CHAPTER 6

Ion Chemistry

6.1 ELECTRON AND PROTON AFFINITIES AND MEASUREMENTS OF GAS PHASE ACIDITY

6.1.1 Electron Affinity

The most fundamental property of a molecule or atom from the perspective of mass spectrometry experiments is their ability to lose or gain electrons and form ions. The energy required for a molecule or atom to gain an electron is known as its *electron affinity* (EA). This results in the formation of a radical-anion according to equation 2.2. The electron affinity of a molecule can be defined by equation 6.1. ΔH_f^0 is the heat of formation of an molecule or ion defined as the heat absorbed or released when one mole of the entity is formed at standard temperatures and pressures (298 K = 25 °C, 1 atmosphere = 1.013×10^5 Pa). Values of ΔH_f^0 can be estimated by simple arithmetic using available thermodynamic data or by *ab initio* molecular orbital calculations.

$$EA(M) = \Delta H_f^0(M) - \Delta H_f^0(M^{-\bullet}) \tag{6.1}$$

Two types of experiments are employed to determine electron affinities. The first of these uses photon detachment methods. Using a crossed photon-molecular beam apparatus, a photon source such as a laser intersects at right angles with a beam of negative ions. The production of neutral molecules according to equation 6.2 is then studied.

$$M^{-\bullet} + h\nu \rightarrow M + e^- \tag{6.2}$$

The neutral molecules produced are detected using a particle multiplier. Ion cyclotron resonance (ICR) mass spectrometers are also used for these measurements where the photon beam runs parallel to the ion motion. Due to the long trapping times, the spatial overlap of the ion

and photon beams is relatively large and photon detachment efficiencies are high. The minimum photon energy required to remove an electron is measured in these experiments. Photon-ion interactions are particularly suited to measurements of electron affinities since the electron binding energies of most negative ions fall in the range of 0.5 to 3.0 eV, corresponding to approximately 400 to 2500 nm.

The second type of experiment used involves a measurement of the energy required to transfer charge between a negative ion and a neutral molecule. In equation 6.3, this *charge transfer* is associated with the transfer of an electron from $A^{-\bullet}$ to B.

$$A^{-\bullet} + B \rightarrow A + B^{-\bullet} \tag{6.3}$$

Experiments to determine whether a series of ions will transfer an electron to a particular molecule enable the electron affinity of the molecule to be bracketed.

As expected, molecules that contain electronegative atoms are more likely to bind electrons and thus will have higher electron affinities. The instability that results from pairing electrons in atomic orbitals, however, has an impact on this trend. The group XV atoms of the periodic table (nitrogen, phosphorous and arsenic) have much lower atomic electron affinities as a consequence of their half-filled *p*-orbitals.

Stabilisation of the negative charge through conjugation can raise the electron affinity of a molecule. The phenoxide radical, for example, has a higher electron affinity (2.4 eV) than other alkoxide radicals due to the delocalisation of the charge on oxygen throughout the aromatic ring.

6.1.2 Gas Phase Acidity and Proton Affinity

Measurements of electron affinities enable other thermodynamic data to be derived. For instance, the enthalpy contribution to the gas phase acidity of a compound can be derived from equation 6.4 where BDE is the *bond dissociation energy* of the M–H bond and IE is the *ionisation energy* for the molecule. The latter is defined as the energy required for the process defined by equation 2.1.

$$\Delta H_{acid}^{0}(M\text{–}H) = BDE(M\text{–}H) - EA(M) + IE(M) \tag{6.4}$$

Equation 6.4 is derived from a thermodynamic cycle produced from a sum of the following two processes (equations 6.5 and 6.6).

$$M\text{–}H \rightarrow M + H \qquad \Delta H_f^0 = BDE(M\text{–}H) \tag{6.5}$$

$$M + H \rightarrow M^- + H^+ \qquad \Delta H_f^0 = E_i(M) - EA(M) \tag{6.6}$$

Since the primary process by which most $[M+H]^+$ ions are formed during ionisation is by the transfer of a proton from one compound to another, a molecule's gas phase acidity is an important property in mass spectrometry. Proton transfer reactions are also among the most important processes in chemical and biochemical transformations and have been studied extensively in solution.

The *gas phase acidity* of a neutral compound MH is defined as the free energy $\Delta G_{acid}{}^0(MH)$ required to effect the forward reaction shown in equation 6.7.

$$MH \rightleftharpoons M^- + H^+ \tag{6.7}$$

The free energy for the reaction has both enthalpy and entropy contributions according to equation 6.8.

$$\Delta G_{acid}{}^0(MH) = \Delta H_{acid}{}^0(MH) - T\Delta S_{acid}{}^0(MH) \tag{6.8}$$

The *proton affinity* (PA) of a neutral molecule M is defined as the energy required to effect the forward reaction shown in equation 6.9. Thus $PA(M) = -\Delta H_{acid}{}^0(MH^+)$.

$$M + H^+ \rightleftharpoons MH^+ \tag{6.9}$$

The traditional approach to measure the gas phase acidity of the compound MH is to react it with a base (B) and measure the degree of formation of the ion BH^+ (equation 6.10).

$$MH + B \rightleftharpoons M^- + BH^+ \tag{6.10}$$

When this measurement is performed in solution, the process is strongly influenced by the solvent medium. Proton transfer reactions with the solvent interfere with and limit the accuracy of such experiments. A mass spectrometer, by comparison, enables the intrinsic reactivity of a molecule to be studied in the absence of solvent and a number of specialised instruments for this purpose have been constructed. These instruments have led to the construction of tables of gas phase acidity data.

6.1.3 Gas Phase Acidity Measurements

Most measurements of gas phase acidities have been performed with high pressure mass spectrometers and both ion cyclotron resonance (ICR) and quadrupole ion trap (QIT) instruments. These latter instruments store ions for sufficient times to effect ion-molecule and ion-ion reactions. Reaction products and rates can be determined using these mass spectrometers.

An example of the former type of mass spectrometer is a *flowing-afterglow instrument*. These devices were originally constructed to study the chemistry of the ionosphere and feature a reaction flight tube along which reactive species can be added in a gaseous form. Their name derives from the visible glow detected within the earlier glass drift tubes from energy lost in exothermic reaction processes. The flight tube is pressurised with helium to collisionally 'cool' the ions formed in the ion source and ensure they are not in an excited (high energy) state. The ions produced in the source drift down the flight tube and react subject to the nature of the molecule added and the reaction time available. The length of the flight tube provides a reaction time domain along which rate constants can be derived.

A common method used to determine the acidity of a gaseous molecule is through bracketing methods. If a molecule MH transfers a proton to base B_1 but not to base B_2, its $\Delta G_{acid}{}^0(MH)$ value will be greater than $\Delta G_{acid}{}^0(B_1H)$ but less than $\Delta G_{acid}{}^0(B_2H)$. In order to rank these acidity measurements, performed on many instruments at various temperatures, on a common $\Delta H_{acid}{}^0$ scale it is necessary to predict the entropy change $\Delta S_{acid}{}^0$ according to equation 6.11.

$$\Delta S_{acid}{}^0(MH) = S^0(H^+) + S^0(M^-) - S^0(MH) \qquad (6.11)$$

For a known value of $S^0(H^+)$, the values of $S^0(M^-)$ and $S^0(MH)$ are the most dissimilar in terms of their rotational contributions. According to theory, the entropy contributions from translational, vibrational and electronic effects can be considered to be identical for M^- and MH and thus cancel each other out. The (usually small) entropy change for the reaction is then estimated from statistical mechanical considerations of rotational entropies. In practice, as these estimates can be unreliable and since most studies are conducted at a single temperature (25 °C), the small entropy contribution to a molecule's gas phase acidity is often ignored.

A problem with bracketing experiments is that the errors in known acidity data are transposed into the measured data for unknowns. An alternate method to determine gas phase acidities is the kinetic method.

6.1.4 Kinetic Method

The application of the *kinetic method* to the measurement of gas phase acidities involves measuring the ratio of product ion signals from the competitive fragmentation of the dimeric precursor ion [A . . . H^+ . . . B]. This ion may undergo metastable decomposition or be activated to dissociate through collision-activated dissociation (CAD) or other process. Two product ions AH^+ and BH^+ are formed with rate constants of k_A and k_B (equation 6.12).

$$[A \ldots H^+ \ldots B] \rightarrow AH^+ + B \text{ with a rate constant } k_A$$
$$\rightarrow A + BH^+ \text{ with a rate constant } k_B \qquad (6.12)$$

The relative abundances of the product ions are related to their differences in acidity $\Delta(\Delta H_{acid})$ (equation 6.13) for a proton dimer at temperature, T. R is the gas constant (8.3×10^3 J K^{-1}).

$$\ln (k_A/k_B) = \ln ([AH+]/[BH+]) \approx \Delta(\Delta H_{acid})/RT \qquad (6.13)$$

A calibration curve based on the ion ratios of several species with known acidities is used to establish measured values. The kinetic method assumes that the competitive dissociations of [A . . . H^+ . . . B] have equal entropies and thus cancel each other out.

The popularity of the kinetic method is the result of several features including a high degree of sensitivity to differences in structure (including isotopically-labelled forms), the close agreement in values obtained by the method with those from other approaches, and the speed with which the analyses can be performed. Since the measurements are performed on a tandem mass spectrometer, it is also not necessary that the samples be pure in order for them to be studied.

6.2 ION-MOLECULE REACTIONS

6.2.1 Types of Ion-Molecule Reactions

There are many types of ion-molecule reactions including electron transfer (equation 6.3), proton transfer (equation 6.9), addition, substitution and elimination reactions. Addition reactions involve the formation of a new covalent bond, while substitution and elimination reactions are also characterised by bond cleavage. Nucleophilic substitution reactions are a class of ion-molecule reactions that have received much

interest given that such processes are common in organic chemistry. In the gas-phase, in the absence of solvent, these reactions proceed along a reaction pathway with two low-energy intermediates shown in square brackets in equation 6.14.

$$N^- + M\text{–}X \rightleftharpoons [N^- \ldots M\text{–}X] \rightleftharpoons [N\text{–}M \ldots X^-] \rightarrow N\text{–}M + X^- \qquad (6.14)$$

It is convenient to present an ion-molecule reaction in terms of a *potential energy diagram* with the reaction co-ordinate on the *x*-axis. The curve (in two dimensions) or surface (in three dimensions) allows a reaction process or series of competing reaction pathways to be viewed in which the energy of the system never passes below the curve or surface.

For the reaction shown in equation 6.14, a double energy minima potential energy profile is constructed (Figure 6.1) featuring a central energy barrier that represents the transition state $[N \ldots M \ldots X]^{-*}$. This transition state may reside at an energy that is above or below that of the reactants.

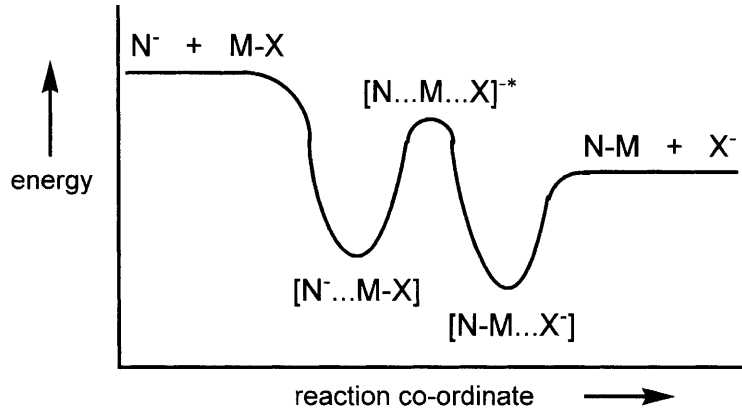

Figure 6.1 *Energy profile for an exothermic ion-molecule reaction without an activation energy barrier*

Gas-phase ion-molecule reactions importantly enable the role of solvent molecules in a chemical transformation to be explored. In the presence of solvent vapour in the mass spectrometer, the reaction of an ion with increasing levels of solvation $M^+(S)_n$ or $M^-(S)_n$ (where S is a molecule of solvent) can be explored.

Historically, most ion-molecule reactions have involved the reaction of singly-charged ions (either positively or negatively charged) and a neutral

molecule though an increasing focus concerns the reaction of multiply-charged ions given their ease of production by electrospray ionisation. The reaction of multiply-charged ions with neutral molecules provides information about the site of the charges within the ion and whether such charged centres are localised or delocalised.

6.2.2 Rates of Ion-Molecule Reactions

Ion-molecule reactions are one of the fastest chemical reactions known. This is a result of attraction between the charge of the ion and the dipole of a polar molecule. This electrostatic interaction is sufficient to overcome many energy barriers to reaction products. As a result, many ion-molecule reactions are exothermic and rapidly proceed even at room temperatures. An exothermic ion-molecule reaction that proceeds without an activation energy barrier has a rate constant k that is equal to the collision-control or diffusion rate (Figure 6.1). That is, the reaction is limited only by the ability of an ion and molecule to encounter one another. As these species do so, an electrostatically-induced or natural ion-dipole interaction occurs resulting in the formation of the ion neutral complex and subsequently products. Collision-controlled rate constants are of the order of 10^{-9} cm^3 molecule^{-1} s^{-1}.

6.2.3 Ion-Neutral Intermediate Complexes

It is common when analysing most ion-molecule reactions in the gas phase to infer the formation of an intermediate complex. *Ion-neutral complexes* have been postulated for many reactions in an attempt to explain the mechanism of formation of unusual product ions observed within mass spectrometers.

Electrostatic considerations demand that when a gas-phase ion encounters a neutral species, its energy initially decreases. Thus an ion-neutral complex is formed before any energy barrier is encountered in order to generate products. In the classical S_N2 nucleophilic substitution reaction where X^- reacts with CH_3Y, the ion-neutral complex formed is represented by $[X\cdots CH_3Y]^-$ (see Figure 6.1). This results in a transition state structure denoted $[X\cdots CH_3\cdots Y]^-$ and the formation of an ion-neutral complex for the product $[XCH_3\cdots Y]^-$. This complex then dissociates to form the products XCH_3 and Y^-. Square brackets are used throughout.

The two components of an ion-neutral complex are associated not by a covalent bond but an ion-dipole attraction. Ion-neutral complexes can be formed from positively or negatively charged ions. The reactants are able to rotate about one another resulting in reactions that would

not be geometrically possible if the partners were covalently bonded. In the gas-phase these species can be relatively long-lived with lifetimes of typically 10–100 μs. Ion-neutral complexes are particularly significant for neutral species with a small dipole moment but a large polarisability. They typically have stabilisation energies in the range of 50 kJ mol^{-1}; that is, some additional 50 kJ mol^{-1} is required for the complex to proceed to a transition state and ultimately to products.

Ion-neutral complexes lose their relevance when solvation is possible. In contrast to the reaction profile above, the S_N2 reaction between X^- and CH_3Y in solution proceeds simply from reactants to the transition structure $[X\cdots CH3\cdots Y]^-$ and then to products.

Ion-neutral complexes have been postulated as intermediates in elaborate mechanisms that attempt to explain the formation of unusual products in gas-phase ionic reactions and rearrangements. Molecular orbital calculations have also been used to implicate ion-neutral complexes in the fragmentation of certain ions. However, since these intermediates cannot be observed directly by spectroscopic methods, their existence is largely inferred rather than strictly proven. Ion-ion and ion-radical intermediate complexes have also been inferred in many gas-phase ion reactions.

6.3 KINETIC ISOTOPE EFFECTS

When the substitution of an atom in a molecule or ion by its isotope alters the reaction rate of that molecule or ion, a *kinetic isotope effect* (KIE) exists. The kinetic isotope effect is measured as the ratio of the rate constants for these reactions at a given internal energy. Where the isotopically-substituted atom is directly involved in bond dissociation or formation, the kinetic isotope effect is a primary one. When the atom is remote from the reaction centre, a secondary kinetic isotope effect is observed.

The value of the kinetic isotope effect provides important information about the particular atoms participating in a reaction, distinguishing hydrogen exchange or scrambling, identifying a stepwise reaction mechanism from a concerted one-step process, and postulating the structure for a transition state.

Most kinetic isotope effects are measured for the substitution of hydrogen with deuterium, *i.e.* k_H/k_D. The value of KIE increases from inverse ($k_H/k_D < 1$) toward normal ($k_H/k_D > 1$) as the "looseness" of the transition state increases. For reactions involving the reversible exchange of isotopes between molecular species, the kinetic isotope effect is given by the equilibrium reaction constant (equation 6.15).

$$MH^+ + A\text{–}D \Leftrightarrow MD^+ + A\text{–}H \qquad K = k_H/k_D \tag{6.15}$$

An intermolecular isotope effect exists where an isotopically-labelled ion has two possible dissociation pathways (equation 6.16).

$$D\text{–}CH_2CH_2Cl^{+\bullet} \rightarrow CDH{=}CH_2^{+\bullet} + HCl \tag{6.16}$$

$$\rightarrow CH_2{=}CH_2^{+\bullet} + DCl$$

Since this reaction occurs from a common precursor, the size of the isotope effect can be predicted from the relative abundances of the product ions.

FURTHER READING

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