acid}}\mathrm{(dication)}} - \Delta H_{\mathrm{acid}}\mathrm{(dication)} \quad (3)$$

where ΔH_{acid}(model) is the gas-phase acidity of a protonated, model monoamine (*i.e.* heptyl amine). Only the underlined terms can be obtained easily from experiment; therefore one is left with a system of two equations and three unknowns. To determine the acidities of dications from bracketing data, one must also obtain a computational or experimental (*i.e.* kinetic energy release)[25] estimate of the RAB.

Combining our calculated ΔH_{acid} for **I** (181.6 kcal/mol) with our estimate of the RAB (18 kcal/mol), we predict a kinetic (bracketing) ΔH_{acid} for **I** of ~200 kcal/mol (eq 3);[26] however, a value of ~190 kcal/mol was reported from Williams' bracketing experiments.[7] This difference may be the result of the combined assumptions in our theoretical model, but there is evidence that a larger kinetic ΔH_{acid} value should have been assigned in the bracketing experiment. The value was assigned on the basis of a rate increase on going from ethanol (PA = 188 kcal/mol, $k = 3.5 \times 10^{-12}$ cm^3/s) to 2-propanol (PA = 191 kcal/mol, $k = 29 \times 10^{-12}$ cm^3/s) as the reference base. However, even with much stronger bases, the proton transfer rates are well below the expected collision rate ($1-2 \times 10^{-9}$ cm^3/s).[27] For example, acetone (PA = 194 kcal/mol) and cyclohexanone (PA = 199 kcal/mol) give rate constants of 8.8×10^{-11} and 3×10^{-10} cm^3/s, respectively. As a result, it seems very likely that the true proton transfer onset or bracket should be set in the vicinity of cyclohexanone.[28] This leads to approximately a 10 kcal/mol increase in the kinetic ΔH_{acid} and gives a value close to the one suggested by our calculations.[29]

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Supporting Information Available: Listing of coordinates of stable species and energies of species used in acidity calculations (4 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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[24] A point charge model is used. In **I** the charge separation is ~10 Å. As the ammonium cation departs from **II**, the distance between the two, charged nitrogens is used. In the region where the proton is transferring from one nitrogen to another, an interpolation based on partial charges is used. The choice of interpolation method does not affect the surface in the vicinity of the rate-determining transition state.

[25] Fenselau has completed kinetic energy release experiments for proton transfers from a dication, but because the location of the acidic sites was not known definitively, a transition structure cannot be inferred: Kaltashov, I. A.; Fenselau, C. C. *J. Am. Chem. Soc.* **1995**, *117*, 9906−9910.

[26] Of course, different bases will give slightly different reverse activation barriers, but this should be a reasonable estimate.

[27] It is difficult to estimate the collision rate for a doubly charged ion of this type. The value given here is certainly an underestimation of the true value and provides a conservative lower bound.

[28] When bracketing, one is searching for a base that effectively leads to a barrierless reaction. Under these circumstances, the rate should approach 50% of the collision limit.

[29] It should be pointed out that this analysis does not account for the experimental observation of slow proton transfers to weaker bases.