JOURNAL OF MASS SPECTROMETRY
J. Mass Spectrom. **33**, 943–949 (1998)

Gas-phase Acidity of Urea

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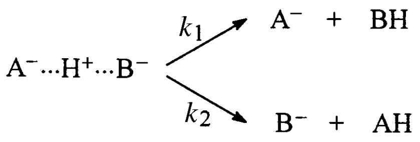
The kinetic method was applied to the estimation of the gas-phase acidity of urea by generating proton-bound dimeric anions comprised of urea and various reference compounds using negative ion desorption chemical ionization and examining their dissociation upon collision in a triple quadrupole mass spectrometer. The individual mass-selected dimers fragment to yield the two deprotonated anions as the only product ions. From the relative product ion abundances, ΔH_{acid} is determined to be 1513.8 ± 12 kJ mol^{-1}, ΔS_{acid} is 85.8 ± 8 J mol^{-1} K^{-1} and ΔG_{acid} is estimated to be 1488.2 ± 14 kJ mol^{-1} at 298 K by using $\Delta G_{acid} = \Delta H_{acid} - T\Delta S_{acid}$, where the ΔH_{acid} and ΔS_{acid} values are determined directly from the kinetic method plots. The experimental ΔH_{acid} value is in good agreement with a value of 1520.5 kJ mol^{-1} obtained from G2 molecular orbital calculations. © 1998 John Wiley & Sons, Ltd.

KEYWORDS: kinetic method; thermochemistry; gas-phase acidity; *ab initio* calculations; urea

INTRODUCTION

We report the application of the kinetic method to the determination of the gas-phase acidity (ΔH_{acid}) of urea, viz. the enthalpy change associated with the deprotonation reaction $H_2NC(O)NH_2 \rightarrow H^+ + H_2NC(O)NH^-$. The corresponding free energy change, i.e. ΔG_{acid}, referred to 298 K as are all data in this paper, is also reported. Urea derivatives are of great biological interest[1–4] and urea itself is widely used to denature proteins in studies of folding/unfolding equilibria.[5–7] Nevertheless, in contrast with extensive condensed-phase studies, little attention has been paid to the gas-phase properties of urea, including thermochemical properties of fundamental importance in understanding its reactivity. The proton affinity and gas-phase basicity of urea were determined recently to be 873.5 ± 5 and 841.6 ± 5 kJ mol^{-1} by using the kinetic method;[8] these results are consistent with equilibrium measurements[4] and with theoretical calculations.[8,9] However, the gas-phase acidity of urea has not been reported in the literature, except for a single value cited as a personal communication from R. W. Taft in Ref. 10. This study was intended to address this deficiency by application of the kinetic method.

The kinetic method is a procedure for estimating thermochemical information based on the rates of competitive dissociations of mass-selected cluster ions.[11,12] The technique involves forming a dimeric species, in this case the proton-bound dimeric anion, $[A^-H^+B^-]$, where A^- and B^- are the reference and unknown anions. The cluster ion is mass-selected and allowed to undergo collision-induced dissociation. Fragmentation yields the corresponding monomeric anions, A^- and B^-.



(1)

Theoretical treatments, given elsewhere,[13–15] show that under appropriate conditions, the acidities of AH and BH can be obtained from the relative abundances $[A^-]$ and $[B^-]$ of the product ions A^- and B^-, according to the approximate relationship

$$\ln\left(\frac{k_1}{k_2}\right) = \ln\frac{[A^-]}{[B^-]} \approx \frac{\Delta(\Delta G_{acid})}{RT_{eff}} \qquad (2)$$

where R is the gas constant and T_{eff} is the effective temperature of the activated dimer, a measure of the excess of the internal energy per degree of freedom.[16] If AH and BH are structurally similar, the entropy difference between the two competitive dissociation channels may be negligible and under these circumstances the logarithm of the ratio of the two reaction rates is simply proportional to the enthalpy difference, $\Delta(\Delta H_{acid})$:

$$\ln\left(\frac{k_1}{k_2}\right) = \ln\frac{[A^-]}{[B^-]} \approx \frac{\Delta(\Delta H_{acid})}{RT_{eff}} \qquad (3)$$

For systems in which the reference compounds are sufficiently different from the compound of unknown thermochemistry, differential entropic contributions will result in the log–linear relationships of Eqns (2) and (3) failing. A simple test for this failure is to vary T_{eff} by varying the activation conditions. If this results in a

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Contract/grant sponsor: US Department of Energy, Office of Basic Energy Science.

Contract/grant sponsor: National Science Foundation; Contract/grant number: CHE 92-23791.

CCC 1076–5174/98/100943–07 $17.50

Received 10 April 1998
Accepted 19 June 1998

change in the measured values of $\Delta(\Delta G_{\mathrm{acid}})$ or $\Delta(\Delta H_{\mathrm{acid}})$, a differential entropic contribution is operating. Under these circumstances, an extended form of the kinetic method[14,15] should be used to separate the enthalpic and entropic values. This is achieved by substituting $\Delta G = \Delta H - T\Delta S$ into Eqn (3), which then becomes

$$\ln\left(\frac{k_1}{k_2}\right) = \frac{\Delta H_{\mathrm{acid}}(\mathrm{AH})}{RT_{\mathrm{eff}}} - \left[\frac{\Delta H_{\mathrm{acid}}(\mathrm{BH})}{RT_{\mathrm{eff}}} - \frac{\Delta(\Delta S)}{R}\right] \quad (4)$$

where the term in the brackets represents an apparent gas-phase acidity of the neutral compound BH, defined by

$$\Delta G^{\mathrm{app}}_{\mathrm{acid}}(\mathrm{BH}) = \Delta H_{\mathrm{acid}}(\mathrm{BH}) - T_{\mathrm{eff}}\,\Delta(\Delta S) \quad (5)$$

where $\Delta(\Delta S)$ is the difference in the entropy change for the two dissociation channels of the dimer to give the products B^- and A^-, respectively. Note that provided the dissociation of the dimer goes through a product-like transition state, $\Delta(\Delta S) \approx \Delta(\Delta S_{\mathrm{acid}}) = \Delta S_{\mathrm{acid}}(\mathrm{BH}) - \Delta S_{\mathrm{acid}}(\mathrm{AH})$, i.e. it equals the difference in the entropy changes for the deprotonation of BH and AH. Since weak bonding and a product-like transition state are normally pre-conditions for application of the kinetic method, this requirement is normally met and entropic differences measured for dissociation of the dimeric ions yield, to a good approximation, entropy differences for deprotonation of the corresponding monomers. The value of the gas-phase acidity, $\Delta H_{\mathrm{acid}}(\mathrm{BH})$, and the entropy change difference, $\Delta(\Delta S_{\mathrm{acid}})$, can be extracted from the linear regression line based on a plot of $\Delta G^{\mathrm{app}}_{\mathrm{acid}}(\mathrm{BH})/RT_{\mathrm{eff}}$ against $1/RT_{\mathrm{eff}}$ (Eqns (4) and (5)).

The kinetic method has been successfully applied to a wide range of chemical systems for the determination of various thermochemical properties, including proton affinity and gas-phase basicity,[17–20] metal ion affinity,[21–25] polyatomic cation affinity,[26–29] ionization energy[30] and electron affinity.[31] The method has recently been applied to stereoisomeric distinction.[32–34] Relevant to this study, the kinetic method has also been applied in the determination of gas-phase acidities of carboxylic acids,[35,36] alcohols[37] and amino acids.[38] In addition, Majumdar *et al.*[39] and Haas and Harrison[40] have demonstrated the application of the kinetic method to the study of stereochemical effects on ΔG_{acid} values. For example, *cis*-2-methylcyclohexanol is found to be more acidic than the *trans* isomer by 4.2 kJ mol^{-1}.[39] The strength of the kinetic method is the simplicity of the procedure, its ready implementation, its sensitivity to small thermochemical differences (0.5 kJ mol^{-1}) and its applicability to polar and non-volatile compounds, including multifunctional and biological molecules. In spite of the strengths and successes of the method, it must be applied with care if reliable data are to be obtained. This study illustrates how this can be achieved in the case of a simple molecule of biological interest.

EXPERIMENTAL

Experiments were performed using a Finnigan TSQ 700 triple quadrupole mass spectrometer (Finnigan MAT, San Jose, CA, USA). All compounds were commercially available (Aldrich Chemical, Milwaukee, WI, USA) and were used without purification. Samples were prepared and introduced by depositing a 1 μl aliquot of a mixture of urea and a reference compound in methanol solution on the rhenium wire filament of a direct evaporation probe. The temperature of the probe was raised from ambient to 300 °C in 1.2 min, then kept constant for 0.5 min before being raised to 1200 °C in 0.2 min to pyrolyze any remaining material. The cluster anion of interest (formally a proton-bound dimer of two anions) was generated in the ion source by negative ion desorption chemical ionization (DCI) using ammonia as reagent gas; it was mass-selected using Q1, and dissociated in Q2 at three different laboratory collision energies, 2, 6 and 10 eV, using argon at a nominal pressure of 0.4 mTorr (1 Torr = 133.3 Pa), which corresponds to single collision conditions.[41] The mass-to-charge ratios are reported here using the Thomson unit (1 Th = 1 Da/unit charge).[42]

Standard *ab initio* molecular orbital calculations were carried out using the G2 procedure in the Gaussian 94 set of programs without any symmetry constraints.[43] As the best known of the precise theoretical models, Gaussian-2 (G2) theory[44] is based on MP2 (FU)/6–31G$*$ geometries using all electrons and the final total energies are calculated at the MP4SDTQ/6–311G$**$ level with corrections from higher level calculations. Thus, gas-phase acidities are generally obtained with an accuracy of 10 kJ mol^{-1} by the G2 method.[45–47]

RESULTS AND DISCUSSION

In order to estimate the gas-phase acidity of urea experimentally, a series of compounds with known acidity[10] were chosen as references. The compounds and their 298 K ΔG_{acid} values, included acetophenone ($\Delta G_{\mathrm{acid}} = 1483.2$ kJ mol^{-1}), 1,1-dimethylurea ($\Delta G_{\mathrm{acid}} = 1484.5$ kJ mol^{-1}), *o*-fluoroaniline ($\Delta G_{\mathrm{acid}} = 1486.6$ kJ mol^{-1}), methyl phenyl sulfone ($\Delta G_{\mathrm{acid}} = 1486.6$ kJ mol^{-1}), *N*-ethylaniline ($\Delta G_{\mathrm{acid}} = 1492.9$ kJ mol^{-1}) and *N*-methylaniline ($\Delta G_{\mathrm{acid}} = 1495.8$ kJ mol^{-1}). Mass selection and collision-induced dissociation of each of the proton-bound anions gave the individual monomeric anions as the only fragment ions. The products arise by the two competitive dissociation channels shown in Eqn (1). This behavior is illustrated by the product ion spectrum shown in Fig. 1. The cluster ion at 166 Th, comprised of urea and the reference compound *N*-methylaniline, dissociates at 6 eV collision energy and gives only two fragments which correspond to deprotonated urea and deprotonated *N*-methylaniline, respectively.

The relatively higher abundance of the deprotonated urea ion indicates that urea releases the proton more easily and, therefore, is more acidic than *N*-methylaniline. Note that this conclusion depends on the two competitive dissociations having similar entropies of activation. However, Fenselau and co-workers[14] and Cerda and Wesdemiotis[15] have published examples of cases in which the reference compounds differ from the analyte and therefore, entropic effects on the competi-

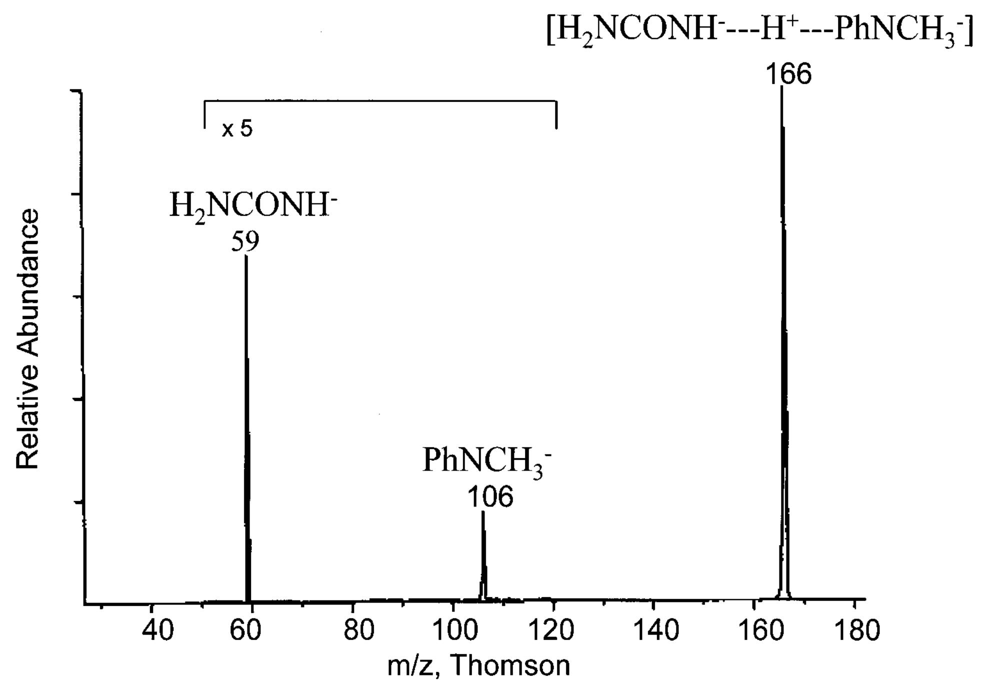


Figure 1. Product ion tandem mass spectrum of the mass-selected anion cluster $[NH_2CONH^-H^+PhNCH_3^-]^-$ at 6 eV collision energy with argon as collision gas.

tive dissociation reaction are large. As noted in the Introduction, these cases can be recognized by the fact that the ion abundance ratio changes with internal energy. However, provided that the difference in the entropies of dissociation $\Delta(\Delta S)$ is constant, ΔH_{acid} can be determined from the plot based on Eqn (4).

The fragmentation of a series of cluster ions, comprised of a reference acid and urea, yielded a set of experimental abundance ratios ($[A^-][B^-]$). A plot of $\ln([A^-][B^-])$ *vs.* the known 298 K ΔG_{acid} values for the reference compounds provided a calibration line with a slope of $1/RT_{eff}$ and an x intercept which should correspond, from Eqn (2), to the gas-phase acidity value (ΔG_{acid}). Such a plot was generated from data taken at three different collision energies and the results are shown in Fig. 2. The effective temperatures of the activated cluster ions are calculated from the slopes of the three regression lines to be 372, 450 and 522 K, respectively. These results reflect the expected trend of increased energy deposition with increased collision

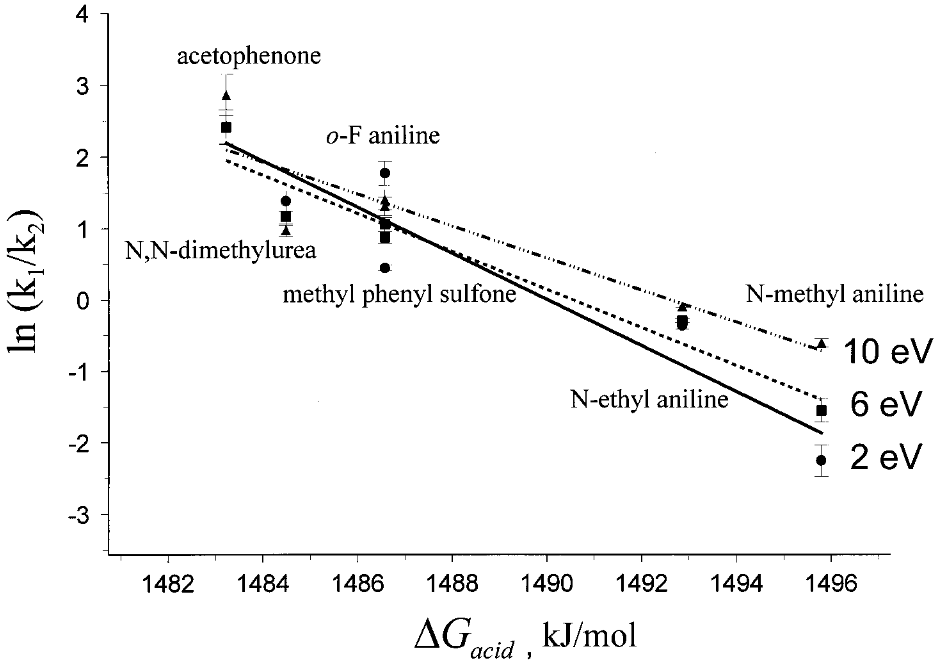


Figure 2. Measured product ion abundance ratio $\ln(k_1/k_2)$ *vs.* gas-phase acidities, ΔG_{acid}, of reference compounds at 2, 6 and 10 eV collision energy.

energy under single-collision conditions.[41] From the three regression lines, the gas-phase acidity of urea, i.e. ΔG_{acid}, is estimated as 1490.0 kJ mol^{-1} for the data taken at 2 eV collision energy, 1490.5 kJ mol^{-1} at 6 eV and 1492.5 kJ mol^{-1} at 10 eV. The small but apparently significant change in ΔG_{acid} is probably due to differential entropic effects, although the fact that the measured ΔG_{acid} values are based on the ΔG_{acid} (298 K) values of reference compounds, whereas the temperature of the activated cluster ion is considerably different from 298 K, might also have an effect. Therefore, the free energy term, ΔG_{acid}, is expected to be obtained more accurately from ΔH_{acid} and ΔS_{acid} using the extended kinetic method, as discussed below.

The existence of a differential entropy effect on the rates of the competitive fragmentations was tested using a second set of plots of $\ln([\mathrm{A}^-]/[\mathrm{B}^-])$ *vs.* ΔH_{acid}(ref). The results are shown in Fig. 3. According to Eqn (3), the gas-phase acidity of urea, i.e. ΔH_{acid}, is estimated as 1520.3 kJ mol^{-1} at 2 eV collision energy, 1520.9 kJ mol^{-1} at 6 eV and 1523.1 kJ mol^{-1} at 10 eV. From these results, one concludes that entropic differences in the two dissociation channels are indeed significant and this precludes use of the simple kinetic method, Eqn (2), to measure ΔG_{acid}, nor can ΔH_{acid} be obtained from the corresponding Eqn (3). Hence, the entropic and enthalpic contributions to $\Delta(\Delta G_{\mathrm{acid}})$ were separated using the double plotting method[14,15] the results of which are shown in Fig. 4. The slope ($1/RT$) and intercept ($\Delta G^{\mathrm{app}}(\mathrm{urea})/RT$) of the $\ln(k_1/k_2)$ plot against ΔH_{acid}(ref) were measured at each collision energy and replotted (Fig. 4). This plot was then used to extract the ΔH_{acid}(urea) value from the slope and the $\Delta(\Delta S_{\mathrm{acid}})$ value from the intercept. The value of ΔH_{acid} determined in this way is 1513.8 kJ mol^{-1}. The estimated overall uncertainty in this value is ± 12 kJ mol^{-1}, the major contribution being the acidity values for the reference compounds which were reported in the literature with a typical uncertainty of 10 kJ mol^{-1}. Meanwhile, $\Delta(\Delta S_{\mathrm{acid}})$ is determined to be -15.3 J mol^{-1} K^{-1}, with an estimated measurement uncertainty of ± 2 J mol^{-1} K^{-1}. The negative sign indicates that deprotonation of urea release more entropy than deprotonation of the reference compounds, a result consistent with the constrained nature of the anion. The average value of ΔS_{acid} for the reference compounds at 298 K is 101.1 J mol^{-1} K^{-1} with a range from 92.7 to 109.5 J mol^{-1} K^{-1} and the difference in these numbers yields an estimate of 85.8 ± 8 J mol^{-1} K^{-1} for ΔS_{acid}(urea). Combining these values and using $\Delta G_{\mathrm{acid}}(\mathrm{urea}) = \Delta H_{\mathrm{acid}}(\mathrm{urea}) - T\Delta S_{\mathrm{acid}}(\mathrm{urea})$, ΔG_{acid}(urea) is calculated to be 1488.2 ± 14 kJ mol^{-1} at 298 K. This ΔG_{acid} value for urea is in excellent agreement with the value of 1487.4 kJ mol^{-1} from Taft's personal communication in Ref. 10. It is also in good agreement with a value of 1489.1 kJ mol^{-1} obtained by extrapolation of the data of Fig. 2 to zero collision energy. Note that the ΔH_{acid}(urea) value determined from the extended kinetic method, 1513.8 ± 12 kJ mol^{-1}, is in agreement with the value of 1520.5 kJ mol^{-1} calculated by the G2 procedure, for which typical accuracies are better than 10 kJ mol^{-1}.

The optimized structures of neutral, protonated and deprotonated urea from G2 calculations are illustrated in Fig. 5. It is obvious that deprotonation elongates the C=O bond from 1.225 Å (neutral) to 1.260 Å (anion) while the C—NH bond shrinks from 1.390 to 1.324 Å owing to resonance stabilization between the carbonyl and amino groups in the anion. The charge is dispersed over the whole anion so electrostatic repulsion causes lengthening of the C—NH$_2$ bond length to 1.488 Å compared with 1.390 Å in the neutral. Thus, in comparison with protonated urea,[8,9] anionic urea shows much stronger resonance effects in the C(O)—NH group, which controls the acidity of urea. Furthermore, this

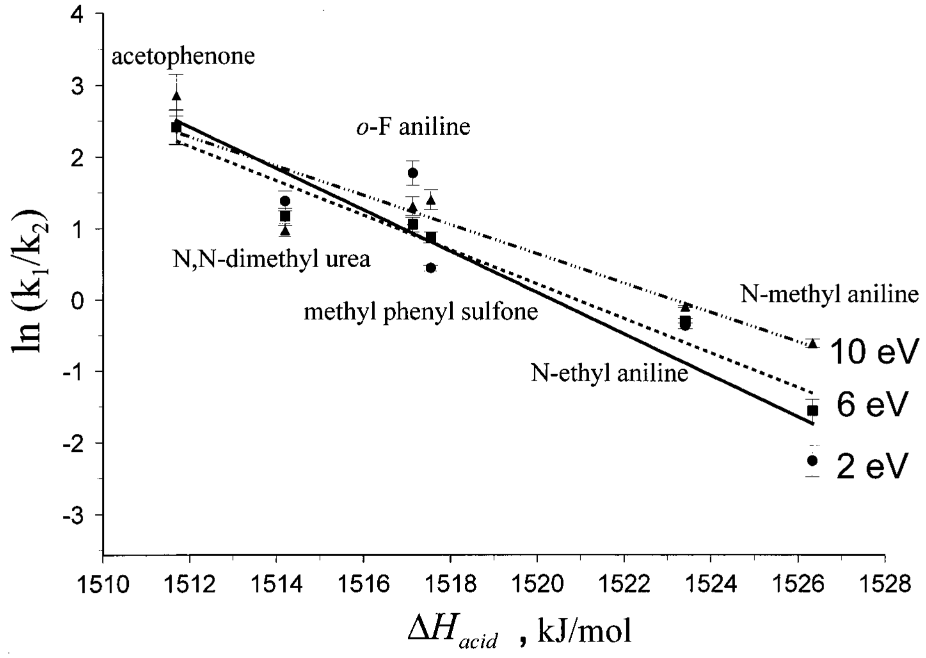


Figure 3. Measured product ion abundance ratio $\ln(k_1/k_2)$ *vs.* gas-phase acidities, ΔH_{acid}, of reference compounds at 2, 6 and 10 eV collision energy.

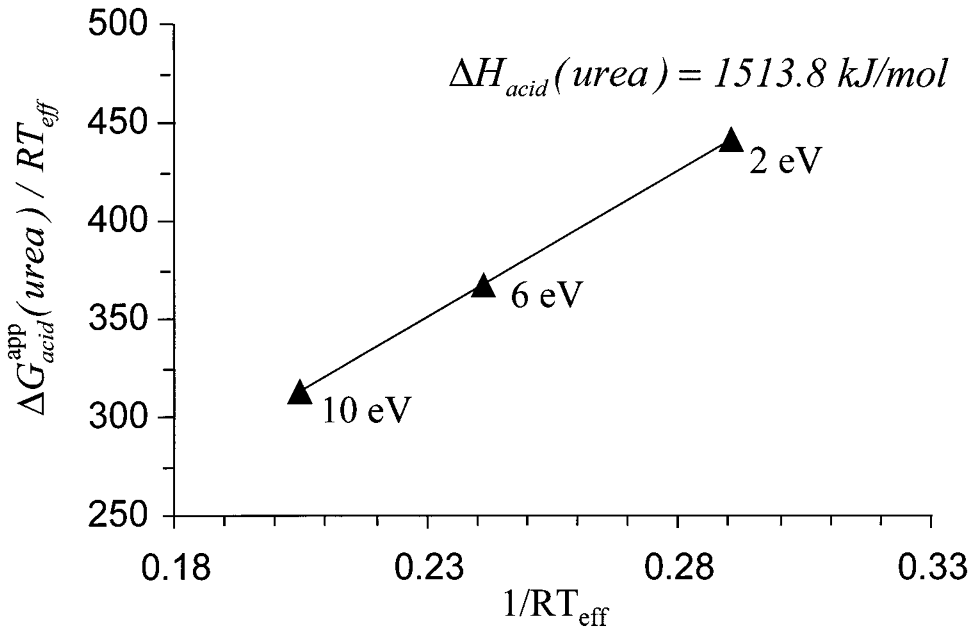
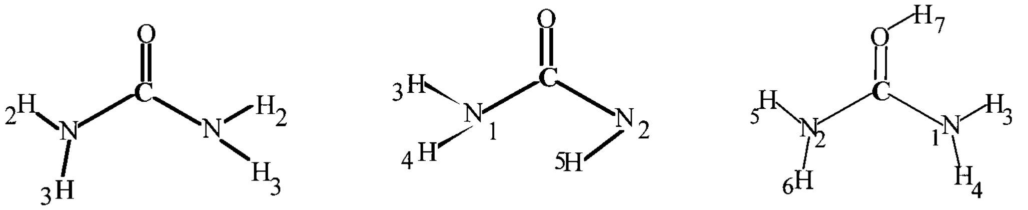


Figure 4. Plot of ΔG^{app}_{acid} (urea)/RT_{eff} vs. 1/RT_{eff} used to determine ΔH_{acid} from the intercept and ΔS_{acid} from the slope.

resonance effect is the predominant factor in determining the acidity of related amides. A similar phenomenon is also observed in thiocarboxamides.[48]

Substitution effects on gas-phase acidity have been widely studied.[49–51] Three kinds of electronic substituent effects, field/inductive (F), resonance (R) and polarizability (P), generally contribute to the effects on acidity. For example, comparison of the acidity of urea ($\Delta G_{acid} = 1488.2$ kJ mol^{-1}) and 1,1-dimethylurea ($\Delta G_{acid} = 1484.5$ kJ mol^{-1}) indicate that methyl substituents cause a decrease in the ΔG_{acid} value (i.e. an increase in acidity) due to changes in polarizability and charge stabilization. Similar trends were found in studies of the effect of alkyl substitution on the gas-phase acidities of alcohols.[39] Replacement of a hydrogen by a methyl group causes a decrease in the ΔG_{acid}



bond length (Å)	
OC	1.225
CN	1.390
NH	1.013

bond angle	
OCN	123.5
CNH$_2$	111.9
CNH$_3$	116.2
NCN	113.0

G2 Energy

-224.934455 hartree

bond length (Å)	
OC	1.260
CN1	1.488
CN2	1.324
N1H3	1.019
N2H5	1.027

bond angle	
OCN1	114.0
OCN$_2$	128.4
CN$_1$H$_3$	105.2
CN$_1$H$_4$	109.4
CN$_2$H$_5$	107.2
N$_1$CN$_2$	117.6

G2 Energy

-224.352457 hartree

bond length (Å)	
OC	1.316
CN$_1$	1.326
CN$_2$	1.319
OH$_7$	0.977
N$_1$H$_3$	1.013
N$_1$H$_4$	1.014

bond angle	
CN$_1$H$_3$	122.1
CN$_2$H$_5$	118.8
N$_1$CN$_2$	122.9
COH$_7$	114.3
CN$_1$H$_4$	121.5
CN$_2$H$_6$	122.9

G2 Energy

-225.264197 hartree

Figure 5. MP2(FU)/6–31G(d) optimized geometries and energies of neutral, deprotonated and protonated urea.

value of the alcohol through increased stabilization of the alkoxide ion. The magnitude of this effect depends on the position of the substitution relative to the charge site.[39,40] Comparing the acidities of urea and acetamide ($\Delta G_{\text{acid}} = 1485.3$ kJ mol^{-1}), one notes that replacement of the amino group by a methyl group causes a small increase in acidity. This can be attributed in part to the increase in the ground-state energy of acetamide, which makes it easier to remove the proton from neutral acetamide.

CONCLUSIONS

This study has demonstrated the applicability of the kinetic method to the estimation of the gas-phase acidity of urea. The kinetic method provides accurate experimental values for reaction enthalpy (ΔH) and entropy (ΔS), which then can be used to calculate the Gibbs free energy (ΔG). The estimated gas-phase acidity (ΔH_{acid}) of 1513.8 $\pm$ 12 kJ mol^{-1} is in good agreement with that from G2 calculations. There are a number of assumptions and uncertainties in the applicability of the kinetic method which have been widely discussed. They include the assumption that absolute rate theory can be used to derive the kinetic method equations, the effects of the non-Boltzmann distribution of internal energies of the activated ions on their fragmentation behavior, the fact that the kinetic method equations are limiting equations which apply only when the excess energy per degree of freedom is large compared with the critical energies for the competitive dissociations and the consequences of the differential entropic effects presented in the Introduction.[12–15] An important finding in this study is that the value of ΔG_{acid} measured by application of the simple kinetic method, Eqn (2), with extrapolation to zero collision energy, 1489.1 kJ mol^{-1}, is in excellent agreement with the value of 1488.2 kJ mol^{-1} obtained by the extended method in which ΔH_{acid} and ΔS_{acid} are used to determine ΔG_{acid}. This is so in spite of the fact that there is obviously a large difference in entropies of the two competitive dissociation reactions. Assuming a temperature of 298 K together with the ΔH_{acid} value of 1513.8 kJ mol^{-1}, the entropy change, ΔS_{acid}(urea), is calculated as 81.5 J mol^{-1} K^{-1}, which is close to the value of 85.8 J mol^{-1} K^{-1} determined from the experiments. The 4.3 J mol^{-1} K^{-1} difference includes some experimental error and may also be due to the range of ΔS_{acid} values of the reference acids (from 92.7 to 109.5 J mol^{-1} K^{-1}). The average ΔG_{acid} value of 1491.0 kJ mol^{-1} from three different collision energies obtained by using Eqn (2) is also slightly different from the value of 1488.2 kJ mol^{-1} at 298 K determined from the extended method using Eqns (4) and (5). This is one contribution to the differential entropic effects in the competitive dissociations. In general, little error will be introduced by using the ΔG values taken at 298 K for the references in Eqn (2) if the entropy changes for the two competitive dissociation channels are similar.[52] However, if the entropy contributions are large, then significant errors might be introduced by this approach. Wu and Fenselau[53] have reported the gas-phase basicity of lysine of 930.1 kJ mol^{-1} obtained from directly using Eqn (2), while a value of 938.5 kJ mol^{-1} at 300 K was calculated from the measured proton affinity (PA) and entropy difference, $\Delta(\Delta S_{\text{H}^+})$, using Eqns (4) and (5). The relatively large difference between the two approaches is ascribed to the large entropy contributions of strong intramolecular hydrogen bonding in the protonated lysine.[53] The fact that the effective temperature of the activated dimer is significantly different from 298 K is a second, but probably minor, source of error in these experiments, which applies whether the original or extended kinetic method is used.

Acknowledgement

This work was supported by the US Department of Energy, Office of Basic Energy Science, and the National Science Foundation, CHE 97-32670. We are grateful to the reviewers for unusually helpful referee reports.

REFERENCES

1. *Chem. Eng. News*, **65**, 21 (1987).
2. J. March, *Advanced Organic Chemistry*, 4th edn. Wiley, New York (1992).
3. G. C. Thomas and S. George, *Chem. Rev.* **97**, 829 (1997).
4. L. Franco, M. Andrei and C. Andrea, *Science* **266**, 801 (1994).
5. D. Neri, M. Billeter, G. Wider and K. Wuthrich, *Science* **227**, 1559 (1992).
6. E. Liepinsh and G. Otting, *J. Am. Chem. Soc.* **116**, 9670 (1994).
7. J. A. Schellman and N. C. Gassuer, *Biophys. Chem.* **59**, 259 (1996).
8. F. Wang, S. Ma, D. Zhang and R. G. Cooks, *J. Phys. Chem.* **102**, 2988 (1998).
9. R. Notario, O. Castano, M. Herreros and J. L. M. Abboud, *J. Mol. Struct. Theochem.* **371**, 21 (1996).
10. S. G. Lias, J. E. Bartmess, J. F. Liebman, J. L. Holmes, R. D. Levin and W. G. Mallard, *J. Phys. Chem. Ref. Data* **17**, Suppl. 1 (1988).
11. S. A. McLuckey, D. Cameron and R. G. Cooks, *J. Am. Chem. Soc.* **103**, 1313 (1981).
12. R. G. Cooks, J. S. Patrick, T. Kotiaho and S. A. McLuckey, *Mass Spectrom. Rev.* **13**, 287 (1994).
13. S. L. Craig, M. Zhang, B. Choo and J. I. Brauman, *J. Phys. Chem. A* **101**, 19 (1997).
14. X. Cheng, Z. Wu and C. Fenselau, *J. Am. Chem. Soc.* **118**, 4844 (1993).
15. B. A. Cerda and C. Wesdemiotis, *J. Am. Chem. Soc.* **118**, 11884 (1996).
16. H. Lee and J. L. Beauchamp, paper presented at the 209th National Meeting of the American Chemical Society, Anaheim, CA, April 2–7, 1995.
17. B. D. Nourse and R. G. Cooks, *Int. J. Mass Spectrom. Ion Processes* **106**, 249 (1991).
18. G. Bojesen and T. Breindahl, *J. Chem. Soc., Perkins Trans. 2* 1029 (1994).
19. A. M. Cardoso, S. M. G. Alexandre, C. M. F. Barros, A. J. Ferrer-Correia and N. M. M. Nibbering, *Int. J. Mass Spectrom.* **172**, 123 (1998).
20. M. Decouzon, J.-F. Gal, M. Herreros, P.-C. Maria, J. Murrel and J. F. J. Todd, *Rapid Commun. Mass Spectrom.* **10**, 242 (1996).

21. K. Eller and H. Schwartz, *Organometallics* **8**, 1820 (1989).
22. L. Z. Chen and J. M. Miller, *J. Organomet. Chem.* **448**, 225 (1993).
23. S. Ma, P. Wong, S. S. Yang and R. G. Cooks, *J. Am. Chem. Soc.* **118**, 6010 (1996).
24. K. Seemeyer, R. H. Hertwig, J. Hrušàk, W. Koch and H. Schwarz, *Organometallics* **14**, 4409 (1995).
25. D. Schröder and H. Schwarz, *J. Orgranomet. Chem.* **504**, 123 (1995).
26. S. S. Yang, G. Chen, S. Ma, R. G. Cooks, F. C. Gozzo and M. N. Eberlin, *J. Mass Spectrom.* **30**, 807 (1995).
27. S. Ma, P. Wong, R. G. Cooks, F. C. Gozzo and M. N. Eberlin, *Int. J. Mass Spectrom. Ion Processes* **163** 89 (1997).
28. F. Cacace, G. de Petris and F. Pepi, *Proc. Natl. Acad. Sci. USA* **94** 3507 (1997).
29. F. Cacace, G. de Petris, F. Pepi and F. Angelelli, *Proc. Natl. Acad. Sci. USA*, **92**, 8635 (1995).
30. P. Wong, S. Ma and R. G. Cooks, *Anal. Chem.* **68**, 4254 (1996).
31. G. Chen and R. G. Cooks, *J. Mass Spectrom.* **30**, 1167 (1995).
32. C. Denekamp, A. Etinger, R. H. Fokkens, N. Khaselev, A. Mandelbaum and N. M. M. Nibbering, *J. Mass Spectrom.* **30**, 1174 (1995).
33. W. Shen, P. Wong and R. G. Cooks, *Rapid Commun. Mass Spectrom.* **11**, 71 (1997).
34. K. Vêkey and G. Czira, *Anal. Chem.* **69**, 1700 (1997).
35. L. G. Wright, S. A. McLuckey, R.G. Cooks and K. V. Wood, *Int. J. Mass Spectrom. Ion Processes* **42**, 115 (1982).
36. S. T. Graul, M. E. Schnute and R. R. Squires, *Int. J. Mass Spectrom. Ion Processes* **96**, 181 (1990).
37. G. Boand, R. Houriet and T. Gäumann, *J. Am. Chem. Soc.* **105**, 2203 (1983).
38. R. A. J. O'Hair, J. H. Bowie and S. Gronert, *Int. J. Mass Spectrom. Ion Processes* **117**, 23 (1992).
39. T. K. Majumdar, F. Clairet, J. C. Tabet and R. G. Cooks, *J. Am Chem. Soc.* **114**, 2897 (1992).
40. M. J. Haas and A. G. Harrison, *Int. J. Mass Spectrom. Ion Processes* **124**, 115 (1993).
41. J. L. Holmes, *Org. Mass Spectrom.* **20**, 169 (1985).
42. R. G. Cooks and A. L. Rockwood, *Rapid Commun. Mass Spectrom.* **5**, 93 (1991).
43. M. J. Frisch, G. W. Trucks, H. B. Schlegel, P. M. W. Gill, B. G. Johnson, M. A. Robb, J. R. Cheeseman, T. Keith, G. A. Petersson, J. A. Montgomery, K. Raghavachari, M. A. Al-Laham, V. G. Zakrzewski, J. V. Ortiz, J. B. Foresman, J. Cioslowski, B. B. Stefanov, A. Nanayakkara, M. Challacombe, C. Y. Peng, P. Y. Ayala, W. Chen, M. W. Wong, J. L. Andres, E. S. Reploge, R. Gomperts, R. L. Martin, D. J. Fox, J. S. Binky, D. J. Defrees, J. Baker, J. P. Stewart, M. Head-Gordon, C. Gonzalez and J. A. Pople, *Gaussian 94, Revision D. 2*. Gaussian, Pittsburgh, PA (1995).
44. L. A. Curtiss, K. Raghavachari, G. A. Trucks and J. A. Pople, *J. Chem. Phys.* **94**, 7221 (1991).
45. B. J. Smith and L. Radom, *J. Phys. Chem.* **95**, 10549 (1991).
46. L. A. Curtiss, K. Raghavachari and J. A. Pople, *J. Chem. Phys*. **98**, 1293 (1993).
47. B. J. Smith and L. Radom, *Chem. Phys. Lett.* **1**, 123 (1997).
48. M. Decouzon, O. Exner, J.-F. Gal and P.-C. Maria, *J. Phys. Org. Chem.* **7**, 511 (1994).
49. R. W. Taft and R. D. Topsom, *Prog. Phys. Org. Chem.* **16**, 1 (1987).
50. W. J. Hehre, C.-F. Pau, A. D. Headley, R. W. Taft and R. D. Topsom, *J. Am. Chem. Soc.* **108**, 1711 (1986).
51. R. W. Taft, J. L. M. Abboud, F. Anvia, M. Berthelot, M. Fujio, J.-F. Gal, A. D. Headley, W. G. Henderson, I. Koppel, J. H. Qian, M. Mishima, M. Taagepera and S. Ueji, *J. Am. Chem. Soc.* **110**, 1797 (1988).
52. A. G. Harrison, *Mass Spectrom. Rev.* **16**, 201 (1997).
53. Z. Wu and C. Fenselau, *Rapid Commum. Mass Spectrom.* **8**, 777 (1994).