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Quantification of gas-phase ion-molecule reactions of complex organic compounds and a study of the factors involved in these determinations by Fourier transform ion cyclotron resonance mass spectrometry

Santos, Ivan, Ph.D.
The Ohio State University, 1987
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QUANTIFICATION OF GAS-PHASE ION-MOLECULE REACTIONS OF COMPLEX ORGANIC COMPOUNDS AND A STUDY OF THE FACTORS INVOLVED IN THESE DETERMINATIONS BY FOURIER TRANSFORM ION CYCLOTRON RESONANCE MASS SPECTROMETRY

DISSertation

Presented in Partial Fulfillment of the Requirements for the Degree Doctor of Philosophy in the Graduate School of the Ohio State University

By

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* * * * * *

The Ohio State University

1987

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Department of Chemistry
To my parents—Juan and Lydia Santos,
my wife—Doris,
and to the memory of her parents—Ben and Leila Robison.
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\[ K_{\text{apparent}} = \frac{[C_8H_8][C_9H_{11}^+]}{[C_9H_{10}][C_8H_9^+]} \]

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Open circles: no ion ejection.
Squares: after ejection of protonated cubane.
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INTRODUCTION

It was long believed that the acid-base properties of compounds in solution would be similar to those properties of the compounds in the gas phase and that the intrinsic acid-base property could be determined from solution experiments. This belief was shattered in the late 1960's with the work of Brauman and Blair. Brauman and Blair showed that toluene was more acidic than H₂O in the gas phase even though H₂O is more acidic than toluene by 20 orders of magnitude in solution. Since that time the effort to determine intrinsic acid-base properties by the study of gas-phase proton transfer reactions has been increasing.

The gas-phase basicity determinations of cubane, dodecahedrane and its mono and 1,16-dimethyl derivatives were needed since little experimental information is available about the fundamental properties of these highly symmetrical molecules, particularly for the dodecahedranes since they were first synthesized only 5-6 years ago.

5-fluorouracil (FU) is one of the most prescribed antitumor drugs of today. The changes that it brings about in RNA when it replaces uracil (U) are not completely clear. The greater acidity of FU over U should bring about changes in normal hydrogen bonding in RNA. Therefore, knowledge of the acidity difference between FU and U
is of value. This acidity difference has been known from aqueous solution studies, but since, the interior of the RNA is known to be hydrophobic, a determination of the acidity difference between FU and U in the gas phase (gas-phase acidity measurements correlate well with measurements in non-aqueous solvents) was needed.
A. INTRODUCTION

There are various types of mass analyzers: magnetic, quadrupole, double focusing, time-of-flight, ion cyclotron resonance (ICR), and Fourier transform ion cyclotron resonance (FT/ICR) [1-4]. Certain spectrometers can be used in combination with other instruments such as laser microprobe, ion microprobe/microscope; etc. [4-6]. What they all have in common is that analysis is based on ionic mass to charge ratio.

ICR spectroscopy differs from the rest in the way the ions move within the instrument and the way the ions are detected. In the ICR, motion of an ion in a static large magnetic field is governed by the Lorentz force on that ion:

\[ \mathbf{F}_{\text{Lorentz}} = q \mathbf{v} \times \mathbf{B} \]  

where \( \mathbf{F}_{\text{Lorentz}} \) is the Lorentz force (in Newtons) on the ion,
\[ q \] the ionic charge (in Coul),  
\[ v \] the ionic velocity (in m/s),  
and \[ B \] the magnetic field induction (in Tesla).

The ion is forced into circular motion perpendicular to both the magnetic field and the ion's velocity; see Figure 1. When the ion is in a stable orbit of radius, \( r \), the Lorentz force equals the centripetal force:

\[ qvB = \frac{mv^2}{r} \]  \hspace{1cm} (2)

The frequency with which this ion circulates is called the cyclotron frequency (\( \omega_0 \)) and is characteristic of the ion. Solving for the angular velocity \( \frac{v}{r} \) (radian/sec), one gets:

\[ \frac{v}{r} = \omega_0 = \frac{(qB)/m}{(\text{radians/sec})} \]  \hspace{1cm} (3)

where \( m \) is the mass of the ion (in kg).

**B. HISTORY AND DEVELOPMENT OF FT/ICR**

The key to the development of ICR stems from the discovery by Lawrence and Livingston in 1932 of the cyclotron resonance principle [7]. This principle showed that the radius and energy of a charged particle moving in a uniform magnetic field increases when a resonant oscillating field is applied at a right angle to the magnetic field. The resonant condition was achieved when the applied frequency was equal to the ion cyclotron frequency; see Figure 2. This principle was used
Figure 1. Lorentz force, $\mathbf{F}_L$, on a moving ion of charge $q$ and mass $m$ in a static uniform magnetic field, $\mathbf{B}$. 
Figure 2. Effect of applied RF signal on a resonant and nonresonant ion. A) The frequency of the applied RF signal is not equal to the cyclotron frequency of the ion, hence, there is no power absorption by the ion and its radius does not increase. B) When the RF frequency and the cyclotron frequency are equal, the ion absorbs power and its radius increases. (figure from Reference [44].)
to accelerate charged particles without the use of high voltages and, thus, helped expand the area of experimental nuclear physics in the 1930's.

Not until the omegatron was developed by Hipple, Sommer, and Thomas in 1949 was the principle of cyclotron resonance used for mass spectrometry [8]. The omegatron was first used by physicists to study particle physics; later, after instumental refinements, it was used as a residual gas analyzer for sampling the upper atmosphere [9]. In the 1960's, Wobschall [10] and later Baldeschwieler [11] developed ICR instruments to study gas-phase ion-molecule reactions [9,12,13].

Most of the ICR instruments of the 1960's and early 1970's were drift cell instruments in which ions generated in one region would drift to the analyzer region due to the crossed electric and magnetic fields; see Figure 3. These drift cells normally operated at pressures of \(10^{-5}\) Torr, and ion residence times were on the order of \(10^{-3}\) seconds [14]. Because of this short ion observation time and magnetic field-swept operation, the mass resolution of these early instruments was poor (a resolution \((m/\Delta m)\) of about 200 at \(m/z = 200\), where \(\Delta m\) is the full width, in mass units, of a mass spectral peak at one half the peak height). Another drawback of the early ICR instruments was their time consuming method of spectra recording. The power absorption of each ion was measured separately (continuous-wave ICR); for example, a spectrum ranging from 15 to 200 amu would take as long as 30 minutes to record [15]. For the ICR to be a useful analytical tool, it should provide
Figure 3. A typical drift cell in which the ions are formed in the source region, then due to a potential applied to the drift plates, D, drift towards the resonance analyzer region. (Figure is from Reference [14].)
exact mass measurements (± 1-2 millimass units) in a short time (preferably 1-2 sec) over a large mass range (~ 18-600 amu).

The problems of speed and mass resolution were solved in the 1970's by instrumental developments that would eventually lead to the development of the Fourier transform ICR mass spectrometer (FT/ICR, FTMS); see Table 1 for the advantages of FT/ICR over continuous-wave ICR. There were four main aspects that had to be developed so that FT/ICR could become the powerful and useful analytical tool that it is today:

1) The first development actually occurred in 1965 when Cooley and Tukey developed the fast Fourier transform algorithm [16]. This algorithm, together with an array processor, makes possible the Fourier transform of a large data set (65,536 points) on a mini-computer in a short time (4-5 sec on the Nicolet 1280).

2) The second innovation was that of the trapped ion cell developed by McIver [17]; see Figure 4. With this cell one could store and detect the ion signal for periods of more than 100 ms, therefore providing higher mass resolution than the drift cell.

3) The third feature that needed to be developed was the fast 128 bit analog-to-digital converter needed to cover the large frequency ranges (a few MHz) that are encountered in ICR [4].

Table 1. Advantages of FT/ICR over continuous-wave ICR.

<table>
<thead>
<tr>
<th>FEATURE</th>
<th>IMPROVEMENT FACTOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPEED</td>
<td>1000-10,000</td>
</tr>
<tr>
<td>SIGNAL-TO-NOISE</td>
<td>100</td>
</tr>
<tr>
<td>RESOLUTION</td>
<td>10,000-100,000</td>
</tr>
<tr>
<td>UPPER MASS LIMIT</td>
<td>15-30</td>
</tr>
</tbody>
</table>
Figure 4. A typical elongated trapped ion cell: the ions are formed and trapped in a single region. (Figure is from Reference [17].)
C. PRINCIPLES OF ION MOTION IN THE ICR

The resultant force on the ion in the ICR cell is given by the following equations (mks units):

\[ F = F_{\text{Lorentz}} + F_{\text{elec}} \] (4)

and

\[ F = m\left(\frac{dv}{dt}\right) = q(v \times B) + qE \] (5)

where
- \( F \) is the total force exerted on the ion,
- \( F_{\text{elec}} \) is the force due to the applied static electric field,
- \( \frac{dv}{dt} \) is the acceleration due to \( F \),
- and \( E \) is the electric field generated by the trapping potentials.

The resultant motion of the ion, due to the total force, is shown in Figure 5. This motion is composed of three oscillating motions (see Figure 6), each with its own characteristic frequency (see Table 2) [20-24]. Equation 3 gives the expression for the cyclotron frequency. The trapping and magnetron frequencies in radians/sec are given by [21,22]:

\[ \omega_{\text{Trap}} = \left[ \frac{2Bq(V_T - V_0)}{ma^2} \right]^{1/2} \] (6)

\[ \omega_{\text{Mag}} = \frac{2qV}{a^2B} \] (7)

where \( \omega_{\text{Trap}} \) is the trapping frequency.
Figure 5. Combination of the cyclotron, trapping, and magnetron motions, resulting in a complicated ion motion in the cell. (Figure is from Reference [25].)
Figure 6. Decomposition of ion motion into three periodic motions. The cyclotron motion is shown in Figure 1. Note that these three motions are not drawn to scale. (Figure is from Reference [25].)
Table 2. Parameters of the three oscillating motions in an ICR for typical charged particles (at 3T and 1V/inch trapping potential).

<table>
<thead>
<tr>
<th>CHARGED PARTICLE</th>
<th>NOMINAL MASS (amu)</th>
<th>CYCLOTRON (MHz)</th>
<th>TRAPPING (kHz)</th>
<th>MAGNETRON (Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ELECTRON</td>
<td>5.5 x 10^{-4}</td>
<td>83,430</td>
<td>6126</td>
<td>224.8</td>
</tr>
<tr>
<td>PROTON</td>
<td>1</td>
<td>45</td>
<td>143</td>
<td>224.8</td>
</tr>
<tr>
<td>H_{2}O^{+}</td>
<td>18</td>
<td>2.5</td>
<td>34</td>
<td>224.8</td>
</tr>
<tr>
<td>(α-METHYLSTYRENE)^+</td>
<td>118</td>
<td>0.4</td>
<td>13</td>
<td>224.8</td>
</tr>
<tr>
<td>(DODECAHEDRANE)^+</td>
<td>260</td>
<td>0.2</td>
<td>9</td>
<td>224.8</td>
</tr>
</tbody>
</table>
the magnetron frequency,
the geometric cell constants,
the trap potential in volts,
the upper and lower plate potentials in volts,
potential of the cell equipotential lines in volts
and the cell dimensions (2.54x10^-2 m)
for the cubic cell.

(I obtained the data for Table 2 from a computer program that was written by Dr. Francis Verdun, a postdoctoral fellow in our research group; this program was based on work by Hunter, Sherman, and McIver [21]. As the ions drift along the z axis (the axis parallel to the magnetic field), they are forced by the trapping potential into harmonic oscillations along the z axis at the "trapping or axial" frequency. The electric field, used to trap the ions, has a radial component perpendicular to the magnetic field. The field of this radial component, \( E_r \), at a radius of \( r \) is given by:

\[
E_r = 2r \frac{V}{a^2}
\]  

(8)

The radial field forces the ion away from the z-axis (the axis parallel to the magnetic field), however, the magnetic field constantly opposes this motion, and thus, the ion slowly drifts about the z-axis at the magnetron frequency [22,25]. The cyclotron motion is given by
Equation 3 and has a corresponding "cyclotron" frequency. It is this last frequency that is used to obtain the mass spectrum.

One needs a mass calibration equation to convert the frequency domain spectrum into a mass spectrum [26-30]. Since frequencies can be measured accurately, one can obtain high mass accuracy; see the calibration spectrum of perfluorotri-n-butylamine in Figure 7.

D. FEATURES OF THE FT/ICR

The instrument used in this work is a Nicolet FTMS 1000. A block diagram of the vacuum system of this instrument is shown in Figure 8. The cell used in this study is a 1" cubic cell [31]; see Figure 9. Table 3 lists the analytical features of FT/ICR mass spectrometry [4]. Many of these features are improvements over those of conventional sector mass spectrometry [3]. These advantages will be explained in the following sections.

1. MECHANICAL SIMPLICITY

In FT/ICR, the ion source and the analyzer are in the same cell, and the events such as ion formation, detection, and mass analysis occur at the same location and are separated only in time. Because of these features, FT/ICR does not require the ion focusing lenses, slits, and high voltages needed by conventional mass spectrometers. Thus, the FT/ICR is more simple to operate and maintain than a conventional mass spectrometer.
<table>
<thead>
<tr>
<th>Calculated Mass (amu)</th>
<th>Observed Mass (amu)</th>
<th>Error (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>68.99466</td>
<td>68.99467</td>
<td>0.1</td>
</tr>
<tr>
<td>118.99147</td>
<td>118.99149</td>
<td>0.1</td>
</tr>
<tr>
<td>130.99147</td>
<td>130.99137</td>
<td>-0.7</td>
</tr>
<tr>
<td>218.98508</td>
<td>218.98506</td>
<td>-0.1</td>
</tr>
<tr>
<td>263.98666</td>
<td>263.98694</td>
<td>1.5</td>
</tr>
<tr>
<td>413.97698</td>
<td>413.97715</td>
<td>0.4</td>
</tr>
<tr>
<td>501.97060</td>
<td>501.96991</td>
<td>-1.4</td>
</tr>
</tbody>
</table>

Figure 7. Spectrum of a standard mass calibrant, perfluorotri-n-butyl-amine, obtained by careful adjustment of the excitation and detection parameters and by keeping the number of ions in the cell as low as possible.
Figure 8. Block diagram of the FTMS 1000 vacuum system.
Figure 9. Cubic 1" ion trapped cell used in this work.
Table 3. Some advantages of FT/ICR for analytical mass spectrometry.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mass Resolution</td>
<td>To 4,000,000 at m/z = 131</td>
</tr>
<tr>
<td>Speed</td>
<td>0.01 - 1 sec/scan</td>
</tr>
<tr>
<td>Chemical Ionization</td>
<td>No reagent gas</td>
</tr>
<tr>
<td>MS/MS/...</td>
<td>One spectrometer</td>
</tr>
<tr>
<td>Upper Mass Limit</td>
<td>95,000 amu possible at 13T</td>
</tr>
<tr>
<td>Slits</td>
<td>None</td>
</tr>
<tr>
<td>High Voltage</td>
<td>None</td>
</tr>
<tr>
<td>Ei/Ci/Laser Ionization</td>
<td>One source</td>
</tr>
</tbody>
</table>
2. HIGH MASS RESOLUTION (m/Δm)

Improved mass resolution, as a rule, implies better precision and more accurate mass measurements. The best resolution with a conventional mass spectrometer is about 150,000 (e.g., Kratos MS-50). With the FT/ICR, however, the best resolution reported is as high as 2x10^8 (at m/z = 40, argon) [32]. It should be noted that this value was obtained from an experiment specifically designed to obtain as high a resolution as possible. A resolution of 100,000 at m/z = 1000, however, is routinely obtainable with the FTMS 1000 [33].

3. UPPER MASS LIMIT

Theoretically, FT/ICR offers the possibility of higher mass limits than those currently available with conventional mass spectrometers (about 10,000 amu with a reasonable working limit of 3-5,000 amu [3]). In ICR mass spectrometry, one can find the radius of the cyclotron motion (r), for an ion in a stable orbit, by setting the Lorentz and centripetal forces equal to each other and by solving for the radius:

\[ r = \frac{mv}{qB} \]  

(9)

Expressing the velocity in terms of the kinetic energy of the ion, one can relate the radius as thus:

\[ r = \left(\frac{m}{qB}\right)\left(\frac{2T}{m}\right)^{1/2} \]  

(10)

where T is the kinetic energy \(mv^2/2\) and has units of J. To determine
an upper mass limit, $m_{ul}$, in terms of the size of the cell, the radius is set equal to the cell dimension, $a$, and one solves for $m_{ul}$.

$$m_{ul} = \frac{q^2 B^2 a^2}{2T} \quad (11)$$

The ions have an additional constraint, however, in that the trapping potential will contribute to the kinetic energy of the ions. As the mass increases so will their kinetic energy and eventually the ions can no longer be trapped, if the kinetic energy is included in Equation 11 then one obtains:

$$m_c = \frac{qB^2 a^2}{8\alpha V_{eff}} \quad (12)$$

where $V_{eff}$ is the trapping voltage corrected for space charge, and $\alpha$ the geometric factor for the cell, i.e., $\alpha = 1.3869$ for cubic cell [21].

The critical mass, $m_c$, represents the highest mass that can be trapped [3]. As can be seen from Equation 12 the magnetic field and size of the cell for the most part limit the critical mass. Gross and Rempel have calculated that the upper mass limit should be 95,000 amu for a 1 V trapping potential in a cubic cell at magnetic field strength of 13 T and at a reasonable working limit of 10% of the critical mass limit [3]. Experiments, however, are routinely done at 1000-4000 amu [34-37], but can be done as high as 8800 amu [36].
4. CHEMICAL IONIZATION

Since the FT/ICR is capable of retaining ions for several seconds (compared to $10^{-4}$ to $10^{-6}$ seconds for conventional MS) [3,9], chemical ionization can be done at a pressure of $10^{-6}$ Torr (rather than at 1 Torr). Since one can avoid cluster formation by running at these low pressures, chemical ionization in the ICR is simpler to interpret than in conventional instruments [9].

5. HIGH-RESOLUTION MS/MS EXPERIMENTS

In a conventional MS/MS experiment, one needs two separate mass analyzers in addition to a separate reaction region. The ions (called parent ions) formed in the source are separated by mass in the first analyzer. The parent ions are allowed to pass from the first analyzer into the reaction region where they undergo collisionally induced fragmentation. These fragment ions, called daughter ions, are then mass analyzed by the second mass analyzer [38]. This technique is useful for identifying individual components in complex mixtures, such as those found in coal liquid [38].

FT/ICR is also capable of doing MS/MS experiments: parent ions are formed, all ions except the parent ions are ejected from the cell, the parent ions are then excited and collide with the buffer gas producing daughter ions, and the mass spectrum obtained is the same as that from a conventional MS/MS experiment. The ability of FT/ICR to selectively eject or excite ions within the same region enables the FT/ICR to do not only MS/MS but up to MS/MS/MS/MS/MS [39,40] experiments; moreover,
whereas it would take five separate mass spectrometers for the conventional MS/MS/MS/MS/MS/MS experiment, only the one FT/ICR instrument is needed. Also, the stored waveform (SWIFT) technique [41-43] makes possible ultra-high mass resolution MS/MS on the FT/ICR, a capability not achievable by conventional MS/MS [44].

Since FT/ICR has advantages over conventional MS/MS (such as those just described and those mentioned in the sections on mechanical simplicity and chemical ionization) and since FT/ICR has the abilities to trap ions for long periods of time and to selectively eject ions, the FT/ICR is the instrument of choice for the study of ion-molecule reactions [4]. These features will be described further in Chapter II.

6. MULTICHANNEL ADVANTAGE

Since the FT/ICR spectrometer is essentially a "multichannel" instrument in the sense that all information in a large spectral bandwidth is obtained simultaneously, the signal-to-noise (S/N) ratio is enhanced over that of a spectrum acquired in the same length of time by conventional ICR or by scanning sector MS [3,45,46]. Because noise is detector limited, as one accumulates N scans, the signal accumulates as N while noise increases only as N^{1/2}. Therefore, one gains a S/N ratio of N^{1/2} in the same time that a scanning instrument takes to cover the same bandwidth; this improvement in signal-to-noise for FT spectrometry is known as the Fellgett advantage [47].

E. ION MANIPULATION

Two very useful techniques of ion manipulation are possible because
of the ability of the ICR to excite ions into cyclotron motion. The first of these techniques is ion ejection, which is based on the radial excitation method; see Figure 10. Ion ejection works on the principle that ions of a given mass-to-charge ratio can be selectively accelerated and, thus, selectively ejected from the cell. An oscillating electric field is chosen so that its frequency equals the cyclotron resonance frequency of the ion to be ejected. The ion absorbs power and increases its orbital radius:

$$r = \sqrt{2} \frac{V_{\text{RMS}}(t/2Bd)}{B}$$  \hspace{1cm} (13)

where \( r \) is the radius of ion motion,
\( V_{\text{RMS}} \) the root mean square voltage of the excitation signal,
\( t \) RF excitation period,
and \( d \) the distance between excitation plates.

If the power absorbed is above a particular value (the dashed line in Figure 10), the ion will be driven into the cell wall where it loses its charge and is, thus, "ejected" from the system. The other ions will not be affected since they are not resonant at that frequency.

Selective ion ejection can accomplish the following:

1) extension of instrumental dynamic range by ejecting abundant ions [42],

2) determination of the relationship between products and reactants of gas-phase ion-molecule reactions [11].
Figure 10. Effect of 3 different levels of power applied during ion excitation. Pulse C has enough power to drive the ion into an orbit that neutralizes the ion at the cell wall. (Figure from Reference [44].)
The second technique of ion manipulation that is useful to the gas-phase reaction chemist also involves ion excitation. In this case, however, the ions are excited with just enough energy so that they will dissociate when they collide with molecules of a reagent gas or with neutrals of the same compound. This technique is known as collision induced dissociation, CID [3,48]. The resulting fragments help to establish structures and to determine the reaction mechanism when these fragments are related to the findings from MS-MS experiments [38].

F. OPERATION OF THE FT/ICR

In modern FT/ICR, all excitation, ion manipulation, and detection events are computer controlled and are separated in time; see Figure 11 for typical experimental pulse sequences. The experimental sequence represents the acquisition of one spectrum, i.e., one scan. In actual practice, many scans are collected to improve the signal-to-noise ratio by signal averaging. In between each scan there is a quench event (QNC) in which a uniform electric field of about 25 V is applied to the trap plates. This field clears the cell of all ions so that none are present in the cell at the start of the scan. During the electron beam event (BEM) ions are formed by electron impact (a current is applied to a rhenium filament for about 20-100 ms at a voltage biased by about -50 V with respect to 0 V at the cell). During the BEM event, one can selectively eject ions of a particular m/z ratio by exciting them at their ICR frequency; this step is referred to as the
Figure 11. Typical experimental pulse sequences. A) Sequence for no ion ejection. B) Sequence for ion ejection.

QNC - Quench duration
QND - Quench delay
BEM - Ion formation
TTX - Ion excitation
TRX - Data acquisition

DL4 - Switching delay
DL1, DL2, and DL3 - Delays for reactions
ET1, ET2, and ET3 - Ion ejection events

The DL And ET events can also be used to trigger pulsed valves and special electronics.
frequency-during-beam event (FDB). All of the various operations such as reactions, ion-ejections, and pulsing of reagent gases take place during the time between QNC and ion excitation.

1. ION EXCITATION

One must supply sufficient power, at the ion cyclotron frequency, to force the ions into orbits that are large enough to be detected. The most commonly used excitation waveform in FT/ICR is a linear frequency sweep that covers the frequency range and, hence, mass range of interest [4,49]. During this event, the excitation waveform is applied to the excitation plates, and all ions are excited into coherent motion. The single frequency excitation waveform used for ion ejection in the FDB event can also be used for excitation of ions in a narrow frequency range.

Since the application of uneven power over a given frequency range during the frequency sweep excitation results in varying relative peak areas, quantification of spectra is difficult [50,51]. In addition, it is difficult to eject selectively an ion close in frequency to others (± 5 KHz) since, with the linear sweep, the frequency cutoff point on either side of the power spectrum is not sharp but has a rolloff on the order of the reciprocal of the excitation period; see Figure 12. A new method of excitation, stored waveform inverse Fourier transform excitation (SWIFT), developed by Marshall, Wang, Ricca, and Chen has largely eliminated these problems [41,43]. Figure 12 shows how much flatter the power application and sharper the frequency cutoff are for SWIFT than they are for frequency sweep excitation [41,43]. The use of
Figure 12. Effect of two different time domain waveforms on power applied in the frequency domain. 
A) Frequency sweep excitation waveform in the time domain gives non-flat power application in the frequency domain. B) SWIFT excitation gives a much flatter power in the frequency domain than that obtained from frequency sweep excitation waveform. (Figure from Reference [44].)
SWIFT excitation/ejection in the low and high resolution modes is shown in Figures 13 and 14 respectively.

2. ION DETECTION

The ions, excited into coherent motion and forced into ion packets that oscillate at the cyclotron frequency of the corresponding ion, induce image currents on the detector plates [52]. The frequency and amplitude (ion intensity) of all the various image currents that make up this time domain signal are amplified, digitized, and stored. The Fourier transform of this signal separates and analyzes the signals and thus allows this data to be presented as a mass spectrum. Two main modes of ion detection are currently used in FT/ICR: the broad band normal mass resolution mode called the direct mode, and the narrow band high resolution mode called the heterodyne mode.

a. DIRECT MODE

The direct mode is the easier and faster way of detecting a large mass range since the time domain signal is digitized directly and then transformed. It is, therefore, the mode used most often for experiments involving large mass range.

b. HETERODYNE MODE

Before proceeding with an explanation of the heterodyne mode, I would like to show the relationship of resolution and acquisition time to the number of time domain points acquired. Resolution (m/Δm)
Figure 13. Comparison of SWIFT vs. frequency sweep excitation waveforms on power applied in the frequency (mass) domain. A) Power spectrum resulting from a frequency sweep excitation. Note the poor selectivity in the mass range 75-80. B) Power spectrum from SWIFT excitation. Note that it is more selective, flatter, and exhibits less rolloff at 60, 70 amu than in A above. (With permission of Reference [44].)
Figure 14. High resolution SWIFT-based ejections. A) Both the $^{13}\text{C}^{12}\text{C}_6\text{H}_7^+$ and $^{12}\text{C}_7\text{H}_8^+$ peaks are excited. B) Only $^{12}\text{C}_7\text{H}_8^+$ is ejected. (With permission of Reference [44].)
increases as the total acquisition time \( T \) increases \([53]\):

\[
m/\Delta m = (qBT/Cm)
\]  

(14)

where \( C \) has the value of 3.8 and 7.6 for absorption and magnitude lineshapes, respectively. Note that all quantities are in MKS units. Since, the sampling theorem states that the highest frequency (Nyquist frequency) in the spectrum must be sampled at a rate of at least 2 points per cycle in order for one to accurately represent the waveform in the digitized data, \( T \) can be increased only to the point at which computer memory is filled \([54]\).

\[
\text{Sampling rate} = 2f_{\text{Nyquist}} = N/T
\]  

or

\[
N = 2Tf_{\text{Nyquist}}
\]  

(15)

(16)

where \( N \) is the number of acquired time domain data points, and \( f_{\text{Nyquist}} \) the Nyquist frequency.

Thus one can see from Equations 14 and 16 that for a given bandwidth, as \( T \) increases, so does data acquisition, and the available computer memory will be used up before high resolution is achieved. If the Nyquist frequency could be lowered, the same computer memory would allow a longer acquisition time, and thus greater resolution. The frequency can be lowered when one uses the heterodyne mode in which the ICR signal, including all frequencies up to the Nyquist frequency, is mixed (multiplied) with a known reference oscillator signal in a suitable non-linear device resulting in a signal composed of both high
(sum) and low (difference) frequencies. Passing the resultant signal through a low pass filter, one eliminates the high frequency. The low frequency band of signals (now carrying ionic m/z information) is sent to the digitizer. These low frequencies allow the digitizer sampling rate to be lower than if the cyclotron frequencies were digitized directly. The lower sampling rate allows the acquisition time to be longer without overflowing the computer memory, thus, higher resolution is obtained.

The mass range when the heterodyne mode is used is small, however. Therefore, every time a different mass range is studied, the instrument must be re-tuned. The effect of tuning the instrument on quantitating spectra is discussed in Chapter III.

G. PRESSURE EFFECTS ON RESOLUTION

As one saw from Equation 14, the longer the observation time, the better the resolution. The signal duration, mostly a function of system pressure, usually limits the observation time. At high pressure there are more neutrals with which the ion can collide and since its signal decays quickly, the available observation period is short and mass resolution is low [3]:

\[
\frac{m}{\Delta m} \leq \frac{(k'qB)(\xi/n)}{(mp)}
\]

(17)

where \( k' \) is a constant characteristic of the cell, in amu·cm³·Torr/Tesla·sec, \( p \) is the neutral pressure in Torr,
and \( \xi/n \) the collision damping frequency
in cm\(^3\)/sec\cdot molecule.

The collision damping frequency can be calculated from [55,56]:

\[
\frac{\xi}{n} = \frac{M}{M+m} k_{\text{ADO}}
\]  

(18)

where \( n \) is the concentration of the neutral in
molecules/cm\(^3\),

\( M \) neutral mass in amu,

\( m \) ion mass in amu,

and \( k \) the collisional rate constant from
ADO theory (discussed in Chapter IV).

in cm\(^3\)/sec\cdot molecule

In general, the decrease in resolution with increasing mass is not a
linear function at very high mass (500–1000 amu) due mainly to
inhomogeneity in the electric field rather than in the magnetic
field [21,22,57–59].
REFERENCES


A. INTRODUCTION

In the early days of mass spectrometry, researchers soon discovered that many of the ions they were observing were coming not only from electron impact but also from ion-molecule reactions [1]. One such example, observed in 1916, was the formation of $H_3^+$:

$$H_2^+ + H_2 \rightarrow H_3^+ + H^+ \quad (19)$$

It was not until after certain developments, such as better sensitivity, better mass resolution, and broader mass range, that the mass spectrometer became an analytical instrument used to study ion-molecule reactions [2-4]. In the early 1950's, much research was done on the formation of $CH_5^+$:

$$CH_4^+ + CH_4 \rightarrow CH_5^+ + CH_3^- \quad (20)$$

Since that time there has been extensive work done in the area of gas-phase ion-molecule reactions [5-21].

The ion-molecule reactions studied in this work have been the
gas-phase proton transfer reactions between two compounds, generalized by:

\[ A^- + BH \rightleftharpoons AH + B^- \]  

(21)

and by:

\[ A + BH^+ \rightleftharpoons AH^+ + B \]  

(22)

These reactions are governed by the acid-base properties of the compounds involved. A close examination of the two classic definitions of acidity and basicity, proposed by Bronsted and Lewis, shows how these definitions relate to the gas-phase Reactions 21 and 22.

According to the Bronsted definition, an acid is a species that loses a proton and a base is one that accepts a proton [22]. This definition can be readily applied to Reactions 21 and 22. The direction of the reaction is determined by the compound with the greater tendency to accept the proton, i.e., the more basic compound [1,23,24]. Reaction 22 can also be viewed according to the Lewis definition [25]:

\[ B: + H^+ \rightleftharpoons B:H^+ \]  

(23)

Lewis proposed that an acid could be defined as an electron pair acceptor and a base as an electron pair donor [26]. The compound with an electron pair will be able to form a strong covalent bond with the proton [26] and will thus be more basic than the other compound. This view of proton exchange is useful when dealing with compounds that contain atoms with an available electron pair, such as oxygen and nitrogen.
Gas-phase determinations of a compound's intrinsic acidity or basicity is in and of itself important [24,27-29]. Moreover, gas phase measurements have been shown to correlate well with properties observed in non-aqueous solvents [23]. From acidity measurements, in particular, one can obtain much information about the extent of hydrogen bonding [23,30-32]. Also, one can determine the process and effect solvation has on these intrinsic properties [13,24,25,33-36].

Unfortunately, most acid-base studies have involved aqueous systems mainly because it was long believed that the acid-base properties of a compound in solution would be the same for that compound in the gas phase [37-43]. However, many startling results were obtained from gas-phase studies that showed the nearsightedness of this belief. One such discovery was that of toluene. In the gas phase, toluene is more acidic than water, and yet water is almost 20 orders of magnitude more acidic in solution [22,44]. Hydrogen bonding between the solvent and either the OH- or phenoxide ion stabilizes the OH- ion more than it does the phenoxide ion [45]. The effect of the stabilization due to hydrogen bonding greatly outweighs the stabilization of the phenoxide ion due to the larger polarizability of the phenoxide ion over that of OH- [45]. In the gas phase, however, the stabilization of the ions due to induced dipoles (polarizability effect) is the predominant effect, and since the benzilic C-H bond strength (85 kcal/mol) is inherently weaker than the O-H bond in H2O (119 kcal/mol) [46], toluene deprotonates more easily than H2O.

Another observation was that of t-butoxide. It too is less basic than methoxide in the gas phase while the reverse is observed in
Discoveries like these were not unique, isolated events but were instead part of a general trend that showed a fundamental difference between gas and solution phase measurements and forced attention on the need to do more gas-phase work [47-49].

B. SOLVATION EFFECTS

An example of this trend is that of the relative order of simple aliphatic alcohols in the gas phase. Their acidity order has been shown to follow their inductive or polarizability order, i.e., t-butyl alcohol > isopropyl > ethyl > methyl. Yet in solution, they follow the Baker-Natham order where methyl alcohol > ethyl > isopropyl > t-butyl [45,50,51]. Part of the reason for this reversal is the stabilizing effect of the alkyl group's polarizability. The alkyl group helps to stabilize a charge on the molecule because there is an induced dipole moment in the alkyl group [50,52-54]. Taft [51] showed, from his study of aliphatic alcohols, that the destabilization of the t-butoxide ion due to the CH₃ inductive effect is smaller than the stabilizing effect from the induced dipole moment of the alkyl groups; for t-butoxide the polarizability effect is about three times larger than the inductive effect. Hence, t-butanol, having more methyl groups than methanol, is better able to accommodate the negative charge incurred from the proton loss than is methanol, and thus accounts for the higher acidity of t-butyl alcohol compared to methanol. The stabilizing effect of the alkyl groups also accounts for the greater gas phase stability of the t-butoxide ion over the methoxide ion, hence, leading to the higher basicity of methoxide compared to t-butoxide.

In solution, however, the methoxide ion is more stable than the
t-butoxide ion, hence, methanol is more acidic than t-butyl alcohol and t-butoxide is more basic than methoxide. The order of solution acidities is due in part to the steric hindrance of the alkyl groups. This steric hindrance causes: 1) blockage of hydrogen bonding between the alcoholic hydrogen and the solvent and 2) shielding of the negative charge on the oxide ion from the solvent [55-57].

However, in measurements of relative basicities of simple aliphatic amines, the same order was obtained in the gas phase as in solution; that is, trimethylamine > dimethylamine > methylamine > ammonia [55,58]. In a later study, it was shown that in an aqueous solvent the tertiary amine is less basic than the primary amine but more basic than ammonia. Otherwise the gas phase order is obeyed [50]. This effect is due to the greater solubility of the primary and secondary amines over that of the tertiary amine. The order is highly dependent on the size of the alkyl group and the size of the solvent molecule [36,50,59].

Solvation factors account for whether or not the following solvated acid-base reactions take place [22,43,44,58,60,61]. These reactions can be viewed as the counterparts of the gas phase Reactions 21 and 22.

\[
\begin{align*}
SH + HX & \rightleftharpoons SH_2^+ + X^- \quad (24) \\
SH + Z & \rightleftharpoons ZH^+ + S^- \quad (25)
\end{align*}
\]

where \(SH\) is the solvent,
\(HX\) the acid under examination,
and \(Z\) the base.
In addition to the intrinsic acid-base property of the compound HX or Z, there are three main contributions to the determination of a compound's acidity or basicity in solution:

1) Solvent acidity-basicity.

If the solvent is very basic, HZ will donate a proton to the solvent very easily. Any acid whose strength is above a certain value will be fully deprotonated and they will all appear to have the same acidity. The solvent is said to have "leveled" the acid's power. When a different solvent is used, the relative order of these acids may change; this is called the "differentiating effect" [43,61].

2) Solvent dielectric constant (ε).

The dielectric constant of the solvent is a measure of the solvent's electrical insulating property and can influence the degree of ionization of Reactions 24 and 25. The energy needed to separate the SH$_2^+$ ion from the X$^-$ ion varies inversely with the dielectric constant [62,63]. Thus, one would expect Equation 24 to occur to a greater extent in water (ε = 80 at 25 °C) than in ethanol (ε = 24) or in benzene (ε = 2). And because the dielectric constant for benzene is so low it would also be expected that the two ions would exist as an ion pair and not as two separate solvated ions [43].

3) Specific solvation interactions.

The ion-dipole interaction between the ion and the solvent and/or the formation of hydrogen bonds between the ion and the solvent can help to stabilize the ion in solution. Because the polarizability effect is less than the effects just described, solvation can outweigh any
influences that the molecule's polarizability may have on its acid-base property. Thus, the acid-base strength order can become reversed in the gas phase. In the gas phase the polarizability effect does not compete with any solvent effects and is thus the dominant factor. However, the effect on solvation of steric hindrance, such as F-strain (caused when compounds with bulky alkyl groups come together), can inhibit solvation and may cause the polarizability effect to be the dominant force [35,43,50,55].

C. ACIDITY-BASICITY DEFINITIONS

The gas-phase acidity of a compound AH (GB(AH)) is defined as the standard free energy change (ΔG°(AH)) for the following reaction [23,64]:

\[ AH \rightarrow A^- + H^+ \] (26)

The gas-phase basicity of compound A (GB(A)) is defined as the negative of the standard free energy change (ΔG°A) for the following reaction [24,65]:

\[ A + H^+ \rightarrow AH^+ \] (27)

What are actually studied in the mass spectrometer are proton transfer reactions between two compounds of interest, such as Reactions 21 and 22. For example, Reaction 27 can be combined with the following protonation reaction of compound B to give the Reaction 22:

\[ B + H^+ \rightarrow BH^+ \quad \Delta G_B^0 \] (28)
The net standard free energy change for Reaction 22, $\Delta G_{\text{netB}}^\circ$, is then given by

$$\Delta G_{\text{netB}}^\circ = \Delta G_A^\circ - \Delta G_B^0 \quad (29)$$

and from the definition of gas-phase basicity, one can obtain

$$\Delta G_{\text{netB}}^\circ = GB(B) - GB(A) \quad (30)$$

By a similar process involving the acidity reaction (Reaction 21) and the acidity definition, one can get:

$$\Delta G_{\text{netA}}^\circ = GA(\text{AH}) - GA(\text{BH}) \quad (31)$$

and hence, $\Delta G_{\text{netA}}^\circ$ is the standard free energy change for Reaction 21.

From Equations 30 and 31, it is obvious that the net standard free energy change gives only a difference in acidity or basicity, thereby providing a relative ordering of the compounds based on their acid-base properties. In Chapter III the calculation of $\Delta G_{\text{net}}^\circ$ is explained.

To understand how absolute values of acidity-basicity are obtained, it is necessary to know how $\Delta G_{\text{net}}^\circ$ relates to other thermochemical data through thermodynamic cycles [23]. Compounds subjected to extensive measurements, other than just mass spectrometric proton transfer reactions, provide these thermochemical data and thus are used as absolute reference standards [65].

The thermochemical cycle involving acidity reactions is:
\[
\begin{align*}
\text{IP(H)} & \quad \text{H} + \text{A}^\cdot \longrightarrow \text{H}^+ + \text{A}^\cdot + e^- \\
D(\text{H-A}) & \quad \downarrow \quad \text{H} \quad \text{D}(\text{H-A}) \quad -\text{EA}(\text{A}^*) \\
\text{HA} & \quad \text{HD}(\text{HA}) \quad \downarrow \quad \text{H}^+ + \text{A}^- \\
\end{align*}
\]

where \( \text{IP(H)} \) is the ionization potential of hydrogen, \( \text{EA}(\text{A}^\cdot) \) the electron affinity of the radical \( \text{A}^\cdot \), \( \text{D}(\text{H-A}) \) the bond dissociation energy of \( \text{HA} \), and \( \text{HD}(\text{HA}) \) the heat of deprotonation of Reaction 26.

The heat of deprotonation is the standard enthalpy of Reaction 26 (\( \Delta H^\circ_{\text{HA}} \)) and, in general, is endothermic by about 300-400 kcal/mol and, therefore, is not directly observed in the mass spectrometer [23]. The measurement of \( \Delta G^\circ_{\text{netA}} \), however, is observable and can be related to the net heat of deprotonation by:

\[
\Delta G^\circ_{\text{netA}} = \Delta H^\circ_{\text{netA}} - T \Delta S^\circ_{\text{netA}} \quad (33)
\]

The entropy changes are commonly approximated by the isoelectronic estimation method where it is assumed that the entropy of the anion is the same as the experimentally measured entropy of the isoelectronic neutral [47,48,66]. Isoelectronic compounds have the same number of electrons and differ only in the charge on their nuclei, e.g., \( \text{NH}_4^+ \), \( \text{CH}_4 \) [67]. Since, in general, the ionization potential of hydrogen is well known (13.595 eV)[46], and since there are extensive tables of bond dissociation energies [68-70] and electron affinities [71,72], the uncertainties in the assignment of absolute acidities is small [23,65].
Unfortunately, as one will see from the thermodynamic basicity cycle, the error in absolute basicities is larger than for the acidities [23,65].

The thermodynamic cycle involving basicity determinations is [23]

\[
\begin{align*}
\text{IP}(B) & \quad \text{IP}(H) \\
B^+ + H & \quad B^+ + H^+ + e^{-} \\
\downarrow D(B^+-H) & \quad \downarrow \text{IP}(B) \\
BH & \quad PA(B) \\
& \quad B + H^+
\end{align*}
\]

(34)

where \(\text{IP}(B)\) is the ionization potential of compound B,
\(D(B^+-H)\) the bond dissociation energy of \(BH^+\),
and \(PA(B)\) the proton affinity of compound B.

The proton affinity of B is defined as the negative of the standard enthalpy change (\(\Delta H^\circ_A\)) for Reaction 27. The difference between the proton affinities of compounds A and B (\(\Delta H^\circ_{\text{netB}}\)) can be determined from a mass spectrometric temperature variation experiment, which will be described in Chapter III. \(\Delta G^\circ_{\text{netB}}\) can usually be determined more easily than the proton affinity difference and is related to the net enthalpy change by the following:

\[
\Delta G^\circ_{\text{netB}} = \Delta H^\circ_{\text{netB}} - T\Delta S^\circ_{\text{netB}}
\]

(35)

The entropy change in the equation above can be estimated from that part of the partition function that has to do with rotational entropy changes as calculated from the symmetry change of the molecule as it undergoes protonation [65,73-77]:
\[
\Delta S_{\text{rot}} = R \ln \frac{\sigma(\text{AH}^+) \cdot \sigma(\text{B})}{\sigma(\text{BH}^+) \cdot \sigma(\text{A})}
\]

where \( \sigma \) is the molecule's symmetry number (the number of pure rotational elements, including the identity element) in the point group of the molecule \([73]\). This method of entropy calculation can also be used to calculate \( \Delta S_{\text{net}} \) in Equation 33 and gives a value that agrees well with the isoelectronic estimation method \([66]\).

In dealing with basicities, the thermodynamic cycle is given by the following \([58,78]\):

\[
\text{PA}(\text{B}) = \Delta H^o_f(\text{B}) + \Delta H^o_f(\text{H}^+) - \Delta H^o_f(\text{BH}^+)
\]

The heat of formation of \( \text{B} \) \( (\Delta H^o_f(\text{B})) \) has been reported in many sources \([65,69,70]\). To set a value for the heat of formation for the proton \( (365.7 \text{ kcal/mol}) \), the assumption was made that the integrated heat capacity of the electron is zero at all temperatures except zero Kelvin (stationary electron model)\([65]\). The values of \( \Delta H^o_f(\text{BH}^+) \) are often obtained by electron impact or photoionization appearance potential measurements of \( \text{BH}^+ \) fragments from large molecules \([79,80]\):

\[
\text{M} \xrightarrow{\text{e}^- \text{ h}\nu} \text{BH}^+ + \text{X} + \text{ne}^-
\]

The problem in these measurements is identifying the exact threshold energy that leads to \( \text{BH}^+ \) formation. Although the thermodynamic data on \( \text{M} \) and \( \text{X} \) is well known, this uncertainty in the value of \( \Delta H^o_f(\text{BH}^+) \), or \( D(\text{B}^+-\text{H}) \) in Equation 34, leads to the larger uncertainty in assignments of absolute basicities over those in absolute acidities \([23]\). Thus, the inherent errors in the values calculated for the various thermodynamic
properties in these cycles determine the uncertainties in the reference standards used to establish absolute acidity-basicity scales from the relative values determined in the mass spectrometric proton transfer reactions.

D. INSTRUMENTATION

Gas-phase transfer reactions have been studied since the late 1960's and early 1970's by three principal methods, which in general give values that agree well [23, 25, 51]:

1) High pressure mass spectrometry (HPMS) [81-84],
2) Flowing afterglow and selected ion flow tube (SIFT) [49, 85-88],
3) Ion cyclotron resonance mass spectrometry - conventional (ICR) and Fourier transform (FT/ICR, FTMS) [28, 29, 89-91].

The HPMS system consists of a chamber where the reactant gases, at several mTorr up to one Torr, are mixed with a buffer gas at 3 to 10 Torr; see Figure 15. The ions are formed by impact with high energy electrons (2 KeV), which are pulsed for about 10-20 microseconds. The ions diffuse through a field free region and pass through slits into the low vacuum chamber, about $10^{-4}$ Torr, where they are accelerated into the analyzer and detected. Since the ratio of ion concentrations in the HPMS can be measured as a function of time, one can do equilibrium experiments. Also, such information as equilibrium constants and forward and reverse rate constants can be obtained.
Figure 15. Block diagram of a typical high pressure mass spectrometer ion source and accelerator.
HPMS has the advantages that a well defined reaction temperature is easy to achieve and that the ions are thermalized by collisional relaxation in a short time because of the high pressure. The main disadvantages of HPMS are: 1) mass discrimination inherent to the system because of the use of slits for ion sampling, 2) collision induced ion decomposition of the ion on its way to the detector because of ion acceleration in the high voltage area, and 3) condensation and clustering reactions due to the high pressure of the system, e.g., proton dimer formation, which interferes with the equilibrium proton transfer reaction. Although the first two problems are not easy to correct for, the third problem can be prevented by running the experiment above 600 K [25].

In the flowing afterglow experiment, see Figure 16, the first reactant is admitted, at a pressure of 0.1 Torr, into the source end of the long flow tube (usually 100 cm long). The ions are formed by a hot cathode discharge, about 50-100 eV for example; the ions are thermalized by the presence of a buffer gas, which is at a pressure of about 0.1 to 5 Torr, in the area where the reactant is admitted. As the ions migrate down the tube, other neutral reactants can be added (at 0.1 Torr) at various points along the tube. Ion-molecule reactions take place as these ions move down the tube (about 10^{-2} s). The final reaction products are detected by standard quadrupole filter-particle counter techniques at the downstream end of the flow tube. Because the ions are detected only at the end of the tube, only the total extent of the reaction is directly observable.
Figure 16. Schematic diagram of a typical flowing afterglow apparatus.
Flowing afterglow offers the advantage that the ions carry no excess energy into the reaction section since they are well thermalized before they interact with the reactants. The main disadvantage of this technique, however, is that just as in HPMS many condensation products can form because of the high pressure. Furthermore, any effects from the formation of multiple primary ions--ions formed before the reaction section of the flow tube--and any reaction intermediates are difficult to ascertain because the ions are detected only at the end of the tube.

To study complex reactions, one can employ a technique called SIFT (selected ion flow tube); see Figure 17. By adding a quadrupole mass filter between the ion formation region and the reaction region, one can allow only one ion at a time to pass into the reaction region. Each time the experiment is repeated, a different ion is passed into the reaction region. Thus, the mechanism for the complex reaction can be pieced together by studying each of these individual reaction steps. Although the ion abundance ratios are not directly observed, the equilibrium constants for proton transfer reactions can be determined because the forward and reverse reaction rate constants can be measured separately.

The basic theory of conventional ICR and FT/ICR has been covered in Chapter 1. Equilibrium measurements can normally be made easily with the ICR technique. The drift cell is useful for rapid determinations of fast proton transfer reactions, and since the drift cell can be operated at pressures of $10^{-4}$ to $10^{-5}$ Torr, the ions can be thermalized fairly quickly. The trapped ion cell is useful for both fast and slow reactions and is particularly useful for slow reactions since the ions can be trapped for a period of many seconds. The low pressure in the trapped
Figure 17. Schematic diagram of a selected ion flow tube (SIFT) apparatus. Single ionic species are injected into the flowing buffer gas by the quadrupole filter at the left.
ion cell (10^-7 to 10^-9 Torr) also eliminates many of the problems associated with dimer formation and other condensation products; the hydrogen bound dimers do not undergo enough collisions at these low pressures to help eliminate their excess energy, and thus, they fall apart before they can interfere in the proton transfer reaction [24].

Due to the low pressures used in the trapped ion cell, sufficient time must be allowed to insure that enough collisions have happened to establish equilibrium and to thermalize the ions [92]. Because of this longer observation time, slow protonation reactions can present a problem when nonreactive ion losses compete for the ions involved in the main reaction [1,23].

The selective ion ejection capability of the ICR is very important in the study of proton transfer reactions. This technique can be used to determine whether a particular reaction occurs, to determine the direction of the reaction, or to check for possible side reactions. Also, one can check that equilibrium has been reached by perturbing the reaction and seeing if equilibrium is reestablished from both directions. In addition, when an ion is continuously ejected during the course of the reaction, the forward and reverse pseudo-first order rate constants can be determined and used to calculate the reaction equilibrium constant. For a further description of these ion ejection techniques see Chapter III.
REFERENCES


CHAPTER III

EXPERIMENTAL DETERMINATION OF GAS-PHASE ACIDITIES AND BASICITIES USING A NICOLET FTMS 1000 ION CYCLOTRON RESONANCE MASS SPECTROMETER

A. INTRODUCTION

There are many problems associated with the determination of gas-phase acidities and basicities. None are so troublesome as: 1) vaporizing enough sample, and 2) maintaining a steady pressure long enough to measure the thermodynamic properties of the proton transfer reactions being studied. In this chapter a discussion will be given of the problems, procedures, and needed equipment associated with sample introduction. Next, the experimental procedures for generating the ions and for measuring the pressure and temperature of the reaction will be given in detail. A description of the bracketing and equilibrium methods used to make the acidity-basicity measurements will conclude this chapter.

B. EXPERIMENTAL PROCEDURES

1. SAMPLE INTRODUCTION

The method of sample introduction depends on whether the sample is
a gas, liquid, or solid. Gases are handled in a straightforward manner: the gas, from either a gas collecting tube or a gas cylinder (equipped with a pressure regulator), is connected directly to the batch inlet system; see Figure 8. The inlet lines are pumped down and purged with gas to remove any air. The gas is then leaked into the system through a precision leak valve: a Varian model 951 valve (standard equipment on this ICR), and a Whitey SS-22RS4 valve (which was added to increase the system's capacity and flexibility). All valves and lines are heated to prevent condensation of samples. Sometimes it is desirable to introduce the compound in well defined pulses rather than as a continuous injection; one can do this by using a pulsed valve (General Valve series 9 pulsed valve). The valve is computer controlled and activated. Of the three states (gases, liquids, and solids) gases are, by their very nature, the easiest to introduce into the system.

Liquid samples, however, are also relatively easy to work with. Less than 0.1 ml of the sample is placed in a glass vial which is then attached to the batch inlet system. To insure that the volatile impurities have been removed from the sample, one should subject the sample to several cycles of freezing (in liquid nitrogen), pumping, and thawing. This procedure is repeated until there is no change in the pressure gauge (Granville-Phillips series 275 vacuum ConveXatron gauge) that monitors the batch inlet system. It usually takes about three such cycles to remove the impurities.

Solids are without question the hardest of the three states to work with. Although most solids are not volatile under the conditions under which this work was done, those that are can be introduced through
the batch inlet system. In general, compounds that have high volatility at room temperature, such as cubane and adamantane, can be handled like a liquid. Others, such as 4-methoxyphenol, that have a melting point between room temperature and about 140 °C can be melted and then treated like a liquid. Between 10 and 100 mg of sample is placed in a glass vial, which is attached to the inlet system, pumped down, and then heated (with heating tape wrapped around the vial) until the solid melts.

Those solids with melting points above 140 °C (the maximum temperature on the inlet system) must be introduced using a solid sample probe; see Figure 18. A capillary tube about 0.25" long, containing 10 to 500 µg of sample, is placed in the tip of the probe and secured with a set screw. The probe is introduced into the vacuum system and brought into contact with the cone of the cell. The probe is equipped with a heater and a platinum resistance thermometer. When the probe tip is heated the sample vaporizes, and the gases enter the cell (where they are ionized) through a hole in the trapping plate; see Figure 19.

2. ION FORMATION

Once the compound is in the gas phase, either the protonated parent cation (for a basicity study) or a deprotonated parent anion (for an acidity study) must be formed. There are two ways of obtaining the protonated parent ion: 1) self-protonation, or 2) protonation by a buffer gas; when needed in most of these studies, methane was used as the buffer gas.

Self-protonation occurs in the following way. The radical cation
Figure 18. Detail showing the probe tip that holds the capillary tube containing the sample.
Figure 19. Detail showing the placement of the probe tip in the cone when in position. The vaporized sample enters the cell through the hole in the trap plate. The cone is electrically isolated from the trap plate.
parent is formed directly from the neutral parent by electron impact. These ions are very acidic and protonate the neutral parent very easily by the following reaction [1]:

\[ M^{+*} + M \rightarrow MH^+ + (M-H) \]  

Ideally, this self-protonation should be quick relative to the time the compounds react so that a good population of protonated parent ions can be built up. To verify that the compound will indeed self-protonate in a short time, one should always run a pure sample first. Figure 20 shows an example of a compound that self-protonates quickly, and Figure 21 shows a compound that under identical conditions does not self-protonate. If there is insufficient self-protonation, a check is made to see if introduction of methane will help protonate the compound. Methane self-protonates very well, and because methane has a very low basicity [2], it will usually transfer a proton to the other compound [1]. Methane can be introduced continuously, or it can be introduced in pulses; low methane concentration minimizes side reactions with the sample. This pulsed valve technique is used only when side reactions are observed, since this method is a more complicated and time consuming procedure than the continuous introduction method.

A typical experimental pulsed valve sequence is shown in Figure 22. Methane is admitted into the system during the QND event, and the time delay DL5 is adjusted so that the pulse maximum arrives when the electrons are going through the cell. The results of a study of the effect of pulsed valve period (QND) and delay (DL5) on pulse travel time is shown in Figure 23; when a narrow pulse is used (QND=10 msec) and
Figure 20. ICR peak area vs. time for isopropyl ether, a compound that undergoes very fast self-protonation to form the protonated ether ion $C_6H_{15}O^+$. Pressure was $2 \times 10^{-7}$ Torr.
Figure 21. ICR peak area vs. time for benzene, a compound that does not undergo self-protonation. Experimental conditions as for isopropyl ether shown in Figure 20.
Figure 22. A typical experimental sequence that would be used when operating with the pulsed valve. All pulse and interval durations can be computer controlled.
Figure 23. ICR signal magnitude vs. pulsed gas introduction period (DL5) for various pulse durations (QND).
when the electron beam is fired immediately after the pulsed valve closes (DL5 = 0), insufficient time has been allowed for the pulse gas to travel to the cell and, therefore, one does not see a signal for argon (the maximum signal occurs when DL5 = 60 msec). The pulsed valve is positioned so that there is a roughing valve between the pulsed valve and the leak valve; see Figure 24. By adjusting the leak rate, pulsed valve working time, and the rate at which the excess sample is pumped away through the roughing valve, one can regulate the pressure burst to get a pressure of between 10\(^{-6}\) to 10\(^{-7}\) Torr during the ion formation event. During the time delay DL6 event, all neutral methane is pumped away from the cell.

The deprotonated anions cannot be formed by electron impact in as straightforward a manner as were the protonated cations [3,4]. Methyl nitrite is used to deprotonate the parent compound. Methyl nitrite is introduced into the cell where it forms methoxide ions by electron impact (0.2 eV) [5]:

\[
\text{CH}_3\text{ONO} + \text{e}^- \rightarrow \text{CH}_3\text{O}^- \quad (40)
\]

\[
0-0.2\text{eV} \quad (m/z = 31)
\]

These ions easily abstract protons from most organic compounds [4,6].

\[
\text{CH}_3\text{O}^- + \text{AH} \rightarrow \text{A}^- + \text{CH}_3\text{OH} \quad (41)
\]

Figure 25 shows a reaction of the methoxide ion with 4-methoxyphenol. A large population of deprotonated anion is formed within about 150 msec,
Figure 24. Block diagram showing the placement of a roughing valve between the leak valve and the pulsed valve. The roughing valve is used to pump away the excess gas that accumulates during the time between pulses.
Figure 25. ICR peak area vs. time for the reaction of methoxide ion and 4-methoxyphenol:

\[
\text{CH}_3\text{O}^- + \text{C}_7\text{H}_8\text{O}_2 \rightarrow \text{CH}_3\text{OH} + \text{C}_7\text{H}_7\text{O}_2^-.
\]

The partial pressures of CH$_3$ONO and 4-methoxyphenol are 1x10$^{-8}$ and 1x10$^{-7}$ Torr, respectively.
and, to reduce the chance of side reactions, one can eject the small amount of methoxide leftover.

The procedure used to generate the methyl nitrite gas was first reported by Bartmess [7] and modified in this study. 90 µl of methanol is placed in a glass side arm vial attached to the inlet system, frozen, and pumped down. The vial is covered at all times with aluminum foil to protect the light sensitive isoamyl nitrite. The vial is kept under vacuum and 10 µl of isoamyl nitrite is syringed into the vial through a rubber septum cap. At first both the methyl and the isoamyl nitrite are present as gases in the vial, thus accounting for the methoxide (m/z = 31) and the isopentoxide (m/z = 87) peaks. After about one hour the methoxide is the predominant ion in the cell.

A further modification of the methyl nitrite generation procedure produces abundant methoxide ion within minutes. This procedure involves freezing the solution (after the introduction of the isoamyl nitrite) and pumping away any unreacted isoamyl nitrite results within about two minutes in a spectrum of predominately methoxide ion; see Figure 26. Bartmess suggests that the methyl nitrite has a lower vapor pressure than isoamyl nitrite and, thus, is formed in greater abundance [7].

The methyl nitrite leaks continuously into the cell at a very low rate. At this point samples can be introduced as previously discussed. If the methoxide ion is not basic enough to efficiently produce the deprotonated hydrocarbon anion from very weak acids such as saturated hydrocarbons, the amide ion (NH$_2^-$), formed by electron impact of ammonia (at about 6 eV) [5], can be used to abstract the proton from the hydrocarbon samples, thereby producing the deprotonated anions
Figure 26. FT/ICR mass spectra showing the relative abundances of the CH$_3$O$^-\text{ion}$ at m/z = 31 and C$_5$H$_{13}$O$^-\text{ion}$ at m/z = 87. A) 5 minutes after the start of Reaction 42. B) 1 hour after the reaction starts. C) 2 minutes after the reaction starts using the freeze-pump method.
needed [8]:

$$\text{CH}_3\text{OH} + (\text{CH}_3)_2\text{CHCH}_2\text{CH}_2\text{ONO} \rightarrow \text{CH}_3\text{ONO} + (\text{CH}_3)_2\text{CHCH}_2\text{CH}_2\text{OH} \quad (42)$$

3. ION EJECTION

One of the features of ICR mass spectrometry that makes it a powerful tool in the study of gas-phase reactions is its ion ejection capability; see Chapter I for description of ion ejection. Recall that the ions of a given frequency (mass-to-charge ratio) can be ejected while the other ions will not be affected since they are not at that resonance frequency. However, the frequency range should be chosen as narrow as possible since ions close in frequency to the ions being ejected can be influenced. To minimize this effect and to get complete ion ejection, one must adjust the radiofrequency pulse height (the power level) and the pulse width (the time the power is left on); see Figure 27. These parameters have to be readjusted for each new set of reactants. It should be noted that for a given frequency window width, the window will cover a larger mass range at high mass than it will at low mass.

When working with negative ions, as in acidity studies, one would like to eject electrons from the cell since they 1) might, under certain conditions, form anions that can compete in the acidity reactions, and 2) cause inaccurate ion intensity measurements due to ion cloud distortion caused by the space charge effect of the excess electrons [4]. If the resonance frequency of an electron (55GHz) [10] was not so
Figure 27. Effect of time-domain pulse width, $T$ (sec), frequency-domain spectral width, $\Delta \omega = 3.8/T$ (sec$^{-1}$)(from Reference [9]).
great as to be beyond the range of our electronics, the electrons could be ejected by the radial ejection technique described above. However, a different technique of charge particle ejection, based on axial ejection, can be used [11]. A frequency corresponding to the electron trapping frequency (which corresponds to oscillating electron motion parallel to the axis of the magnetic field) is applied to the trap plates, and the electrons are ejected when they hit these plates; see Figure 5 and 9. The needed electronic circuitry (unavailable on this ICR) was designed and built by Tom L. Ricca (Campus Chemical Instrument Center of The Ohio State University). Leaving the trapping potential (dc potential of minus one volt) unaffected, the new circuit switches in (computer controlled) and superimposes upon this dc voltage a several volt peak-to-peak oscillating field, see Figure 28, at the electron trapping frequency of about 6 MHz [10]. Since the trapped ion ICR frequencies differ from this frequency, and because there is still a negative dc potential at the trap plates, only electrons are ejected.

Using this axial ejection circuitry, I am able to completely eject H$_2$O$^+$ (at 6 V p-p) with little effect on the neighboring ions of N$_2^+$ and O$_2^+$; see Figure 29. Since this circuitry is designed to work optimally at high frequency (about 6 MHz), the ejection waveform for H$_2$O$^+$ (at 34 KHz) is not ideally sinusoidal. Since the electrons are ejected at high frequency, and since the trapping frequencies of the ions in the cell are about 10$^3$ times lower than that of the electron, there is no interference with these ions. Figure 30 shows a proposed method for electron measurement after the BEM event is off; the required circuitry
Figure 28. A) Trap voltage configuration for a normal experiment.
B) 6 MHz oscillating voltage is applied to the trap plates during electron ejection. The -1 V dc potentials are applied continuously to prevent ion loss.
Figure 29. FT/ICR mass spectra showing the axial ejection of water (m/z = 18) at 34 KHz trapping frequency. The three spectra are at the following power levels: (Top) 0 V, (Middle) 2 V, (Bottom) 6 V.
Figure 30. A) Trap voltage configuration for a normal experiment. B) Voltage configuration for measuring the electron current at the collector.
is being built and will be used routinely in experiments where complete
electron ejection must be confirmed. The experimental sequence used for
routine electron ejection is shown in Figure 31.

4. TEMPERATURE AND PRESSURE DETERMINATIONS

The cell temperature is regulated by the main chamber dc heaters.
The large volume of the main chamber helps keep the cell temperature
constant to within 1-2 °C over 5-6 hr. The chamber heater is very
efficient, easy to control (by an Omega 4001JC controller), and variable
from 30 to 350 °C. The absolute temperature of the cell is measured by
a wire wound platinum resistance thermometer, which is accurate to
within ± 1.8 °C at 300 °C [12]. This thermometer has been mounted free
so that it will respond quicker to temperature changes than if it were
mounted in a metal block that can retain heat. A type J Iron-Constantan
thermocouple measures the main chamber temperature.

The cell temperature must remain constant throughout the
experiment, and all experiments are run at a temperature of at least
150 °C. This temperature level takes into account the heating effect
due to the electron filament. This filament alone can heat up the cell
to 80-110 °C depending upon the amount of current supplied; as a rule,
the older a filament is, the higher the filament current needed. Thus,
the effect of filament heat becomes negligible when the experiment is
run at 150 °C or more since the temperature is being stabilized by the
main chamber heaters.
Figure 31. A typical experimental sequence used for electron ejection.
The cell pressure is measured using a nude Bayard-Alpert ionization gauge, mounted 1 m away and at right angles to the cell (this mounting configuration minimizes the interference in the pressure measurement from the strong magnetic field found at the cell).

Now that the sample has been introduced, and after the temperature and pressure have stabilized, one is ready to start the experimental methods for acid-base gas-phase determinations. By "bracketing" the unknown compound with compounds of known acidity-basicity, one can get an approximate value of its acidity-basicity. Knowing this approximate value, one can later make a more accurate determination by an equilibrium study.

C. BRACKETING EXPERIMENTS

The first bracketing experiments were conducted by Munson who was studying the relative basicities of various polar organic compounds [13]. His experiment centered around the concept that ion-molecule reactions occurring in a mass spectrometer proceed with no or very little activation energy [1]; therefore, the observed reactions are either thermoneutral or exothermic [14-16]. With this criterion and the following equations and reactions

\[ B + H^+ \rightarrow BH^+ \] (43)

\[ \Delta H^\circ_{rx} = \Delta H^\circ_f(BH^+) - \Delta H^\circ_f(H^+) - \Delta H^\circ_f(B) \] (44)

\[ PA(B) = - \Delta H^\circ_{rx} \] (45)
an upper bound can be set on the heat of formation, \( \Delta H_f^0(BH^+) \) of the BH\(^+\) ion, and since the heats of formation of the other species are known, a lower bound on the proton affinity of B, PA(B), can also be set [13].

There are, however, several occasions when a bracketing experiment is needed. Bracketing, as already mentioned, is useful for a quick approximation of the acidity-basicity of the unknown compound. Furthermore, when the partial pressures of the compounds cannot be accurately determined, as is sometimes the case for solid samples, the equilibrium method cannot be used. Thus, the only values one can get are by bracketing the sample between compounds of known acidity-basicity. Also, if the protonated parent ion (BH\(^+\)) undergoes either a fast reaction with the parent compound or some alternate side reaction, it may be impossible to establish an equilibrium proton transfer reaction with the reference compound [2].

The main complication of the bracketing experiment occurs when there is an energetically more favorable path available for the reactants to take rather than the exothermic proton transfer reaction path. Care must be taken to insure that the protonated parent ion is actually the product of the proton transfer reaction. Ion ejection can verify whether the reaction is proceeding in the direction predicted when one path is exothermic and the other endothermic. Also, ion ejection can verify if there are any competing side reactions.

Experimentally, after the electron impact and self-protonation steps, neutral species (A and B) and protonated parent ions (AH\(^+\) and BH\(^+\)) are present in the cell. Allowing all of them to react in one
experiment would be equivalent to seeing which reaction, 46 or 47, is the dominant path.

\[
A + BH^+ \xrightarrow{?} AH^+ + B \quad (46)
\]

\[
A + BH^+ \xleftarrow{?} AH^+ + B \quad (47)
\]

In addition to this experiment, each protonated parent is ejected, before any reactions take place, in two separate experiments [17].

\[
A, B, AH^+ \xrightarrow{} N. R. \quad (48)
\]

\[
A, B, BH^+ \xrightarrow{} AH^+ \quad (49)
\]

Suppose that Reaction 48 occurs after BH\(^+\) is ejected. Since there is no BH\(^+\) formed, B must be less basic than A. Next, as a verification step, AH\(^+\) is ejected in Reaction 49. Since AH\(^+\) is again the product formed, B must indeed be less basic than A. The experiment is continued by reacting A with different reference bases until compound C is found such that it is more basic than A.

\[
AH^+ + C \xrightarrow{} CH^+ + A \quad (50)
\]

The basicity value of A lies somewhere between the values of B and C, the two bracketing reference compounds [13,18] see Figures 32 and 33. At best, the bracketing method can give only relative values for a determination of the true acidity-basicity. The equilibrium constant for the transfer reaction must then be determined [2,19].
Figure 32. FT/ICR negative-ion mass spectra from the bracketing experiments, showing that uracil is more acidic than 4-methoxyphenol (Top) and less acidic than difluoroacetic acid (Bottom). These experiments were done at $10^{-7}$ Torr and at a reaction time of 5 seconds. The direction of the reaction was verified by ion ejection of the deprotonated ions.
Figure 33. FT/ICR mass spectra of approximately equal amounts of uracil and 5-fluorouracil. Top spectrum is from the reaction:

\[ \text{FU} + U^- \xrightarrow{\text{reaction}} U + FU^- \]

Bottom spectrum is from the reaction:

\[ U + FU^+ \xrightarrow{\text{reaction}} FU + UH^+ \]
D. EQUILIBRIUM EXPERIMENTS

The equilibrium experiments are based on the determination of various thermodynamic parameters for the proton transfer reaction of unknown compound (A or AH) with a reference compound (B or BH)

\[ A + BH^+ \rightleftharpoons AH^+ + B \]  
\[ A^- + BH \rightleftharpoons B^- + AH \]

The standard free energy change for the above reactions is given by

\[ \Delta G^0_{rx} = -RT \ln K_{eq} \]  

where the equilibrium constant is either

\[ K_{eq} = \frac{[B][AH^+]}{[A][BH^+]} \]  
\[ K_{eq} = \frac{[B^-][AH]}{[A^-][BH]} \]

One can then relate these reaction free energy changes to the acidity-basicity difference by Equations 30 and 31.

1. TEMPERATURE DEPENDENCE OF THE EQUILIBRIUM CONSTANT

As one can see from Equation 53, the temperature must be accurately known, and should remain constant throughout the experiment. Therefore, all equilibrium reactions are carried out at one
temperature; for example, all the cubane and dodecahedrane work was done at 155 °C. The equilibrium constant is also temperature dependent

\[
\ln K_{eq} = -\frac{\Delta H_0}{RT} + \int_0^{T_1} \Delta C_p dT \tag{56}
\]

where \(\Delta H_0\) is the heat of reaction at zero Kelvin, \(\Delta C_p\) the change in heat capacity from zero to temperature \(T_1\), and \(T_1\) the temperature of the reaction.

The contribution to the change in \(K_{eq}\) with temperature from the heat capacity integral in Equation 56 is typically negligible when compared to the change in \(\Delta G^0\) occurring directly from the change in temperature.

For enthalpy changes of 0.5-3 kcal/mol, the error in \(K_{eq}\) due to temperature variations of 400-600 K is about ±0.2-0.9%. The corresponding error in the basicity determinations is about ±0.02 to 0.07 kcal/mol. Temperature enters into the rate constant determination when the equilibrium constant is calculated from the ratio of the forward to reverse rate constant for the Reactions 51 and 52. The temperature dependence of the rate constant is given by the generalized Arrhenius equation [20]

\[
k = A T^n \exp(-E_a/RT) \tag{57}
\]
where \( k \) is the specific rate constant, 
\[ A \] the pre-exponential factor, 
\[ E_a \] the activation energy, 
and \( n \) is determined experimentally.

2. PARTIAL PRESSURE CORRECTIONS

The concentrations of the neutral compounds \( A \) and \( B \) can be determined from their partial pressures measured with a nude Bayard-Alpert hot cathode ionization gauge; see the schematic diagram shown in Figure 34. This gauge operates by emitting electrons from a cathode filament (+30 V); these electrons accelerate toward the anode (+180 V). The anode forms a cylinder of spiral wire filament around the thin wire collector (0 V). The ion current is proportional to the ion number density, which in turn is proportional to the pressure [21]. An absolute pressure measurement using this gauge is subject to a 50-100% error [21]. Calibrating the gauge helps to minimize this error; however, at low pressures, the error can still be quite large, up to 30% [22]. The absolute pressure, important in the measurement of absolute rate constants, is, however, not needed in this study. Fortunately, determination of the pressure ratio in Equation 53 or the ratio of the specific rate constants, requires only the ratio of partial pressures of the neutrals [23].

For equilibrium methods, two precautions must be taken into account with the ionization gauge. First, the gauge surfaces must be "degassed" of any adsorbed material. Adsorbed material will cause a pressure burst.
Figure 34. Typical hot cathode Bayard-Alpert ionization gauge. The collector monitors the current from the ions generated by electron impact of the neutral gas.
when it is ejected from the surface during electron impact. This adsorbed material is baked off by passing a large current through the gauge's anode (degassing). This procedure is repeated until the gauge pressure returns to the background pressure within 2-3 min after turning off the current.

The second and most important precaution is to take into account the pressure corrections that are needed for different chemical sensitivities toward ionization. The amount of ion current needed for electron impact depends upon the nature of the gas, since different compounds have different ionization sensitivities [21,23]. The absolute chemical sensitivity of a gas can vary by 30% or more depending on the gas and the gauge construction [24]. However, by using a ratio of the compound's chemical sensitivity to that of nitrogen, a common gas used in gauge calibrations, one can reduce the variation in ratio to only about 7% [23] for the following equations

\[ R_X = \frac{S_X}{S_{N_2}} \]  

\[ P_{true} = \frac{P_{obs}}{S_X} \]  

where \( R_X \) is the relative sensitivity of compound \( X \) and \( S_X/ S_{N_2} \) is the ratio of absolute sensitivities of compound \( X \) (\( S_X \)) and that of nitrogen (\( S_{N_2} \)). The true pressure (\( P_{true} \)) is the observed pressure (the actual gauge reading, \( P_{obs} \)) divided by the absolute chemical sensitivity of the gas being measured. The partial pressure ratio of \( P_1 \) to \( P_2 \) is given by
The remaining parameter to be calculated is the relative sensitivity of the compounds used. For most compounds, this value can be determined by the method, developed by Bartmess [23], which is based on the relationship

$$R_x = 0.36\alpha + 0.3$$  \hspace{1cm} (61)

where $\alpha$ is the compound's molecular polarizability. This polarizability can be calculated by either of two methods. One method, developed by Miller and Savchik, uses the calculation based on the average molecular polarizability [25],

$$\alpha = \frac{4}{N} \cdot (\Sigma \tau_A)^2$$  \hspace{1cm} (62)

where $\tau_A$ is the atomic hybrid component, and $N$ the total number of electrons in the molecule.

It should be noted that this method is not just an addition of atomic polarizabilities but takes into account the hybrid state of the atoms, and therefore, the molecule's bonding character. This method has been shown to give values that agree well with experimental values [25].

The other method, developed by Otvos and Stevenson, uses the mean square radius of a compound's valence electrons as a measure of the
compound's polarizability [26]. From Table 4, one can compare the values obtained from both methods. Cubane and styrene, C9H8 isomers, are very different in their bonding and valence electron characteristics, and it is reasonable to expect that their chemical sensitivities would be different. Since the method of Otvos and Stevenson does not take bonding characteristics into account, the difference in relative sensitivities does not show up as it does in the Miller-Savchik method.

Table 4. Relative ionization sensitivities

<table>
<thead>
<tr>
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<th>MILLER-SAVCHIK METHOD</th>
<th>OTVOS-STEVENSON METHOD</th>
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</thead>
<tbody>
<tr>
<td>CUBANE</td>
<td>6.509</td>
<td>5.520</td>
</tr>
<tr>
<td>STYRENE</td>
<td>5.294</td>
<td>5.520</td>
</tr>
</tbody>
</table>

The actual mechanics of calculating the partial pressures of the samples with one ionization gauge is relatively easy for samples that are sufficiently volatile to be introduced through the batch inlet. Compound A is leaked into the system and allowed to stabilize. Since it is the only compound in the system, the pressure reading of the ionization gauge represents the initial partial pressure (P_A^0) of the compound. Next, compound B is leaked in, and the pressure is again
allowed to stabilize. The pressure reading \((P_T)\) is now the sum of the partial pressures of A and B. Accordingly, the partial pressure of B \((P_B^0)\) is the difference between \(P_T\) and \(P_A^0\). One can determine the partial pressure of B at the end of the experiment by shutting off A; the resulting pressure reading being, therefore, due only to compound B. During the experiment, the pressure is closely monitored and if it fluctuates by more than 5-10% of the initial pressure, the measurement is stopped. The leak valve from B is closed to see if the pressure from A is the same as it was at the beginning of the experiment. If it is the same, the flow rate of B has to be readjusted; if it is not, the entire process must be repeated. When \(P_T\) does not change during the experiment, and if \(P_B'\) is different from \(P_B^0\), an average partial pressure for each compound is reported. The error in the final value of the standard free energy of Equation 53 is about 0.1 kcal/mol for those samples introduced through the leak valves.

For those samples that cannot be introduced via the batch inlet system, the partial pressure determinations are less straightforward and are more difficult than the procedure just described. One can expect errors of 20-60% in the partial pressure measurements; these errors carry over into the free energy calculations as an error of about 0.2-0.7 kcal/mol. There are two main reasons why these solids are difficult to work with: 1) it is difficult to maintain a steady pressure, and 2) it is difficult to determine their partial pressures accurately.

The worst scenario occurs when both A and B are solids and must be
introduced via the solids probe. The problem of maintaining a steady sample pressure depends upon how well the temperature of the probe tip can be controlled. Since the probe heater control is very poor, it is difficult to maintain a steady pressure. If a steady pressure can be maintained, one can determine, from the positive ion spectra, the relative partial pressures of A and B from the relative peak intensities of the parent ions. This procedure has the advantage of being fast and easy; however, it also suffers from two complications:

1) If the two compounds have vastly different volatility, one will volatilize completely before the other. A satisfactory solution to this problem was developed. A stainless steel sleeve was placed around the probe tip and secured with a set screw; see Figure 35. As the temperature of the probe increases, the mass of the sleeve helps to establish a thermal gradient between the probe tip and the face of the sleeve. Because of this thermal gradient, when the compound of higher volatility is placed on the face of the sleeve and the one of lower volatility is placed in the probe tip, both compounds volatilize at about the same time.

2) If one parent ion reacts very fast, the parent ion peak intensity will not indicate its true partial pressure, as for uracil and 5-fluorouracil. The parent ion undergoes self-protonation so fast, as does the subsequent proton transfer reaction between uracil and 5-fluorouracil, that very few parent ions are present even when the time delay between ion formation and detection is as little as 60 μs; see Figure 36.
Figure 35. Probe adaptation for simultaneous detection of two solids of different volatility. The high volatility sample is placed on the sleeve face, which heats slower than the less volatile compound in the probe tip.
Figure 36. FT/ICR positive ion mass spectrum of an electron-ionized mixture of uracil and 5-fluorouracil. Fast proton transfer occurs between uracil and 5-fluorouracil after only 60 µsec between ion formation and ion detection.
Eventually, I developed the following technique which maintains a steady pressure in the $10^{-7}$ Torr range and, moreover, allows the partial pressures of A and B to be measured directly. A large amount of the more volatile sample (5-10 mg) is placed in the probe tip. By quickly heating the tip, one can vaporize enough sample to coat the cone of the cell. The probe is withdrawn and the cell heated using the chamber heaters. In this manner, the sample can be volatilized in a controlled fashion and also be maintained at a steady pressure because of the stable temperature afforded by the main heaters. Using the "sleeve-probe" method for uracil, one cannot maintain a steady pressure for more than 10 min; however, with this method just described, the pressure can be maintained in the low to mid $10^{-7}$ Torr range for about two hours.

Once the pressure has stabilized, the pressure is measured, and the probe, containing the compound of lower volatility, is introduced into the chamber. The probe is then heated, and by a combination of the probe heater and the chamber heater, a steady chamber pressure is achieved. Knowing the total pressure of the system and the partial pressure of the first compound, one can determine the partial pressure of the second. If the pressure changes during the experiment, it is impossible to determine which compound is causing this change. Usually, by the end of the experiment, the second compound has also coated the cell making it impossible to check the partial pressure of the first compound by just withdrawing the probe containing the second compound (as was done for the samples regulated by the leak valves).
The disadvantage of this technique is that it requires at least 3-5 mg of sample, nearly ten times what was needed for the previous techniques. For the dodecahedrane studies, only 1-2 mg of 1,16-dimethyldodecahedrane was available and therefore this technique could not be used. Nevertheless, this method should prove very useful for equilibrium studies when the samples must be introduced via the solids probe.

3. ION INTENSITY - MEASUREMENTS AND CORRECTIONS

Measuring the protonated parent ion ratio is fairly straightforward and involves measuring the area of the mass spectral peak of the protonated parent ions. For this study the direct mode is better to use than the heterodyne mode; see Chapter I. Even though the heterodyne mode has higher resolution, the heterodyne mode requires retuning the ICR. Thus, the detection bandwidth, and the excitation and detection parameters would have to be adjusted each time a new set of compounds were run. The relative peak intensities, however, can be affected by changing the detection bandwidth and these excitation parameters, as shown in Figures 37 and 38. Note that as the excitation power increases, the high mass peaks are enhanced relative to the low mass ones. This phenomenon may in part be due to the position of the ion cloud in the cell before and after excitation [27-29].

The excitation level is expressed as the attenuation of a maximum 30 V(p-p) excitation signal and is expressed in terms of decibels (dB) [30]. For example, an attenuation level of zero means that full excitation power is being applied to the excitation plates. From the
Figure 37. FT/ICR positive-ion mass spectra of perfluorotri-n-butylamine, all detected at 1 MHz bandwidth. A) 0 dB excitation power attenuation. B) 1 dB excitation power attenuation. C) 4 dB excitation power attenuation.
Figure 38. FT/ICR positive-ion mass spectra of perfluorotri-n-butylamine, all detected at 2.6 MHz bandwidth. A) 0 dB excitation power attenuation. B) 1 dB excitation power attenuation. C) 4 dB excitation power attenuation.
equation defining power attenuation, one gets

$$dB(\text{power}) = 10 \cdot \log\left(\frac{P_{\text{out}}}{P_{\text{in}}}\right)$$  \hspace{1cm} (63)

where $P_{\text{out}}/P_{\text{in}}$ is the ratio of the output to input power.

The variation in peak intensity with excitation parameters is a consequence of the frequency sweep excitation, which gives an uneven application of power to the cell over a given frequency range. One can see from Figure 39 (top figure) that the power is not flat over the indicated frequency range; Figure 39 (bottom figure) shows an optimally flat power spectrum. However, by keeping the excitation parameters the same for a series of experiments, one can get a variation in peak intensity that is consistent from run to run. Furthermore, a compound, such as chloroform or bromoform, can be used for calibration, to adjust the excitation parameters until the compound's correct isotope ratio is obtained. This helps to ensure that the experimental peak intensities are correct; see Table 5. The theoretical values in Table 5 were calculated using a program modified by Dr. Steve Mullen [32].
Figure 39. FT/ICR excitation magnitude spectra. Typical magnitude applied by the use of a frequency sweep excitation. Uniform power at all frequencies as it would be for the optimally flat magnitude shown in (B)(from Reference [31]).
Table 5. Isotopic ratios achievable from the FTMS 1000. Chloroform, CHCl₃, loses a Cl to form the CHCl₂⁺ ion, with a mixture of $^{35}$Cl and $^{37}$Cl, to give peaks at m/z = 83, 85, and 87. Bromoform, CHBr₃, loses a Br to form CHBr₂⁺ ion, with mixtures of $^{79}$Br and $^{81}$Br, to give peaks at m/z = 171, 173, and 175.

<table>
<thead>
<tr>
<th>MASS RATIO</th>
<th>MASS SPECTRAL PEAK AREA RATIO</th>
<th>MASS SPECTRAL PEAK AREA RATIO</th>
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</thead>
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<tr>
<td></td>
<td>CALC.</td>
<td>EXP.</td>
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<tr>
<td>83/85</td>
<td>1.54</td>
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REFERENCES


A. INTRODUCTION

In this chapter, I will present several methods for achieving and verifying equilibrium. The importance of establishing that the proton transfer reaction has come to equilibrium and not just steady state cannot be overemphasized. Under certain conditions, explained later in this chapter, a steady state condition could give constant ion ratios when Equations 54 and 55 are used, which in turn gives a constant product to reactant ratio over time that can be misinterpreted as the equilibrium constant. Changes in product or reactant ion concentrations by mechanisms other than the proton transfer reaction will be discussed and their effect on the equilibrium measurement evaluated.

B. GAS-PHASE ION-MOLECULE COLLISIONS

To achieve equilibrium, one must ensure that a sufficient number of collisions occur so that the ion and neutral temperatures are in thermodynamic equilibrium with the temperature of the cell (i.e., the ions are thermalized) [1,2]. In addition, there should be sufficient reactive collisions so that equilibrium is achieved in a reasonable time (2-20 s) [3,4]. The basic parameters of pressure,
electron current, and reaction time can be estimated once the number of ions in the cell and their collision frequencies have been estimated.

1. ESTIMATE OF THE NUMBER OF IONS

The positive ion current can be calculated for a given electron beam current from the following equation [5]:

\[ \frac{I^+}{I^-} = \sigma l P \]  

(64)

where \( I^+ \) is the positive ion current, in A,
\( I^- \) the electron beam current, in A,
\( \sigma \) the ionization cross section, in ions cm\(^{-1}\) electron\(^{-1}\) torr\(^{-1}\),
\( l \) the length, in cm, that the electron beam travels,

and \( P \) the corrected gas pressure, in Torr,  
(described in Chapter III).

In this work, the ionization cross section was approximated from the values established by Tate and Smith [6] and Lampe and Franklin [7]; it is commonly expressed in units of ions formed per electron per cm of travel per Torr of pressure [8]. I approximated \( \sigma \) (70.5) by averaging the values of a variety of compounds used in this research.

The positive ion current is calculated to be about 3x10\(^{-12}\) A for an electron beam current of 300 nA. For an electron beam of about 30 msec duration, 6x10\(^5\) ions are formed in the cell. From the ideal gas law, the number of neutrals in the cell (at 145 °C) is calculated to
be about $10^{11}$ at 3x10^{-7} Torr.

The experimental conditions are set so that the neutral to ion ratio is about $2\times10^5$, insuring that the population of neutrals stays fairly constant during the course of the reaction [3]. This constancy is imperative for kinetic and continuous ion ejection studies. Furthermore, this number of neutrals provides a collision rate (with the cell wall) of $2\times10^4$ collisions per second and thus helps insure that the neutrals are well thermalized. This thermalizing process is essential for dissipation of any excess kinetic energy the neutrals or ions may have before the proton transfer reactions are measured. The energy change measured in the proton transfer reaction is thus due entirely to the energetics of the reaction and not to excess translational energy changes [1,3,9].

2. COLLISION FREQUENCY

In general, for proton transfer reactions, a constant product to reactant ratio is achieved in about 30-100 ion-molecule collisions [3,4,10,11]. Given the number of ions in the cell, one can calculate the collision frequency to estimate how long the reaction takes to reach equilibrium. The collision frequency of an ion with a neutral ($Z_{\text{ion}}$) is given by:

$$Z_{\text{ion}} = \rho_{\text{neu}}Q(v)v_r$$  \hspace{1cm} (65)

where $\rho_{\text{neu}}$ is the neutral number density, in molecules/cm$^3$, $Q(v)$ the collision cross section, in cm$^2$, and

$$v_r$$
and \( v_r \) the relative velocity of the ion and neutral, in cm/s.

The collision rate constant \( (k_c) \) is given by:

\[
  k_c = Q(v)v_r
\]

The simplest way to calculate the collision frequency is from the hard sphere model. In this model, a uniform particle has no characteristics such as charge, polarizability, or dipole moment. In the hard sphere model, a collision is purely elastic; see Figure 40 [12]. The collision cross section for the hard sphere model is given by:

\[
  Q(v) = \pi b^2
\]

The impact parameter, \( b \), is simply the distance between the centers of the two particles. Obviously, since the collision occurring in the cell involves an ion and a polarizable neutral molecule, the hard sphere calculation provides only a lower limit to the collision frequency.

The Langevin theory [13] of ion-molecule collisions takes into account the polarizability of the neutral. The collision of an ion-neutral pair is shown in Figure 41. This type of collision is also known as an orbiting collision since an ion approaching a neutral at a distance of \( b_0 \) orbits the ion at a radius shown by the dashed circle, but does not collide with the neutral. When the ion approaches closer than \( b_0 \), it spirals towards the neutral and collides with it.
Figure 40. Diagram of a hard sphere collision. The collision is elastic and occurs at a distance characterized by the impact parameter \(b\).
Figure 41. Langevin collision between an ion and a neutral molecule (from Reference [14]).
Thus, by inducing a dipole in the neutral, the ion will collide with the neutral under conditions that would not lead to a collision in the hard sphere model [14]. As one can see from the equation for the Langevinian collision cross section, the larger the polarizability, the more collisions:

$$Q(v) = \left[ \frac{(2\pi q)}{v_r} \right] (a/\mu)^{1/2}$$  \hspace{1cm} (68)

where $q$ is the charge on the ion, in esu,

$\alpha$ the polarizability of the neutral, in cm$^3$,

and $\mu$ the reduced mass of the colliding particles,

in g; $\mu = \frac{m_1 m_2}{m_1 + m_2}$

The Langevin model, however, does not account for the presence of a permanent dipole moment in the neutral and the actual collision cross section is larger than that predicted by Equation 68.

Thread and Hamill [15] and Moran and Hamill [16] attempted to include the effect of the permanent dipole by assuming that the ion locks in on the dipole and that the dipole orientation is fixed during the approach and collision. Their assumption was that the angle between the dipole and the line of centers of collision is zero.

It was later recognized by Bowers and Laudenslager [17] that the permanent dipole moment has a smaller effect on ion-molecule cross section than that predicted by the totally locked dipole model. The ion field does not completely quench the rotational angular momentum of the polar molecule, and only partial locking of the dipole moment occurs [18].
The average dipole orientation (ADO) theory, for calculation of collision cross section, takes into account this partial locking phenomenon [18,19]. In the ADO theory, the degree of locking is dependent upon the polarity of the molecule; the larger the dipole moment, the greater the locking. The degree of locking is accounted for in the calculation of the cross section by experimentally determining the locking parameter \( c \) a value between 0 and 1:

\[
Q(N) = \left[\frac{(2\pi q)}{\nu_r \mu^1/2}\right]\left[\alpha^{1/2} + c\mu_D(2/\pi kT)^{1/2}\right]
\]  

(69)

where \( c \) is the locking constant,

- \( \mu_D \) the electric dipole moment, in esu·cm,
- \( k \) the Boltzmann constant, in erg/K,
- and \( T \) the temperature, in K.

The values of the collision rate, collision frequency, and collision cross section for the various theories described above are summarized in Table 6. Even the ADO collision theory usually predicts frequencies that are low by about 30-60% [20,21], and therefore, the final corrected collision frequency is about 18 collisions per second. It will take, therefore, about 2-5 seconds to reach 30-100 collisions at 3x10^{-7} Torr. It must be remembered that these numbers are rough approximations and are only intended to provide some reasonable experimental starting parameters. A reaction, conducted under the conditions just described, is shown in Figure 42. The reaction comes to equilibrium in about 2-4 seconds at a pressure of 3x10^{-7} Torr. According to Equation 65, the collision frequency is
Table 6. Comparison of collision parameters for three collision models at about 150 °C and 3x10^{-7} Torr.

<table>
<thead>
<tr>
<th>MODEL</th>
<th>ION-MOLECULE COLLISION FREQUENCY (1/s)</th>
<th>COLLISION CROSS-SECTION (cm²)</th>
<th>COLLISION RATE CONSTANT (cm³/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HARDSPHERE</td>
<td>2.2</td>
<td>7.8x10^{-15}</td>
<td>3.3x10^{-10}</td>
</tr>
<tr>
<td>LANGEVIN</td>
<td>9.0</td>
<td>3.2x10^{-14}</td>
<td>1.3x10^{-9}</td>
</tr>
<tr>
<td>ADO</td>
<td>12.1</td>
<td>4.3x10^{-14}</td>
<td>1.8x10^{-9}</td>
</tr>
</tbody>
</table>
Figure 42. Pressure effect on an equilibrium reaction between isopropyl ether and α-methylstyrene. At a pressure of $6 \times 10^{-7}$ Torr, the reaction comes to equilibrium faster than at $3 \times 10^{-7}$ Torr.
proportional to the neutral number density, hence, equilibrium is reached more quickly when the pressure is increased; see Figure 42.

C. ACHIEVING AND VERIFYING EQUILIBRIUM

Equilibrium can be verified by several different experiments. The duration of the reaction can be varied and the product to reactant ratio monitored to determine if this ratio remains constant over time. The initial concentrations can be changed, or the system, already at equilibrium, can be perturbed. If the product to reactant ratio remains the same, the reaction is at equilibrium.

1. TIME VARIATION

For verifying equilibrium, one of the simplest and most reliable methods is to vary the reaction period and monitor the product to reactant ratio as time increases. If this ratio attains a constant value, the reaction has come to equilibrium [4,9,11]. Since the neutrals are in greater abundance than the ions, the neutral concentration is virtually constant during the course of the reaction. A plot of the intensity of the two protonated bases in Equation 70 versus time can verify whether or not a constant product to reactant ratio has been achieved. The product to reactant ratio contains both the ion ratio and the neutral ratio. Because neutral concentration remains constant over time, the neutral ratio remains constant over time and a plot of the product to reactant ratio versus time or a plot of the ion ratio versus time will be constant for an equilibrium reaction; see
Figures 43 and 44. Thus, from now on I will refer to the product to reactant ratio as simply the ion ratio.

As was mentioned at the start of this chapter, the ion ratio can be constant in time and yet be due to a steady state condition rather than an equilibrium state. Steady state exists when the system does not change in time, and yet there is an irreversible flow of product or reactant through the system, such as the irreversible loss of AH⁺ in the following example [22]:

\[
A + BH^+ \overset{k_1}{\underset{k_{-1}}{\rightleftharpoons}} AH^+ + B \tag{70}
\]

\[
AH^+ + C \overset{k_2}{\rightarrow} D \tag{71}
\]

in which C is a fragment or an impurity that does not appear in the product to reactant ratio calculation from Reaction 70. If the side Reaction 71 does not occur and if the forward rate constant, \(k_1\), is much larger than \(k_{-1}\), the ion ratio, \(AH^+/BH^+\), will be constant at equilibrium and much greater than one. A constant ion ratio, arising from a steady state condition, can be obtained if the rate constant \(k_2\) in Reaction 71 is of such a magnitude as to compensate for the small \(k_{-1}\) rate constant. Even if Reaction 70 had not reached equilibrium, it would be possible for one to observe a constant ratio, but this value would lead to an incorrect "equilibrium constant". Since this "equilibrium constant" is used to calculate the free energy change, this value would also be incorrect.

To ensure that the ratios seen in Figures 43 and 44 represent a
Figure 43. Product to reactant ion concentration ratio versus reaction period for the reaction of 2,4-dimethyl-3-pentanone with n-butyl ether. This reaction is very fast and comes to equilibrium quickly. Verification of equilibrium comes from the constancy of the product to reactant ratio over a long reaction period.
Figure 44. Product/reactant ICR spectral peak area ratio for the protonated bases versus reaction period for the reaction of 2,4-dimethyl-3-pentanone with n-butyl ether. At equilibrium, the ion ratio is constant over time.

Circles: peak area of the protonated 2,4-dimethyl-3-pentanone.
Crosses: peak area of the protonated n-butyl ether.
true equilibrium situation, one must force the system to change, to see if equilibrium can be reestablished from both sides of Reaction 70. If equilibrium is so reestablished, Reaction 70 has indeed reached equilibrium [9].

2. CHANGING THE INITIAL CONCENTRATIONS

The concentration of the neutrals, can be changed by changing their partial pressures, and the concentrations of the protonated bases by either ejecting ions, changing the electron current, or changing the ionization potential. The protonated bases are formed by self-protonation:

\[ \text{M}^{+*} + \text{M} \rightarrow \text{MH}^+ + (\text{M-H})^* \]  

(72)

The electron current determines how many radical cations (\(\text{M}^{+*}\)) are generated. These cations are very acidic and easily protonate the parent neutral (M) to form the protonated base (\(\text{MH}^+\)) [23,24]. Thus, changes in the electron current or ionization potential alter the number of ions formed by electron impact. The variation in spectral peak intensity of the \(\text{C}_{10}\text{H}_{15}^+\) ion from adamantane as a function of the ionization potential is shown in Figure 45.

a. PRESSURE VARIATION

A system at equilibrium should withstand pressure changes in the neutral ratio of up to a a factor of five to seven and still return to the same equilibrium state as a reaction with equal neutral partial
Figure 45. Spectral peak area of adamantane (C_{10}H_{15}^+) ion versus ionization potential.
pressures [3,25]. If the reaction is at equilibrium, an increase in the collision rate will not change equilibrium. One can increase the number of collisions without changing the neutral ratio by adding a buffer gas (such as methane) thus increasing the total reaction pressure [3,9]. Adding methane to the very fast reaction between 2,4-dimethyl-3-pentanone and n-pentyl ether, illustrated in Figure 46, has no effect on equilibrium. Both reactions, one with and one without methane, reach the same equilibrium constant after 0.5 sec. In this research, equilibrium was verified by this method; typical data for reactions of various compounds are presented in Table 7. The small changes in \( \Delta G^\circ \) (standard deviation of about 0.1 kcal/mol) for these reactions help one to prove that equilibrium was achieved.

b. ELECTRON CURRENT AND IONIZATION POTENTIAL VARIATIONS

In general, the effect of the electron current on the number of molecular ions formed is linear for the range of electron currents used in this research (40-400 nA) [26]. Increasing the electron current increases the number of molecular ions, and one can see from Equation 72 that increasing the concentration of molecular ions increases the concentration of protonated species.

The concentration of molecular ions can also be changed by varying the ionization potential of the electron beam. This technique, however, is not as straightforward as the technique of increasing the electron current since it is not a linear relationship [27]; see Figure 45. Nonetheless, an increase in ionization potential changes the concentration of protonated parent ions.
Table 7. Effects of pressure variations on $\Delta G^\circ$ for the reactions of α-methylstyrene with 2-methylfuran, 2-methylfuran with isopropyl ether, and acetophenone with α-methylstyrene.

<table>
<thead>
<tr>
<th>REACTING COMPOUNDS</th>
<th>PRESSURE (Torr x 10^7)</th>
<th>REACTION $\Delta G^\circ$ (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-METHYLSTYRENE</td>
<td>2-METHYLFURAN</td>
<td></td>
</tr>
<tr>
<td>1.4</td>
<td>0.3</td>
<td>-2.3</td>
</tr>
<tr>
<td>1.4</td>
<td>0.7</td>
<td>-2.6</td>
</tr>
<tr>
<td>1.4</td>
<td>1.0</td>
<td>-2.4</td>
</tr>
<tr>
<td>1.4</td>
<td>1.5</td>
<td>-2.3</td>
</tr>
<tr>
<td><strong>AVERAGE</strong></td>
<td></td>
<td><strong>-2.4 ± 0.2</strong></td>
</tr>
<tr>
<td>2-METHYLFURAN</td>
<td>ISOPROPYL ETHER</td>
<td></td>
</tr>
<tr>
<td>1.5</td>
<td>0.3</td>
<td>-0.40</td>
</tr>
<tr>
<td>1.5</td>
<td>0.6</td>
<td>-0.38</td>
</tr>
<tr>
<td>1.5</td>
<td>1.0</td>
<td>-0.33</td>
</tr>
<tr>
<td>1.5</td>
<td>1.5</td>
<td>-0.35</td>
</tr>
<tr>
<td><strong>AVERAGE</strong></td>
<td></td>
<td><strong>-0.36 ± 0.03</strong></td>
</tr>
<tr>
<td>ACETOPHENONE</td>
<td>α-METHYLSTYRENE</td>
<td></td>
</tr>
<tr>
<td>1.3</td>
<td>0.2</td>
<td>-3.1</td>
</tr>
<tr>
<td>1.3</td>
<td>0.5</td>
<td>-3.1</td>
</tr>
<tr>
<td>1.3</td>
<td>1.0</td>
<td>-3.1</td>
</tr>
<tr>
<td>1.3</td>
<td>1.5</td>
<td>-3.2</td>
</tr>
<tr>
<td>1.3</td>
<td>1.7</td>
<td>-3.1</td>
</tr>
<tr>
<td>1.3</td>
<td>2.0</td>
<td>-3.0</td>
</tr>
<tr>
<td><strong>AVERAGE</strong></td>
<td></td>
<td><strong>-3.1 ± 0.07</strong></td>
</tr>
</tbody>
</table>
If the reaction is at equilibrium, there should be no change in the apparent equilibrium constant when one runs the proton transfer reaction at various ionization potentials or at various electron currents. The reaction between 2,4-dimethyl-3-pentanone and methyl benzoate (see Figure 47) illustrates that the apparent equilibrium constant does not change as the beam voltage varies from 20-90 V. Because the beam potential (at 10 V) is just above the ionization potential of these compounds, few parent ions are formed, and therefore, the population of protonated bases is small. Equilibrium cannot be established since this small number of protonated bases does not provide the needed number of reactive collisions with the neutrals [3].

The same reaction is used to illustrate how variation of the electron current affects equilibrium as shown in Figure 48. The error in the electron current is small (about 5 nA), and each point represents the average apparent equilibrium constant from three different reaction periods. The overall error due to changes in the electron current is only about 0.05 kcal/mol for the free energy change of this proton transfer reaction. The error in the final relative gas-phase basicity measurement due to electron current and beam voltage variations is less than 0.1 kcal/mol.

c. ION EJECTION

Ion ejection allows the reaction to approach equilibrium from both sides. One of the protonated bases from Reaction 70 is completely ejected from the system at the start of the reaction, and therefore
Figure 46. Effect of methane addition to an equilibrium reaction of 2,4-dimethyl-3-pentanone with n-pentyl ether. The partial pressure of the two reacting compounds is $1.5 \times 10^{-7}$ Torr. Circles: reaction without methane. Crosses: reaction with methane at a pressure of $5 \times 10^{-7}$ Torr.
Figure 47. Effect of ionization potential on the apparent equilibrium constant for the reaction of 2,4-dimethyl-3-pentanone with methyl benzoate.
Figure 48. Effect of electron current on the apparent equilibrium constant for the reaction of 2,4-dimethyl-3-pentanone with methyl benzoate. Each point represents an average constant from reaction periods of 0.9, 1.1, and 1.3 seconds. The error due to the electron current in the relative basicity measurement is \( \pm 0.05 \) kcal/mol.
the initial base concentration is zero. The same apparent equilibrium constant is obtained from the time variation experiment and from two ion ejection experiments for the reaction between 2,4-dimethyl-3-pentanone and n-butyl ether; see Figure 49. Since all apparent equilibrium constants agree, equilibrium is confirmed [9].

A different method of checking equilibrium involves the ejection of one of the bases after equilibrium is established. If the system is truly at equilibrium, given time it will return to its original equilibrium state. The reaction shown in Figure 50 (the same reaction shown in Figure 49) was perturbed by ejecting the protonated n-butyl ether at 0.25 s. The reaction returned to the same equilibrium constant as was obtained in the non-perturbed experiment.

By comparing Figures 49 and 50, one can also see that the same equilibrium constant is obtained, whether the ions are ejected at the start of the reaction time (initial ion ejection) or after the reaction reaches equilibrium (post equilibrium ion ejection). Two ejection experiments, one occurring at 3 ms and the other at 0.25 s, are shown in Figure 51; the equilibrium constants obtained are the same for both. From an experimental point of view, the initial ion ejection experiment is easier to do than post equilibrium ion ejection since the overall reaction period is shorter. This factor is important for a reaction that requires several seconds since there is less time for the pressure to fluctuate and cause errors in the measurement of the neutral concentrations.

One must apply sufficient rf power to the ions to get complete ion ejection. By taking a scan immediately after ejection but before a
Figure 49. Approach to equilibrium for the reaction of 2,4-dimethyl-3-pentanone with n-butyl ether. The apparent equilibrium constant is plotted versus reaction period for three experiments:
Open circles: no ion ejection.
Squares: after ejection of protonated n-butyl ether.
Solid circles: after ejection of protonated 2,4-dimethyl-3-pentanone.
Perturbation of an equilibrium reaction between 2,4-dimethyl-3-pentanone and n-butyl ether by ion ejection. The protonated n-butyl ether is ejected 0.25 s after the start of the reaction; equilibrium is subsequently established.

Circles: no ion ejection.
Crosses: after ejection of protonated n-butyl ether.
Figure 51. Comparison of initial and post equilibrium ion ejection for the reaction between 2,4-dimethyl-3-pentanone with n-butyl ether. The time at which the protonated n-butyl ether ion is ejected does not affect the attainment of equilibrium.

Circles: protonated n-butyl ether ejection at 3 ms.

Crosses: protonated n-butyl ether ejection at 250 ms.
reaction occurs, one can verify that complete ion ejection has taken place. The top spectrum in Figure 52 is an example of such a scan for the reaction between α-methylstyrene and acetophenone. Note also that as time increases, the spectra from the two ejections become identical.

The importance of allowing a reaction to undergo sufficient collisions for equilibrium is demonstrated by a comparison of the spectra obtained in Figures 53 and 54 for the reaction between 5-fluorouracil and 1,1,1-trifluoro-2,4-pentanedione. Note that the reaction periods are 3 seconds and 7 seconds for Figures 53 and 54, respectively. The top spectrum in both figures is where no ejection occurs, the middle spectrum is where the (5-fluorouracil-H+) anion is ejected, and the bottom spectrum is where (1,1,1-trifluoro-2,4-pentanedione-H+) anion is ejected. As can be seen from the spectra in Figure 53, 3 seconds is insufficient time for equilibrium to be reached; thus the three spectra are not identical (in other words, they do not have the same ion abundance ratios). In Figure 54, however, the three spectra are identical, indicating that seven seconds provides time for sufficient collisions for equilibrium.

3. THERMODYNAMIC CONSISTENCY

Standard free energy changes are state functions. The first law of thermodynamics states that state functions are path independent. The free energy change for a given reaction is independent of the reactions that make up that energy difference, and can be illustrated by the three
Figure 52. Spectra of initial ion ejection and return to equilibrium. The top spectra are taken immediately after ion ejection, thus verifying complete ion ejection, in the reaction between α-methylstyrene and acetophenone.
Figure 53. Negative ion spectra for the reaction of 5-fluorouracil (C₄H₃N₂O₂F) with 1,1,1-trifluoro-2,4-pentadione (C₅H₅O₂F₃) at three seconds.
A. no ion ejection.
B. ejection of C₄H₂N₂O₂F⁻.
C. ejection of C₅H₅O₂F₃⁻.
Figure 54. Negative ion spectra for the reaction of 5-fluorouracil (C₄H₃N₂O₂F) with 1,1,1-trifluoro-2,4-pentadione (C₅H₅O₂F₃) at seven seconds.

A. no ion ejection.
B. ejection of C₄H₂N₂O₂F⁻.
C. ejection of C₅H₅O₂F₃⁻.
reactions presented in Table 8. Reaction 75 can be obtained by adding Reactions 73 and 74. $\Delta G^\circ$ for Reaction 73 can be obtained in the same way. The predicted $\Delta G^\circ$ value from adding Reactions 73 and 4.11 is $-1.0$ kcal/mol, precisely what is found experimentally. The $\Delta G^\circ$ values (with standard deviation of $\pm 0.2$ kcal/mol) for Reactions 73-75 are averages of time variation, ion ejection, and pressure variation experiments.

One can establish an internally consistent set of free energy changes for the compounds being studied; see Figure 55. Compared to the accepted tolerance of $0.2$ kcal/mol in relative free energy changes, my value of $0.14$ kcal/mol is considered excellent [28]. This internal consistency provides additional strong verification of equilibrium [4,9,11]. This tolerance in relative free energy changes is also the error of the relative gas-phase basicities; see Equation 30.

D. ION LOSSES

The ion ratio is observed as a function of time for equilibrium measurements. Ideally, the ion concentration changes only because of proton transfer. Ion concentration can change, however, because of several reasons: 1) non-reactive ion losses during the reaction and excitation periods [29-31] and 2) competing side reactions [4,9]. Several ways to minimize these problems will be discussed in the following sections.

1. NON-REACTIVE ION LOSSES
   a. DURING EXCITATION
Table 8. Consistency of state function, $\Delta G^\circ$, for three reaction pairs.

<table>
<thead>
<tr>
<th>REACTION NUMBER</th>
<th>$\Delta G^\circ$(exp) (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>73</td>
<td>C$<em>7$H$</em>{14}$OH$^+$ + C$_8$H$_8$O$_2$ $\leftrightarrow$ C$<em>7$H$</em>{14}$O + C$_8$H$_8$O$_2$H$^+$</td>
</tr>
<tr>
<td>74</td>
<td>C$_8$H$<em>8$O$<em>2$H$^+$ + C$</em>{10}$H$</em>{22}$O $\leftrightarrow$ C$_8$H$<em>8$O$<em>2$ + C$</em>{10}$H$</em>{22}$OH$^+$</td>
</tr>
<tr>
<td>75</td>
<td>C$<em>7$H$</em>{14}$OH$^+$ + C$<em>{10}$H$</em>{22}$O $\leftrightarrow$ C$<em>7$H$</em>{14}$O + C$<em>{10}$H$</em>{22}$OH$^+$</td>
</tr>
</tbody>
</table>
Figure 55. Self-consistent (to within less than + 0.2 kcal/mol) set of gas-phase basicities ($\Delta G^\circ$), in kcal/mol. Basicity decreases from top to bottom of scale.
The motion of an ion in the cubic cell is composed of radial and axial motions [32]. Although most of the power during excitation is applied to the radial motion of the ion, enough power goes into the axial motion so that some of the ions are excited enough to overcome the trapping potentials and are ejected from the cell [30,32,33]. This axial loss of ions during excitation may also account for the accentuation of high masses at high excitation power levels; see Chapter III [31].

The effect of high mass accentuation becomes more of a problem as the mass difference between the ions becomes larger [31]. Most of this work deals with ions that differ in mass by about only 20-40 amu. In these cases the above effect can be ignored. The mass difference between dodecahedrane and the reference compounds, however, is about 120 amu and this effect may not be overlooked. Under these conditions, it is important to find an excitation level where this effect is minimized. By using compounds such as chloroform or bromoform whose natural isotopic abundances are known, one can find the excitation level which corresponds to their correct peak intensity ratios. In other words, one uses them as standards to optimize the excitation level.

b. DURING REACTION

Ion loss that occurs before excitation and along the axis parallel to the magnetic field has been investigated and termed "ion evaporation" by Rempel, Huang, and Gross [30]. Ion evaporation results from ion-molecule collisions that impart enough translational energy to the ion for it to overcome the trapping potentials.
The spectral peak area of the benzene parent ion as a function of the time period between ion formation and excitation is presented in Figure 56. The signal characteristically increases as the ion cloud evolves and relaxes to the Z-axis. Ion cloud evolution is a complicated process dependent upon pressure, trap potential, and the number of ions [30]. When the cloud reaches maximum relaxation, it is compact and well defined, and hence an optimum signal is obtained [30,33]. As time increases, ion evaporation becomes apparent. As a barrier to ion loss, one can use trap potentials of 0.75 V or higher [30].

To maintain efficient trapping, one must maintain a clean cell. Materials coating the trap plates attenuate and distort the trap potentials [30]; if the cell is dirty, the signal will decay rapidly. For maximum trapping efficiency due to cell cleanliness, Rempel [30] found that the signal should decay to no more than 50% of the maximum benzene parent ion signal over 8-10 s for their experimental conditions listed in Figure 56. The results from a typical routine cleanliness test are presented in Figure 56.

The total number of ions should remain constant if no additional ions are generated during the reaction. Therefore, the total ion intensity should remain constant over time. Moini and Eyler have reported, however, that the total ion intensity does not remain constant over time for certain excitation levels [31]. This effect may be in part due to the location of the ions within the cell at the time of excitation and their location after excitation. If the ion cloud is located in the cell where the electric fields perturb the motion of the
Figure 56. Clean cell test (heterodyne mode). The spectral peak area for C\textsubscript{6}H\textsubscript{6}\textsuperscript{+} is monitored as a function of the time between ion formation and detection. Spectra were obtained with a C\textsubscript{6}H\textsubscript{6}\textsuperscript{+} mass resolution (m/Δm) of 32,000 at a pressure of 8x10\textsuperscript{-9} Torr with a trap potential of +0.24 V.
excited ion cloud, the signal will not be as great as the signal obtained when the ion cloud is located where the electric fields do not perturb the ion cloud [33,34]. One can minimize this effect by finding an excitation level at which ion intensity remains constant over time.

2. REACTIVE ION LOSSES

Generally, for proton transfer reactions, most ion losses occur from competing side reactions [31]. One of the most prevalent side reactions encountered in this study is proton bound dimer formation [10,11,25]:

\[
\begin{align*}
A + BH^+ &\rightarrow (AHB)^+ \quad (76) \\
A + AH^+ &\rightarrow (AHA)^+ \quad (77)
\end{align*}
\]

The fate of the dimer formed in Reaction 76 can be as follows:

\[
\begin{align*}
(AHB)^+ &\rightarrow AH^+ + B \quad (78) \\
(AHB)^+ &\rightarrow \text{other products} \quad (79)
\end{align*}
\]

The same is true for the dimer in Reaction 77. In either case, if the dimer dissociates, as in Reaction 79, the protonated bases in Reactions 76 and 77 are lost from further proton transfer reactions.

One can minimize the formation of bound dimers by operating at low pressures and high temperatures. A pressure of low to mid $10^{-7}$ Torr is high enough to provide enough collisions to attain equilibrium of proton transfer reactions, yet low enough to prevent the many collisions needed for stabilization of the proton bound dimer [10]. I find that
above 150 °C dimer formation does not present a problem in reaching equilibrium. The reaction between 2,4-dimethyl-3-pentanone and n-butyl ether illustrates how I arrived at this temperature. At 32 °C, this reaction does not reach equilibrium (see Figure 57) because the overwhelming reaction taking place is proton bound dimer formation—see Figure 58. Note that both bases are involved and that all three possible dimers are formed. Note also that for short reaction times, the protonated bases are the dominant species. The reaction time is too short for enough collisions to occur, and since it is through these collisions that the excess dimer energy is removed, the dimer can not be stabilized [10]. As the temperature increases, the internal energy of the dimer also increases leading to quicker dissociation than at lower temperatures; see Figure 59 [23]. Finally, at 157 °C, the proton transfer reaction reaches equilibrium; see Figure 60.
Figure 57. Non-equilibrium reaction between 2,4-dimethyl-3-pentanone with n-butyl ether at 32 °C. The apparent equilibrium constant is not constant over time.
Figure 58. Formation of proton bound dimers in the reaction of 2,4-dimethyl-3-pentanone with n-butyl ether at 32 °C.
Figure 59. Effect of temperature on the proton bound dimer reactions between 2,4-dimethyl-3-pentanone and n-butyl ether.
Figure 60. Equilibrium reaction between 2,4-dimethyl-3-pentanone and n-butyl ether at 157 °C. The proton bound dimer reaction no longer competes effectively with the H⁺ transfer reaction.
REFERENCES


21. Su, T. Private Communication


31. Moini, M.; Eyler, J.R. Private Communication


A. INTRODUCTION

For over two decades the chemotherapeutic activity of 5-fluorouracil (FU) (see Figure 61) has been known and today it is one of the most common anti-tumor drugs [1,2]. 5-fluorouracil is metabolized to 5-fluoro-2'-deoxyuridine monophosphate which inhibits thymidylate synthetase thereby inhibiting DNA synthesis and impairing the replication of tumor cells [1]. Furthermore, 5-fluorouracil is known to replace normal uracil (U) in RNA [3,4]. The disruption of normal base-pairing schemes in RNA and normal biosynthetic pathways involving uracil have, in part, been attributed to the greater acidity of the N-3 proton of 5-fluorouracil than that of uracil [5].

The acidity difference between uracil and 5-fluorouracil is well known in solution (1.3 pH units) [4,6-8] and many structural and chemical properties due to fluorination in solution have been well documented [4,9,10]. However, these conclusions may not be strictly
Figure 61. Structures of uracil (left) and 5-fluorouracil (right). The standard numbering system for uracils is shown in the left hand structure. In the nucleoside the sugar moiety is attached to the n-1 position.
applicable to the interior of the RNA helix since it has parts isolated from aqueous solution. Thus, the determination of the acidity difference between uracil and 5-fluorouracil in the gas-phase should be of interest and was, therefore, the subject of this study.

B. DETERMINATION OF GAS-PHASE ACIDITIES OF 5-FLUOROURACIL AND URACIL

The acidity difference between these two nucleic acids can be determined by evaluating the free energy change of the following reaction:

\[ \text{FU}^- + \text{U}^- \rightleftharpoons \text{U} + \text{FU}^- \]  

(80)

where \( \text{U}^- \) and \( \text{FU}^- \) are the deprotonated anions of \( \text{U} \) and \( \text{FU} \) respectively.

1. DIRECT REACTION BETWEEN 5-FLUOROURACIL AND URACIL

In the gas-phase, 5-fluorouracil is more acidic than uracil; see the top spectrum in Figure 33. The equilibrium ratio of \( \text{FU}^-/\text{U}^- \) is very large, indicating that Reaction 80 lies far to the right. The direction of the reaction was confirmed by ion ejection of both \( \text{FU}^- \) and \( \text{U}^- \). To insure that the observed \( \text{FU}^-/\text{U}^- \) ratio is not a function of ionization of excess 5-fluorouracil, reactions were run with the partial pressure of 5-fluorouracil roughly equal to that of uracil, and with excess uracil; the results obtained in both cases are the same. The \( \text{FU}^-/\text{U}^- \) ratio is too large to permit an accurate measurement of the equilibrium constant. Furthermore, equilibrium is difficult to establish since the minor component (uracil) does not provide and maintain a sufficient number of reactive collisions.
2. REACTION OF 5-FLUOROURACIL AND URACIL WITH REFERENCE ACIDS

Since the direct reaction between 5-fluorouracil and uracil did not serve to quantitate their acidity difference, they were reacted individually with various reference acids. From these reactions the acidity of the nucleic acids can be determined. The acidities of the reference acids used in this study were determined by Fujio, McIver, and Taft [11] using ICR mass spectrometry.

a. 5-FLUOROURACIL EQUILIBRIUM REACTION

Equilibrium for the reaction of 5-fluorouracil and 1,1,1-trifluoro-2,4-pentanedione was established after 5 sec and maintained up to 9 sec. Ion ejection experiments at 7 sec confirmed this equilibrium; see Figure 54. A spectrum was taken immediately after ion ejection of FU\(^-\) (m/z = 129): see middle spectrum in Figure 62. The absence of a peak at m/z = 129 confirms total FU\(^-\) ejection. The gas-phase acidity of 5-fluorouracil (321.1 kcal/mol) is calculated from the free energy change (-2.1 kcal/mol) for the reaction between 5-fluorouracil and 1,1,1-trifluoro-2,4-pentanedione and the known acidity of the reference acid (323.2 kcal/mol).

b. URACIL BRACKETING EXPERIMENTS

Establishing an equilibrium reaction for uracil has not yet been accomplished. Since uracil vaporizes at a very high temperature (about 300 °C, much higher than that of 5-fluorouracil), the experiment must be run at a high temperature causing large ion losses (due to the
Figure 62. Verification of complete ion ejection for the reaction of 5-fluorouracil (C$_4$H$_3$N$_2$O$_2$F) with 1,1,1-trifluoro-2,4-pentadione (C$_5$H$_5$O$_2$F$_3$). A spectrum is taken with minimal delay (~60 µs) between ion ejection at m/z = 129 and ion detection. This procedure insures that enough RF power is applied at m/z = 129 to completely eject the ion from the cell.
large kinetic energy of the ions at the high temperatures) and also causing decomposition of some of the reference acids. Thus, the small signal because of large ion-losses requires the acquisition of many scans to get a good signal to noise ratio. Since many scans (about 40) are needed and since each scan takes about 7 sec, several minutes are needed to run a reaction. A reaction period of this length makes it difficult for one to accurately measure the partial pressure of uracil. Since establishment and confirmation of equilibrium was difficult, bracketing reactions were carried out between uracil and a variety of acids, some of which are listed in Table 9; see Figure 32. The gas-phase acidity of uracil was bracketed between that of difluoroacetic acid and 2-cyanophenol; see Figures 32 and 63.

The acidities for the reference acids in Table 9 are based on the value of 343.0 ± 2 kcal/mol for phenol [11]. The absolute acidities for 5-fluorouracil and uracil will thus have an error of at least 2 kcal/mol. Since the uracil value is based on a bracketing experiment, the error of the relative placement of uracil in Table 9 is ± 1.6 kcal/mol (i.e., the acidity difference between difluoroacetic acid and 2-cyanophenol)[12,13]. The error in the relative acidity determination of 5-fluorouracil (± 0.7 kcal/mol) is due mostly to the large errors in the measurement of its partial pressure.

C. COMPARISON OF THE GAS-PHASE AND SOLUTION-PHASE ACIDITY DIFFERENCE BETWEEN 5-FLUOROURACIL AND URACIL

Even though 5-fluorouracil is more acidic than uracil in both the gas and solution phases, the magnitude of the acidity difference is much
Figure 63. FT/ICR mass spectrum of the bracketing reaction between uracil and 2-cyanophenol.
Table 9. Gas-phase acidities of uracil and 5-fluorouracil. The absolute values are based reference acids anchored to phenol, $343.0 \pm 2$ kcal/mol \[11\]. Acidity increases from top to bottom of scale.

<table>
<thead>
<tr>
<th>Compound</th>
<th>$\Delta G^\circ_{\text{acid}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-METHOXYPHENOL</td>
<td>344.2</td>
</tr>
<tr>
<td>PHENOL</td>
<td>$343.0 \pm 2$ kcal/mol</td>
</tr>
<tr>
<td>BENZOIC ACID</td>
<td>334.0</td>
</tr>
<tr>
<td>3,5-DICHLOROPHENOL</td>
<td>328.6</td>
</tr>
<tr>
<td>2-CYANOPHENOL</td>
<td>328.2</td>
</tr>
<tr>
<td>URACIL</td>
<td>$326.6 \pm 1.6$ kcal/mol</td>
</tr>
<tr>
<td>DIFLUOROACETIC ACID</td>
<td>325.0</td>
</tr>
<tr>
<td>1,1,1-TRIFLUORO-2,4-PENTANEDIONE</td>
<td>323.2</td>
</tr>
<tr>
<td>5-FLUOROURACIL</td>
<td>321.1</td>
</tr>
</tbody>
</table>
larger in the gas phase than in the solution phase. Reaction 80 is a competing reaction between two deprotonating reactions:

\[
\text{HFU} + \text{H}_2\text{O} \rightleftharpoons \text{H}_3\text{O}^+ + \text{FU}^- \quad (81)
\]

\[
\text{H}_2\text{O} + \text{HU} \rightleftharpoons \text{U}^- + \text{H}_3\text{O}^+ \quad (82)
\]

Each has an associated \( K_a \):

\[
K_a(\text{FU}) = \frac{[\text{FU}^-][\text{H}^+]}{[\text{FU}]} \quad (83)
\]

\[
K_a(\text{U}) = \frac{[\text{U}^-][\text{H}^+]}{[\text{U}]} \quad (84)
\]

The equilibrium constant for Reaction 80, \( K_{eq(1)} \), is determined from the ratio of these \( K_a \)’s:

\[
K_{eq(1)} = \frac{K_a(\text{FU})}{K_a(\text{U})} \quad (85)
\]

From the pKa values of 5-fluorouracil (pKa = 8.15) and uracil (pKa = 9.45)\[4,6\], the \( K_{eq(1)} \) in solution is approximately 20.

From the expression of the free energy change for Reaction 80 (\( \Delta G^\circ_1 \)), \( K_{eq(1)} \) in the gas phase can be evaluated:

\[
G^\circ_1 = -RT\ln K_{eq(1)} \quad (86)
\]

The free energy change in Reaction 80 (about -5.5 kcal/mol; see Table 9) gives a \( K_{eq(1)} \) of approximately 430. From a ratio of the two \( K_{eq(1)} \) values (gas and solution phase \( K_{eq(1)} \)’s), one sees that
5-fluorouracil is about 20 times more acidic in the gas phase than it is in solution. The acidity of uracil will increase upon fluorination due to the electron withdrawing effect of fluorine [14]. McIver [15] and Taft [16] found, however, that the effect of fluorination on the acidity of a compound in an aqueous solution is greatly reduced by as much as a factor of five. Aue and Bowers [17] showed that hydrogen bonding between the solvent and the neutrals attenuates the inductive effect of fluorine. In addition to the above effects the basicity of the solvent must be taken into account. If the solvent is much more basic than FU or U (as is the case for water as a solvent) then the solvent will tend to compress the acidity difference between the two nucleic acids since both are easily ionized [18,19]. The absence of solvent compression and the presence of the full electron withdrawing effect of fluorine gives rise to a larger acidity difference in the gas phase than in solution.

The free energy change for Reaction 81 or 82 can be written as:

$$
\Delta G^\circ = -2.3RT \cdot (pK_a)
$$

therefore, for Reaction 80 $\Delta G^\circ_1$ is:

$$
\Delta G^\circ_1 = -5.5 = -2.3RT[pK_a(FU) - pK_a(U)]
$$

Using Equation 88, one finds a $pK_a$ difference of 2.6 pH units in the gas phase; this is twice the difference in solution.

The strength of the hydrogen bond (A-H ....B) between the proton donor (AH) and the proton acceptor (B), has been linked, in part, to the acidity of AH; the larger this acidity, the stronger the hydrogen bond [20-23]. Hydrogen bonding plays a crucial part in the helical structure of RNA [20,24], and since hydrogen bonding in the gas phase has been
found to be quite strong (about 15–30 kcal/mol)[26], more than likely
the hydrogen bonding of 5-fluorouracil in RNA is stronger than
previously predicted.

d. ELECTRON AFFINITY OF THE 5-FLUOROURACIL RADICAL

The energetics of the acid ionization reaction (Reaction 81) for
5-fluorouracil (C₄H₃N₂O₂F) can be thought of as the sum of three
thermodynamic processes [25]:

\[
\begin{align*}
C_4H_3N_2O_2F & \rightarrow C_4H_2N_2O_2F^\circ + H^\circ \quad \Delta H_8^\circ \quad (89) \\
H^\circ & \rightarrow H^+ + e^- \quad \Delta H_g^\circ \quad (90) \\
e^- + C_4H_2N_2O_2F^\circ & \rightarrow C_4H_2N_2O_2F^- \quad \Delta H_{10}^\circ \quad (91)
\end{align*}
\]

where \( \Delta H_8^\circ \) is the enthalpy change of the homolytic bond
dissociation reaction for the N-H bond in
FU (D(FU[N-H])),
\( \Delta H_g^\circ \) the ionization potential of hydrogen
(IP(H^\circ)),
and \( \Delta H_{10}^\circ \) the negative of the electron affinity of the
FU radical (-EA(FU^\circ))[26].

The enthalpy change for Reaction 81 (\( \Delta H^\circ_{acid} \)) is the sum of the
enthalpy changes \( \Delta H_8^\circ \) through \( \Delta H_{10}^\circ \). The electron affinity of FU^\circ can
be expressed thus:

\[
EA(FU^\circ) = D(FU[N-H]) + IP(H^\circ) - \Delta H^\circ_{acid} \quad (92)
\]
Before the electron affinity can be calculated, the entropy change in Reaction 81 ($\Delta S_2^\circ$) must be calculated and the bond dissociation energy for the N-H bond in 5-fluorouracil must be known. The entropy for Reaction 81 can be estimated:

$$\Delta S_2^\circ = S^\circ(\text{FU}^-) + S^\circ(\text{H}^+) - S^\circ(\text{FU})$$ (93)

The entropy of the free proton ($S^\circ(\text{H}^+)$) can be calculated from the Sakur-Tetrode equation and is about 26 eu at 298 K [27]. This value can be used for reactions at 450 K since the change in heat capacity over this temperature range is negligible [27-30]. Thus, for the calculation of $\Delta S_2^\circ$, the quantity of interest is the entropy change given by $S^\circ(\text{FU}^-) - S^\circ(\text{FU})$. The entropy for each species can be calculated from the translational ($S^\circ_{\text{tran}}$), rotational ($S^\circ_{\text{rot}}$), vibrational ($S^\circ_{\text{vib}}$), and electronic ($S^\circ_{\text{el}}$) entropies:

$$\Delta S^\circ_{\text{compd}} = S^\circ_{\text{tran}} + S^\circ_{\text{rot}} + S^\circ_{\text{vib}} + S^\circ_{\text{el}}$$ (94)

The electronic entropy change is very small [31], and for molecules over about 30 amu the translational entropy change is less than 0.1 eu. The rotational entropy change is due primarily to changes in internal and external rotations because of deprotonation of the neutral acid. These changes in external rotations are changes in rotational symmetry. For Reaction 81 the change in external rotation is zero; see Chapter II. These changes for compounds similar to those used in this study have been experimentally determined to be about -6 eu [30,31], mostly due to changes in internal rotations. The total $\Delta S_2^\circ$ at 456 K, therefore, is about 20 eu. Experimental $\Delta S_2^\circ$ determination of compounds similar to
ours and where rotational symmetry changes are also zero have yielded $\Delta S^\circ_2$ values of about 20–30 eu [29]. Therefore a reasonable estimate of $\Delta S^\circ_2$ in our reaction is 25 ± 5 eu; hence with a value of 321.1 kcal/mol for $\Delta G^\circ_2$ (see Table 9):

$$\Delta H^\circ_{\text{acid}} = \Delta G^\circ - T\Delta S^\circ$$

(95)

one can determine that $\Delta H^\circ_{\text{acid}}$ is 332.6 ± 3 kcal/mol.

The entropy change in Reaction 81 can be determined by the following experiment. A proton transfer reaction between 5-fluorouracil and a reference acid (AH) is carried out:

$$\text{FU} + \text{A}^- \rightleftharpoons \text{AH} + \text{FU}^-$$

(96)

The $y$-intercept of the plot of $R\ln K_{eq}$ versus $1/T$ gives the entropy change for this reaction ($\Delta S^\circ_{\text{net}}$). If the entropy change of the following reference acid deprotonation reaction:

$$\text{AH} \rightleftharpoons \text{A}^- + \text{H}^+$$

(97)

is known, the entropy change for Reaction 81 can be calculated from the following relationship:

$$\Delta S^\circ_2 = \Delta S^\circ_{\text{net}} - \Delta S^\circ_{\text{AH}}$$

(98)

Before this temperature variation experiment can be done, however, the solids inlet system must be redesigned so that the partial pressure of the solid can be controlled more precisely than is presently possible.

The bond dissociation energy of the N-H bond in 5-fluorouracil has been estimated from other nitrogen compounds like pyrrole, and several
secondary amines [30,32]. This bond dissociation energy is approximately 90 kcal/mol ± 10 kcal/mol. The ionization potential for hydrogen is well known, 313.6 kcal/mol [32]. From Equation 92 one calculates the electron affinity of the 5-fluorouracil radical EA(FU*) to be 70 ± 13 kcal/mol. The value of EA(FU*) is compared to that of other well known compounds in Table 10 [29,30,33,34].

To interpret the measured values in terms of hydrogen bonding and structural changes in the RNA helix, two points must be addressed: 1) which proton, N-1 or N-3, is being deprotonated since in RNA only the N-3 proton is available, and 2) to what extent does the lactam/lactim tautomerism influence the measured acidity of the uracil compounds. I attempted to address these two points by comparing the results from the reaction of 5-fluorouracil and 1,1,1-tri-fluoro-2,4-pentanedione with the reaction of 5-fluorouridine and 1,1,1-tri-fluoro-2,4-pentanedione. 5-fluorouridine was chosen since it is the nucleoside that would be in RNA and only the N-3 proton is available; however, 5-fluorouridine did not yield a large amount of the deprotonated anion parent, and the predominant peak was instead that of FU-fragment. Perhaps the best way to deal with these points is to look at the reaction of the 1 and 3 methylated uracil nucleic acids and compare their reactions with the reference acids to the reactions of the non-methylated uracils with those same reference acids since the methylated uracils will not fragment like 5-fluorouridine.

In general, the predominant tautomeric form, Figure 64, is the lactam form, which is present in the gas-phase at about 70-95%. For the methylated bases, however, the uracils should be almost totally in
Table 10. Comparison of the electron affinity for FU* (= 70 kcal/mol) to various compounds. References: a:[33], b:[29], c:[30], d:[34].

<table>
<thead>
<tr>
<th>(RH)</th>
<th>EA(R*) (kcal/mol)</th>
<th>REFERENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>DICHLOROACETIC ACID</td>
<td>98</td>
<td>a</td>
</tr>
<tr>
<td>HCN</td>
<td>88</td>
<td>c</td>
</tr>
<tr>
<td>HCl</td>
<td>83</td>
<td>a</td>
</tr>
<tr>
<td>HF</td>
<td>80</td>
<td>a</td>
</tr>
<tr>
<td>HBr</td>
<td>78</td>
<td>a</td>
</tr>
<tr>
<td>HI</td>
<td>71</td>
<td>a</td>
</tr>
<tr>
<td>H₂S</td>
<td>53</td>
<td>b</td>
</tr>
<tr>
<td>t-BUTYL ALCOHOL</td>
<td>45</td>
<td>b</td>
</tr>
<tr>
<td>H₂O</td>
<td>42</td>
<td>b</td>
</tr>
<tr>
<td>CH₃CN</td>
<td>35</td>
<td>c</td>
</tr>
<tr>
<td>C₆H₆</td>
<td>25</td>
<td>d</td>
</tr>
<tr>
<td>NH₃</td>
<td>17</td>
<td>c</td>
</tr>
<tr>
<td>CH₄</td>
<td>2</td>
<td>d</td>
</tr>
</tbody>
</table>
Figure 64. Two major tautomeric forms of uracil.
the lactam form since the aromaticity gained by the right hand structure is lost [35-37]; see Figure 64.
PART II
GAS-PHASE BASICITIES OF CUBANE AND DODECAHEDRANE
PARENT AND METHYL DERIVATIVES

A. INTRODUCTION

Since the synthesis of cubane by Eaton and Cole in 1964 [38] and of
dimethyl and parent dodecahedrane by Paquette in 1981 and 1982,
respectively [39-41], there has been much interest in the chemical and
physical properties of these compounds [42-48]. I have determined the
gas-phase basicity of cubane and the dodecahedranes and the heats of
formation of C_{20}H_{20}^+ and C_{20}H_{19}^+.

Cubane was introduced through a liquid inlet; dimethyl and parent
dodecahedrane were introduced with the solids probe; and mono-methyl-
dodecahedrane was generated in the mass spectrometer by electron-
ionization of dimethyl-dodecahedrane. The basicities of cubane and the
three dodecahedranes were referred to a recalibrated self-consistent set
of eight reference bases; see Figure 55. n-Propyl ether was chosen
as an anchor for the relative basicity scale shown in Figure 55, thus
making possible the assignment of absolute gas-phase basicities for
these compounds; see Table 11. n-propyl ether is a secondary standard
base in the compilation of Lias, Liebman, and Levin [12] and as such
its value has been rigorously referenced to primary standards such as
ethylene and isobutene. The gas-phase basicities of
Table 11. Gas-phase basicities determined from ionized binary mixtures of the designated compounds. The relative basicities for all but the dodecahedrane are self-consistent to within ±0.2 kcal/mol; the absolute errors are ±3 kcal/mol relative to a basicity of 194.5 kcal/mol for n-propyl ether [12]. The origin of the larger imprecision for dodecahedrane ±1 kcal/mol and its methyl and dimethyl derivatives ±3 kcal/mol is discussed in the text.

<table>
<thead>
<tr>
<th>COMPOUND</th>
<th>GAS-PHASE BASICITY (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,16-DIMETHYLDODECAHEDRANE</td>
<td>202</td>
</tr>
<tr>
<td>α-METHYLSTYRENE</td>
<td>201.4</td>
</tr>
<tr>
<td>CUBANE</td>
<td>200.7</td>
</tr>
<tr>
<td>ISO PROPYL ETHER</td>
<td>199.4</td>
</tr>
<tr>
<td>n-PENTYL ETHER</td>
<td>198.4</td>
</tr>
<tr>
<td>2,4-DIMETHYL-3-PENTANONE</td>
<td>197.3</td>
</tr>
<tr>
<td>METHYL BENZOATE</td>
<td>197.0</td>
</tr>
<tr>
<td>METHYLDODECAHEDRANE</td>
<td>197</td>
</tr>
<tr>
<td>n-BUTYL ETHER</td>
<td>196.8</td>
</tr>
<tr>
<td>DODECAHEDRANE</td>
<td>196.6</td>
</tr>
<tr>
<td>METHYL TRIMETHYLACETATE</td>
<td>195.7</td>
</tr>
<tr>
<td>METHYL CYCLOPROPANECARBOXYLATE</td>
<td>194.9</td>
</tr>
<tr>
<td>n-PROPYL ETHER</td>
<td>194.5</td>
</tr>
</tbody>
</table>
standards have been calculated from well established heats of formation for their parent and protonated parent compounds. The heats of formation were obtained from numerous ionization potential and appearance potential measurements. The gas-phase basicity of n-propyl ether is $194.5 \pm 3$ kcal/mol [12].

B. Cubane

The FT/ICR mass spectra obtained for ionized binary isobaric mixtures of cubane with either α-methylstyrene or isopropyl ether are shown in Figure 65. The peaks at $m/z = 117$ and 101 in Figure 65 represent $(M-H)^+$ from α-methylstyrene and isopropyl ether, respectively. The doublet at $m/z = 104$ can be resolved into the $M^+$ molecular ion from cubane and $(M+2H)^+$ from isopropyl ether. The present basicity determinations are unaffected by ejection of the above ions; thus, those ions do not affect the results. It is qualitatively clear that protonated cubane is more abundant (i.e., higher basicity) than protonated isopropyl ether, but less abundant (i.e., lower basicity) than α-methylstyrene.

Once cubane had been bracketed between α-methylstyrene and isopropyl ether, the gas-phase basicity of cubane could be determined quantitatively with respect to α-methylstyrene; see Figure 66. As seen in Figure 49, equilibrium was approached without (open circles) and following ejection of either of the two protonated parents (squares and solid circles). From the averaged equilibrium constants (after $>20$ s equilibration period) of the three routes to equilibrium, the gas-phase
Figure 65. Fourier transform ion cyclotron resonance mass spectra of isobaric binary ionized mixtures of cubane and isopropyl ether (top) or α-methylstyrene (bottom), detected 45 sec after ion formation. The relative peak heights of the protonated parent ions at m/z = 105, 103, and 119 clearly show that cubane has a gas-phase basicity lower than that of α-methylstyrene and higher than that of isopropyl ether. The m/z = 101, 117 peaks are (M-H)+ from isopropyl ether and α-methylstyrene, respectively. The doublet at m/z = 104 peaks was clearly resolved into cubane M+ parent and a very small amount of (M + 2H)+ from isopropyl ether.
\[
\begin{align*}
\text{C}_9\text{H}_{11}^+ & \quad ((\text{CH}_3)_2\text{CH})_2\text{O} \\
\text{C}_8\text{H}_9^+ & \quad \text{C}_6\text{H}_{15}^+ \\
\end{align*}
\]
Figure 66. Approach to equilibrium for the proton transfer reaction between cubane (C₈H₈) and α-methylstyrene (C₉H₁₀). The apparent equilibrium constant,

\[ K_{\text{apparent}} = \frac{[\text{C₈H₈}] [\text{C₉H₁₁}^+]}{[\text{C₉H₁₀}] [\text{C₈H₉}^+]} \]

is plotted as a function of time following ion formation.

- Open circles: no ion ejection.
- Squares: after ejection of protonated cubane.
- Solid circles: after ejection of protonated α-methylstyrene.
basicity of cubane was found to be 0.7 ± 0.2 kcal/mol lower than that of α-methylstyrene. Based on an absolute gas-phase basicity of n-propyl ether as 194.5 ± 3 kcal/mol [12], the absolute gas-phase basicity of cubane is 200.7 ± 3 kcal/mol.

Preliminary semi-empirical (MNDO) [49] and ab initio (HF/3-21G) [50] calculations predict the relative energies for cubane protonated at different sites: corner < edge < face < center. Thus, the most likely site for protonation of cubane is a corner.

C. Dodecahedranes

The larger relative error (± 1 kcal/mol vs. ± 0.2 kcal/mol reported for dodecahedrane (Figure 55) is due to the larger uncertainty in the measurement of its partial pressure. The dodecahedranes were introduced by a solids probe, from which the sample pressure in the high-vacuum chamber was controlled by heating the probe tip. Because there is no valve between the ICR excitation/detection cell and the sample tip, no fine control of pressure is possible. Moreover, the small amount of sample on the probe tip is exhausted at a partial pressure of about 5x10^-8 Torr, at which the rate of approach to equilibrium is inconveniently slow. Therefore, methane was added to the reaction as a buffer gas to increase the chamber pressure to about 3-5x10^-7 Torr and to provide a source of protons. In this way, it was possible to equilibrate a binary mixture of dodecahedrane and methyl benzoate to give a relative basicity difference of 0.4 kcal/mol; however, due to
Inaccurate partial pressure measurements, the relative error is about ±0.7 to 1.0 kcal/mol. The absolute gas-phase basicity of dodecahedrane is 196.6 ± 4 kcal/mol.

The available quantities of methyl- and dimethyldodecahedrane were too small to permit multiple quantitative equilibrations with reference bases. Therefore, their reported basicities (197 ± 5, 202 ± 5 kcal/mol for methyl and dimethyl derivatives, respectively) were based on bracketing experiments (with correspondingly larger errors) to establish whether or not proton transfer to a reference base took place.

D. Total Strain Energy

Table 12 shows the direct relation between gas-phase basicity and total strain energy for representative cycloalkenes. On the basis of strain energy alone cubane (166 kcal/mol) would be expected to exhibit much greater basicity than other hydrocarbons, including the dodecahedrane (70 kcal/mol) corresponding to only about 17% as much strain energy per carbon as cubane [20,51-53].

Dodecahedrane should have little bond angle strain since its angles are close to the tetrahedral value of about 109.5 °C; however, major torsional strain results from the precise eclipsing of all the C-H bonds [52,54]. 1,16-dimethyldodecahedrane is slightly distorted from its D₃d symmetry -- dodecahedrane has full Ih symmetry -- due to elongation along the axis passing through the dodecahedrane center and connecting the two methyl groups. This elongation is caused by steric crowding of
Table 12. Effect of total strain energy on gas-phase basicity. All quantities in kcal/mol. Strain energies from references [20,51,53], gas-phase basicities from [12].

<table>
<thead>
<tr>
<th>COMPOUND</th>
<th>TOTAL STRAIN ENERGY</th>
<th>STRAIN ENERGY PER CARBON ATOM</th>
<th>GAS-PHASE BASICITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYCLOHEXANE</td>
<td>1.4</td>
<td>0.2</td>
<td>161</td>
</tr>
<tr>
<td>CYCLOHEXENE</td>
<td>2.5</td>
<td>0.4</td>
<td>181.5</td>
</tr>
<tr>
<td>CYCLOBUTENE</td>
<td>30.6</td>
<td>7.6</td>
<td>183</td>
</tr>
<tr>
<td>CYCLOPROPENE</td>
<td>54.5</td>
<td>18.2</td>
<td>190</td>
</tr>
<tr>
<td>DODECAHEDRANE</td>
<td>70</td>
<td>3.5</td>
<td>196.6</td>
</tr>
<tr>
<td>CUBANE</td>
<td>166</td>
<td>20.8</td>
<td>200.7</td>
</tr>
</tbody>
</table>
the protons, resulting in bond angles which are less than 108 °C (sharper than in dodecahedrane) and hence greater strain energy than that for dodecahedrane [39,51]. Although the experimental cubane basicity is indeed higher than those for other hydrocarbons, it is only slightly higher than those of dodecahedrane and methylidodecahedrane, and is actually lower than that of 1,16-dimethylidodecahedrane.

E. Polarizability

Gas-phase basicity also varies directly with molecular polarizability, as seen for the series of primary amines in Table 13 [12,20]. Polarizability varies directly with alkyl chain length. Since the calculated polarizabilities of the dodecahedranes are much larger than for cubane (about 2.5:1), the increased polarizability of the dodecahedranes evidently offsets their lower strain energies (relative to cubane) in determining the gas-phase basicities. The relative basicity order among the unsubstituted, methyl-, and 1,16-dimethylidodecahedranes is consistent with the predicted small increases in polarizability and torsional strain introduced by the attachment of methyl groups.

The gas phase basicities of cubane (200.7 kcal/mol) and the dodecahedranes (196.6-202 kcal/mol are strikingly higher than for most saturated hydrocarbons (e.g., cyclohexane (161 kcal/mol)[12]. Although the high basicity of cubane is consistent with its high bond strain energy, the remarkably high basicity of dodecahedrane cannot
Table 13. Gas-phase basicities of primary amines, n-(C\(_x\)H\(_{2x+1}\))NH\(_2\) [12]. Basicity increases directly with polarizability, which in turn varies directly with alkyl chain length.

<table>
<thead>
<tr>
<th>ALKYL CHAIN LENGTH</th>
<th>GAS-PHASE BASICITY (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>205.7</td>
</tr>
<tr>
<td>2</td>
<td>208.5</td>
</tr>
<tr>
<td>3</td>
<td>210.1</td>
</tr>
<tr>
<td>4</td>
<td>210.6</td>
</tr>
<tr>
<td>5</td>
<td>211.1</td>
</tr>
<tr>
<td>6</td>
<td>211.1</td>
</tr>
<tr>
<td>7</td>
<td>211.2</td>
</tr>
<tr>
<td>8</td>
<td>212.0</td>
</tr>
</tbody>
</table>
arise from strain alone, and at present must be ascribed to its high polarizability.

F. CALCULATION OF HEATS OF FORMATION FROM APPEARANCE POTENTIALS

The appearance potentials for \( \text{C}_2\text{H}_{20}^+, \text{C}_2\text{H}_{19}^+, \text{C}_{10}\text{H}_{16}^+, \text{C}_{10}\text{H}_{15}^+, \) and \( \text{C}_2\text{H}_4^+ \) (a reference compound) are reported in Table 14; see also Figures 67 to 69. The appearance potentials were measured by electron impact in the FT/ICR mass spectrometer. Since the electron beam is not precisely monoenergetic, there is an error of at least 0.35 eV in all measurements [55,56]. The remainder of the error in the measurements comes from inability to determine the threshold appearance potential accurately [56].

The most common method to determine the threshold potential is use the initial onset method, where the appearance potential is taken as the minimal electron energy at which ion intensity is first detected [56,57]. The initial onset method is remarkably accurate as long as the pressure is constant [55,58]. Since the ionization experiments can be done at low pressures and since it is easier to maintain a constant low pressure (low \( 10^{-8} \) Torr) of a solid than a high pressure (\( 10^{-7} \) Torr) (see Chapter III), maintaining a constant dodecahedrane pressure was not difficult.

The Warren extrapolated difference technique [55] is an improved method for measuring appearance potentials. The basis of the Warren method is that the initial curvature of the plot of ion abundance vs.
Table 14. Appearance potentials of several organic compounds. Cubane is included for comparison to adamantane and dodecahedrane. Cubane values from reference KC66.

<table>
<thead>
<tr>
<th>NEUTRAL</th>
<th>ION</th>
<th>APPEARANCE POTENTIAL (eV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETHYLENE</td>
<td>C$_2$H$_4^+$</td>
<td>10.7 ± 0.45</td>
</tr>
<tr>
<td>ADAMANTANE</td>
<td>C$<em>{10}$H$</em>{16}^+$</td>
<td>9.8 ± 0.45</td>
</tr>
<tr>
<td></td>
<td>C$<em>{10}$H$</em>{15}^+$</td>
<td>10.8 ± 0.45</td>
</tr>
<tr>
<td>DODECAHEDRANE</td>
<td>C$<em>{20}$H$</em>{20}^+$</td>
<td>9.6 ± 0.45</td>
</tr>
<tr>
<td></td>
<td>C$<em>{20}$H$</em>{19}^+$</td>
<td>11.2 ± 0.65</td>
</tr>
<tr>
<td>CUBANE</td>
<td>C$_8$H$_8^+$</td>
<td>8.74 ± 0.15</td>
</tr>
<tr>
<td></td>
<td>C$_8$H$_7^+$</td>
<td>9.5 ± 0.11</td>
</tr>
</tbody>
</table>
Figure 67. FT/ICR Mass spectral peak areas vs. ionization energy. Dodecahedrane, C_{20}H_{20}, is ionized by electron impact to yield C_{20}H_{20}^{+} and C_{20}H_{19}^{+}. Argon is a calibrant gas.
Figure 68. FT/ICR Mass spectral peak areas vs. ionization energy. Adamantane, C\textsubscript{10}H\textsubscript{16}, is ionized by electron impact to yield C\textsubscript{10}H\textsubscript{16}\textsuperscript{+} and C\textsubscript{10}H\textsubscript{15}\textsuperscript{+}. Argon is a calibrant gas.
Figure 69. FT/ICR Mass spectral peak areas vs. ionization energy. Ethylene, C₂H₄, is ionized by electron impact to yield C₂H₄⁺. Argon is a calibrant gas.
electron energy is due to the electron beam energy spread; hence the appearance potential is measured from the rising linear portion of the curve [55]. Therefore, if the linear portions of the two ionization curves (a compound of interest and a calibrant gas) are made parallel, then the true appearance potential difference can be obtained [55,56,57]. The two curves for C_{10}H_{16}^+ and A^+ Figure 68, (argon was used as a calibrant gas in all experiments since its ionization potential, 15.755 eV, is well known [32]) will be used to demonstrate the good agreement between the initial onset and the Warren methods. The data for the argon curve is multiplied by 2.06 to make the slopes of the linear portions of both curves equal. The appearance potential difference is determined from a plot of the voltage difference between the curves vs. the peak intensity by extrapolating to zero voltage difference. The initial onset method yielded an appearance potential of 9.7 eV for C_{10}H_{16}^+ and the Warren method a value of 9.9 eV. Thus, the threshold potential can be measured to within about 0.1 eV using the initial onset method: this error was about 0.3 eV for C_{20}H_{19}^+ due to the gentle rise of the curve and poor signal-to-noise ratio of the dodecahedrane experiments.

Appearance potentials measured by electron impact are complicated by the presence of the reactant and product excited states. Therefore, all the measurements were done with a trap potential of 60 mV (the usual trap voltages are about 1 V) (2.54 cm between the trap plates). Low trap voltages allow ions of kinetic energy larger than about 0.06 eV to escape from the cell and thus help insure that the ions are close to their translational ground states.
G. Calculation of the Heats of Formation of \( \text{C}_{20}\text{H}_{20}^+ \) and \( \text{C}_{20}\text{H}_{19}^+ \)

The heat of reaction for the ionization of a neutral \( M \) is given by:

\[
M \rightarrow A^+ + B^* + e^- \quad (99)
\]

\[
\Delta H_{rx} = \Delta H_f(A^+) + \Delta H_f(B^*) - \Delta H_f(M) \quad (100)
\]

The \( \Delta H_f(M) \) for the compounds studied were obtained from literature [60-62]. The appearance potential energy for \( A^+ \) is equal to \( \Delta H_{rx} \) [59]. The thermal energy of the electron is not taken into account in calculation of the heat of formation at temperatures other than 0 K, since the integrated heat capacity of the electron is taken to be zero at all temperatures > 0 K; i.e., the stationary electron convention [12,63]. The heat of formation of hydrogen is 52.1 kcal/mol at 25 °C [61]. Since the present measurements were made at about 60 °C, the change in heat capacities over this temperature range can be ignored, and therefore the heats of formation at 25 °C were used without corrections [27,58]. The heats of formation of the ions can be calculated from:

\[
\Delta H_f(A^+) = AP - 52.1 - \Delta H_f(M) \quad (101)
\]

where \( AP \) is the measured appearance potential in kcal/mol. The values of \( \Delta H_f(A^+) \) for the ions in Table 14 are given in Table 15. The cubane values in Tables 14 and 15 were calculated from the work by Kybett...
Table 15. Heats of formation (kcal/mol) for compounds in Table 14. Heats of formation for the C\textsubscript{8}H\textsubscript{8}+ and C\textsubscript{g}H\textsubscript{7}+ ions were calculated from values in reference KC66. References for \(\Delta H^\circ_{\text{fNEUTRAL}}\): a:[60], b:[62], c:[61], and d:[42].

<table>
<thead>
<tr>
<th>NEUTRAL</th>
<th>ION</th>
<th>(\Delta H^\circ_{\text{fION}})</th>
<th>(\Delta H^\circ_{\text{fNEUTRAL}})</th>
<th>REF.</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETHYLENE</td>
<td>C\textsubscript{2}H\textsubscript{4}+</td>
<td>258.6 ± 10.4</td>
<td>-112.5</td>
<td>b,c</td>
</tr>
<tr>
<td>ADAMANTANE</td>
<td>C\textsubscript{10}H\textsubscript{16}+</td>
<td>193.6 ± 10.4</td>
<td>-32.3</td>
<td>a,b</td>
</tr>
<tr>
<td></td>
<td>C\textsubscript{10}H\textsubscript{15}+</td>
<td>164.3 ± 10.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DODECAHEDRANE</td>
<td>C\textsubscript{20}H\textsubscript{20}+</td>
<td>215.8 ± 10.4</td>
<td>-5.5</td>
<td>a</td>
</tr>
<tr>
<td></td>
<td>C\textsubscript{20}H\textsubscript{19}+</td>
<td>200.6 ± 15.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CUBANE</td>
<td>C\textsubscript{8}H\textsubscript{8}+</td>
<td>350.2 ± 4.0</td>
<td>+148.7</td>
<td>a,d</td>
</tr>
<tr>
<td></td>
<td>C\textsubscript{8}H\textsubscript{7}+</td>
<td>315.6 ± 4.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
[42] and are included for comparison with the present values. Ethylene was used as a standard since its ionization potential and the $C_2H_4^+$ heat of formation (10.5 eV and 253-260 kcal/mol, respectively) are well known [56,62,64-66]. The appearance potential of $C_{10}H_{16}^+$ has been previously determined to be 9.25 eV [66] and the heat of formation of $C_{10}H_{15}^+$ has been estimated by Kebarle [67] from chloride transfer reactions as -159 kcal/mol. The present value of 164.3 kcal/mol is intermediate between the value determined by Kebarle and the value for butyl benzene ($C_{10}H_{15}^+$) of 167-170 kcal/mol, although rearrangement of the adamantyl cation to butyl benzene is not likely [63,68]. The dodecahedryl cation ($C_{20}H_{19}^+$), even though distorted to something like $D_{3d}$ symmetry by the Jahn-Teller effect [52] will still retain the same connectivity as the parent neutral [52,63,69].
REFERENCES


49. Bartmess, J.E. Private Communication.


58. Holmes J.L. Private Communication.


63. Lias, S.G. Private Communication.


68. Fort, R.C. Jr.; Schleyer, P.R. Chem. Rev. 1964, 64, 277-300.

CHAPTER VI

VACUUM SYSTEM REDESIGN AND RENOVATION

A. INTRODUCTION

The original Nicolet FTMS-1000 vacuum system consisted of a Balzers TPU 270 turbopump backed by an Alcatel 2012 A mechanical pump. The turbopump cannot be placed close to the chamber because the magnetic field interferes with the rotation of the metal turbine blades that spin at over 20,000 rpm. The tolerances of the components within the pump are small, and if the blades get out of balance, they could destroy the pump. Since the pump must be placed away from the chamber, effective pumping speed is reduced. To increase pumping speed and to achieve a low base pressure, I redesigned the vacuum system and added an Air Products HV202-8C cryopump. This new system achieves the following:

1) increases the mass resolution by lowering the base pressure, and thus a lower chamber pressure results; see Equation 17.
2) increases the effective pumping speed thereby allowing:
   a) the gas from a pulsed valve experiment to be pumped away faster, thus shortening the cycle period of the experimental sequence; see Figure 22.
b) Pumpdown time following probe introduction to be shortened, thus allowing more samples to be run. Also, less time is spent pumping down between the introduction of two samples by the solids probe, and therefore a more reliable pressure measurement can be made since the pressure from the first sample is constant.

B. CALCULATION OF EFFECTIVE PUMPING SPEED

The effective pumping speed at the cell is always less than the intrinsic pumping speed (pumping speed with the inlet blanked off) of the pump due to restrictions (such as bends, long lengths of pipe,) between the cell and the pump [1-3]. The effective pumping speed is given by [2,4]:

\[
\frac{1}{S_{\text{eff}}} = \frac{1}{S} + \frac{1}{C_T} \tag{6.1}
\]

where \( S_{\text{eff}} \) is the effective pumping speed (in l/s), \( S \) the intrinsic pumping speed (in l/s), and \( C_T \) the total conductance at some point (in l/s).

The total conductance at a particular point in the system can be calculated from the individual conductances of each component in the system. For components in series the total conductance is given by:

\[
\frac{1}{C_T} = \frac{1}{C_1} + \frac{1}{C_2} + \cdots \tag{6.2}
\]

and for components in parallel:
\[ C_T = C_1 + C_2 + \cdots \]  

where \( C_1, C_2, \cdots \) are the individual conductances \([1,3]\).  

C. EXAMPLE OF SPECIFIC CONDUCTANCE CALCULATIONS  

The original vacuum system configuration will be used as example to demonstrate conductance calculations; see Figure 70. The system is composed of two lengths of pipe: section \( L_1 \) contains two bends and two straight sections of short pipe, section \( L_2 \) is just one straight pipe with no bends, and the diameter of each pipe segment is 4" (10.2 cm). One of two equations is used to determine conductance (1/s) in a pipe \([1,3]\):

\[ C = 12.1 \frac{d^3}{L} \]  
\[ C = 11.6 a'A \]  

where \( d \) is the pipe diameter (in cm),  
\( L \) the pipe length (in cm),  
\( a' \) the Clausing factor for short pipes,  
\( A \) the cross-sectional area of the pipe (in cm\(^2\)).

Equation 105 is used in situations where \( L > 15d \) \([1,3]\). The ratio of \( L/d \) for the present example never exceeds ten, thus Equation 106 must be used. The Clausing factor is based on the \( L/d \) ratio and can be obtained from published tables \([3,4]\). For \( l/d = 0 \), \( a' \) is 1, and Equation 106 reduces to the equation for the conductance through an aperture of
Figure 70. Schematic diagram of Nicolet FTMS-1000 vacuum system configuration.

\[ L_1 = L_a + L_b \]
area A.

The use of Equation 105 or 106 depends on whether or not the gas is in a state of molecular flow [3,5]. Two criteria are used to determine whether molecular flow exists: 1) the Knudsen number (Kn) should be greater than one [3] given:

\[ Kn = \frac{1}{d} \]

where \( d \) is the mean free path of the gas, and 2) the product of the pipe diameter and the gas pressure should less than \( 7 \times 10^{-3} \) Torr·cm. For this example (at \( 3 \times 10^{-7} \) Torr and 150 °C) this product is about \( 1 \times 10^{-6} \) Torr·cm, and Kn is about 1300. Thus, the present system is in the molecular flow regime.

The conductances for the two sections, \( L_1 \) and \( L_2 \), are calculated as follows. Bends are treated as additions to the true length, and thus the effective length for \( L_1 \) (\( L_{\text{eff}}(1) \)) is given by [1]:

\[ L_1 < L_{\text{eff}}(1) < L_1 + 2.66n r \]

where \( n \) is the number of bends in the section, and \( r \) is the radius of the pipe (in cm).

In the present example, the longest possible \( L_{\text{eff}}(1) \) is 85.5 cm. The ratio of this length to pipe diameter is 8.4; thus the Clausing factor is about 0.13. From Equation 106, the conductance \( C_1 \) is calculated to be about 122 l/s. The Clausing factor for section \( L_2 \) is about 0.17 and \( C_2 \) is about 160 l/s. Therefore, as seen from Equation
103, total conductance is about 69 l/s. The intrinsic pumping speed for
the turbopump is 300 l/s, and thus the effective pumping speed at the
cell calculated from Equation 102 is 56 l/s for air at 20 °C.

For the new vacuum system, I replaced the 4-way cross with a more
versatile 6-way cross that allows more equipment to be adapted to the
ICR mass spectrometer. The new cross was machined by The Ohio State
University Department of Physics machine shop from a solid piece of high
grade stainless steel to eliminate the many complex welds needed in a
6-way cross. Since the cryopump is not affected by the magnetic field,
it can be mounted directly to the cross with only a gate valve (Vat
Series 10 model DN 200, conductance 7500 l/s) separating the cryopump
from the chamber, thereby minimizing loss in conductance to the
cryopump; see Figure 71. The diameter of the pipe leading to the
turbopump was increased from 4" to 6" and a gate valve was added between
the turbopump and the main chamber. The effective pumping speed was
increased to about 140 l/s when only the cryopump is used and to about
200 l/s when both the cryopump and the turbopump are used.

To minimize the unwanted introduction of water into the system when
it is opened to the atmosphere, I added a regulator and a 3-way valve to
the inlet system allowing 2-4 psi of dry nitrogen to flow through the
existing probe inlet roughing valves; see Figure 72. Furthermore, I
designed and built an evacuated probe storage tube, which can also be
brought up to atmosphere with dry nitrogen since it is plumbed into the
inlet vacuum system. All these modifications have shortened the
pumpdown time (to about mid 10^-8 Torr) from 30 min to 5-10 min.
Figure 71. Schematic diagram of the new vacuum system. Dry nitrogen is used to purge the cryopump during pump regeneration.
Figure 72. Schematic diagram of the solids/liquid inlet system modification. This modification allows dry nitrogen to be supplied to the solid probe storage tube and main vacuum chamber during times when the system is brought up to atmosphere.
REFERENCES


APPENDIX

Computer programs
PROGRAM BASICITY

REAL INT(50), INTP(50), INTM(50), INMP(50)
REAL IONRATE(50), REX(50), INVTEMP(50)
DIMENSION TEMP(50), PREAD(50), PREAD(50)
DIMENSION CORIN(50), CORIN(50), PRESS(50), PRESS(50)
DIMENSION TEM(50), RANKD(50), DELTAG(50)
CHARACTER SUBSTR, REWR, RESPONSE, DIITLE
CHARACTER NAME(50), NAME(50), SPECNAME(50), NAME(50)
CHARACTER CMOD(20)
READFLG = 0
CHNGFLG = 0
PRINT *, 'BASICITY version 4.00, 06.04'
PRINT *, 'Do you want to Read or Write a file'
READ(1,4000) REWR
IF(SUBSTR(REWR,1,1).UN.EQ.'R') THEN
  READFLG = 0
  GOTO 122
ELSEIF(SUBSTR(REWR,1,1).UN.EQ.'W') THEN
  GOTO 10
ELSE
  PRINT *, 'Please answer again R/W'
  GOTO 1
ENDI
10 PRINT *, 'Enter the # of specs run with the same compd.'
  READ(1,4100) NSPECS
  PRINT *, 'Enter the data title for this data set'
  PRINT *, 'Enter the data title for this data set'
  READ(1,4200) DITLE
  CALL COMPCODE(NLARR,NAME,RENAM,RENAM,CMPD)
  DO 100 I=1,NSPECS
    WRITE(2,4300)
    PRINT *, 'Enter the remarks of this spectrum'
    PRINT *, 'Enter the remarks of this spectrum'
    READ(1,4300) SPECNAME
    IF (I.EQ.1) THEN
      PRINT *, 'Enter the temperature in degrees.
      READ(1,45000) TEMPC(1)
      PRINT *, 'Enter the pressure reading for 1 M atm.
      READ(1,46000) PREAD(1)
      PRINT *, 'Enter the pressure reading for 2 M atm.
      READ(1,47000) PREAD(1)
    ELSE
      WRITE(5,48000) TEMPC(I)
      READ(1,46000) IMPTEMP
      IF (IMPTEMP.EQ.0.0) THEN
        TEMPC(I) = IMPTEMP
ELSE
    TEMPC(1) = TMP-TEMPC
ENDIF

WRITE(2,5700) PREAD1(1-1)
READ(1,4600) TMPPRI
IF(TMPPRI.EQ.0) THEN
    PREAD1(I) = PREAD1(I-1)
ELSE
    PREAD1(1) = TMPPRI
ENDIF

WRITE(2,5800) PREAD2(1-1)
READ(1,4600) TMPPRI
IF(TMPPRI.EQ.0) THEN
    PREAD2(I) = PREAD2(I-1)
ELSE
    PREAD2(1) = TMPPRI
ENDIF

PRINT *, 'Enter the peak intensity for #1 M ion'
READ(1,4600) INTM1(I)
PRINT *, 'Enter the peak intensity for #1 MH ion'
READ(1,4600) INTMH1(I)
PRINT *, 'Enter the peak intensity for #2 M ion'
READ(1,4600) INTM2(I)
PRINT *, 'Enter the peak intensity for #2 MH ion'
READ(1,4600) INTMH2(I)

CONTINUE

PRINT *, 'Do you wish to make any changes?'
READ(1,4500) RESPONSE
IF(SUBSTR(RESPONSE,1,1).EQ.'Y') THEN
    CHNGFLG = 1
    GOTO 300
ELSE IF(SUBSTR(RESPONSE,1,1).EQ.'N') THEN
    GOTO 200
ELSE
    PRINT *, 'Please answer again Y/N'
    GOTO 150
ENDIF

DO 300 1=1,NSPECS
    CORIN(I) = INTMH1(I) - 0.0108*NCARR1*INTM1(I)
    CORIN2(I) = INTMH2(I) - 0.0108*NCARR2*INTM2(I)
    PRESS(I) = PREAD(I)/RSENT1
    PRESS2(I) = PREAD(I)/RFPNT2
    IONRATIO(I) = CORIN2(I)/CORIN1(I)
    KEL(I) = KEL1(I)*PRESS1(I)/PRESS2(I)
    TEMP(I) = TEMPE1(I) + 273.15
    INVTEMP(I) = 1/TEMP(I)
    RLNKED(I) = 0.987*LOG(KEL(I)) + 10000
    DELTAG(I) = -1*TEMP(I)*RLNKED(I)

CONTINUE

IF(READ(1,4500).EQ.1) AND,
* (CHNGFLG.EQ.0) THEN
    GOTO 330
END
ENDIF
325 PRINT *, 'Enter the filename for the data set '
   READ(1, 4700) (FLNAME(K),K=1,J)
   IF (SUBSTR(REWR,1,1).EQ. 'N') THEN
      IF (READFLG.EQ.1) THEN
         GOTO 1000
      ELSE
         GOTO 2000
      ENDIF
   ELSEIF (SUBSTR(REWR,1,1).EQ. 'L') THEN
      GOTO 1000
   ELSEIF (SUBSTR(REWR,1,1).EQ. 'W') THEN
      GOTO 1000
   ENDIF
   C
   ***** ****  PRINT SECTION ***** ****
   C
330 CALL OUTDEVCD(J)
   WRITE(J,5500)
   WRITE(J,4300) DTITLE
   WRITE(J,5000) FLNAME, CMPD(1), CMPD(2)
   WRITE(J,5100)
   WRITE(J,5200)
   DO 335 I=1,NSPECS
      WRITE(J,5300) I, SPECNME(I), DELTAG(I), KEQ(I), TEMPK(I),
         TEMPK(I), ALNKED(I), INVTMP(I), IONRT10(I)
   CONTINUE
   WRITE(J,5500)
   C
350 PRINT *, 'Do you have any more data set to calculate? '
   READ(1,4000) RESPONSE
   IF (SUBSTR(RESPONSE,1,1).EQ. 'Y') THEN
      GOTO 1
   ELSEIF (SUBSTR(RESPONSE,1,1).EQ. 'N') THEN
      GOTO 3500
   ELSE
      PRINT *, 'Please answer again Y/N ',
      GOTO 350
   ENDIF
   C
   ***** ****  WRITE SECTION ***** ****
   C
1000 OPEN (11, FILE=FLNAME, STATUS='UNKNOWN')
   WRITE(11,4400) NSPECS
   WRITE(11,4200) DTITLE
   WRITE(11,4100) NCRAD
   WRITE(11,4100) NCRAD
   WRITE(11,4100) RSEN!
   WRITE(11,4600) RSEN!
   DO 1000 I=1,NSPECS
      WRITE(11,4500) SPECNME(I)
      WRITE(11,4600) TEMPK(I)
      WRITE(11,4600) TEMPK(I)
      WRITE(11,4600) IREAD1(I)
      WRITE(11,4600) INI1(I)
      WRITE(11,4600) INI1(I)
      WRITE(11,4600) INI3(I)
      WRITE(11,4600) INI3(I)
CONTINUE
PRINT *,'DATA WRITTEN'
CLOSE(11,STATUS='KEEP')
WRITE(6,5500)
GOTO 330

C
C          ********** READ SECTION **********
C
C 200 CONTINUE
OPEN(11,FILE=FILENAME,STATUS='OLD')
READ(11,4100) NSPECS
READ(11,4200) DTITLE
READ(11,4100) NCARB1
READ(11,4100) NCARB2
READ(11,4600) RSENT1
READ(11,4600) RSENT2
DO 2020 I=1,NSPECS
   READ(11,4300) SPECNAME(I)
   READ(11,4600) TEMPC(I)
   READ(11,4600) PREAD1(I)
   READ(11,4600) PREAD2(I)
   READ(11,4600) INTMI(I)
   READ(11,4600) INTMH(I)
   READ(11,4600) INTMC(I)
2020 CONTINUE
PRINT *,'DATA READ'
CLOSE(11,STATUS='KEEP')
READFLG = 1
WRITE(6,5500)
GOTO 150

C
C          ********** CHANGE SECTION **********
C
C 3000 PRINT *,'How many changes do you want to make?'
READ(11,4100) NCHANGES
DO 3100 I=1,NCHANGES
   PRINT *,' NCARB1 No. of carbons in # 1 compd'
   PRINT *,' NCARB2 No. of carbons in # 2 compd'
   PRINT *,' RSENT1 Relative ion gauge rent # 1 compd'
   PRINT *,' RSENT2 Relative ion gauge rent # 2 compd'
   PRINT *,' DTITLE Data title for data set'
   PRINT *,' SPECNAME Spectrum name and/or remarks'
   PRINT *,' TEMPC Temperature of the reaction'
   PRINT *,' PREAD1 Apparent press reading # 1 compd'
   PRINT *,' PREAD2 Apparent press reading # 2 compd'
   PRINT *,' INTMI Peak intensity for the # 1 M ion'
   PRINT *,' INTMC Peak intensity for the # 2 M ion'
3100 CONTINUE
PRINT *, '11 INTM1 Peak intensity for the #1 MH ion'
PRINT *, '12 INTM2 Peak intensity for the #2 MH ion'
PRINT *, '13 INTM3 Peak intensity for the #3 MH ion'
PRINT *, 'Enter the # of the item you want changed'
READ(1,4100) ITEMNO
IF (ITEMNO.GT.5) THEN
  PRINT *, 'Enter the reaction # of the change'
  READ(1,4100) NRX
ENDIF
IF (ITEMNO.EQ.1) THEN
  WRITE(2,4100) NCARBI
  PRINT *, 'Enter new NCARBI value (RET) if no change'
  READ(1,4100) K
  IF (K.NE.0) NCARBI = K
ELSEIF (ITEMNO.EQ.2) THEN
  WRITE(2,4100) NCARB2
  PRINT *, 'Enter new NCARB2 value (RET) if no change'
  READ(1,4100) K
  IF (K.NE.0) NCARB2 = K
ELSEIF (ITEMNO.EQ.3) THEN
  WRITE(2,4100) RSENT1
  PRINT *, 'Enter new RSENT1 value (RET) if no change'
  READ(1,4100) F
  IF (F.NE.0) RSENT1 = F
ELSEIF (ITEMNO.EQ.4) THEN
  WRITE(2,4100) RSENT2
  PRINT *, 'Enter new RSENT2 value (RET) if no change'
  READ(1,4100) F
  IF (F.NE.0) RSENT2 = F
ELSEIF (ITEMNO.EQ.5) THEN
  WRITE(2,4500) DTITLE
  PRINT *, 'Enter new DTITLE (RET) if no change'
  PRINT *, '
  READ(1,4200) T
  IF (T.NE.0) DTITLE = T
ELSEIF (ITEMNO.EQ.6) THEN
  WRITE(2,5400) SPECNME(NRX)
  PRINT *, 'Enter new SPECNME (RET) if no change'
  PRINT *, '
  READ(1,4300) T
  IF (T.NE.0) SPECNME(NRX) = T
ELSEIF (ITEMNO.EQ.7) THEN
  WRITE(2,4600) TEMPC(NRX)
  PRINT *, 'Enter new TEMPC value (RET) if no change'
  READ(1,4400) F
  IF (F.NE.0) TEMPC(NRX) = F
ELSEIF (ITEMNO.EQ.8) THEN
  WRITE(2,4600) TREAD1(NRX)
  PRINT *, 'Enter new TREAD1 value (RET) if no change'
  READ(1,4400) F
  IF (F.NE.0) TREAD1(NRX) = F
ELSEIF (ITEMNO.EQ.9) THEN
  WRITE(2,4600) TREAD2(NRX)
PRINT 'Enter new PREAD value (REI) if no change'
READ(1,4600) F
ELSEIF (ITEMNO.EQ.10) THEN
WRITE(2,4600) INTM1(NRX)
PRINT 'Enter new INTMI value (REI) if no change'
READ(1,4600) F
ELSEIF (ITEMNO.EQ.11) THEN
WRITE(2,4600) INTM2(NRX)
PRINT 'Enter new INTM2 value (REI) if no change'
READ(1,4600) F
ELSEIF (ITEMNO.EQ.12) THEN
WRITE(2,4600) INTM3(NRX)
PRINT 'Enter new INTM3 value (REI) if no change'
READ(1,4600) F
ELSEIF (ITEMNO.EQ.13) THEN
WRITE(2,4600) INTM4(NRX)
PRINT 'Enter new INTM4 value (REI) if no change'
READ(1,4600) F
ENDIF
CONTINUE
3100 PRINT ',  Do you have any more changes to make?'
READ(1,4600) RESPONSE
IF(SUBSTR(RESPONSE,1,1).EQ.'Y') THEN
GOTO 3000
ELSEIF (SUBSTR(RESPONSE,1,1).EQ.'N') THEN
GOTO 2000
ELSE
PRINT ', Please answer again: Y/N'
GOTO 3150
ENDIF
3000 PRINT ' Program BASICITY is over.'
STOP
4000 FORMAT(A3)
4100 FORMAT(15)
4200 FORMAT(80)
4300 FORMAT(A3)
4400 FORMAT(IX,' for spectrum #',1X,15)
4500 FORMAT(1X,80)
4600 FORMAT(F8.5)
4700 FORMAT(3A5)
4800 FORMAT(A15)
4900 FORMAT(1X,'DATA: ',1X,80)
5000 FORMAT(1X,'DATA: ',1X,80)
5100 FORMAT(1X,'DATA: ',1X,80)
5200 FORMAT(1X,'DATA: ',1X,80)
5300 FORMAT(1X,'DATA: ',1X,80)
5400 FORMAT(1X,15)
5500 FORMAT(7)
5600 FORMAT(1X,'Keep old temperature (RET) or enter new',1X,
*F6.1,2X)
5700 FORMAT(1X,'Keep old #1 pressure (RET) or enter new',1X,
*F7.2,2X)
5800 FORMAT(1X,'Keep old #2 pressure (RET) or enter new',1X,
*F7.2,2X)
END
C ****** BASEREAD ******
C ****** THIS PROGRAM READS THE INPUT DATA FOR THE
C ****** PROGRAM BASICITY.
C ****** BASEREAD, FOR ******
C ****** 5.20 86.01 ******
C
C PROGRAM BASEREAD
REAL INTMI(50), INTHM(50), INTMH(50), INTMIC(50)
REAL IDNRT10(50), RED(50), INVTMP(50)
DIMENSION TEPG(50), PREDI(50), PREAD(50)
DIMENSION CORNI(50), CORN(50), PESS1(50), PRESS(50)
DIMENSION TEMP(50), RLENK(50), DELTAG(50)
CHARACTER SUBAM*3, REMA*3, RESPONSE*3, DTITLE*80
CHARACTER *100, *5, 40NAME(5)*5, SPECNME(50)*20
READFLG = 0
CHNGFLG = 0
PRINT *, 'BASEREAD version 5.20 86.01'
PRINT *,
100 PRINT *, 'Enter the filename for the data set ',
READ(11,4700) (4NAME(K),K=1,3)
C
C ****** *********** READ SECTION *********** ******
C
OPEN(11,FILLNAME,STATUS='OLD')
READ(11,4100) NSPECT
READ(11,4200) DTITLE
READ(11,4100) NCARB
READ(11,4100) NCARE
READ(11,4600) RSENT
READ(11,4600) RSENT.
DO 300 I=1,NSPECT
  READ(11,4300) SPECNME(I)
  READ(11,4600) TEMPG(I)
  READ(11,4800) PREDI(I)
  READ(11,4800) PREAD(I)
  READ(11,4600) INTM1(I)
  READ(11,4600) INTMH(I)
  READ(11,4600) INTHM(I)
  READ(11,4600) INTMIC(I)
  CONTINUE
  PRINT *, 'DATA READ'
CLOSE(11,STATUS='KEEP')
READFLG = 1
WRITE(2,5500)
CALL OUTDEV(I)
WRITE(2,5500)
WRITE(2,6500) DTITLE
WRITE(2,6500) NCARB, RSENT
WRITE(2,6500) NCARE, RSENT.
WRITE(2,5500)
DO 300 I=1,NSPECT
  WRITE(2,5500) SPECNME(I), INTM1(I)
  WRITE(2,5500) TEMPG(I), INTMH(I)
  WRITE(2,5500) PREDI(I), INTMIC(I)
  WRITE(2,5500) PREAD(I), INTM1(I)
  WRITE(2,5500) RSENT
WRITE (J, 5500)
CONTINUE
WRITE (J, 5500)
C
PRINT *, 'Do you have any more data set to calculate?'
READ (1, 4000) RESPONSE
IF (SUBSTR (RESPONSE, 1, 1).EQ. 'Y') THEN
  GOTO 100
ELSE IF (SUBSTR (RESPONSE, 1, 1).EQ. 'N') THEN
  GOTO 3500
ELSE
  PRINT *, 'Please answer again Y/N'
  GOTO 400
ENDIF
C
PRINT *, 'Program BASICITY is over.'
STOP

FORMAT (A5)
FORMAT (I5)
FORMAT (A80)
FORMAT (A20)
FORMAT (1X, A80)
FORMAT (F8.3)
FORMAT (3AS)
FORMAT (6AS)
FORMAT (7)
FORMAT (I, A73)
FORMAT (I, 'NCARB1',EX, 16, T30, 'HSENT1', T37, F5.3)
FORMAT (I, 'NCARB2', EX, 16, T30, 'HSENT2', T37, F5.3)
FORMAT (I, 'DATA', EX, A10, T30, 'INTM1', T37, F8.3)
FORMAT (I, 'TEMPC', EX, F6.2, T30, 'INTM2', T37, F8.3)
FORMAT (I, 'PREAD1', EX, F6.2, T30, 'INTM3', T37, F8.3)
FORMAT (I, 'PREAD2', EX, F6.2, T30, 'INTM4', T37, F8.3)
END
**CARBICOR**

**CORRECTS AN ION FOR 13 CARBON UP TO M-3 IONS**

**FORTRAN CARBICOR.FLP**

**3 .58 85.91**

**PROGRAM CARBICOR**

```fortran
REAL M, M1, M2, M3
CHARACTER QUIT3, SUBSTR3, COPY3, TITLE3, PRTYPE3
PRINT *, 'CARBICOR version 3.2 85.91'
WRITE(2,3000)

***** THIS SECTION Assigns DEVICE CODE FOR OUTPUT *****

WRITE(2,3000)
1 PRINT *, 'Do you want a hard copy of the data?'
READ(1,2500) COPY
IF(SUBSTR(COPY,1,1).EQ.'Y') THEN
   PRINT *, 'What type of printer do you have LP or CP?'
   READ(1,2500) PRTYPE
   IF(SUBSTR(PRTYPE,1,1).EQ.'L') THEN
      J=3
   ELSEIF(SUBSTR(PRTYPE,1,1).EQ.'C') THEN
      J=9
   ELSEIF(SUBSTR(COPY,1,1).EQ.'N') THEN
      J=2
   ELSE
      PRINT *, 'Please answer printer type again'
      GOTO 1
   END IF
   WRITE(2,3000)
10 PRINT *, 'Enter the number of carbons'
READ(1,11000) NCH
CC=0.0108*FLOAT(NCH)
PRINTF *, 'How many calculations at this carbon ?'
READ(1,11000) N
DO 30 I=1,N
   M=0
   M1=0
   M2=0
   PRINT *, 'Enter the data title'
   READ(1,12000) TITLE
   PRINT *, 'Enter the following intensities,'
   PRINT *, 'M ION '
   READ(1,11000) M
   PRINT *, 'M-1 ION '
   READ(1,11000) M1
   PRINT *, 'M-2 ION '
   READ(1,11000) M2
   PRINT *, 'M-3 ION '
   READ(1,11000) M3
```

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MTRUE=M1*M2*CC*CC/CC*MC*MC*MC
WRITE(J,14000) DTITLE,MTRUE
WRITE(J,14000)
PRINT *,"Do you want to quit?"
READ(I,13000) QUIT
IF(SUBSTR(QUIT,1,1).EQ.,'N') THEN
  GOTO 10
ELSE
  STOP
ENDIF
1000 FORMAT(I3)
1100 FORMAT(F10.4)
1200 FORMAT(A30)
1300 FORMAT(F8.3)
1400 FORMAT(A30,F8.3)
2000 FORMAT(I7)
2500 FORMAT(A3)
STOP
END
COMPCODE

SUBROUTINE THHI HEIURN6 (MIN T) t ) i  t  AHHON5 X
SEN SITIV ITIE S F 'Q H  T H E  COMPOUND C U U E  EN )  E  H E  L )
7 14 66. t . » 3

SUB RO UT INF COMPCODE (NCARBl ,  NCAHRC, R b E  N (  1  ,  R SI N  I.C M C U )
DIMENSION NCARBS (  1  >  ,  flSENISI E,n)
CHARACTER CMPDCDDL (  1  5u) * 3, L IIM E I)* .'., H I  SI' ONSf • 3, 6UBSTR»3
CHARACTER CMPD(C>»3
DATA LMFDCODfc/
1  '  NE'  ,  *  TE1  ,  '  D M *  BA' ,  '  PA'  ,  '  AN'  ,  '  MR'  ,  '  DF'  ,
2' EY', ' BA', ' CY', ' HR', ' MP', ' AS', ' CU', ' IE', ' BN',
3' TH', ' FE', ' MF', ' AT', ' DP', ' MB', ' BE', ' NH', ' ND',
4'MC', ' MI', ' PA', ' SI', ' HO', ' PO', ' ET', ' DO', ' MH',
5'MA', ' MCF', ' AC', ' ME', ' PH', ' MX', ' NP', ' UX', ' TBB',
6'PX', ' BE', ' TB', ' HE', ' BZ', ' HA', ' DD', ' MD',
7'HC', ' TME', ' DMA', ' DE', ' DPE', ' DFH', ' MS', ' DEF', ' DO',
8'MTH', ' URT', ' FUR', ' UD', ' FUD', ' TFE', ' DCA', ' CY', ' MEY',
9'CT', ' MCT' /
DATA NCARBS/
AB, 4, 2, 3, 7, 8, 6, 15, 6,
B4, 6, 4, 7, 6, 9, 8, 4,
CS, 10, 5, 8, 7, 8, 8, 0, 0,
DS, 6, 6, 8, 6, 5, 4, 7,
E3, 6, 3, 6, 8, 10, 8, 10,
FB, 8, 8, 7, 6, 6, 8, 2, 21,
GI0, 6, 9, 15, 12, 16, 9, 4, 20,
HI, 4, 4, 9, 9, 5, 2, 4, 5,
19, 19/
DATA RSENIS/
AS, 7, 7, 7, 3, 4, 4, 3, 2, 108, 5, 5, 6, 5, 3, 6, 3, 4, 2, 9, 16, 4, 4, 8, 8,
BS, 378, 5, 400, 3, 191, 8, 033, 4, 397, 5, 353, 6, 509, 4, 791, 3, 837,
C4, 303, 7, 469, 5, 556, 5, 376, 5, 351, 5, 619, 6, 120, 1, 114, 1, 114,
DS, 374, 4, 218, 4, 711, 5, 309, 4, 103, 3, 509, 3, 500, 3, 404, 4, 872,
E2, 845, 4, 507, 5, 573, 2, 801, 4, 871, 5, 374, 6, 271, 5, 74, 6, 705,
FS, 374, 2, 153, 5, 374, 4, 710, 4, 107, 4, 046, 5, 709, 8, 509, 15, 709,
G8, 105, 5, 649, 7, 377, 10, 832, 9, 105, 11, 497, 6, 039, 3, 464, 14, 905,
H1, 480, 3, 780, 3, 748, 7, 496, 7, 856, 5, 856, 3, 605, 3, 995, 4, 651,
18, 106, 8, 758/
NOCOMPS = 74
DO 100 K=1, ,
WRITE (2,1000) K
READ (1,11000) COMPD
CMRD(K) = COMPD
DO 200 I=1, NOCOMPS
IF (COMPD(K).EQ.CMPCODE(I)) THEN
IF (K.EQ.1) THEN
NCARBl = NCARBS(I)
RSEN1 = RSENIS(I)
GOTO 100
ELSE IF (K.F0.) THEN
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NCARB= NCARB(I)
RSENT= RSENT(I)
RETURN
ENDIF
ENDIF
100 CONTINUE
GOTO 200
RETURN

200 PRINT*, 'No matches on your entry. Please check it.'
IF (SUBSTR(RESPONSE,1,1),EQ.'Y') TH
GOTO 10
ELSEIF (SUBSTR(RESPONSE,1,1),EQ.'N') THEN
GOTO 100
ELSE
PRINT *, 'Please answer again: Y/N'
GOTO 200
ENDIF
200 PRINT*, 'Please enter manually the following.'
IF (K.EQ.1) THEN
PRINT *, 'Enter the # of carbons in compd #1'
READ(1,4100) NCARB
PRINT *, 'Enter the rel. sensitivity of compd #1'
READ(1,4600) RSENT
GOTO 100
ELSEIF (K.EQ.2) THEN
PRINT *, 'Enter the # of carbons in compd #2'
READ(1,4100) NCARB
PRINT *, 'Enter the rel. sensitivity of compd #2'
READ(1,4600) RSENT
ENDIF
RETURN
1000 FORMAT(1X,'Enter the code for compound #',IX,11,2X)
1100 FORMAT(A1)
1200 FORMAT(IX,12,IX,A3,IX,1,IX,2,IX)
4100 FORMAT(15)
4600 FORMAT(F6.3)
END

END
C ***** OUTDEVCD *****
C ***** THIS SUB ASSIGNED DEVICE CODE FOR OUTPUT *****
C **** 3 & 86.01 ****
C

SUBROUTINE OUTDEVCD(J)
CHARACTER COPY*3,PRTYPE*3,STR*3
1 PRINT *, 'Do you want a hard copy of the data?'
READ(1,1000) COPY
IF (SUBSTR(COPY,1,1).EQ.'Y') THEN
2 PRINT *, 'What type of printer do you have LP or CP?'
READ(1,1000) PRTYPE
IF (SUBSTR(PRTYPE,1,1).EQ.'C') THEN
J=9
ELSEIF (SUBSTR(PRTYPE,1,1).EQ.'L') THEN
J=10
ELSE
PRINT *, 'Please answer printer type again'
GOTO 2
ENDIF
ELSEIF (SUBSTR(COPY,1,1).EQ.'N') THEN
J=3
ELSE
PRINT *, 'Please answer again'
GOTO 1
ENDIF
1000 FORMAT(A3)
RETURN
END
PROGRAM RELSENT
DIMENSION RSENT(40), ALFA(40), NELEC(40), SUMTAN(40)
DIMENSION N(10), NAMAT(10), NATOMS(10), NHYBRIDE(10)
CHARACTER NAME(40)*25, CLASS(40)*2
PRINT *, 'RELSENT version 4.27 86.01'
PRINT *, 'Enter the # of molecules you have to call.'
READ(1,1000) NMOLCE
DO 100 1=1,NMOLCE
   WRITE(2,1500) I
   READ(1,1000) NAME(I)
   PRINT *, 'For this molecule how many different hybride atoms do you have?'
   READ(1,1000) NYHPAMS
   DO 200 J=1, NYHPAMS
      PRINT *, J, 'H single bond'
      PRINT *, J, 'C single bond'
      PRINT *, J, 'C double bond -defins aromatic'
      PRINT *, J2, 'C triple bond'
      PRINT *, J, 'N single bond NH3, all amines'
      PRINT *, J, 'N part. dbl bond w/ pair aromatic'
      PRINT *, J, 'N part. dbl bond w/ pair aniline'
      PRINT *, J, 'N triple bond'
      PRINT *, J, 'O single bond'
      PRINT *, J, 'O double bond carbonyls'
      PRINT *, J, 'O part. dbl bond foran ring w/dbl bond'
      PRINT *, J, 'O single bond'
      PRINT *, J, 'S single bond'
      PRINT *, J, 'S triple bond'
      PRINT *, J, 'S double bond'
   END
   PRINT *, 'Enter the # of the hybride atom'
   READ(1,1000) NHYBRIDE(I)
   IF (NYHYBRIDE(I),GT,19) THEN
      PRINT *, 'Please enter a number less than 19'
      GOTO 10
   ELSE
      END!
   PRINT *, 'Enter the # of atoms that hybride type'
      READ(1,1000) NAMAT(I)
   END
   CONTINUE
DO 300 J=1, NTYPATS
    IF (NHYBRIDE(J), ED, 1) THEN
        TAU(J) = 1.314
        N(J) = 1
        GOTO 300
    ELSEIF (NHYBRIDE(J), ED, 2) THEN
        TAU(J) = 1.294
        N(J) = 6
        GOTO 300
    ELSEIF (NHYBRIDE(J), ED, 3) THEN
        TAU(J) = 1.428
        N(J) = 6
        GOTO 300
    ELSEIF (NHYBRIDE(J), ED, 4) THEN
        TAU(J) = 1.293
        N(J) = 6
        GOTO 300
    ELSEIF (NHYBRIDE(J), ED, 5) THEN
        TAU(J) = 1.425
        N(J) = 7
        GOTO 300
    ELSEIF (NHYBRIDE(J), ED, 6) THEN
        TAU(J) = 1.266
        N(J) = 7
        GOTO 300
    ELSEIF (NHYBRIDE(J), ED, 7) THEN
        TAU(J) = 1.220
        N(J) = 7
        GOTO 300
    ELSEIF (NHYBRIDE(J), ED, 8) THEN
        TAU(J) = 1.304
        N(J) = 7
        GOTO 300
    ELSEIF (NHYBRIDE(J), ED, 9) THEN
        TAU(J) = 1.290
        N(J) = 8
        GOTO 300
    ELSEIF (NHYBRIDE(J), ED, 10) THEN
        TAU(J) = 1.216
        N(J) = 8
        GOTO 300
    ELSEIF (NHYBRIDE(J), ED, 11) THEN
        TAU(J) = 1.079
        N(J) = 8
        GOTO 300
    ELSEIF (NHYBRIDE(J), ED, 12) THEN
        TAU(J) = 1.064
        N(J) = 9
        GOTO 300
    ELSEIF (NHYBRIDE(J), ED, 13) THEN
        TAU(J) = 1.120
        N(J) = 17
        GOTO 300
    ELSEIF (NHYBRIDE(J), ED, 14) THEN
        TAU(J) = 5.077
        N(J) = 35
        GOTO 300
GOTO 300
ELSEIF (NHYBRIDE(J), EQ. 15) THEN
  TAU(J) = 8.820
  N(J) = 53
  GOTO 300
ELSEIF (NHYBRIDE(J), LD. 16) THEN
  TAU(J) = 3.000
  N(J) = 16
  GOTO 300
ELSEIF (NHYBRIDE(J), ED. 17) THEN
  TAU(J) = 2.400
  N(J) = 16
  GOTO 300
ELSEIF (NHYBRIDE(J), EQ. 18) THEN
  TAU(J) = 2.982
  N(J) = 16
  GOTO 300
ELSEIF (NHYBRIDE(J), ED. 19) THEN
  TAU(J) = 3.367
  N(J) = 16
ENDIF
300 CONTINUE
SUMTAU(I) = 0.0
NELEC(I) = 0
DO 400 J = 1, NTYPATOMS
  SUMTAU(I) = SUMTAU(I) + TAU(J)*NATOMS(J)
  NELEC(I) = NELEC(I) + N(J)*NATOMS(J)
400 CONTINUE
ALFA(I) = 4/NELEC(I)*SUMTAU(I)**(:
CALL SENSEITAL(I, ALFA, NELEC, RSENT, CLASS)
100 CONTINUE
CALL OUTDEVCD(K)
WRITE(K, 1200)
DO 500 I = 1, NMOLECS
  WRITE(K, 1300) NAME(I), RSENT(I), NELEC(I), ALFA(I), CLASS(I)
WRITE(K, 2000)
500 CONTINUE
WRITE(K, 2000)
STOP
1000 FORMAT(15)
1100 FORMAT(A25)
1200 FORMAT(1X,'Name',2X,'Rsent',2X,': ele1',2X,': Mol Pos1',
  4X,'Class')
1300 FORMAT(1X,AE3,1X,F7.5,3X,13,4X,F7.3,8X,AE)
1400 FORMAT(F10.5)
1500 FORMAT(1X,'Enter the name of molecule N',1X,1,2X)
1600 FORMAT(1X)
END
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ELSE IF (SUBSTR(CMPDTYP, 1, 1).EQ.'AR') THEN
  SLOPE = 0.05
  YINTCPT = 2.6
ELSE IF (SUBSTR(CMPDTYP, 1, 1).EQ.'NG') THEN
  SLOPE = 0.047
  YINTCPT = 0.4
ELSE IF (SUBSTR(CMPDTYP, 1, 1).EQ.'AL') THEN
  SLOPE = 0.067
  YINTCPT = 0.346
ELSE IF (SUBSTR(CMPDTYP, 1, 1).EQ.'C') THEN
  SLOPE = 0.051
  YINTCPT = 0.83
ELSE IF (SUBSTR(CMPDTYP, 1, 1).EQ.'CH') THEN
  SLOPE = 0.038
  YINTCPT = 1.282
ELSE IF (SUBSTR(CMPDTYP, 1, 1).EQ.'E') THEN
  SLOPE = 0.071
  YINTCPT = 0.635
ELSE IF (SUBSTR(CMPDTYP, 1, 1).EQ.'NI') THEN
  SLOPE = 0.084
  YINTCPT = 0.181
ELSE IF (SUBSTR(CMPDTYP, 1, 1).EQ.'T') THEN
  SLOPE = 0.088
  YINTCPT = 0.201
ENDIF
300  RSENT(1) = FNC*SLOPE + YINTCPT
RETURN
1000  FORMAT(A2)
1100  FORMAT(F10.5)
1200  FORMAT(I5)
END
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