INTEGRATING MASS SPECTROMETRY AND COMPUTATIONAL CHEMISTRY
INTEGRATING MASS SPECTROMETRY AND COMPUTATIONAL CHEMISTRY: A STUDY OF DISSOCIATION REACTIONS OF RADICAL CATIONS IN THE GAS PHASE

By
Richard Lee, B. Sc.

A Thesis
Submitted to the School of Graduate Studies
In Partial Fulfillment of the Requirements
for the Degree
Master of Science

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ABSTRACT

The organic ions studied in this thesis were generated in the rarefied gas phase of the mass spectrometer by electron ionization of selected precursor molecules. The characterization of their structure and reactivity was probed by using a variety of tandem mass spectrometry techniques. These include metastable ion spectra to probe the dissociation chemistry of the low energy ions and collision experiments to establish the atom connectivity of the ions. The technique of neutralization-reionization mass spectrometry (NRMS) was used to probe the structure and stability of the neutral counterparts of the ions. Computational results involving the CBS-QB3 model chemistry formed an integral component in the interpretation of the experimental findings.

The above approach was used to study proton-transport catalysis in the formaldehyde elimination from low energy 1,3-dihydroxyacetone radical cations. Solitary ketene-water ions, CH$_2$C(=O)OH$_2^+$, do not readily isomerize into its more stable isomer, CH$_2$C(OH)$_2^+$. A mechanistic analysis using the CBS-QB3 model chemistry shows that metastable 1,3-dihydroxyacetone radical cations will rearrange into hydrogen-bridged radical cations [CH$_2$C(=O)O(H)-H•••OCH$_2$]**, where the CH$_2$=O will catalyze the transformation of CH$_2$C(=O)OH$_2^+$ into CH$_2$C(OH)$_2^+$.

Metastable pyruvic acid radical cations, CH$_3$C(=O)COOH**+, have been shown to undergo decarboxylation to yield m/z 44 ions, C$_2$H$_4$O**, in competition with the formation of CH$_3$C=O$^+$ + COOH$^-$ by direct bond cleavage. Collision induced dissociation experiments agree with an earlier report that oxycarbene ions CH$_3$COH** are formed but they also suggest the more stable isomer CH$_3$C(H)=O** may be co-generated. Using the CBS-QB3 model chemistry, a mechanism is proposed to rationalize these results.

Next, the isomeric ions CH$_3$O-P=S** and CH$_3$S-P=O** were characterized and differentiated by tandem mass spectrometry. Metastable CH$_3$O-P=S** and CH$_3$S-P=O** ions both spontaneously lose water to yield m/z 74 cyclic product ion [-S-CH=]P**. Using the CBS-QB3 model chemistry a mechanism is proposed for the water loss from CH$_3$O-P=S**
and CH$_3$S-P=O$^{+*}$. Our calculations also show that these two isomers communicate via a common intermediate, the distonic ion CH$_3$S-P-OH$^{+*}$, prior to the loss of water.

The final component of this work details the computational study addressing the long standing question on the mechanism for the water elimination from metastable ethyl acetate radical cations. The CBS-QB3 results show that low energy ethyl acetate ions isomerize into ionized 4-hydroxy-2-butanone prior to the loss of water.
ACKNOWLEDGEMENTS

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<table>
<thead>
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<th>Abbreviation</th>
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<tr>
<td>B</td>
<td>magnetic sector</td>
</tr>
<tr>
<td>B3LYP</td>
<td>hybrid Hartree-Fock/density functional theory</td>
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<tr>
<td>CCSD(T)</td>
<td>coupled cluster singles doubles and triples</td>
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<td>CI</td>
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<td>CBS-QB3</td>
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<td>EI</td>
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<td>ESA (E)</td>
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<td>eV</td>
<td>electron Volt (1 eV = 23.061 kcal mol⁻¹ or 96.487 kJ mol⁻¹)</td>
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<td>ffr</td>
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<td>IE</td>
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<td>KER</td>
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<td>MI</td>
<td>metastable ion</td>
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<td>MP</td>
<td>Möller-Plesset(perturbation theory)</td>
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<td>MS</td>
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<td>NDMA</td>
<td>N,N-dimethylaniline</td>
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<tr>
<td>m/z</td>
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<td>NR(MS)</td>
<td>neutralization-reionization(mass spectrometry)</td>
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<tr>
<td>ZAB-R</td>
<td>BEE three-sector mass spectrometer</td>
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<td>ZPVE</td>
<td>zero-point vibrational energy</td>
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Chapter 1

1.1 Introduction, scope of this thesis

The gas phase ion chemistry described in this thesis focuses on the study of relatively small organic ions. To generate these ionic species a mass spectrometer is used. The techniques used to probe their structure and reactivity are tandem mass spectrometry and computational chemistry. The ions that are generated in the mass spectrometer are radical cations. In certain cases the ions can be generated in the source by direct electron ionization (EI) of its gaseous neutral counterpart. An alternative method to direct EI is dissociative electron ionization of a judiciously selected precursor molecule. An important detail of these experiments is the pressure in the ion source. The source pressure must be kept low to ensure that the ions do not interact with molecules via ion-molecule reactions. This implies that the chemistry and reactivity of the ions is observed in a “solvent-free” environment.

Radical cations generally have stable isomers of conventional or unconventional structure. Radical cations of unconventional structure include the following: (i) distonic ions, where the charge and radical are located on separate atoms within the same ion, (ii) ion-dipole complexes, ionic species which are stabilized by the charge of the ionic component and the dipole of the neutral component and (iii) hydrogen-bridged radical cations (HBRC’s), species where the ionic and neutral components interact through a hydrogen bond. The methanol radical cation, CH₃OH⁺⁺, has a only one stable isomer of unconventional structure: the distonic ion *CH₂OH₂⁺ [1]. In contrast, ionized formic acid H-C(=O)OH⁺⁺, has four stable isomers: the ion-dipole complex, [H₂O⋯CO]⁺⁺, the hydrogen-bridged radical cations [OC⋯H⋯OH]⁺⁺ and [CO⋯H⋯OH]⁺⁺, and the ionized carbene, HO-C-OH⁺⁺ [2].
The radical cations which are generated in the low pressure experiments do not necessarily retain their structure connectivity. The internal energy content of these ions may be so high that isomerization into one or more stable isomers takes place, frequently via a H-shift rearrangement. In contrast, there are many systems where the energy barrier for unimolecular H-shifts are too high for interconversion to another isomer to occur. However, recent studies by our group and other research laboratories have shown that such high rearrangement barriers can be lowered if the ion is allowed to form an encounter complex with a carefully chosen neutral molecule. In our experimental arrangement this is achieved by carrying out the reaction under chemical ionization (CI) conditions, where the source pressure is greater by a factor of c. 10 000 compared to a conventional electron ionization experiment. This reaction, where a single (solvent) molecule assisted isomerization of a given radical cation into a more stable isomer takes place, has been coined "proton-transport catalysis" and is further discussed in detail in Section 1.

Chapter 2 describes the above situation. It focuses on the metastable dissociation of the 1,3-dihydroxacetone radical cation, HOCH₂C(=O)CH₂OH⁺. Upon dissociation it yields C₂H₄O₂⁺ ions via loss of formaldehyde. These ions were determined to have the structure connectivity of the enol of acetic acid, CH₂=C(OH)₂⁺. Our calculations indicate that the initial complex that is formed is the hydrogen-bridged radical cation [O=C-CH₂OH...H...OCH₂]⁺. Solitary CH₂=C(=O)OH₂⁺ ions do not readily communicate with their more stable isomer CH₂=C(OH)₂⁺ because the interconversion barrier lies too high but prior to dissociation, the CH₂=O molecule catalyzes the rearrangement.

Chapter 2 also deals with the dissociation of low-energy (metastable) pyruvic acid radical cations, CH₃C(=O)-C(OH)=O·+. The most prominent reaction is a decarboxylation which yields C₂H₄O⁺ ions. The identity of these ions was determined to be the ionized carbene CH₃COH⁺ rather than its more stable isomer CH₃C(H)=O⁺, ionized acetaldehyde. Our computational study on the mechanism for the dissociation of ionized pyruvic acid suggests that the HBRC CH₃CO-H⁺...O=C=O is initially formed. In contrast to the CH₂O mediated isomerization in dihydroxyacetone, the carbon dioxide molecule in the above
HBRC cannot accommodate the transformation of CH$_3$COH$^+$ into CH$_3$C(H)=O$^+$. The barrier for the isomerization is significantly lowered but it does not become low enough for efficient proton transport catalysis.

The characterization and behaviour of CH$_3$S-P=O$^+$ and CH$_3$O-P=S$^+$ is discussed in Chapter 3. Experiments involving collision-induced dissociation (CID) and neutralization-reionization (NR) mass spectrometry are used to probe the structure, stability and reactivity of these ions in the gas phase. Both isomers spontaneously lose H$_2$O to form the same cyclic product ion, [-S-CH=]P$^+$ and computational results suggest that these two ions communicate through a common intermediate. The dehydration reaction of CH$_3$S-P=O$^+$ involves a double hydrogen transfer, while the water loss from CH$_3$O-P=S$^+$ requires a skeletal rearrangement.

Chapter 4 describes the unimolecular chemistry of the ethyl acetate radical cation and in particular the generation of ionized methyl vinyl ketone, CH$_3$C(=O)CH=CH$_2$$^+$ via the spontaneous loss of water from low-energy (metastable) ethyl acetate ions. The mechanism of this reaction has been shrouded in mystery for the past 20 years although a great number of studies have been conducted. It will be shown that this reaction occurs via the potential energy surface of ionized 4-hydroxy-2-butanone, CH$_3$C(=O)CH$_2$CH$_2$OH$^+$. This Chapter is an example of theory and experiment working in concert to elucidate a complex yet transparent mechanism which involves 7 steps to describe the water elimination from ionized ethyl acetate.

The next two sections of this Chapter provides the non-expert reader with the background information on the mass spectrometry based techniques and the computational chemistry methods employed in the studies reported in this thesis.

Section 1.2 gives a brief introduction to the instrumentation used in the various experiments; a state-of-the-art tandem magnetic sector mass spectrometer. This section will also discuss the various techniques used to generate and characterize the ions and the computational chemistry used to assist in the interpretation of the experimental results.

Section 1.3 presents a brief overview of the methods to perform ion-molecule reactions under chemical ionization conditions. It focuses on the importance of the
various parameters that influence molecule-assisted isomerization reactions of radical cations.

1.2 The generation and characterization of ions by tandem mass spectrometry

*The VG Analytical ZAB-R Mass Spectrometer*

Several sophisticated mass spectrometric techniques used in conjunction with computational chemistry allowed for the characterization of ions generated in the ion source of the mass spectrometer.

A schematic diagram illustrating the various components of our ZAB-R mass spectrometer is shown in Fig. 1. The instrument is a multi-sector mass spectrometer and is comprised of an ion source and three mass analyzers: a magnetic sector (B) followed by two electrostatic analyzers (E). This mass spectrometer is of reverse geometry, with a BEE configuration in that the magnetic sector precedes the electrostatic analyzers. The sectors are separated by field-free regions (ffr) where there is no external field to alter the flight path of the ion-beam. Within these regions are collision cells, which can be pressurized by various gases to perform sophisticated experiments such as collision-induced dissociation (CID) and neutralization-reionization (NR) mass spectrometry.
The compound of interest is introduced into the ion source as a vapour directly via a leak valve or a direct insertion probe. Electrons which are generated from a tungsten filament are accelerated into the source by a potential difference of c. 70 V between the filament and the ion source [3]. Ions are generated by the “collision” of the accelerated electrons and the neutral vapour molecules as the electrons travel towards the trap, an electrode with a slightly higher potential. Ionization occurs by direct contact or close contact of the electrons with the neutral molecule. Removal of an electron from the neutral sample molecule leads to the formation of an ion. This method of ion generation is termed electron (impact) ionization (EI). The ion that is generated is positively charged and the process occurs as: $M + e^- \rightarrow M^{+} + 2e^-$, where $M$ is the neutral sample molecule, $e^-$ is an electron and $M^{+}$ represents the radical cation that is generated. The resulting $M^{+}$ species is an odd-electron ion because almost all organic molecules contain an even number of electrons.

Electron ionization takes place within $10^{-16}$ sec, which is much faster than the movement of the nuclei in the molecule: the fastest molecular vibrations require $10^{-14}$ sec. [3]. Therefore, during the ionization process the nuclei can be viewed as stationary.
This situation can be described as a vertical ionization process that is governed by the Frank-Condon principle. If there is excess energy from the ionization process, i.e. the energy imparted by the electron is greater than the ionization energy of the molecule, the excess energy materializes as internal energy in the form of transitions to excited vibrational, rotational and electronic states. The excess energy imparted by the electrons is different for every ion that is generated, resulting in a wide range of internal energies. Consequently only a fraction of the ions dissociate, by direct bond cleavage or rearrangement, whereas the others remain intact.

The incipient ions reside in the source for c. 1 μs and takes them c. 10 μs to reach to the detector. For molecular ions to dissociate in the source, they must do so within 1 μs which is equivalent to a minimum rate constant, k, of $10^6$ sec$^{-1}$. The internal energy content of a given ion dictates the type of reactions it can undergo. For example, rearrangement reactions generally have a maximum rate constant of $10^{10}$ sec$^{-1}$ compared to direct bond cleavage reactions which have a maximum rate constant of $10^{14}$ sec$^{-1}$. Ions which dissociate in the source – the “unstable” ions - do so with a rate constant of $10^6 < k < 10^{14}$ sec$^{-1}$. Ions that do not dissociate prior to reaching the detector because their internal energy is insufficient are deemed to be “stable”. Such ions are characterized by a rate constant of $k < 10^4$ sec$^{-1}$. The fraction of ions that dissociates with a rate constant in the range of $10^4 < k < 10^6$ sec$^{-1}$ has just enough internal energy to dissociate en route to the detector. These low-energy ions are termed metastable ions and their dissociation chemistry can be studied in the field-free regions of the mass spectrometer.

Two well established statistical theories describe the relationship between the rate constant, k, to the internal energy of an ion: the Quasi-Equilibrium Theory (QET) and the Rice, Rampsberger, Kassel and Marcus (RRKM) Theory. In the most basic representation of the QET, the dissociation reactions of ions can be described by the following equation: $k = \nu [e_i - \epsilon_0/e_i]^{s-1}$, where ν is the frequency factor, $\epsilon_i$ is the internal energy of the dissociating ion, $\epsilon_0$ is the activation energy and s represents the number of effective oscillators of the ion [3].
Metastable Ion spectra

Metastable ion (MI) spectra are generated by mass selecting the ion of interest with the magnet. As the beam of ions traverse through the magnet from the ion source, a magnetic field is imposed on the beam in a direction that is perpendicular to the flight path of the ions [3]. The path of the ions through the magnet can be represented by the following equation: \( r = \frac{mv}{Be} \), where \( r \) is the radius of the circular path, \( m \) mass of the ion, \( v \) the velocity of the ion, \( e \) the charge, and \( B \) the strength of the magnetic field. The radius of the path can be viewed as proportional to the momentum. The magnet can be viewed as a momentum separator. The magnetic field separates the ions by the following relationship: \( \frac{m}{z} = \frac{B^2 r^2}{2v} \) [3]. Once the precursor ions, \( m_1^{++} \), are selected, they are transmitted into the 2ffr where a small fraction spontaneously dissociates into the products \( m_2^{++} \) and \( m_3 \). The translational energy of the precursor ion, \( m_1^{++} \), is distributed among the products based on their mass, by the following mass-weighted relationship: \( \frac{m_2}{m_1} V_{\text{acc}} \), where \( V_{\text{acc}} \) is the accelerating voltage. This allows for the first ESA to function as a mass analyzer based on the translational energy of the product ions. The initial main beam of ions contains a mixture of stable and metastable ions, and generally not more than 1% of the main beam contributes to the overall intensity of the peaks in the MI spectrum.

Fig. 2. A schematic diagram demonstrating the events in a metastable ion experiment.
A general observation in MI mass spectra is the broadening of the fragment ion peak with respect to the main beam of non-dissociating ions [3]. The broadening of the peaks is caused by the conversion of internal energy of the precursor ion $m_1^{++}$ into kinetic energy of the products $m_2^{++}$ and $m_3$. Figure 2 illustrates the dissociation of metastable ions in the second field-free region.

A reverse activation energy may also contribute to the kinetic energy content of the products. The energy diagram of Fig. 3 depicts an endothermic dissociation reaction with a barrier for the reverse reaction. The minimum amount of internal energy required to observe the dissociation of $m_1^{++}$ in the metastable time-frame is represented by $\epsilon_{\text{min}}$ [3]. To satisfy the energetic requirements, $\epsilon_{\text{min}}$ must be larger than the forward activation energy, $\epsilon_o$. The excess energy, $\epsilon_{\text{excess}}$, is the difference between the $\epsilon_{\text{min}}$ and $\epsilon_o$. The energy for the reverse barrier is represented by $\epsilon_{\text{rev}}$. The difference between the enthalpy of formation of the reaction products and the activated complex is equal to the barrier. The reverse activation energy, along with the excess energy contributes to the kinetic energy of the products.

Fig. 3. A potential energy diagram for an endothermic reaction in the gas phase.
During the energy conversion, from internal energy to translational energy, a kinetic energy release (KER) may result [3]. The kinetic energy release is a result of contributions from the reverse activation energy and excess energy of the activated complex. Direct bond cleavage reactions are generally not associated with a significant reverse activation energy. Reactions that do have a significant reverse activation energy are rearrangements reactions, where the products are a stable ionic species and a neutral molecule [3]. The broadening of the metastable peaks relative to the main beam can be observed in the MI spectrum. Metastable peaks associated with a large kinetic energy release may have a flat-topped or dish shaped peak but reactions with a small kinetic energy release are characterized by peaks of a Gaussian shape [3]. Metastable peak shapes can provide information on the structure of the fragmenting ion, as well as the distribution of the internal energy of the fragmenting ion into translational energy of its products [5]. The kinetic energy release can be calculated by the following relationship: \[ T_{0.5} = \frac{m_1^2}{16m_2m_3}(V_{\text{acc}})[(\Delta E_{0.5})^2/E^2], \] where \( V_{\text{acc}} \) is the accelerating voltage, \( \Delta E_{0.5} \) is the width of the metastable peak at half height, and \( E \) represents the sector voltage of the transmitted ions.

Collision-Induced Dissociation spectra

Collision-induced dissociation reactions provide valuable information on the structure (atom connectivity) of the precursor ion. To generate a CID spectrum, the ions of interest are accelerated from the ion source by 8 kV and then they are mass selected by the magnet. The selected beam of ions is then transmitted into the 2ffr, where one of the collision chambers is pressurized with a suitable collision gas such as helium or oxygen. Figure 4 shows the collision events during a CID experiment. A portion of the fast moving ions collides with a gas molecule and, as it does so, a small fraction of the ion’s translational energy is converted into internal energy. The internal energy distribution of the collisionally activated ions is fairly broad. This generally leads to a range of dissociation reactions and more often than not, direct bond cleavage reactions dominate.
over rearrangement reactions. Thus the CID spectrum of a given ion is generally characterized by a number of direct bond cleavage reactions and/or rearrangement reactions whereas its MI spectrum may only display one or two low energy rearrangement processes.

![Diagram](cid_diagram.png)

Fig. 4. Schematic diagram illustrating the events in a collision-induced dissociation experiment.

The intensity distribution of the peaks in a CID mass spectrum depends on a number of factors such as the type of collision gas, its pressure and also the translational energy of the ions. Typical collision gases are helium, argon, nitrogen and oxygen. Of these helium is most commonly used because it does not readily neutralize the ions and it causes less scattering. All experiments reported in this thesis use oxygen as the collision gas. CID mass spectra generated with oxygen are similar in appearance to those obtained using helium. However, they sometimes display weak peaks resulting from high energy reactions that are not seen in CID spectra obtained with other collision gases [6].

As mentioned earlier, the pressure of the collision cell can affect the CID experiment. The pressure of the collision gas dictates if the ion undergoes a single collision or multiple collisions. In the experiments conducted in this thesis, the pressure of the collision gas was kept sufficiently low to ensure that only single collision reactions take place. A remote ionization gauge located outside the collision was used to monitor the pressure of the collision gas. Monitoring the main beam intensity can provide an estimate of the pressure within the collision cell. To avoid multiple collision reactions, the optimal conditions are set to reduce the main beam to c. 60 – 70% [7]. If the collision
cell pressure is too high and multiple collision reactions occur, structure-specific information may be lost [7].

As noted earlier, the translational energy of the collisionally activated ions can also affect the appearance of the CID spectrum. As the translational energy of an ion is increased, the range of internal energy also increases, resulting in more collision induced fragmentation [7]. An estimate of the energy transferred during a collision can be obtained from the following relationship: \( E_{\text{max}} = \frac{h}{a} (2eV/m)^{1/2} \), where \( h \) denotes Planck’s constant, \( a \) represents the interaction distance, \( eV \) is the ion’s translational energy and \( m \) is the mass of the ion [7]. The size of the collision gas can also affect the appearance of the CID spectrum.

Neutralization-Reionization spectra

Neutralization-reionization (NR) mass spectrometry has become an important technique in studying the stability of elusive and highly reactive neutrals that are normally difficult to generate because of their propensity toward unimolecular dissociation or bimolecular rearrangement [8a]. Below in Fig. 5, the major elements of a NR experiment are shown.

![Fig. 5. Schematic diagram illustrating the events in a neutralization-reionization experiment.](image)

To conduct a NR study, ions are first generated in the source from an appropriate precursor ion. The ions of interest are then selected by the magnet and allowed to enter
the 2ffr. The fast moving ions are then subjected to two consecutive collisions with the appropriate target gases. The first collision cell is pressurized with the neutralizing gas, N,N′-dimethylaniline (or Xe), that neutralizes the ions by electron transfer. Ions that are not neutralized are deflected away by a positively charged deflector electrode, positioned between the two collision cells in the 2ffr. The fast moving neutral molecules are then reionized as they travel through the second collision cell which is pressurized with oxygen gas. Some of the reionized ions will fragment in this collision cell. The reionized ions are then analyzed by the first ESA and detected by the first photomultiplier detector. If the NR spectrum displays a peak corresponding to the original mass-selected ion, then the neutral counterpart of the ion is deemed to be a stable species on the μs timescale.

As previously mentioned, xenon can be used effectively for neutralization despite the fact it has a rather high ionization energy (12.2 eV). Implying that the neutralization process is often an endothermic process. This does not inhibit the neutralization process because the translational energy of the ions compensates for the energy deficiency [8b]. Typically a “hard” target gas such as helium is used for the collisional reionization process: \( AB + He \rightarrow AB^+ + He + e^{-} \). However, using such a hard target gas can result in extensive dissociation during the reionization process. Oxygen is a softer target gas which causes less fragmentation. The reionization process with \( O_2 \) involves the following reaction: \( AB + O_2 \rightarrow AB^+ + O_2^{-} \). One aspect of using helium as the collision gas is the large amount of information on the structure (atom connectivity) of the neutral species compared to oxygen, but oxygen does allow for a higher yield of “survivor” ions.
Fig. 6. A schematic diagram illustrating the events in a neutralization-reionization/collision-induced dissociation experiment.

A NR/CID experiment can provide information on whether the neutral species has retained its original structure connectivity or that it has rearranged into a more stable isomer prior to reionization. To perform a NR/CID experiment, the reionized species, the "survivor ions", are mass selected with the first ESA and transmitted into the 3ffr. The collision cell in this ffr is pressurized with oxygen and the mass selected ions are induced to dissociate by high energy collisions. The dissociating ions are then separated according to their m/z values by scanning the second ESA.

To determine whether the neutral species has retained its structure, the NR/CID spectrum is compared to the 3ffr CID spectrum of the source generated ions. If the two spectra are closely similar, there is strong evidence that the neutral molecule has retained its structural identity. If, on the other hand, there is a discrepancy between the spectra, it may be tentatively concluded that the neutral has isomerized into a more stable isomer. Definitive evidence that a given neutral has rearranged into a more stable isomer comes from a comparison with a reference CID spectrum of the more stable isomer. It should be noted in this context that NR/CID and CID spectra will also be different if the source generated ions consist of a mixture of isomers and/or contain isobaric impurities [9].
Another method to probe the stability of a neutral species is to perform a collision-induced dissociative ionization (CIDI) experiment. In this experiment neutrals generated from a spontaneous dissociation reaction are studied. A precursor ion is transmitted into the 2ffr by mass selecting it by the magnet. A small fraction of the selected ions undergoes unimolecular dissociation en route to the collision chamber [10]. The precursor ions \( m_1 \) and the product ions \( m_2 \) are deflected away by the deflector electrode so that only the fast moving neutral species enter the collision cell. The collision cell is pressurized with \( \text{O}_2 \) which reionizes the neutral species. The reionized neutrals and their dissociation products are then separated according to their m/z values by scanning the first ESA to generate a CIDI spectrum. The structure of the ionized neutrals can be further probed by mass selecting the ionized neutrals with ESA1 and transmitting these ions into the 3ffr, where they are collisionally induced to dissociate by pressurizing the 3ffr collision cell with \( \text{O}_2 \).

Fig. 7. A schematic diagram illustrating the events in a collision-induced dissociative ionization experiment.
In conjunction with the results from a mass spectrometric analysis, computational chemistry is often used as a complementary aid in determining the structure of a species and the mechanism of its formation [11].

Several types of model chemistries are available but the one used in the studies of this thesis is the CBS-QB3 method [12]. This model chemistry allows for the calculation of the absolute enthalpies of formation for minima and transition states. The CBS-QB3 method is a Complete Basis Set Quadratic (CBS-Q) configuration interaction model chemistry with an empirical correction/pair correlation energy extrapolation function that incorporates density functional theory, B3LYP (B3), to optimize the geometry. The B3LYP geometry optimization uses the extensive 6-311G(2d,d,p) basis set to describe the orbitals. This model chemistry involves a composite approach comprised of four calculations at varying levels of theory to determine the final energy of the structure that is examined.

The first part of the calculation involves the optimization in terms of bond angles and bond lengths of the input geometry (the initial guess) of an ion or neutral of a given atom connectivity. In this step, density functional (B3LYP) theory is used to search for the geometry that corresponds with the lowest energy on the potential energy surface (PES). The structure is optimized once all the forces converge to zero [13]. The converged structure may correspond to a minimum or a transition state.

The energy calculated at this point is not used but rather the optimized structure is used for the subsequent steps to determine its absolute heat of formation at 0 K and 298 K. In this step, the vibrational frequencies of the optimized structure are also calculated. For any non-linear polyatomic molecule or ion there are 3N-6 vibrational frequencies, where N is the number of atoms. In a transition state, one of these frequencies corresponds to the negative imaginary frequency of the transition state vibration. The zero point energy (ZPE) of the neutral molecule, ion or transition state can be determined from the frequencies [14].
The subsequent steps in the CBS-QB3 method involve calculating the energy by electron correlation methods. The second step following the geometry optimization calculates the energy by coupled-cluster theory, CC. Coupled-cluster theory is the highest order electron correlation method used in the CBS-QB3 model. This is a many body perturbation theory approach [15] which takes into account the single, double and triple excitations, CCSDT. The next two steps incorporate the so-called Møller-Plesset (MP) level of theory. Within MP type calculations there are various orders of electron-correlation [16]. The third and fourth steps of the CBS-QB3 method, utilize the MP4 and MP2 levels of theory respectively.

The final energy is then calculated and presented as $E(\text{CBS-QB3})$ in the output file. The $E(\text{CBS-QB3})$ value uses the MP2 generated energy which is corrected with the energy determined from the CCSD(T) and MP4 steps. This final energy represents the total energy of the species at 0 K. To determine the heat of formation at 298 K, $\Delta H^0_{298}$, the following relationship must be used:

$$
\Delta h_{298} = \Delta h_0^{\text{exp}} - E_{\text{AT}} + E(\text{CBS-QB3}) + E_{\text{thermal}} - ZPE - \Delta H_{298}^{\text{exp}}
$$

where $\Delta h_0^{\text{exp}}$ represents the sum of all the experimental $\Delta h_0$ values of each atom in the molecule or ion, $E_{\text{AT}}$ denotes the total atomization energies for each type of atom in the structure, $E_{\text{thermal}}$ is the thermal energy correction, ZPE is the zero point vibrational energy and $\Delta H_{298}^{\text{exp}}$ represents the sum of the experimentally derived values for each of the atoms in the species. A list of $\Delta h_0^{\text{exp}}$ and $\Delta H_{298}^{\text{exp}}$ values for first and second-row elements has been compiled by Nicolaides et al. [17].

A validation study on the accuracy of the CBS-QB3 method for ionic dissociations has been reported [18]. It proposes that the calculated heats of formation are reliable to 1-2 kcal mol$^{-1}$ for minima and 2-5 kcal mol$^{-1}$ for transition states. The accuracy of the energies can be affected by the so-called spin contamination. Spin contamination can be viewed as a mixture of spin states resulting from too much spin polarization [19b]. The inclusion of spin contamination generally results in a higher energy due to the addition of a higher spin state. A large spin contamination can also result in a change of the geometry. The total spin value, $S^2$, can be found in the output file. If there is no spin
contamination this value should be equal to \( s(s + 1) \), where \( s \) denotes the number of unpaired electrons multiplied by \( \frac{1}{2} \). An acceptable level of spin contamination is that the value lies within 10\% of the \( s(s + 1) \) value [19b].

All calculations were performed with the Gaussian suite of programs implemented on both a desktop PC as well as on the SharcNet (McMaster University) cluster of computers.

1.3 Ion-Molecule Reactions and Proton-Transport Catalysis

The study of bimolecular reactions of ions and neutrals in the gas phase is an extensive field of research [20]. To study such reactions chemical ionization (CI) conditions must be used. In CI experiments the source pressure typically ranges from \( 10^{-4} \) to \( 10^{-5} \) Torr to ensure that the species of interest experience multiple collisions prior to exiting the source [4]. To pressurize the source, a reagent gas, \( R \), is introduced which is initially ionized by collision with fast moving electrons. Once the reagent gas is ionized, it has the option to react with other reagent molecules or sample molecules, \( M \), to generate various ionic species [4]. Shown below are the possible routes of reaction and the potential encounter complexes:

\[
\begin{align*}
R + e^- & \rightarrow R^{*+} + 2e^- \\
R^{*+} + M & \rightarrow [R\cdots M]^+^+ \quad \text{(ion-dipole complex)} \\
R^{*+} + R & \rightarrow [R\cdots R]^+^+ \quad \text{(dimer radical cation)} \\
R^* + R & \rightarrow RH + [R-H]^+ \\
RH^+ + M & \rightarrow [R\cdots H\cdots M]^+ \quad \text{(proton bound mixed dimer)} \\
RH^+ + M & \rightarrow [R\cdots H\cdots R]^+ \quad \text{(proton bound dimer)} \\
R^{*+} + M & \rightarrow [R\cdots H\cdots (M-H)]^+^+ \quad \text{(hydrogen-bridged radical cation)}
\end{align*}
\]
Encounter complexes of ions and neutrals result when the two species interact via electrostatic forces and/or hydrogen bonding. An ion-dipole complex is an encounter complex between an ion and the dipole of a neutral molecule that is stabilized by the electrostatic forces. Proton-bound dimers (PBDs) \([R\cdots H\cdots R]^+\) and \([R\cdots H\cdots M]^+\) are generated from the interaction of the protonated reagent \(RH^+\) with a neutral molecule. When a reagent ion interacts with a hydrogen atom of a neutral molecule, a hydrogen-bridged radical cation (HBRC) of the type \([R\cdots H\cdots(M-H)]^+\) can be formed, where the two species are connected by a bridging hydrogen. The dimer radical cations formed between a reagent radical cation and a neutral molecule are either ion-dipole complexes or HBRCs.

**Stabilization Energy**

Before the widespread adoption of computational chemistry, the heat of formation of proton-bound dimers was experimentally determined through an empirical relationship between the proton affinity (PA) of the separate molecules and the bond dissociation energies of the PBD.

A proton-bound dimer is an even electron ion because neither of its components has lost an electron but is bound together by a proton. When the two bridged molecules are the same then a symmetrical PBD is generated, such as the proton bound dimer of water, \([H_2O\cdots H\cdots OH_2]^+\). In an asymmetrical PBD, the two bridged species are different, such as the proton-bound dimer of water and methanol, \([H_2O\cdots H\cdots O(H)CH_3]^+\).

An empirical relationship for the heat of formation of \(O\cdots H\cdots O\) proton-bound dimers has been developed by Meot-Ner [22] along with Larson and McMahon [21]. These researchers were able to study the exchange equilibria of a great number of PBDs with carefully selected bases in high pressure CI type experiments. Gibbs free energy and bond dissociation energies can also be obtained from the solvent-exchange equilibria.

The empirical relationships developed by the two groups are not exactly the same, as the PBD species studied were different. For the stabilization energy (SE) of a PBD,
Meot-Ner [22] derived the empirical relationship $SE(\text{kcal mol}^{-1}) = 30.4 - 0.30[\Delta PA]$ whereas Larson and McMahon [21] derived $SE(\text{kcal mol}^{-1}) = 30.8 - 0.46[\Delta PA]$. The first term represents the average bond dissociation energy of a set of symmetrical PBDs. In both equations the first term is slightly different due to the different PBD species studied. The second term denotes the slope of the bond dissociation vs. $\Delta PA$ plots.

The determination of the stabilization energy of a symmetrical PBD differs from that of an asymmetric proton-bound dimer. If the PBD is symmetric the stabilization energy is obtained from the expression: $\Delta H_{i}(\text{product}_1) + \Delta H_{i}(\text{product}_2) - \Delta H_{i}(\text{PBD}^+)$. In a symmetrical PBD like for example $[\text{H}_2\text{O} \cdots \text{H} \cdots \text{OH}_2]^+$, there is only one possibility for the products, $\text{H}_3\text{O}^+ + \text{H}_2\text{O}$, and their heats of formation are well established. The $\Delta PA$ is the same for each component water molecule so $\Delta PA$ is zero and as a result the stabilization energy is 30.0 kcal mol$^{-1}$. This value can be used to obtain the $\Delta H$ of the proton-bound dimer.

When the PBD is asymmetrical, as in $[\text{H}_2\text{O} \cdots \text{H} \cdots \text{O(H)CH}_3]^+$, the proton-bound dimer between water and methanol, there are two possible combinations of dissociation products, $\text{H}_3\text{O}^+ + \text{CH}_3\text{OH}$ and $\text{H}_2\text{O} + \text{CH}_3\text{OH}_2^+$. In this situation, the lowest energy combination is used to derive the enthalpy of formation of the PBD, as indicated in the Figure below:
Meot-Ner has also studied \([\text{N}\cdots\text{H}\cdots\text{O}]^+\) and \([\text{N}\cdots\text{H}\cdots\text{N}]^+\) proton-bound dimers [22]. For these, the expressions for the stabilization energy (kcal mol\(^{-1}\)) are 30.0 – 0.26[ΔPA] and 23.2 – 0.25[ΔPA] respectively.

The empirically derived expressions for the stabilization energy of proton-bound dimers have also been applied to hydrogen-bridged radical cations. An example of a HBRC is the radical cation \([\text{CH}_3\text{O}\cdots\text{H}\cdots\text{OH}_2]^+\), where the hydroxyl hydrogen of methanol provides the bridging hydrogen. Employing the same empirical expression, \(SE = 30.0 – 0.30[ΔPA]\), a good estimate of the enthalpy of formation of this O···H···O bridged HBRC can be calculated. For HBRCs the ΔPA term represents the difference in proton affinity of the radical (CH\(_3\)O\(^+\)) and the molecule (H\(_2\)O). As with asymmetric PBDs, there are two combinations of dissociation products in HBRCs of which the lowest energy pair is used to determine its heat of formation..

_Catalyzed Isomerization Reactions_

A great number of studies have been reported which demonstrate that the interconversion of isomeric ions can be catalyzed by interaction with a suitable neutral molecule [20]. These catalyzed isomerization reactions often involve distonic ions. Distonic ions are radical cations in which the charge and the radical reside on different atoms [20]. They tend to be more stable than their conventional counterparts but the two types of ions are often separated by a large energy barrier. This high energy barrier enables independent observation of the two isomeric species. The archetypal example of this type of reaction is the rearrangement of ionized methanol, CH\(_3\)OH\(^+\), into the more stable methylene oxinium ion, \(^*\text{CH}_2\text{OH}_2^+\) [23,24]. As solitary ions these two isomers cannot interconvert because of a prohibitively high 1,2-H shift barrier. Nevertheless, this reaction readily occurs with a single water molecule acting as the catalyst.

This type of reaction is termed proton-transport catalysis (PTC) [25]. The mechanism for the rearrangement of a convention radical cation, \([\text{H-X-Y}]^{+\dagger}\), into its more stable counterpart, \([\text{X-Y-H}]^{+\dagger}\), occurs via a three step proton transfer process:
\[
B + [H-XY]^{**} \rightarrow B\cdots H^+\cdots [XY]^* \\
B\cdots H^+\cdots [XY]^* \rightarrow B\cdots H^+\cdots [YX]^* \\
B\cdots H^+\cdots [YX]^* \rightarrow B + [H-YX]^{**}
\]

The neutral molecule, B, acts as a "base" to abstract a proton from [H-XY]^{**}. The second step in the mechanism illustrates how the base acts as a catalyst to "transport" the proton from the high energy site to the low energy site. In order for this reaction to proceed the PA of the base must be higher than the PA of XY* at the X site but lower than at the Y site. The weakly bound complex, B\cdots H^+\cdots [XY]^*, allows for the rotation of the XY molecule within the ion. In the case where the PA[B] is lower than the PA[XY*] at X, the B\cdots H^+\cdots [YX]^* encounter complex cannot be formed. If, on the other hand, PA[B] is greater than the PA[XY*] at Y, the intermediate complex, B\cdots H^+\cdots [XY]^*, will dissociate into undesirable products, HB* and [X-Y]^*. Based on extensive computational studies, Radom and co-workers have developed a criterion for efficient PTC: the PA[B] must be intermediate between PA[X] and PA[Y] for successful PTC [20b].
References


Chapter 2a

Formaldehyde mediated proton-transport catalysis in the ketene-water radical cation CH$_2$=C(=O)OH$_2$$^{+}$

Abstract

Previous studies have shown that the solitary ketene-water ion CH$_2$=C(=O)OH$_2$$^{+}$ (1) does not isomerize into CH$_2$=C(OH)$_2$$^{+}$ (2), its more stable hydrogen shift isomer. Tandem mass spectrometry based collision experiments reveal that this isomerization does take place in the CH$_2$=O loss from *low energy* 1,3-dihydroxyacetone ions (HOCH$_2$)$_2$C=O$^{+}$.

A mechanistic analysis using the CBS-QB3 model chemistry shows that such molecular ions rearrange into hydrogen-bridged radical cations [CH$_2$C(=O)O(H)–H⋯OCH$_2$]$^{+}$ in which the CH$_2$O molecule catalyzes the transformation 1 → 2 prior to dissociation. The barrier for the unassisted reaction, 29 kcal mol$^{-1}$, is reduced to a mere 0.6 kcal mol$^{-1}$ for the catalysed transformation. Formaldehyde is an efficient catalyst because its proton affinity meets the criterion for facile proton-transport catalysis.
1. Introduction

A very recent review elegantly demonstrates that the application of mass spectrometric techniques to the study of elementary ion reactions has led to remarkable progress in the characterization of detailed aspects of the kinetics, thermodynamics, and mechanisms of molecular transformations catalyzed by ions in the gas-phase [1].

This active field of research has greatly benefited from the selected-ion flow tube (SIFT) studies of D.K. Böhme and his research group [1]. This is also true for the related area of research which studies ionic transformations catalyzed by molecules in the gas-phase. As pointed out in Böhme’s early review on this topic [2], a pair of solitary ionic isomers whose interconversion barrier is prohibitively high may be induced to interconvert via proton transfer in an encounter complex with a neutral molecule having the correct proton affinity (PA). This process is commonly called proton-transport catalysis (PTC). As a result the higher energy isomer may be transformed into its thermodynamically more stable counterpart.

For example [3], a large 1,2-H shift barrier prevents the conversion of ionized hydroxycarbene into ionized formaldehyde: HCOH" → CH₂=O". The barrier exceeds the energy required for loss of H" by direct bond cleavage, so even high energy ions will dissociate rather than interconvert. However, when a neutral molecule is allowed to interact with HCOH"+, proton-transport catalysis (PTC) may promote its isomerization into the lower energy CH₂=O" isomer. The molecule may act as a base (B) and accept a proton from one site of the HCOH" substrate, and then donate it back to a different site, as illustrated in Eq. 1: HCOH" + B → HCO-H"•••B (a) → HC=O•••HB+ → O=C(H)•••HB+ → O=C(H)-H"•••B (b) → CH₂=O" + B (1).

Criteria for successful proton-transport catalysis have been further developed by Radom and co-workers [4]. The most important criterion states that a smooth isomerization for the reaction of Eq. 1 occurs if the PA of the base B lies between the PA of HCO' at O and at C. If PA(B) is too low, proton abstraction will not take place. If PA(B) is too high, the incipient ion BH' will not release the proton: dissociation to HCO' + BH' will ensue instead. As reported recently [5], the criterion can be significantly
extended downwards to include bases of lower PA with a concomitant increase of the barrier height.

Several examples of ion-molecule reactions in the gas phase are now available [6] where interaction of a radical cation with a single, judiciously chosen, “solvent” molecule leads to its transformation into a more stable isomer. Key intermediates in these reactions are hydrogen-bridged radical cations (HBRCs) [7] of the type (a) and (b) in Eq. 1. However, we note that not all such catalyzed transformations involve transport of a proton rather than a hydrogen atom [6c] and also that these transformations may take place in the dissociative ionization of molecules [3].

In the context of studies on proton transport catalysis, the Böhme group presented intriguing experimental and computational results on the water-catalyzed hydrolysis of the ketene radical cation at the 2004 Trent Conference in Mass Spectrometry [8]. Ketene ions were allowed to react with water in the SIFT mass spectrometer and one aspect of their study dealt with the water catalyzed isomerization of the incipient ketene-water ion, \( \text{CH}_2\text{C(=O)OH}_2^+ \) (1), into its thermodynamically more stable isomer \( \text{CH}_2\text{C(OH)}_2^+ \) (2), the enol ion of ionized acetic acid, \( \text{CH}_3\text{C(=O)OH}^+ \) (3).

The criterion for efficient PTC for the transformation \( \text{CH}_2\text{C(=O)OH}_2^+ \) (1)\( \rightarrow \) \( \text{CH}_2\text{C(OH)}_2^+ \) (2) stipulates[*] that the base has a PA in the range of 166–183 kcal mol\(^{-1}\) and hence water (PA = 167 kcal mol\(^{-1}\)) is a suitable catalyst. The PA of the formaldehyde molecule, 170 kcal mol\(^{-1}\) [10b], also satisfies the PTC criterion. Thus it may be expected that formaldehyde can also efficiently catalyse the isomerization.

This information inspired us to re-examine the generation of 1 as the product ion of the dissociative ionization of 1,3-dihydroxyacetone: \((\text{HOCH}_2)_2\text{C}=\text{O}^+ \) (DHA-1) \( \rightarrow \) \( \text{CH}_2\text{C(=O)OH}_2^+ \) (1) + \( \text{CH}_2\text{=}\text{O} \). In 1986, Postma et al. [9] provided experimental and supporting computational evidence that the source generated \( \text{C}_2\text{H}_2\text{O}_2^+ \) ions of this dissociation have the connectivity of ketene-water type ions 1. The ion undergoes one major unimolecular dissociation, loss of \( \text{H}_2\text{O} \) to yield \( \text{CH}_2\text{C}=\text{O}^+ \). This process is associated with a very small kinetic energy release, indicative of a species in which a
water molecule is attached to ionized ketene by an ion-dipole bond. Loss of water also wholly dominates the collision induced dissociation (CID) mass spectrum, which is characteristically different from that of any other C$_2$H$_4$O$_2^+$ isomer, including CH$_2$=C(OH)$_2^+$ (2). Thus, there is little doubt that the source generated m/z 60 C$_2$H$_4$O$_2^+$ ions from DHA-1 are (largely) ketene-water type ions 1.

Appearance energy measurements of the m/z 60 ion [9] yielded an apparent heat of formation of 138 kcal mol$^{-1}$ which was interpreted to correspond to the formation of 1 at the thermochemical threshold. This implies that the abundant loss of CH$_2$=O from low-energy ions DHA-1 – the MI spectrum of DHA-1 is dominated by a simple Gaussian shaped peak [11] at m/z 60 corresponding with a T$_{0.5}$ value of 25 meV – would also yield C$_2$H$_4$O$_2^+$ ions of structure 1.

This proposal could be verified by analyzing the CID mass spectrum of the m/z 60 ions generated from metastable DHA-1 ions. Such an experiment could not be performed with the instrumentation of the study of ref. 9 but our three-sector ZAB-R magnetic deflection instrument does have this capability.

The result of this experiment is shown in Figure 1a. The spectrum is virtually identical with that of enol ions CH$_2$=C(OH)$_2^+$ (2), see Figure 1b. It is incompatible with the formation of the ketene-water isomer CH$_2$=C(=O)OH$_2^+$ (1) whose $^{18}$O isotopomer CH$_2$=C(=O$^{18}$)OH$_2^+$ yields the spectrum of Fig. 1c. This spectrum shows a specific loss of H$_2^{16}$O, confirming that ions 1 do not communicate with ions 2 prior to dissociation.

Thus, the formaldehyde loss from low-energy DHA-1 ions does not yield ketene-water ions 1 but rather enol ions 2, possibly by a formaldehyde-catalyzed isomerization 1 → 2. The derived heat of formation of 138 kcal mol$^{-1}$ for the m/z 60 product ion generated in the formaldehyde loss (see above) is not compatible with the threshold formation of 2 (122 kcal mol$^{-1}$, see Table 1) but could result from an energy barrier in the rearrangement.

$^*$using $\Delta H$ [CH$_2$COOH] = -61.6 kcal mol$^{-1}$ [10a], $\Delta H$ (1a) = 138.5 kcal mol$^{-1}$ (Table 1), $\Delta H$ (2) = 121.8 kcal mol$^{-1}$ (Table 1).
This intriguing result prompted us to explore the mechanism of the formaldehyde loss from low-energy 1,3-dihydroxyacetone ions using computational chemistry. During the past five years we have successfully used the CBS-QB3 method [12] in mechanistic studies of proton-transport catalysis in various organic radical cations [13]. We therefore decided to use this CBS variant, which uses density functional geometries and frequencies in the calculations, as the primary computational tool in probing the mechanism for the formaldehyde elimination from metastable ions DHA-1.

It will be shown that proton-transport catalysis indeed accounts for the formation of enol ions 2 in the formaldehyde loss from low-energy 1,3-dihydroxyacetone radical cations.

2. Experimental and theoretical methods

The experiments were performed with the VG Analytical ZAB-R mass spectrometer of BEE geometry (B, magnet; E, electric sector) [14] using an electron ionization source at an accelerating voltage of 8 kV. Metastable ion (MI) mass spectra were recorded in the second field free region (2ffr). The CID mass spectra of the 2ffr metastable peaks were obtained in the 3ffr using O₂ as collision gas (Transmittance, T = 70%). The reference CID mass spectrum of the enol ion of acetic acid of Fig. 2b was
obtained via the dissociative ionization of butyric acid. The spectrum of Fig. 2c was obtained in the context of a previously reported study of ionized oxalacetic acid: it pertains to the decarbonylation of metastable $\alpha$-hydroxy($^{18}$OH) acrylic acid ions into $\text{CH}_2=\text{C}(=\text{O}^{18})\text{OH}_2^{\text{+}}$ as indicated in Scheme 3 of ref. 15. All spectra were recorded using a PC-based data system developed by Mommers Technologies Inc. (Ottawa).

The 1,3-dihydroxyacetone sample was of research grade (Aldrich) and used without further purification.

The calculations were performed with the CBS-QB3 model chemistry [12] using Gaussian 2003, Rev C.02 [16] and (for selected transition state searches) GAMESS-UK [17]. In this model chemistry the geometries of minima and connecting transition states are obtained from B3LYP density functional theory in combination with the 6-311G(2d,d,p) basis set (also denoted as the CBSB7 basis set). The resulting total energies and enthalpies of formation for minima and connecting transition states (TS) in the 1,3-dihydroxy acetone system of ions are presented in Table 1. Spin contaminations were within an acceptable range. Figure 3 displays the optimized geometries for the principal species.

### Table 1. Enthalpies of formation (kcal mol$^{-1}$) and total energies (Hartree) derived from CBS-QB3 calculations.

<table>
<thead>
<tr>
<th>Isomer</th>
<th>$E_{\text{total}}$ (0 K)</th>
<th>$\Delta H^0_{298}$</th>
<th>Isomer</th>
<th>$E_{\text{total}}$ (0 K)</th>
<th>$\Delta H^0_{298}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>DHA-1</td>
<td>-342.75044</td>
<td>92.9</td>
<td>1a</td>
<td>-228.38018</td>
<td>138.5</td>
</tr>
<tr>
<td>DHA-2</td>
<td>-342.73670</td>
<td>102.2</td>
<td>1b</td>
<td>-228.38058</td>
<td>138.4</td>
</tr>
<tr>
<td>DHA-3</td>
<td>-342.74391</td>
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<td>TS DHA-2→7</td>
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<td>CH$_3$=O</td>
<td>-114.34411</td>
<td>-27.3</td>
</tr>
</tbody>
</table>

[a] lowest energy conformer; experimental value = 120 kcal mol$^{-1}$ [10c]; [b] lowest energy conformer; experimental value = 142.5 kcal mol$^{-1}$ [10c]; [c] experimental value = 210.2 kcal mol$^{-1}$ [10c]
3. Results and discussion

3.1. The structure and stability of the ketene-water ion and the relationship with its hydrogen-shift isomers $\text{CH}_2=\text{C}(\text{OH})_2^+$ (2) and $\text{CH}_3-\text{C}(=\text{O})\text{OH}^+$ (3).

In the early ab initio calculations of Postma et al. [9], the standard 4-31G basis set was used to optimize the geometries of various configurations of the ketene-water ion. Our CBS-QB3 calculations agree with their findings that ion 1a and the hydrogen-bridged radical cation 1b, whose optimized geometries are shown in Fig.3, represent the most stable configurations. The two ions have similar energies and our calculations further agree that the barrier for the interconversion 1a/1b is negligible (see Table 1). At internal energies in excess of only a few kcal mol$^{-1}$ above 1a/b, the water molecule can freely move from carbon to carbon. The sum of the product energies relative to 1a was calculated to be 15 kcal mol$^{-1}$ [9] which reasonably agrees with our CBS-QB3 result of 13.4 kcal mol$^{-1}$.

The optimized geometry of 1a shown in Figure 3a points to a description of the ion as a (ketene)ion – (water)dipole complex. Using the simple equation for the ion-dipole stabilization energy – $SE$ (kcal mol$^{-1}$) = $68.8 \mu / r^2$, with $\mu$ = dipole moment (D) and $r$ = distance (Å) between the charge and the dipole – one obtains $SE$ (1a) = 27 kcal mol$^{-1}$, much larger than the CBS-QB3 derived value of 13.4 kcal mol$^{-1}$. However, the above equation does not account for repulsive effects associated with an ion-dipole interaction. That such a repulsive destabilizing effect operates in 1a follows from an inspection of the geometries of the ketene ion in 1a and 1b, see Fig. 3a. In 1b the ketene ion has a linear configuration but in 1a repulsion of the oxygen atoms’ lone pairs causes the ion to adopt an energetically less favourable “bent” structure. In a Valence Bond type of description, structure 1a suffers from some contribution of the distonic form $'\text{CH}_2-\text{C(OH}_2^+)'=\text{O}$, raising the total energy.
Fig. 2 Energy level diagram derived from CBS-QB3 calculations describing the formation of enol ions 2 via loss of CH$_2$=O from metastable 1,3-dihydroxy-acetone ions.
Postma et al. [9] further reported that point calculations for other geometries related to H₂O motion about the ends of the ketene ion showed barriers to such motion. One such motion leads to an isomer of the connectivity H₂O—CH₂=C=O⁺⁺ having an O—C bond length of 2.839 Å, which was calculated to lie ~ 6 kcal mol⁻¹ above 1a. This structure is probably not a minimum on the PES: when we optimized its geometry with the CBS-QB3 method, a minimum was located with corresponds with the distonic ion H₂O-CH₂=C=O⁺⁺ (1c), having an O—C bond of 1.533 Å (see Figure 3). This ion is only marginally stable – it lies 22 kcal mol⁻¹ higher in energy than 1a and requires only 2.5 kcal mol⁻¹ to rearrange into energy rich ions 1a which subsequently dissociate – but it does play a role in the mechanism discussed in the next section.

Our computational results, see Table 1, further show that the unassisted isomerization of ions 1a into the enol of acetic acid ion 2 is prohibitively high: the associated energy barrier of 29 kcal mol⁻¹ lies well above the energy required for dissociation by direct bond cleavage into CH₂=C=O⁺⁺ + H₂O. The same holds true for the isomerization 1a → 3. Thus solitary ketene-water ions do not communicate with their 1,3-hydrogen shift isomers CH₂=C(OH)₂⁺⁺ (2) and CH₃-C(=O)OH⁺⁺ (3).

**Fig.3a.** Optimized geometries (CBSB7 basis set) of stable configurations on the potential energy surface of the ketene-water radical cation

3.2. *The loss of formaldehyde from low energy 1,3-dihydroxyacetone ions.*

We will use the energy diagram of Fig. 2 as a guide in the discussion of our proposed mechanism for the formation of enol ions 2 from metastable 1,3-dihydroxyacetone ions. Starting from ion DHA-1, we see that elongation of the HOCH₂—C(=O) bond with the concomitant formation of a new O-H bond may lead to the
hydrogen-bridged radical cation DHA-2 via a low energy barrier. Ion DHA-2 then rearranges, via a barrier which is calculated to lie at 113 kcal mol\(^{-1}\), into a ter-body complex, ion DHA-3. The height of this barrier is very close to the enthalpy calculated for the dissociation level 1a + CH\(_2\)=O, 112 kcal mol\(^{-1}\), and this supports – see Introduction – our alternative interpretation of the AE measurements of Postma et al.[9], namely that the experimental AE actually corresponds to a barrier, i.e. TS DHA-2/3.

Once ions DHA-3 have been formed, they may undergo a barrierless rearrangement involving the migration of the OH...O=CH\(_2\) moiety to the carbon atom of the carbonyl group of the ketene part to form HBRC DHA-4. A rotation of the OH...O=CH\(_2\) moiety yields its more stable conformer DHA-5, via a TS lying only 2 kcal mol\(^{-1}\) above DHA-4. A formal 1,3-H shift assisted by the CH\(_2\)=O molecule in DHA-5, the proton-transport catalysis step, then yields DHA-6, the desired precursor ion for the generation of 2 + CH\(_2\)=O. The TS connecting DHA-5 and DHA-6 lies at 85 kcal mol\(^{-1}\), well below the energy requirement for dissociation into 2 + CH\(_2\)=O, at 95 kcal mol\(^{-1}\).

It was stated in the Introduction that since formaldehyde fulfils the PA criterion, the transformation should be smooth, i.e. the barrier for proton-transport catalysis should be low. Indeed, as can be seen from Fig. 2 and Table 1, the barrier for the isomerization is reduced from 29 kcal mol\(^{-1}\) for the solitary ions to a mere 0.6 kcal mol\(^{-1}\) for the formaldehyde assisted transformation showing that formaldehyde is an efficient catalyst.

Loss of formaldehyde by a simple O-H--O=CH\(_2\) bond elongation in ions having the structure of TS DHA-2/3 is not expected to occur because the resulting ketene-water isomer 1c lies, see Table 1, far too high in energy. On the other hand, once ions DHA-3 are formed they are proposed to undergo a facile rearrangement into ions DHA-4 and these could dissociate by direct bond cleavage into 1a + CH\(_2\)=O. This reaction, however, is not observed for the dissociation of the metastable DHA ions – these exclusively yield 2 + CH\(_2\)=O – and we propose that the following kinetic argument provides a rationale.

For simplicity, we assume that a model involving only three isomers suffices. These are DHA-1, DHA-3 and DHA-6, where DHA-3 may dissociate into 1a + CH\(_2\)=O, whereas DHA-6 may yield 2 + CH\(_2\)=O. In this model the barrier between DHA-3 and
Fig. 3b. Selected optimized geometries (CBSB7 basis set) for stable intermediates and transition states involved in the formaldehyde elimination from ionized 1,3-dihydroxyacetone (DHA-1).

- DHA-1
- DHA-2
- DHA-3
- DHA-4
- DHA-5
- DHA-6a
- DHA-6b
- DHA-7
- TS DHA-1/2
- TS DHA-2/3
- TS DHA-2/7
- TS DHA-3/4
- TS DHA-4/5
- TS DHA-5/6
DHA-6 is essential for the product yields: if the corresponding TS (TS DHA-3/4) would lie near the dissociation limit for 1a + CH₂=O (and thus also near the rate-determining TS DHA-2/3), the isomerization DHA-3 to DHA-6 and the dissociation DHA-3 to 1a + CH₂=O would both fall into the microsecond time frame. In this case the formation of DHA-6 would compete with the dissociation into 1a + CH₂=O and both products should be found in the MI spectrum. However, our calculations show that the activation energy for the interconversion DHA-3 to DHA-6 is very small indeed. Therefore the isomerization into DHA-6 will be very fast and the same holds for the dissociation of DHA-6 into 2 + CH₂=O. In this scenario all reactions are fast except the one corresponding to the first isomerization.

A similar argument applies to the dissociation of DHA-6a. This ion can fragment to 2 + CH₂=O at 95 kcal mol⁻¹, but the counterpart constituents CH₂OH⁺ + 'CH₂COOH are also energetically accessible. This dissociation level lies at 112 kcal mol⁻¹ when one uses ΔH [CH₂COOH] = -61.6 kcal mol⁻¹ as proposed in the compilation of ref. 10a; it becomes even lower, 108 kcal mol⁻¹, if the CBS-QB3 derived value of -57.3 kcal mol⁻¹ is used for the radical. Nevertheless, the formation of CH₂OH⁺ + 'CH₂COOH is not observed at all because dissociation of DHA-6a into 2 + CH₂=O will be much faster.

As can be seen from Fig. 2, DHA-6a is the global minimum. It has been shown [7] that Mautner’s correlation equation for proton bound dimers [18] also applies to hydrogen-bridged radical cations and can be used to estimate their ΔfH from known dissociation limits.

For O•••H•••O hydrogen-bridged radical cation A-H••·B⁺⁺ one obtains [7]:

ΔfH [A-H••·B⁺⁺] = 0.70{ΔfH [AH⁺⁺] + ΔfH [B]} + 0.30{ΔfH [HB⁺⁺] + ΔfH [A]} - 30.4 (kcal mol⁻¹),

where AH⁺⁺ + B is the cheaper dissociation threshold. Using this equation we obtain ΔfH [DHA-6] = 69 -70 kcal mol⁻¹, which is in agreement with the CBS-QB3 result of 72 kcal mol⁻¹. Note that association of formaldehyde with the cis-cis conformer of 2 leads to a stable complex with a double hydrogen bridge, see structure DHA-6b in Figure 3, whose enthalpy lies at 71 kcal mol⁻¹.
Finally we note that ion DHA-2 could in principle rearrange into DHA-7, the precursor ion for the formation of HBRC 4 and CO. The heat of formation of the decarbonylation products 4 + CO actually lies lower in energy than that of 1a + CH₂=O but the TS connecting DHA-2 and DHA-7 lies at 116 kcal mol⁻¹, 3 kcal mol⁻¹ higher in energy than TS DHA-2/3. Thus the fact that the decarbonylation reaction has a significant reverse activation energy may explain why this process is not detected in the MI spectrum of 1,3-dihydroxyacetone.

4. Conclusions

Tandem mass spectrometry based collision experiments reveal that low energy 1,3-dihydroxyacetone ions (DHA-1) dissociate by loss of formaldehyde to produce the ionized enol of acetic acid, i.e. HOCH₂C(=O)CH₂OH⁺ → CH₂=C(OH)₂⁺ + CH₂=O. The mechanism of this seemingly unintelligible reaction has been elucidated with the help of the CBS-QB3 model chemistry. Key intermediate in this dissociation is the ketene-water ion associated via a hydrogen bridge with a formaldehyde molecule, 'CH₂-C(=O)-O'H-H O=CH₂ (DHA-4/5 in Fig. 2). This ion can undergo an almost barrier-free proton-transport catalysis to produce CH₂=C(OH)₂⁺ associated with formaldehyde (the global minimum) which then dissociates.

Formation of DHA-4, see Fig. 2, is also mechanistically intriguing. After hydrogen bridging of the two hydroxyl groups and concomitant C-C cleavage in DHA-1, HBRC DHA-2 is formed. Next the hydrogen of the H-bridge moves towards the O(H) group and the entire H-O-H•••O=CH₂ moiety can shift from the ketene methylene carbon atom to its carbonyl carbon atom to produce DHA-4. This rearrangement constitutes the rate-determining step; hence all subsequent reactions will be fast precluding the formation of higher energy products such as the ketene-water ion-dipole complex itself. The calculated energy of the rate-determining transition state, 113.0 kcal mol⁻¹, is in excellent agreement with that (112.5 ± 1.0 kcal mol⁻¹) derived from the experimental appearance energy.
References

Chapter 2b

Does proton transport catalysis play a role in the decarboxylation of ionized pyruvic acid?

Abstract

Mass spectrometric studies have shown that metastable pyruvic acid radical cations, \( \text{CH}_3\text{C}(=\text{O})\text{COOH}^+ \) (1), undergo decarboxylation into \( \text{C}_2\text{H}_4\text{O}^+ \) ions in competition with the formation of \( \text{CH}_3\text{C}=\text{O}^+ + \text{COOH}^- \) by direct bond cleavage. Recent work on metastable glyoxilic acid radical cations, \( \text{HC}(=\text{O})\text{COOH}^+ \), revealed that the \( \text{CO}_2 \) molecule formed in its decarboxylation catalyses the isomerization of the incipient oxycarbene ion \( \text{HCOH}^+ \) into its more stable \( \text{CH}_2=\text{O}^+ \) isomer. This raises the question whether the decarboxylation of 1 also involves proton-transport catalysis by \( \text{CO}_2 \). This may be the case, but only to a minor extent. Our collision experiments agree with an earlier report that oxycarbene ions \( \text{CH}_3\text{COH}^+ \) are formed but they also indicate that the (slightly) more stable isomer \( \text{CH}_3\text{C}(\text{H})=\text{O}^+ \) may be co-generated. A mechanistic analysis using the CBS-QB3 model chemistry provides a rationale. Ions 1 can rearrange into the (more stable) hydrogen-bridged radical cations \( [\text{CH}_3\text{CO}-\text{H}&&\text{O}=\text{C}=\text{O}]^+ \) (2a). However, the barriers for this reaction and that of a subsequent \( \text{CO}_2 \) assisted isomerization of 2a into \( [\text{CH}_3\text{C}(=\text{O})-\text{H}&&\text{O}=\text{C}=\text{O}]^+ \) (2b) lie 6-7 kcal mol\(^{-1}\) above the dissociation level of \( \text{CH}_3\text{COH}^+ + \text{CO}_2 \). Thus ions 2a are not prone to rearrange by proton-transport catalysis but they rather dissociate into \( \text{CH}_3\text{COH}^+ + \text{CO}_2 \).
1. Introduction

For the HCOH'/'CH$_2$=O' system of ions, interconversion does not take place at all with the solitary ions because the barrier is much higher than the lowest energy direct bond cleavage reaction. However, in a recent study from our group [1], it was shown that proton-transport catalysis by CO and CO$_2$ does lead to the isomerization of HCOH' into its (slightly) more stable 1,2-H shift isomer CH$_2$=O'. Collision experiments show that CH$_2$=O' is cleanly generated in the decarbonylation of low-energy (metastable) glyoxal ions O=CH-CH=O'. Likewise, glyoxilic acid ions, HC(=O)COOH', decarboxylate into CH$_2$=O', albeit in admixture with some HCOH'. A mechanistic analysis using the CBS-QB3 model chemistry indicates that the above ions first rearrange into hydrogen-bridged radical cations, [HCO-H•••C=O]' and [HCO-H•••O=C=O]', respectively. As mentioned above, solitary ions HCOH' do not isomerize but the CO or CO$_2$ molecule in the above complexes catalyses this transformation prior to dissociation. Carbon monoxide is the better catalyst because its proton affinity is closer to Radom's criterion for efficient proton-transport catalysis as discussed in Chapter 2a.

These results prompted us to re-examine the dissociation chemistry of ionized pyruvic acid, CH$_3$C(=O)COOH' (1), which also undergoes a spontaneous decarboxylation in the metastable time-frame [2]. If the reaction is catalysed by CO$_2$ – as in ionized glyoxilic acid – the m/z 44 [C$_2$H$_4$O]' product ion would be CH$_3$C(H)=O' rather than its higher energy isomer CH$_3$COH' [3,4] as proposed in ref. 2. As with the HCOH'/CH$_2$=O' system of ions, solitary ions CH$_3$COH' and CH$_3$C(H)=O' cannot interconvert because the barrier is much higher than the lowest energy direct bond cleavage reaction [3].

As pointed out in ref. 2, a study reported in 1983 by Terlouw et al., it had earlier been concluded that the decarboxylation of ionized pyruvic acid yielded [C$_2$H$_4$O]' ions having the vinyl alcohol structure CH$_2$=C(H)OH'. This was because the broad metastable peak for H' loss from the (source generated) ion was the same as that for ions known to possess the structure CH$_2$=C(H)OH', the most stable isomer of the family of [C$_2$H$_4$O]' isomers [3]. The study of ref. 2. further noted that ab initio calculations by Bouma et al.
these results have been confirmed by the higher level calculations published in 1998 by Bertrand and Bouchoux [3]—indicate that CH$_2$=C(H)OH$^+$ ions isomerize to CH$_3$COH$^+$ as the reacting configuration leading to the formation of CH$_3$C=O$^+$. Thus the metastable peak for loss of H$^+$, instead of being solely characteristic of CH$_2$=C(H)OH$^+$ ions, is indicative of either these and/or CH$_3$COH$^+$.

In this context we note that the calculations of ref. 3 indicate that loss of H$^+$ from CH$_3$COH$^+$ is associated with a large reverse activation energy [3]. This provides a rationale why loss of H$^+$ from CH$_2$=C(H)OH$^+$ and CH$_3$COH$^+$ is associated with a broad metastable peak whose $T_{0.5}$ value—the kinetic energy release as obtained from the width at half height of the peak [6]—is c. 500 meV [7]. In contrast, loss of H$^+$ from the isomer CH$_3$C(H)=O$^+$ has a only a small reverse activation energy [3] and the $T_{0.5}$ value is 43 meV [7].

Distinguishing the CH$_2$=C(H)OH$^+$ / CH$_3$COH$^+$ pair of isomers therefore, it was argued [2], must rest upon examination of ions of low internal energy content, preferably those generated via metastable dissociation of their precursors. Using a magnetic deflection mass spectrometer of BE geometry it was then shown that the collision induced (CID) mass spectrum of the [C$_2$H$_4$O]$^+$ product ions generated from metastable pyruvic acid ions dissociating in the first field region is characteristic of ions CH$_3$COH$^+$ and not of reference ions of structure CH$_2$=C(H)OH$^+$.

From appearance energy (AE) measurements on both the metastable and the source generated ions it was further proposed [2] that $\Delta H^{0}_{298} \text{[CH}_3\text{COH}]^+ = 206.7 \pm 5$ kcal mol$^{-1}$ [2,8a]. The rather large uncertainty in the proposed value stems from the uncertainty in the AE of the metastable peak (10.7 ± 0.2 eV) and the fact that for the source generated ions - AE ≥ 10.4 eV (energy selected electrons) - only a lower limit could be assessed because of $^{13}$CCH$_3$O$^+$ contributions (AE m/z 43 (CH$_3$CO$^+$) = 10.28 ± 0.05 eV (energy selected electrons) [8e]). However, it has been argued that the experimentally derived enthalpy of the oxycarbene ion is too high and that the result derived from theoretical calculations using the Gaussian 2 (G2) method, 199.5 kcal mol$^{-1}$, is closer to reality [3,4]. We will evaluate this proposal in Section 3 but we first note that
in the decarboxylation study of ref. 2 the (co)generation of ionized acetaldehyde, \( \text{CH}_3\text{C}(\text{H})=\text{O}^+ \), whose well-established \( 
abla H^0_{298} \) value of 196.2 kcal mol\(^{-1}\) [4,8a/b] lies in between that of \( \text{CH}_3\text{COH}^+ \) and \( \text{CH}_2=\text{C}(\text{H})\text{OH}^+ \), has not been explicitly considered.

![Fig. 1 Metastable ion spectrum of ionized pyruvic acid. Inset (a) partial 3ffr CID spectrum of \( \text{CH}_3\text{COH}^+ \) and inset (b) partial 3ffr CID reference spectrum of \( \text{CH}_3\text{C}(\text{H})=\text{O}^+ \) from ionized acetaldehyde.](image)

Figure 1 shows the metastable ion (MI) spectrum of ionized pyruvic acid obtained under conditions of good energy resolution. The spectrum displays two peaks: a peak at m/z 43 corresponding with the formation of \( \text{CH}_3\text{C}=\text{O}^+ \) by loss of \( \text{COOH}^- \) and a peak at m/z 44 corresponding with the decarboxylation. The width of the very narrow m/z 43 peak is that of the main beam of ions so that only an upper limit for the kinetic energy release can be derived: \( T_{0.5} \leq 0.5 \text{ meV} \). Such a small energy release is indicative for dissociation via ion-dipole complexes. The peak at m/z 44 is of simple Gaussian shape [6] and the associated \( T_{0.5} \) value is 15 meV. We further note that the intensity of the m/z 43 peak increases strongly when a collision gas is introduced whereas this has hardly any effect on the m/z 44 peak intensity. The CID mass spectrum of these m/z 44 ions was recorded in the 3ffr and the structure characteristic part of the spectrum is shown in inset (a) of Fig. 1. The intensity distribution of the peaks in this spectrum is very close to that reported in ref. 2 and indeed characteristically different from that of vinyl alcohol type ions \( \text{CH}_2=\text{C}(\text{H})\text{OH}^+ \). On the other hand, see inset (b) of Fig. 1, the m/z 24-30 region of the CID mass spectrum of acetaldehyde reference ions \( \text{CH}_3\text{C}(\text{H})=\text{O}^+ \) is not so different from that of ions of putative structure \( \text{CH}_3\text{COH}^+ \) that the possibility can be dismissed that the
spectrum of inset (a) represents ions CH₃COH⁺ in admixture with some CH₃C(H)=O⁺. Unfortunately, a reference CID mass spectrum of the isomerically pure oxycarbene ion is not available: the dissociative ionization of pyruvic acid is the only reported source of this ion.

The experimental results presented in Fig. 2 lend support to the proposal that the m/z 44 ions generated by the decarboxylation of metastable pyruvic acid ions are not pure ions CH₃COH⁺ but rather CH₃COH⁺ in admixture with CH₃C(H)=O⁺. Fig. 2a displays the m/z 43 peak obtained by the collision induced dissociation of source generated m/z 44 ions from ionized pyruvic acid. The spectrum was obtained in the third field free region using the maximum energy resolution available with the second electrostatic analyser (10 V for 4 keV ions). It is seen that the m/z 43 CID peak is much broader than that of the main beam of ions indicating that the collision induced loss of H⁺ is associated with a large kinetic energy release. The peak has a simple non-composite shape [6] and the large T₀.₅ value derived from its width at half height, 730 meV, leaves little doubt that we are dealing with CH₃COH⁺ and not with a CH₃COH⁺/CH₃C(H)=O⁺ mixture of ions. (As pointed out above, T₀.₅ = 500 meV for loss of H⁺ from source generated ions that decompose spontaneously; the larger kinetic energy release observed in the CID experiments simply results from “collisional broadening” caused by the larger internal energy content of the dissociating ions.)

In contrast, the peak at m/z 43 displayed in Fig. 2b, which refers to the collision induced H⁺ loss from the metastably generated m/z 44 ions, is considerably less broad and the associated T₀.₅ value is only 200 meV. We tentatively suggest that this peak is a composite consisting of a broad component that corresponds with loss of H⁺ from ions CH₃COH⁺ and a narrow component that stems from loss of H⁺ from ions CH₃C(H)=O⁺. A more detailed analysis is required to substantiate this claim. This would involve analysis of the peak shape for the collision induced loss of H⁺ from ionized acetaldehyde and that for loss of D⁺ from the m/z 45 [C₂H₅DO]⁺ ions generated by the decarboxylation of metastable ions CH₃C(=O)COOD⁺.

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Thus, the experiments show that metastable pyruvic acid ions competitively dissociate into $\text{CH}_3\text{C}=\text{O}^+$ + COOH$^+$ and $\text{C}_2\text{H}_4\text{O}^+$ + CO$_2$. The decarboxylation reaction yields oxycarbene ions $\text{CH}_3\text{COH}^+$ but some $\text{CH}_3\text{C}(\text{H})=\text{O}^+$ may also be co-generated, possibly by proton-transport catalysis. Section 3 provides a mechanistic analysis of these intriguing reactions using computational results obtained from the CBS-QB3 model chemistry and related theoretical approaches.

![Figure 2](image)

**Fig. 2** Partial CID spectrum of (a) source generated m/z 44 ions and (b) metastably generated 44 ions from ionized pyruvic acid.

### 2. Experimental and theoretical methods

All mass spectrometric experiments were performed with the VG Analytical ZAB-R mass spectrometer. Details of the geometry of this three-sector (BEE) instrument have been reported elsewhere [7]. Typical operating conditions were 70 eV ionizing electron energy and 8 or 10 kV accelerating voltage. The pyruvic acid sample (Aldrich, research grade) was introduced via an all quartz direct insertion probe whose sample reservoir was cooled with an ice water mixture. The spontaneous and collision induced dissociations of the mass selected pyruvic acid ions were monitored in the second field free region (2ffr) by recording their metastable ion (MI) and collision induced dissociation (CID) mass spectra. These spectra (Fig. 1a/b) were obtained at a fairly high
energy resolution by setting the half-height width of the main beam of 8000 eV ions at 4V. The kinetic energy releases were estimated from the width at half-height of the appropriate metastable peak, by means of the standard one-line equation after applying the usual correction for the width at half-height of the main beam [8]. The partial CID mass spectrum of inset (a) in Fig. 1, which refers to the m/z 44 product ions generated from 10 keV metastable pyruvic acid ions in the 2ffr, was obtained in the 3ffr. Since these product ions have 5 keV of translational energy, the reference spectrum of source generated acetaldehyde ions in inset (b) was obtained at an accelerating voltage of 5 kV. To facilitate comparison with the spectra reported in ref. 2, in these experiments helium rather than oxygen was used as the collision gas.

The calculations were performed with the CBS-QB3 [10a] model chemistry using Gaussian 98, Rev A.11.3 [11] and Gaussian 2003, C.02 [12]. For selected species the Gaussian 3 (G3) model [13] and the higher level (computationally much more demanding) CBS-QCI/APNO method [10b] were also used. The resulting enthalpies of formation (298 K) for minima, transition states and dissociation levels for the pyruvic acid system are presented in Table 1 while the potential energy diagram derived from the CBS-QB3 calculations is presented in Figure 3. Spin contaminations were within an acceptable range. The optimized structures of the principal species are displayed in Fig. 4.

3. Results and discussion

In the discussion of our mechanistic analysis we will use the CBS-QB3 derived potential energy diagram of Fig. 3 and the compilation of theoretical and experimental results of Table 1 as a guide.

The computations indicate that ions 1a and 1b represent the two most stable conformers of ionized pyruvic acid. They both have the carbonyl groups in a trans position and a long O=C—C=O bond: 1.91 Å and 1.77 Å respectively, see Fig. 4. These long-bonded species should be viewed as one-electron bonded species [14] rather than ion-dipole type complexes. However, HO-C=O' has a large dipole moment (3.0 – 3.7 D,
from the model chemistries of this study) and conversion of ions 1a/b with (acetyl)ion-(COOH')dipole complexes is expected to take place en route to their dissociation into CH₃C=O⁺ + COOH⁺.

For neutral pyruvic acid, calculations were performed on two conformers which both have (except for two of the methylic hydrogens) almost planar geometries with the carbonyl groups in the trans position. The one of lowest energy has the hydroxylic H bridging with the keto-carbonyl in a geometry closely similar to that derived from microwave experiments [15]. The geometry of this neutral conformer, 1a(N), corresponds to that of ion 1a apart from the O=C-C=O bond which has the expected typical value of 1.55 Å. This implies that upon vertical ionization, the incipient ions 1a have a considerably shorter O=C-C=O bond length and also a higher energy than the long-bonded species 1a. In line with this, the vertical ionization energy of pyruvic acid, 10.42 eV, - as determined in the photoelectron spectroscopy study of McGlynn and Meekes [8g] - is considerably higher than its (estimated) adiabatic value, 9.9 eV [8c]. Our CBS-QB3 (and also G3) calculations, see Table 1, yield a gratifyingly close adiabatic ionization energy of 10.0 eV for the pyruvic acid conformer 1a(N).

The energies of ionized pyruvic acid’s conformers 1a and 1b are very close but clearly only 1a can serve as the reacting configuration for the decarboxylation. In contrast, both conformers may dissociate by direct bond cleavage into CH₃C=0⁺ + COOH⁺. Considering that the associated kinetic energy release is very small (see above), this reaction undoubtedly takes place at the thermochemical threshold. As seen in Table 1, all levels of theory and experiment agree that this threshold lies at 111 – 113 kcal mol⁻¹. The measured AE for this reaction, AE (m/z 43) = 10.28 ± 0.05 eV [8e], leads to 110 kcal mol⁻¹ as the apparent heat of formation of the reaction products at 298 K if one uses the relationship \( AE^{\text{expt}}_{298} \) (m/z 43) = \( \Delta H^{0}_{298} [\text{CH}_3\text{C}=\text{O}]^+ + \Delta H^{0}_{298} [\text{COOH}]^- - \Delta H^{0}_{298} [\text{pyruvic acid}] \) with \( \Delta H^{0}_{298} [\text{acid}] \) = -127.0 kcal mol⁻¹. The latter value is an empirical estimate that does not account for the stabilization provided by hydroxylic H bridging which theory predicts to be c. 2.5 kcal mol⁻¹, see the results of Table 1. Applying this correction term lowers \( \Delta H^{0}_{298} [\text{pyruvic acid}] \) to -129.5 kcal mol⁻¹ and brings down the
apparent heat of formation of the reaction products at 298 K to the unrealistic value of 107 kcal mol\(^{-1}\). However, another correction term may have to be considered. This is the so-called Traeger-McLoughlin correction term \(\Delta H_{\text{cor}} = \Delta H_{298} \text{ (reaction products)} - 1.48\), whose basis is discussed in detail in Chapter 4 and ref. 16. This correction term raises the apparent heat of formation of the reaction products at 298 K by typically 5 ± 2 kcal mol\(^{-1}\) [17]. For the present system the \(\Delta H_{298}\) component (representing heat capacity terms, obtained from the CBS-QB3 calculations) is 3.9 kcal mol\(^{-1}\) so that \(\Delta H_{\text{cor}}\) becomes 2.4 kcal mol\(^{-1}\). Thus, if both corrections are applied the apparent heat of formation of the reaction products at 298 K remains at 110 kcal mol\(^{-1}\), close to the thermochemical threshold derived from theory and experiment.

Fig. 3 Energy level diagram derived from CBS-QB3 calculations describing the elimination of carbon dioxide from ionized pyruvic acid radical cations ions. The numbers refer to \(\Delta H_{298}\) values in kcal mol\(^{-1}\).
Next we consider the competing decarboxylation. Starting from ion $1a$, a simple 1,4-H shift involving transfer of the hydroxylic H atom to the carbonyl oxygen atom of the acetyl moiety, yields the distonic ion $[\text{CH}_3\text{C(OH)COO}]^+$, $1c$. However, for metastable ions, decarboxylation from $1c$, which is calculated to be a minimum on the potential energy surface, can be ruled out: $\Delta U H^0_{298} (1c) = 127.0 \text{ kcal mol}^{-1}$, much higher than the energy level for dissociation into $\text{CH}_3\text{C}=\text{O}^+ + \text{COOH}^+$. A much more economical route involves a 1,4-H transfer with a concomitant cleavage of the O=C–C=O bond. This yields ion $2a$, a hydrogen-bridged radical cation (HBRC). The transition state is calculated to lie at 112 kcal mol$^{-1}$, i.e. at a par with the energy requirement for dissociation into $\text{CH}_3\text{C}=\text{O}^+ + \text{COOH}^+$. HBRC $2a$, $[\text{CH}_3\text{C-O-H-\cdots-O=C=O}]^+$, may then dissociate by direct bond cleavage into the oxycarbene “Z” conformer $3a_1$ (see Figure 4 for its geometry) and CO$_2$. Both the CBS-QB3 and the G3 method predict that the “Z” conformer $3a_1$ is less stable than its “U” shaped counterpart $3a_2$, by c. 4 kcal mol$^{-1}$. Surprisingly, the higher level CBS-QCI/APNO approach leads to exactly the opposite: it predicts $\Delta U H^0_{298}$ values for $3a_1$ and $3a_2$ of 198.9 and 203.1 kcal mol$^{-1}$ respectively!

This unexpected unusually large discrepancy with the results of the other model chemistries requires a detailed further analysis which we plan to perform in due course in collaboration with Prof. P.J.A. Ruttink. Since this discrepancy concerns the stability of the oxycarbene conformer ($3a_1$) that connects with the precursor ion that undergoes decarboxylation ($1a$), the associated transition state ($\text{TS } 1a \rightarrow 2a$ at 112 kcal mol$^{-1}$ in Fig. 3) may also be lower, by a few kcal mol$^{-1}$, if indeed the lower value for $\Delta U H^0_{298} [3a_1]$ predicted by the CBS-QCI/APNO method is reliable.

However, irrespective of the outcome of the above analysis – which is primarily of importance for a kinetic analysis of the degree of competition between the formation of $\text{CH}_3\text{C}=\text{O}^+ + \text{COOH}^+$ and the decarboxylation pathway(s) – it seems likely that at higher levels of theory TS $1a \rightarrow 2a$ will remain higher in energy than its dissociation products. This implies that the AE measured for this reaction with energy selected electrons, $\geq 10.4$ eV, (see above, note that in these experiments ions are sampled that dissociate in the lower millisecond timeframe) would refer to the barrier for the rearrangement rather than
the thermochemical threshold of the dissociation products. This may well be the case:
the standard equation $AE_{298}(m/z 44) = \Sigma \Delta H^o_{298}[\text{dissociation products}] - \Delta H^o_{298} [\text{pyruvic acid}]$ with $\Delta H^o_{298} [\text{acid}] = -129.6$ kcal mol$^{-1}$ (CBS-QB3 value of Table 1) yields a minimum energy requirement of $\geq 110$ kcal mol$^{-1}$ for the dissociation. This value lies slightly above the calculated thermochemical threshold (108.7 kcal mol$^{-1}$) and slightly below the calculated barrier (111.6 kcal mol$^{-1}$). For the decarboxylation of the metastable ions (which dissociate in the microsecond timeframe) the measured AE is considerably higher, $10.7 \pm 0.2$ eV, (see above) and the associated minimum energy requirement for dissociation now becomes $117 \pm 4.5$ kcal mol$^{-1}$. Taking the lower limit of this rather crude experiment, 112.5 kcal mol$^{-1}$, as the most plausible value, the calculations at all levels of theory still agree that the experiment probes the transition state energy rather than the thermochemical threshold of the dissociation products.

Returning to the energy diagram of Fig. 3, we note that HBRC 2a could rearrange into HBRC 2b, $[\text{CH}_3\text{C}(=\text{O})-\text{H} \cdots \text{O}=\text{C}=\text{O}]^+$, via a formal 1,2-H shift and then decarboxylate to yield the acetaldehyde radical cation 3b. The calculated barrier for this CO$_2$ assisted rearrangement $3a_1 \rightarrow 3b$, is c. 10 kcal mol$^{-1}$ lower than that for the unassisted isomerization but it is still substantial, 21 kcal mol$^{-1}$. This is not unexpected considering that the PA of CO$_2$ (129 kcal mol$^{-1}$ [8c]) lies far below that prescribed by Radom’s criterion (discussed in Chapter 1) for a base that enables efficient proton-transport catalysis. For our system the PA of such a base should lie in the range 159 – 167 kcal mol$^{-1}$ (from a standard calculation of PA(CH$_3$C=O’) @ O and PA(CH$_3$C=O’) @ C, using the CBS-QB3 data of Table 1).

Nevertheless, the calculated isomerization barrier 2a$\rightarrow$2b of 113 kcal mol$^{-1}$ may just be low enough to allow, as the experiments indicate, a small fraction of ions 2a to undergo a CO$_2$ assisted dissociation into ions 3b but a detailed kinetic analysis is required to substantiate this possibility.

As an aside we note that the CBS-QB3 derived stabilization energy (SE) of HBRC 2a, $[\text{CH}_3\text{C-O-H} \cdots \text{O}=\text{C}=\text{O}]^+$, is 17.2 kcal mol$^{-1}$ : from $\Sigma \Delta H^o_{298}[3a_1 + \text{CO}_2] - \Delta H^o_{298} [2a]$. The SE becomes 18.9 kcal mol$^{-1}$ if one substitutes $\Delta H^o_{298}[\text{CO}_2]$ (CBS-QB3) by its well-
established experimental heat of formation. As discussed in Chapter 1, the SE for O•••H•••O type HBRCs can also be derived from the empirical relationship developed by Mautner [18,14]: \[ \text{SE} = 30.4 - 0.30(\Delta PA) \text{ kcal mol}^{-1} \]. The PA of the CO_{2} component is experimentally well-established: 129.3 kcal mol^{-1} [8c]. The PA of the other component, CH_{3}C=O' @ O, is calculated as 159.2 kcal mol^{-1} from \( \Delta H_{298}^{o}[H^+](\text{expt}) + \Delta H_{298}^{o}[\text{CH}_{3}C=O'](\text{expt}) - \Delta H_{298}^{o}[3a_{1}] \) (CBS-QB3). Thus \( \Delta PA = 30 \text{ kcal mol}^{-1} \) and the "Mautner" SE becomes 21.4 kcal mol^{-1}, in only fair agreement with the CBS-QB3 derived stabilization energy.

In summary, we propose that the CBS-QB3 derived energy diagram of Figure 3 provides a solid basis for the rationalization of the dissociation chemistry of metastable pyruvic acid radical cations. However, a complete mechanistic picture requires (i) complementary experiments to substantiate our proposal that proton-transport catalysis indeed plays a (minor) role in the decarboxylation; (ii) further analysis of the conflicting theoretical results regarding the structure and stability of the most stable oxycarbene conformer and (iii) probing the dynamics of the competing reactions featuring in the energy diagram. This would involve analysis of the system in terms of the statistical approach used in RRKM theory [19]. However, we note that a mere RRKM treatment of our system may not be adequate if, indeed, the dissociation of ionized pyruvic acid into CH_{3}C=O^{+} + COOH^{-} involves the participation of ion-dipole complexes [20].
Table 1. Enthalpies of formation (kcal mol\(^{-1}\)) derived from CBS-QB3, Gaussian 3 (G3) and CBS-QCI/APNO (APNO) calculations pertaining to the dissociation chemistry of ionized pyruvic acid

<table>
<thead>
<tr>
<th>Compound</th>
<th>CBS-QB3</th>
<th>CBS</th>
<th>G3</th>
<th>APNO</th>
<th>Exp.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(E_{\text{tot}}) (0 K)*</td>
<td>(\Delta H_0)</td>
<td>(\Delta H_{298}^0)</td>
<td>(\Delta H_{298}^0)</td>
<td>(\Delta H_{298}^0)</td>
</tr>
<tr>
<td>CH(_3)(=O)COOH</td>
<td>-341.94328</td>
<td>-126.2</td>
<td>-129.6</td>
<td>-128.3</td>
<td>-129.4</td>
</tr>
<tr>
<td>CH(_3)(=O)COOH(^{+})</td>
<td>-341.57578</td>
<td>104.4</td>
<td>101.5</td>
<td>103.5</td>
<td>-</td>
</tr>
<tr>
<td>CH(_3)(=O)COOH(^{+})</td>
<td>-341.57688</td>
<td>103.7</td>
<td>100.9</td>
<td>103.5</td>
<td>-</td>
</tr>
<tr>
<td>CH(_3)(=O)(\cdots)COOH(^{+})</td>
<td>-341.59262</td>
<td>93.8</td>
<td>91.5</td>
<td>92.5</td>
<td>-</td>
</tr>
<tr>
<td>ID-1</td>
<td>-341.58951</td>
<td>95.8</td>
<td>93.6</td>
<td>94.5</td>
<td>-</td>
</tr>
<tr>
<td>CH(_3)=O-H(\cdots)O=O(^{+})</td>
<td>-341.55954</td>
<td>114.6</td>
<td>111.6</td>
<td>112.6</td>
<td>?</td>
</tr>
<tr>
<td>TS 1a(\rightarrow)2a</td>
<td>-341.55781</td>
<td>115.7</td>
<td>113.0</td>
<td>-</td>
<td>?</td>
</tr>
<tr>
<td>[CH(_3)CO(O)OH](^{+})</td>
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<td>130.1</td>
<td>127.0</td>
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<td>-</td>
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<td>CH(_3)C-OH(^{+})</td>
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<td>207.3</td>
<td>204.5</td>
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<td>CH(_3)C-OH(^{+})</td>
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<td>CH(_3)=CH-OH(^{+})</td>
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<td>196.9</td>
<td>197.1</td>
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<tr>
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<td>183.9</td>
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<tr>
<td>TS 3a(\rightarrow)3b</td>
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<td>238.1</td>
<td>235.7</td>
<td>235.5</td>
<td>-</td>
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<tr>
<td>CH(_3)C-OH(^{+}) (3a(_1)) + CO(_2)</td>
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<td>207.3</td>
<td>204.5</td>
<td>203.7</td>
<td>198.9</td>
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<tr>
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<td>199.4</td>
<td>196.9</td>
<td>197.1</td>
<td>196.0</td>
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<td>-95.7</td>
<td>-95.8</td>
<td>-95.3</td>
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<tr>
<td>CH(_3)=O(^{+}) + HO-C=O(^{-})</td>
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<td>158.1</td>
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<td>159.8</td>
<td>158.1</td>
<td>157.8</td>
<td>156.9</td>
</tr>
<tr>
<td>HO-C=O(^{-}) (2A(_\text{a}), trans conf.)</td>
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<td>-44.5</td>
<td>-45.2</td>
<td>-44.5</td>
<td>-44.9</td>
</tr>
<tr>
<td>CH(_3)=O(^{-})</td>
<td>-152.94202</td>
<td>10.0</td>
<td>-2.5</td>
<td>-</td>
<td>-2.4 h</td>
</tr>
<tr>
<td>CH(_3)O-C-OH(^{+}) (4a(_1)) + CO</td>
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<td>157.0</td>
<td>153.7</td>
<td>154.6</td>
<td>-</td>
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<tr>
<td>CH(_3)O-C-OH(^{+}) (W)</td>
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<td>158.5</td>
<td>155.1</td>
<td>-</td>
<td></td>
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<tr>
<td>CO</td>
<td>-113.18196</td>
<td>-27.6</td>
<td>-26.8</td>
<td>-26.7</td>
<td>-26.4</td>
</tr>
</tbody>
</table>

* \(E_{\text{tot}}\) (0 K) in Hartree.

(a) Expt. value from ref 8e, an estimate based upon Benson additivity terms; the older estimate of ref. 2 uses -131 kcal mol\(^{-1}\); the calculated value refers to the lowest energy conformer which has the hydroxyllic H bridging with the keto-carbonyl. The non H-bridged conformer yielded -127.0 kcal mol\(^{-1}\); (b) Refs. 3 and 4 propose a value of 199.5 kcal mol\(^{-1}\) based upon G2 type calculations, our G2 value is 202.1 kcal mol\(^{-1}\), see text for further discussion; (c) Expt. value from ref. 8a/b; (d) Expt. value from ref. 3, the computed values refer to the most stable anti conformer; (e) Expt. value from ref. 2, having an uncertainty of ± 5 kcal mol\(^{-1}\), see text for further discussion; (f) Expt. value from ref. 8f, the compilation of ref. 8d reports 156 kcal mol\(^{-1}\); (g) Expt. value from ref. 8e, the compilation of ref. 8d reports -46.5 ± 0.7 kcal mol\(^{-1}\) for the trans isomer and an (unrealistic) value of -52.5 kcal mol\(^{-1}\) for the cis isomer. Its CBS-QB3 value is -43.2 kcal mol\(^{-1}\); (h) ref. 8d; (i) Expt. value from ref. 2, the G2 type calculations of ref. 4 yield 153.0 kcal mol\(^{-1}\) (conformer not specified).
Fig. 3. Selected optimized geometries for stable intermediates and transition states involved in the carbon dioxide elimination from ionized pyruvic acid (1a).

1a

1.768

1b

1.902

ID-1

2.397

2a

1.538

2b

1.738

2c

1.569

TS 1a/2a

1.581

1.722

1.051

TS 2a/2b

3a1 (CBS-QB3)

3a1 (G3)

3a1 (APNO)

3a2

3b

1.514

3c

1.406

TS 3a/3b

1.318

1.223
References

[12] M.J. Frisch et.al., Gaussian 03, Revision C.02, Gaussian Inc., Wallingford, CT, 2004
Chapter 3

The characterization of isomeric CH₃O-P=S⁺⁺ (1a) and CH₃S-P=O⁺⁺ ions and the mechanism of their spontaneous water loss

This Chapter describes the characterization of isomeric ions CH₃O-P=S⁺⁺ (1a) and CH₃S-P=O⁺⁺ (1b). A previous study on low energy CH₃O-P=O⁺⁺ ions reports that this ion undergoes a decarbonylation reaction as the predominate process to generate m/z 50 ions, HP-OH₂⁺. However, the sulphur analogues appear to have their own unique chemistry. Low energy ions 1a and 1b spontaneously lose water to yield m/z 74 cyclic product ion [-S-CH=]P⁺⁺. Using the CBS-QB3, model chemistry a mechanism is proposed for the water loss from ions 1a and 1b. Dehydration of 1b formally involves two H-shifts and a ring closure, while water elimination from 1a involves a skeletal rearrangement. Our calculations also show that these two isomers communicate via a common intermediate, the distonic ion CH₂S-P-OH⁺⁺ (1c), prior to the loss of water.
1. Introduction

The study of organophosphorus compounds in the gas phase is an active research topic in the chemistry field mainly because of their integral role in the chemistry of pesticides and insecticides. Recently there has been a great deal of research focused on the mechanisms for decomposition of organophosphorus compounds upon ionization in the gas-phase [1-3].

Recent studies dealing with the dissociation of organophosphorus ions in the gas-phase have used tandem mass spectrometry in conjunction with computational chemistry to probe the associated ion structures and reaction mechanisms [2-4]. In this approach, a collision induced dissociation (CID) experiment, in which a mass-selected ion is collisionally energized to induce dissociation, often provides conclusive information about the structure (atom connectivity) of the ion of interest. The technique of neutralization reionization mass spectrometry (NR) [5] may provide useful complementary information, particularly where it concerns the isomeric purity of the ions [2]. This technique is also eminently suited to probing the structure and stability of elusive neutral species in the gas-phase [2].

Heydorn et al. previously reported the identity of the isobaric ions, CH₃O-P=O⁺ and CH₃O-P-NH₂⁺ (m/z 78), from the insecticide acephate [2]. It was found that the m/z 78 ions of acephate consist of the CH₃O-P=O⁺ and CH₃O-P-OH⁺ isomers in admixture with the isobaric ion CH₃O-P-NH₂⁺. As a result the CID spectrum of the m/z 78 ions from acephate is not pure, and neither is the NR spectrum. Consequently the “survivor” ion signal is not indicative of the stability of the CH₃O-P=O neutral as originally proposed by Srinivas and co-workers [3]. This is further supported by the computations that Heydorn and co-workers performed [2]: these indicate that the CH₃O-P-NH₂⁺ ion may indeed have a stable neutral counterpart. Moreover, the “survivor” CID spectrum was found to be different from that of pure CH₃O-P=O⁺ ions. The stability of the CH₃O-P=O neutral was, however, ascertained by performing a collision-induced dissociative ionization (CIDI) experiment on an ion, C₆H₅-(=O)(H)OCH₃⁺, which loses CH₃O-P=O neutrals. The resulting CID spectrum of the m/z 78 ions generated in the CIDI experiment of the above
precursor agrees with that of independently generated CH$_3$O-P=O$^+$ ions, thus attesting to the stability of CH$_3$O-P=O as a neutral species. A follow-up study on the mechanism of the remarkable decarbonylation of the low energy (metastable) CH$_3$O-P=O$^+$ ions [5], established that there are a great many stable isomers of the CH$_3$O-P=O$^+$ ion.

Based on these observations we decided to explore the sulphur analogs of CH$_3$O-P=O$^+$, namely CH$_3$O-P=S$^+$ (1a) and CH$_3$S-P=O$^+$ (1b) ions, using computational chemistry and tandem mass spectrometric techniques. Some aspects of the dissociation chemistry of the CH$_3$S-P=O$^+$ ion and its neutral counterpart have recently been reported by Vivekananda et al. [3]. In their study they report that CH$_3$S-P=O$^+$ ions have a stable neutral counterpart, with a heat of formation of -60.1 kcal mol$^{-1}$. The presence of the sulfur atom in this system appears to have introduced its own chemistry. Metastable ions CH$_3$O-P=S$^+$ (1a) and CH$_3$S-P=O$^+$ (1b) spontaneously eliminate water and do not decarbonylate.

2. Experimental

The experiments were performed with the VG Analytical ZAB-R mass spectrometer of BEE geometry (B, magnet; E, electric sector). Metastable ion (MI) mass spectra were recorded in the second field free region (2ffr); collision-induced dissociation (CID) mass spectra were recorded in the 2 and 3ffr using oxygen as collision gas (Transmittance, T = 70%). The CID mass spectra of the 2ffr metastable peaks were obtained in the 3ffr using O$_2$ as collision gas. CID spectra of reference ions having a translational energy close to that of the product ions resulting from (MI or CID) dissociations in the 2ffr, were also obtained in the 3ffr. Neutralization-reionization mass spectra were recorded using N,N-dimethylaniline as the reducing agent and oxygen gas for reionization [5]. All spectra were recorded using a PC-based data system developed by Mommers Technologies Inc. (Ottawa).

Samples of O-methyl phosphorodichloridothioate, CH$_3$O-P(=S)Cl$_2$ (I), S-methyl phosphorodichloridothioate, CH$_3$S-P(=O)Cl$_2$ (II) and methamidophos,
CH₃O(CH₃S)P(=O)NH₂, were prepared as outlined by J.A. Lubkowitz and co-workers [6]. The reagents used for these syntheses were commercially available (Sigma-Aldrich) and of research grade. Dimethyl chlorothiophosphate, (CH₃O)₂P(=S)Cl was of research grade from Sigma-Aldrich and used without further purification.

Structures and energies of the CH₃S-P=S** and CH₃O-P=S** ions and neutrals pertinent to this study, connecting transition states and dissociation products were probed by the standard CBS-QB3 model chemistry [7]. The calculations were performed using Gaussian 98 Revision A11.3 [8]. The calculated energies are presented in Table 1a/b and the potential energy diagrams of Figures 3 and 4. Frequency calculations gave the correct number of negative eigenvalues for all minima and transition states. Spin contamination was within the acceptable range. Figure 5 displays the optimized geometries for the principal species

![Fig. 1. Metastable ion spectrum of (a) CH₃O-P=S** and (b) CH₃S-P=O**.](image-url)
3. Results and Discussion

3.1 Characterization of the ions CH$_3$O-P=S$^\ddagger$, 1a, and CH$_3$S-P=O$^\ddagger$, 1b, and their neutral counterparts

Ion 1a, CH$_3$O-P=S$^\ddagger$, was generated from two independent precursor ions: (i) from ionized O-methyl phosphorodichloridothiolate, CH$_3$OP(=S)Cl$_2$, I, by two consecutive Cl$^-$ losses and (ii) by loss of Cl$^-$ and CH$_3$O$^\ddagger$ from ionized dimethyl chloro-thiophosphate, (CH$_3$O)$_2$P(=S)Cl. The CID spectra of the m/z 94 ions generated by the two routes were closely similar. The CID spectrum of 1a (see Fig. 2a) displays a characteristic base peak at m/z 63, PS$^+$, the result of a direct bond cleavage. Other intense signals are present at m/z 31 (CH$_2$OH$^+$), m/z 47 (loss of PO$^-$), m/z 62 (CH$_3$OP$^+$), m/z 64 (loss of H$_2$C=O), m/z 76 (loss of H$_2$O), and m/z 79 (S=P=O$^\ddagger$). The presence of a peak at m/z 62, which is a direct bond cleavage reaction resulting from the loss of a S atom from 1a, serves as evidence that ions 1a maintain their structure connectivity.

As in the case of 1a, ions 1b, CH$_3$S-P=O$^\ddagger$, were generated by two different routes: (i) by two consecutive Cl$^-$ losses from ionized S-methyl phosphorodichloridothiolate, CH$_3$SP(=O)Cl$_2$, II, and (ii) from the collision induced dissociation of the m/z 125 CH$_3$SP(=O)CH$_3$ ions generated from ionized acephate. The closely similar CID mass spectra of the resulting m/z 94 ions are, see Fig. 2b, characteristically different from the CID mass spectrum of 1a. The CID spectrum of 1b ions shows a base peak at m/z 47 (CH$_2$SH$^+$), followed by peaks at m/z 63 (PS$^+$) and m/z 76 ((=-HC-S-)P$^\ddagger$).

In the CID spectrum of 1b, the base peak at m/z 47 corresponds to CH$_2$SH$^+$ ions. To generate the CH$_2$SH$^+$ cation directly from ion 1b, an energetically costly 1,2-H shift is required, which is unlikely. Alternatively, ion 1b may undergo a 1,4-H shift to form its more stable distonic ion counterpart, 1c, CH$_2$S-P-OH$^\ddagger$. The calculations, see Fig. 3 and Table 1, indicate that the formation of the distonic ion is reasonable since the barrier for the 1,4-H shift lies only 2 kcal mol$^{-1}$ above 1b. This ion can then rearrange via a 1,3-H shift to form the ion-dipole complex, 1e, [CH$_2$SH$^\cdots$PO]$^\ddagger$, the immediate precursor ion for the generation of CH$_2$SH$^+$ + PO$^\ddagger$. 

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The CID spectra indicate that ions 1a maintain their structural integrity, while 1b ions preferentially isomerize into their distonic counterpart, ions 1c, CH$_2$S-P-OH$^+$. The computational results agree with the experimentally observed behaviour of ions 1a and 1b.

The MI spectrum of ion 1a shows one prominent reaction, the elimination of H$_2$O to yield m/z 74 ions, and only a minor peak at m/z 47, see Fig. 1a. The kinetic energy releases of both these reactions are small, 26.1 meV and 6.5 meV, for m/z 74 and 47, respectively and are not indicative of any significant reverse activation energy.
The m/z 74 product ion of the water loss was identified to be the cyclic ion, \( \text{P}[-\text{C(H)-S-}]^+ \). Three stable CHSP\(^+\) structures were calculated, of the three the cyclic ion \( \text{P}[-\text{C(H)-S-}]^+ \) was calculated to be the most stable CHSP\(^+\) isomer lying at 247.7 kcal mol\(^{-1}\), see Table 1b. Remarkably, the MI spectrum of ion 1b is virtually identical to the MI spectrum of 1a, see Fig. 1b. The kinetic energy releases of both these reactions are small, similar to 1a, 29.2 meV and 3.3 meV, for m/z 74 and 47, respectively.

The m/z 74 product ion was found to be the same cyclic ion, \( \text{P}[-\text{C(H)-S-}]^+ \). The mechanism of the water loss and the communication of ions 1a and 1b were probed by theory, uncovering a complex system of isomers. The details of the mechanism of communication between ions 1a and 1b and their water loss will be discussed in Section 3.2 and 3.3, respectively.

To characterize neutral 1a and 1b molecules, experiments involving neutralization-reionization mass spectrometry (NRMS) \(^{[5]}\) were conducted. In the NRMS experiments the beam of mass selected m/z 94 ions was neutralized by charge-exchange with N,N-dimethylaniline. The subsequent beam of neutral molecules was then re-ionized by collision with O\(_2\) gas. The NR spectrum of neutral 1a, see Fig. 2c, displays a sizable peak at m/z 94, expected to correspond to re-ionized CH\(_3\)O-P=S molecules. This is indeed the case as demonstrated by the CID spectrum of the m/z 94 survivor ions shown in Fig. 2e. A comparison of the survivor CID spectrum of Fig. 2e with the CID spectrum of Fig. 2a leaves little doubt that the re-ionized m/z 94 ions correspond to CH\(_3\)O-P=S\(^+\). The heat of formation of 1a was calculated to be -45 kcal mol\(^{-1}\), see Table 1, in agreement with the NR results.

The NR spectrum of 1b shows a fairly strong peak at m/z 94, see Fig. 2d. Comparison of the survivor CID spectrum of 1b to its 3ffe CID spectrum, see Fig. 2b, it can be concluded that these ions are of different structure. The CID spectrum of the survivor CH\(_3\)SP=O\(^+\) ions has a fairly intense peak at m/z 76 of almost equal intensity to the base peak at m/z 47 but the 3ffe CID of source generated 1b ions show the peak at m/z 76 is nearly half the intensity of the base peak. This result implies the neutral counterpart
of ion 1b is not stable on the µs time scale and may undergo a facile isomerization into its
distonic counterpart upon ionization.

3.2 Communication between ions 1a and 1b

The CID spectra of ions 1a and 1b indicate that the isomeric ions do not easily
communicate. However, their respective MI spectra do show that the two ions may lose
water via a sufficiently low interconversion barrier. In both cases, the MI spectrum
displays an intense base peak at m/z 76 (loss of H2O) and a minor peak at m/z 47, see
Fig.1. The loss of water from these two isomers suggests that ions 1a and 1b
communicate via a common intermediate.

A 1,3-CH3 shift would be an obvious route of communication between ions 1a
and 1b but this appears to be a very energy demanding process, requiring 54 kcal mol\(^{-1}\),
see Fig. 3 and Table 1. Thus, there must be an alternative pathway connecting these two
isomers. In order for these two ions to communicate, the pathway must lie below the
energy for the formation of CH3SH\(^+\) + PO\(^-\), as indicated in the energy diagram of Fig. 3.

We will use the energy diagram of Fig. 3 as a guide in the discussion of the
proposed mechanism for the communication of 1a and 1b. Starting from ion 1a, a 1,4-H
shift may lead to the formation of its distonic ion 1d, via a TS calculated to lie at 187 kcal
mol\(^{-1}\). Elongation of the O-P bond and the concomitant formation of an O-H bond may
lead to the hydrogen-bridged radical cation, 1f, via a TS lying at 194 kcal mol\(^{-1}\). A
rotation of the CH2OH moiety of HBRC 1f yields a slightly more stable ion, 1g, via a
barrier of 9 kcal mol\(^{-1}\). Ion 1g can then rearrange into ion 1h by breaking the S–O bond
and forming a C-S bond. Once ions 1h have been formed, a formal 1-3-CH2 shift will lead
to the stable distonic ion, 1c. The transition state at 200 kcal mol\(^{-1}\) connecting ions 1h and
1c is quite high in energy but it lies is still below the dissociation level of CH3SH\(^+\) + PO\(^-\).
Ion 1b can undergo a 1,4-H shift to form its distonic counterpart 1c, via a TS lying only 2
cal mol\(^{-1}\) above 1b. Ion 1c is the common intermediate shared by ions 1a and 1b prior to
their water elimination and it will be shown in the next section that the water elimination proceeds via ion 1c.

Fig. 3 Energy level diagram derived from CBS-QB3 calculations describing the communication between metastable CH₃O-P=S⁺⁺ (1a) and CH₃S-P=O⁺⁺ (1b) ions. The numbers refer to Δ_H^0 values in kcal mol⁻¹.
3.3 Spontaneous water loss from ions 1a and 1b

In the previous section it was shown that ions 1a and 1b can communicate via a common intermediate 1c, and we will describe the water elimination beginning with ion 1c. The energy diagram of Fig. 4 will act as a guide to describe the water loss. Starting from ion 1c, a bond formation between C and P may lead to the formation of the cyclic ion 1j, via a fairly high barrier of 20 kcal mol⁻¹. A formal 1,3-H shift in ion 1j then yields the ion-dipole complex 1k, H₂O···P[-C(H)-S]-⁺, the direct precursor ion for the formation of P[-C(H)-S]-⁺ + H₂O. The barrier 1j → 1k lies at 202 kcal mol⁻¹, close to the level for the dissociation products CH₂SH⁺ + PO⁺.

Finally we note that the TS connecting 1j and 1k can compete with a 1,3-H shift from 1c to yield the ion-dipole complex 1e, which serves as the direct precursor to the generation of CH₂SH⁺ + PO⁺ at 201 kcal mol⁻¹. The barrier for TS 1c → 1e lies at the same level as TS 1j → 1k. Although the energy barrier of both competing 1,3-H shifts lie at the thermochemical threshold, the water elimination is the predominant reaction with a minor loss of PO⁺, see Fig. 1a/b. This result can be rationalized by comparing the energy levels of the dissociation products. Ions 1c with enough energy will preferentially dissociate into [-S-P-CH₂]⁺ + H₂O because the energy difference between the 1,3-H shift transition states and their respective dissociation products is greater for TS 1c → 1j → 1k than 1c → 1e, as a result the loss of PO⁺ competes poorly with the water elimination reaction.
Fig. 4 Energy-level diagram derived from CBS-QB3 calculations describing the water elimination from metastable CH$_3$O-P=S$^+$ (1a) and CH$_3$S-P=O$^+$ (1b) ions. The numbers refer to $\Delta H_{298}^0$ values in kcal mol$^{-1}$.

Conclusion

The structure, stability and isomerization behaviour of isomeric ions 1a, CH$_3$O-P=S$^+$, and 1b, CH$_3$S-P=O$^+$, was probed using the CBS-QB3 model chemistry. From neutralization-reionization experiments on ions 1a and 1b, it follows that ion 1a has a stable neutral counterpart, as predicted by theory. The NR experiments of 1b do not show it has a stable neutral counterpart in the gas-phase. The communication between low energy 1a and 1b ions and their mechanism of the water was established by theory. The details of the mechanism of water elimination process revealed that ions 1a and 1b
communicate via ion 1c, CH$_2$S-P-OH$^{++}$, prior to H$_2$O loss. The water elimination proceeds via ion 1c, which can isomerize into 1k, the direct precursor ion to yield [-S-P-CH$_3$]** and water.

References

Appendix to Chapter 3

Fig. 5. The CBS-QB3 optimized geometries for CH$_3$O-P=S$^{++}$ 1a, CH$_3$S-P=O$^{++}$ 1b ions and selected transition states.

1a (s) 1a (a) 1b (s)

1b (a) 1c (s) 1c (a)

1d (s) 1d (a) 1e

1f   1g   1h

1i   1j   1k

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Fig. 5. cont

Figures 5.1a to 5.1k showing various molecular structures with bond lengths indicated.
Table 1a. Enthalpies of formation derived from CBS-QB3 calculations of stable isomers and connecting transition states involved in the water loss from CH$_3$O-P=S$^\text{+}$, 1a, and CH$_3$S-P=O$^\text{+}$, 1b.

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<th>Ionic Species</th>
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<th>ZPE</th>
<th>$\Delta H^\text{0}_0$</th>
<th>$\Delta H^\text{0}_{298}$</th>
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Table 1b. Relative energies, $E_{\text{rel}}$ (kcal/mol), of dissociation reactions of ion $1c^{\bullet\bullet}$ derived from CBS-QB3 calculations.

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<td>12.99</td>
<td>-22.4</td>
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<tr>
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<td>2.39</td>
<td>2.4</td>
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<td>CH$_3^+$</td>
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<td>19.17</td>
<td>262.2</td>
<td>261.3</td>
</tr>
</tbody>
</table>

*E$_{\text{total}}$ in Hartrees, all other values in kcal/mol, including the ZPVE scaled by 0.99.
Chapter 4

The water elimination from the ethyl acetate radical cation: Answers from theory to a longstanding mechanistic problem

Abstract

Previous experimental studies of the water elimination from ionized ethyl acetate (EA-1) and its enol, CH$_2$C(OH)OC$_2$H$_5^{**}$ (EA-2) provide no mechanistic proposals but note that the reaction is complex because all hydrogen atoms and both oxygen atoms participate. Loss of H$_2$O is the predominant process observed for the metastable ions, yielding ionized methyl vinyl ketone, CH$_3$C(=O)CH=CH$_2^{**}$ (MVK), as the product ion. Metastable keto-alcohol ions CH$_3$C(=O)CH$_2$CH$_2$OH$^{**}$ (HB-1) also abundantly lose H$_2$O, yielding MVK at the thermochemical threshold. Using the CBS-QB3 model chemistry and complementary RRKM calculations, we have examined plausible mechanisms for the water elimination from metastable ions EA-1/2 and HB-1. Our calculations support the proposal that (i) ions HB-1 dissociate into MVK at the thermochemical threshold via a 1,4-H shift and a consecutive [1,2]-hydroxycarbene shift and (ii) ions EA-1/2 undergo a three-step isomerization reaction into HB-1, which serves as the precursor for the ensuing water elimination. It is further shown that synergy between theory and experiment leads to a complex yet transparent mechanistic picture of ionized ethyl acetate’s isomerization and dissociation behaviour which accounts for the labelling results.
Introduction

Since the inception of electron ionization (EI) mass spectrometry as a powerful method for the structure analysis of organic molecules in the mid 1950’s, the gas-phase ion chemistry of ethyl acetate has been studied extensively. Two dissociations of the ethyl acetate radical cation, \( \text{CH}_3\text{C(=O)OCH}_2\text{CH}_3^{+} \) (EA-1), have received particular attention: EA-1 \( \rightarrow \text{C}_2\text{H}_5\text{O}^+ + \text{C}_2\text{H}_3^* \) and EA-1 \( \rightarrow \text{C}_4\text{H}_6\text{O}^{**} + \text{H}_2\text{O} \). Peaks at m/z 61 and 70 resulting from these rearrangement reactions prominently feature in the ester’s conventional EI mass spectrum, as shown in Fig. 1a.

![Fig. 1: 70 eV EI mass spectra of ethyl acetate (item a) and its 4-hydroxy-2-butanone isomer (item b).](image)

In 1962, Godbole and Kebarle [1] using deuterium labeling found that the acetyl methyl group remained intact during the formation of \( \text{C}_2\text{H}_5\text{O}^+ \), while hydrogen atoms were randomly transferred from the ethyl group. In 1977, Benoit, Harrison and Lossing
[2] concluded that the m/z 61 product ion is carbonyl protonated acetic acid, \(\text{CH}_3\text{C(OH)}_2^+\), rather than its higher energy isomer \(\text{CH}_3\text{C(=O)OH}_2^+\) [3] and that the keto ester ion EA-1 may isomerize to its more stable [4] enol form \(\text{CH}_2=\text{C(OH)OCH}_2\text{CH}_3^{**}\) (EA-2) prior to dissociation. Dissociation into \(\text{CH}_3\text{C(OH)}_2^+\) has become a textbook example of a “McLafferty + 1” rearrangement [5]. The first step of the proposed mechanism [5] leads to the distonic ion \([\text{CF}_3\text{C(OH)OCH}_2\text{CH}_2]^{**}\) (EA-3) via a 1,5-H shift in EA-1. A consecutive 1,3-H shift from the terminal \(\text{CH}_2\) group to the ether O atom in EA-3 then initiates the \(\text{C}_2\text{H}_3^+\) loss. We will examine this proposal in more detail in Section 1.3 of the Results and Discussion.

The elimination of \(\text{H}_2\text{O}\) into ions \(\text{C}_4\text{H}_6\text{O}^{**}\) (m/z 70) has been studied in much greater detail [6-8] than the \(\text{C}_2\text{H}_3^+\) loss, but its mechanism is still shrouded in mystery. Loss of water represents the unimolecular reaction of lowest energy requirement for ionized ethyl acetate [7,8]. In line with this, it is the predominant process observed for metastable [9] ions EA-1 dissociating in the \(\mu\text{s}\) time-frame: loss of \(\text{C}_2\text{H}_3^+\) competes unfavourably as its metastable peak is only 0.02 as intense as that for the \(\text{H}_2\text{O}\) loss process [7].

The reaction was first studied by Yeo [6] in 1970. He studied both metastable ions and ions dissociating in the source and found that deuteriums on the ethyl group more readily end up in the neutral water fragment than do the deuteriums on the acetyl group. The degree of hydrogen exchange becomes greater as the lifetime of the precursor ion increases, that is when the internal energy content of the ion becomes lower. Yeo proposed that the intra- and inter-alkyl H-H exchange reactions take place from the unrearranged keto ion EA-1 and that the actual mechanism for \(\text{H}_2\text{O}\) loss involves ring closure of EA-1 into the 2-hydroxy-2-methyloxetane ion, as depicted in Scheme 1.

![Scheme 1](image-url)
The cyclic ion would then undergo H$_2$O elimination yielding ionized 2-methyloxetene, the four-membered ring-closed form of ionized methyl vinyl ketone, CH$_3$C(=O)CH=CH$_2$** (MVK). Yeo formulated this proposal some twenty years before the role of distonic ions as stable key intermediates was fully established [10]. A more plausible formulation of the cyclization step in his mechanism would involve formation of the distonic ion EA-3 as the first step (as in the mechanism for C$_2$H$_3$• loss discussed above), followed by cyclization. We further note that Yeo’s proposal remains speculative because there is no experimental evidence for the proposed product ion structure.

In 1981, Holmes et al. [7] investigated the H$_2$O loss from EA-1 and its independently generated enol EA-2, employing most of the presently available methodology for the detailed study of unimolecular ionic dissociations [11]. These included metastable ion (MI) and collision induced dissociation (CID) mass spectra, appearance energy (AE) measurements using electron ionization (EI), thermochemical data [12] and analysis of D- and $^{18}$O-labelled isotopologues. Shortly thereafter, Baer and co-workers [8] used photoionization (PI) to study the energetics of the five primary dissociations of EA-1; in addition, they studied the rate of the H$_2$O elimination using photoion-photoelectron coincidence (PIPECO) experiments in conjunction with RRKM/QET calculations.

Although these two papers contain a wealth of experimental observations on ethyl acetate’s gas-phase ion chemistry, they do not provide a clear mechanistic picture of the H$_2$O loss. The most important results and conclusions pertaining to the H$_2$O elimination are the following:

(i) Holmes et al. [7] found that metastable enol ions EA-2 also abundantly lose H$_2$O and deduce from their D- and $^{18}$O-labelling experiments that the reaction probably occurs via the reacting configuration(s) of the less stable keto tautomer EA-1. The isomers have different CID spectra - see Fig. 2a/b of this study - but this does not imply that keto ions cannot partially tautomerize: the CID spectrum of EA-1 is not necessarily that of a single ionic species.
Fig. 2 CID mass spectra of the radical cations of ethyl acetate, its enol and the 4-hydroxy-2-butanone isomer (HB-1), items (a), (b) and (c) respectively. Partial spectra of CH$_3$C(=O)$_{18}$OC$_2$H$_5$ and CH$_3$C(=O)$_{18}$CH$_2$CH$_2$OH are shown in the insets of (a) and (c) respectively. Item (d) represents the CID mass spectrum of the m/z 70 product ion generated by the loss of water from metastable ion HB-1.

(ii) Analysis of $^{18}$O labelled ions [7] showed that for ion source decompositions and all metastable ion observation times the keto and enol O atoms in both EA-1 and EA-2 are similarly preferentially lost: ion source 65%, metastable ions 70 – 90%. It is likely that this process has a lower energy requirement than the H$_2$O loss which involves the ester O atom. This is because (i) the associated kinetic energy release [9] is lower than that for the ester O atom and (ii) the degree of exchange becomes increasingly less important at longer ion lifetimes, which is just the opposite of the H atom exchange results [6,7]. These data indicate that there is a significant barrier to O atom migration, whereas the H atoms have no significant barrier for exchange but do so at a slow rate because of circuitous (high entropy) pathways (7,8).

(iii) From their analysis of the CID spectra of various C$_4$H$_6$O$^{**}$ isomers (13), Holmes et al. (7) conclude that CH$_3$C(=O)CH=CH$_2$ $^{**}$ (MVK) is generated by H$_2$O loss from
either metastable ions EA-1 and EA-2 or those fragmenting in the ion source. They further note that the CID results do not exclude that a minor fraction of the ions would be CH$_2$=C(OH)CH=CH$_2$**, the enol of MVK which is 13 kcal mol$^{-1}$ lower in energy than MVK (11a). They entertained this possibility because their AE measurements on EA-1 yielded an apparent $\Delta H^0_{298} = 190$ kcal mol$^{-1}$ for the C$_7$H$_6$O$^{**}$ ion which lies below the proposed value for MVK, 195 kcal mol$^{-1}$ [13a].

(iv) Baer and co-workers [8] note that this enthalpy difference is on the border line of being significant. They conclude from their experiments on EA-1 that MVK ions – for which they derive $\Delta H^0_{298} = 194$ kcal mol$^{-1}$ - are also generated at threshold. They further conclude that EA-1 isomerizes to a more stable structure prior to dissociating, possibly the enol ion EA-2.

In the summary of their paper Baer and co-workers state: “we know the energy of the isomerized molecular ion, but not its structure; we suspect that the transition state is cyclic; and we believe that the product ion is MVK. With all this information it should be possible to derive a mechanism and determine the structure of the molecular ion. However, as was already pointed out by Holmes et al. the loss of H$_2$O is a very complicated reaction”. Yeo’s mechanistic proposal of Scheme 1 is mentioned in these studies but not discussed.

At the time the above studies were published, the use of ab initio MO calculations as a complementary tool in studying structures and reactions of gas-phase organic ions was only in its infancy. However, theory steadily progressed and in 1989 a review of structures and reactions of gas-phase ions [10b] stated that the computational results of Heinrich et al. on ionized methyl acetate [14] offer some hope that the chemistry of ionized ethyl acetate may some day be understood. A hydrogen-bridged radical cation [15], CH$_3$-CH=O•••H•••OCH=CH$_2$**, was suggested to play a key role in the water elimination from EA-1. It was also stressed that ab initio calculations are required to solve this problem but that, considering the size of the system and the number of possible intermediates, this would be a formidable task.
Fortunately, the following decade witnessed a development in methodology and computing power short of a revolution, enabling computational chemistry to become a key player in the field of gas-phase ion chemistry [11]. The G-3 variant of the Gaussian methods of Pople and co-workers [16] and the CBS-QB3 variant of the complete basis set methods of Petersson and co-workers [17] provide absolute enthalpies of chemical accuracy for medium sized ions and neutrals. This makes both model chemistries attractive for a study of ethyl acetate's gas-phase ion chemistry. During the past five years we have successfully used the CBS-QB3 method in mechanistic studies of organophosphorus ester ions [18] and proton-transport catalysis in various organic radical cations [19]. We therefore decided to use this CBS variant, which uses density functional geometries and frequencies in the calculations, as the primary computational tool in probing the elusive mechanism for the $\text{H}_2\text{O}$ elimination from metastable ions $\text{EA-1}$ and $\text{EA-2}$.

It will be shown that synergy between theory and experiment leads to a complex yet transparent mechanistic proposal for the $\text{H}_2\text{O}$ elimination into $\text{MVK}$ which satisfies the energetic constraints imposed by experiment and accounts for the labelling results.

**Experimental and theoretical methods**

The experiments were performed with the VG Analytical ZAB-R mass spectrometer of BEE geometry (B, magnet; E, electric sector) [29]. Metastable ion (MI) mass spectra were recorded in the second field free region (2ffr); collision-induced dissociation (CID) mass spectra were recorded in the 2 and 3ffr using oxygen as collision gas (Transmittance, $T = 70\%$). The CID mass spectra of the 2ffr metastable peaks were obtained in the 3ffr using $\text{O}_2$ as collision gas. For these experiments the maximum available accelerating voltage, 10 kV, was used. CID spectra of reference ions having a translational energy close to that of the product ions resulting from (MI or CID) dissociations in the 2ffr, were also obtained in the 3ffr. All spectra were recorded using a PC-based data system developed by Mommers Technologies Inc. (Ottawa).

Ethyl acetate, methyl vinyl ketone, and 4-hydroxy-2-butanone were of research grade (Aldrich) and used without further purification. The $^{18}\text{O}$-labelled ester
CH$_3$C(=O)$^{18}$OCH$_2$CH$_3$ was synthesized on a microscale by esterification of acetic acid with C$_2$H$_5^{18}$OH (MSD Canada); samples of CH$_3$C(=O$^{18}$)OCH$_2$CH$_3$ and CH$_3$C(=O$^{18}$)CH$_2$CH$_2$OH were prepared by exchange of the carbonyl oxygen of the unlabelled precursors with H$_2^{18}$O (Prochem 90 atom%) under slightly acidic conditions.

The calculations were performed with the CBS-QB3 model chemistry [17] using Gaussian 2003, Rev C.02 [30] and (for selected transition state searches) GAMESS-UK [31]. In this model chemistry the geometries of minima and connecting transition states are obtained from B3LYP density functional theory in combination with the 6-311G(2d,d,p) basis set (also denoted as the CBSB7 basis set). The resulting total energies and enthalpies of formation for minima and connecting transition states (TS) in the ethyl acetate (EA), acetoin (AC) and 4-hydroxy-2-butanone (HB) systems of ions are presented in Table 1a/b. Computational and experimental enthalpies for various dissociation products are presented in Table 2. We have also used the G3 model chemistry [16b] to calculate the enthalpies of the species of Table 2: agreement with the results of the CBS-QB3 method (and experiment) was quite satisfactory, within ±1-2 kcal mol$^{-1}$.

Spin contaminations were within an acceptable range. The correct identity of transition states was verified (where not trivially evident) by means of Intrinsic Reaction Coordinate (IRC) calculations using the algorithm implemented in Gaussian 2003.

For several facile isomerization reactions, including EA-1a → EA-3a in Fig. 3, the CBS-QB3 energy of the TS is calculated to be slightly lower than that of the least stable of the connecting isomers. This may happen since transition states are more sensitive to correlation effects than minima and the ZPE also tends to favour transition states.

However, the TS connecting HB-1b and HB-2a, see Fig. 3 and Table 1b, is calculated to lie much lower in energy: 4.5 kcal mol$^{-1}$ below that of HB-1b. Here, the discrepancy between the B3LYP/CBSB7 energies and the final CBS-QB3 results is probably due to the fact that the B3LYP and the MP2 parts of the CBS-QB3 calculation disagree about the geometry of the transition state. We have compared the contributions to the CBS-QB3 energy for HB-1b and two transition states relating to this isomer. It was found that for HB-1b and TS HB-1a → 1b the various contributions are nearly the same.
but this is not case for TS HB-1b $\rightarrow$ 2a. Here, the $\Delta E$(MP2) contribution is much larger and the effect is enhanced in the $\Delta E$(CBS) component, which is based on the MP2 energies. In contrast, the $\Delta E$(MP4) contribution for this TS is smaller. This analysis suggests that for this transition state the MP2 method is not reliable enough to give satisfactory results.

Figure 5 displays the optimized geometries for the principal species. The complete set of computational results is available from the authors upon request.

RRKM theory [23] was used to calculate microcanonical rate constants. The harmonic frequencies and rotational constants were taken from the B3LYP/CBSB7 part of the CBS-QB3 calculations. The internal energies were calculated from the CBS-QB3 heats of formation at 0 K.

The extended RRKM model used is that described by Baer and Hase [23]. Here several reaction steps are combined to get an overall rate constant. As will be discussed in a separate publication (in preparation) this procedure also makes it possible to compare the yields of various dissociation products.

We have also compiled data comparing CBS-QB3, G3B3, and G3 calculated energies on selected ions and transition states as seen in Table 4. The energies calculated by G3B3 were all systematically lower than their CBS-QB3 counterparts by 4 kcal mol$^{-1}$. The discrepancy can be attributed to the basis set used in the geometry optimization step of the model chemistries. Both model chemistries use B3LYP DFT method to optimize the geometry but CBS-QB3 employs a much larger basis set, 6-311G(2d,d,p), whereas, G3B3 uses a smaller basis set, 6-31G(d). The smaller basis set can account for the slight energy difference since the geometry optimization using G3B3 is not has refined as CBS-QB3.

**Results and discussion**

**1.1. Experimental and theoretical preliminaries**

In our computational quest of plausible mechanisms for the H$_2$O elimination from EA-1 and EA-2 we focussed on the behaviour of the metastable ions. For such ions the experiments [7,8] stipulate that none of the stable intermediates or connecting transition
states of a viable calculated mechanism should lie significantly higher in energy than the thermochemical threshold for the formation of MVK + H₂O. The experimental and calculated enthalpies for this threshold are close: 137 ± 3 and 139 kcal mol⁻¹ respectively, see Table 2. The experimental value suffers from a rather large uncertainty because the heat of formation of neutral methyl vinyl ketone has not been measured with great precision. The computed enthalpies of the stable structures (minima) presented in Tables 1 and 2 of this study are expected to be reliable to 2 kcal mol⁻¹ [17,18a]; for the uncertainty in computed barrier heights we affix ± 4 kcal mol⁻¹ as a conservative estimate [18a].

As mentioned in the Introduction, Holmes et al. [7] in their detailed experimental study do not propose a mechanism for the water loss from EA-1/2. However, they do make the intriguing suggestion that the isomeric 4-hydroxy-2-butanone ion, CH₃C(=O)CH₂CH₂OH⁺, HB-1, is a participating structure in the complex behaviour of the keto and enol ions of ethyl acetate. This suggestion is based upon their observations that metastable ions HB-1 readily lose H₂O, with a small kinetic energy release, and that the source generated ions HB-1, see Figure 1b, also generate m/z 61 ions CH₃C(OH)₂⁺. The CID mass spectrum of HB-1, see Fig. 2c, also displays a m/z 61 peak, supporting the idea that EA-1/2 and HB-1 can (inter)convert via a fairly low energy route. There is no mechanistic proposal for the loss of H₂O from HB-1 but, as will be discussed in Section 1.2, there is little doubt that the product ion generated is MVK and that the reaction occurs at the thermochemical threshold.

We decided to further explore the idea that ions EA-1/2 can access the potential energy surface (PES) that describes the water elimination from HB-1. Ions EA-1 may well undergo a facile isomerization into distonic ions EA-3 or EA-4 as depicted in Scheme 2. Ion EA-3 could in principle connect to the PES of HB-1 via a well-documented skeletal rearrangement, the [1,3]-hydroxycarbene shift [10b]. In this rearrangement the CH₃-C-OH moiety of EA-3 migrates, via a cyclic transition state, to the radical position, yielding [CH₃C(OH)CH₂CH₂O⁺, a 1,5-hydrogen-shift isomer of HB-1. Our computational results for this reaction sequence are presented in the energy-level diagram of Fig. 4a which will
be discussed in detail in Section 1.4. Here we note that the barrier for the hydroxycarbene shift is too high to account for the loss of water at the thermochemical threshold.

Table 1. Enthalpies of formation derived from CBS-QB3 calculations of stable isomers and connecting transition states involved in the water loss from the ethyl acetate (EA) radical cation.

<table>
<thead>
<tr>
<th>Ionic species (a)</th>
<th>B3LYP/ CBSB7 E(total)</th>
<th>CBS-QB3 [0 K] E(total)</th>
<th>ZPE</th>
<th>$\Delta H^0$</th>
<th>$\Delta H^{298}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>EA-1a (Fig. 3a/4a)</td>
<td>-307.43701</td>
<td>-306.83417</td>
<td>71.2</td>
<td>132.4</td>
<td>126.5</td>
</tr>
<tr>
<td>EA-1b (Fig. 4b)</td>
<td>-307.43573</td>
<td>-306.83503</td>
<td>71.4</td>
<td>131.9</td>
<td>126.3</td>
</tr>
<tr>
<td>EA-2a (Fig. 5)</td>
<td>-307.46197</td>
<td>-306.86357</td>
<td>72.8</td>
<td>114.0</td>
<td>108.0</td>
</tr>
<tr>
<td>EA-2b (Fig. 4a)</td>
<td>-307.45361</td>
<td>-306.85647</td>
<td>72.6</td>
<td>118.3</td>
<td>112.4</td>
</tr>
<tr>
<td>EA-2c (Fig. 4a)</td>
<td>-307.45268</td>
<td>-306.85569</td>
<td>72.7</td>
<td>118.9</td>
<td>113.0</td>
</tr>
<tr>
<td>EA-3a (Fig. 3a/4a)</td>
<td>-307.45400</td>
<td>-306.85444</td>
<td>72.6</td>
<td>119.7</td>
<td>113.9</td>
</tr>
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<td>EA-3b (Fig. 3a/4a)</td>
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<td>-306.85565</td>
<td>71.8</td>
<td>118.9</td>
<td>113.3</td>
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<td>EA-4a (Fig. 4b)</td>
<td>-307.45513</td>
<td>-306.85827</td>
<td>71.4</td>
<td>117.3</td>
<td>111.7</td>
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<td>EA-4b (Fig. 4b)</td>
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<td>-306.86186</td>
<td>71.4</td>
<td>115.1</td>
<td>109.5</td>
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<tr>
<td>EA-4c (Fig. 4b)</td>
<td>-307.45945</td>
<td>-306.85995</td>
<td>71.4</td>
<td>116.3</td>
<td>110.7</td>
</tr>
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<td>EA-5 (Fig. 4a)</td>
<td>-307.42616</td>
<td>-306.82384</td>
<td>70.1</td>
<td>136.1</td>
<td>131.1</td>
</tr>
<tr>
<td>EA-6a (Fig. 4a)</td>
<td>-307.41941</td>
<td>-306.82415</td>
<td>69.3</td>
<td>138.6</td>
<td>133.6</td>
</tr>
<tr>
<td>EA-6b (Fig. 5)</td>
<td>-307.41997</td>
<td>-306.82469</td>
<td>68.2</td>
<td>138.4</td>
<td>133.6</td>
</tr>
</tbody>
</table>

| TS EA-1a → 3b     | -307.43426            | -306.83666             | 69.4 | 130.9       | 124.5         |
| TS EA-3a → 3b     | -307.39355            | -306.83688             | 70.2 | 130.7       | 125.1         |
| TS EA-3a → 5      | -307.42543            | -306.82502             | 69.7 | 138.1       | 132.8         |
| TS EA-5 → HB-1b   | -307.41738            | -306.82077             | 69.8 | 140.8       | 135.3         |
| TS EA-3b → 6a     | -307.41335            | -306.81679             | 66.0 | 143.2       | 138.1         |
| TS EA-6a → 6a (b) | -307.41768            | -306.82381             | 68.8 | 138.2       | 133.6         |
| TS EA-3a → 3c     | -307.43466            | -306.83390             | 70.7 | 132.5       | 126.9         |
| TS EA-3c → 2b     | -307.42637            | -306.83177             | 70.1 | 133.8       | 127.1         |
| TS EA-3a → HB-5b  | -307.39355            | -306.79996             | 71.9 | 153.9       | 147.3         |
| TS EA-1b → 4a     | -307.42702            | -306.83023             | 68.9 | 134.9       | 128.8         |
| TS EA-4a → 4b     | -307.44507            | -306.84473             | 70.2 | 125.8       | 120.0         |
| TS EA-4b → 4c     | -307.43112            | -306.83260             | 70.1 | 133.4       | 127.4         |
| TS EA-4c → 2c     | -307.41198            | -306.81925             | 69.4 | 141.8       | 135.4         |
| TS EA-4c → AC-2a  | -307.39971            | -306.80465             | 70.8 | 151.0       | 144.8         |
| TS AC-2a → AC-1a  | -307.41178            | -306.81565             | 68.9 | 144.1       | 137.9         |
| AC-1a (Fig. 4b)   | -307.44905            | -306.84929             | 71.2 | 122.9       | 117.6         |
| AC-1b (Fig. 5)    | -307.45270            | -306.85452             | 71.4 | 119.7       | 114.2         |
| AC-2a (Fig. 4b)   | -307.42693            | -306.82804             | 71.8 | 136.3       | 130.3         |
| TS AC-1b → HB-3c  | -307.40616            | -306.81321             | 68.6 | 145.5       | 139.3         |

(a) E(total) in Hartrees, all other components, including the ZPE scaled by 0.99, in kcal mol$^{-1}$. (b) the transition state for the O-equilibration, see Figure 3a.
Table 2. Energetic data for dissociation reactions of the radical cations of ethyl acetate and 4-hydroxy-2-butane derived from CBS-QB3 calculations and experimental observations (a).

<table>
<thead>
<tr>
<th></th>
<th>CBS-QB3</th>
<th>CBS</th>
<th>CBS</th>
<th>Exp.</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>E(total) [0K]</td>
<td>ΔH°</td>
<td>ΔH° 298</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH₃C(O)OCH₂CH₃⁺</td>
<td>-306.83503</td>
<td>131.9</td>
<td>126.3</td>
<td>125 ± 1</td>
<td>8</td>
</tr>
<tr>
<td>CH₃C(O)OCH₂CH₃</td>
<td>-307.20745</td>
<td>-101.8</td>
<td>-107.7</td>
<td>-106.1</td>
<td>12a</td>
</tr>
<tr>
<td>CH₃C(O)CH₂CH₂⁺^+  + H₂O</td>
<td>139.2 (b)</td>
<td>137±3 (c)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH₃C(O)CH=CH₂⁺</td>
<td>-230.83494</td>
<td>-22.3</td>
<td>-26.2 (b)</td>
<td>-27.4</td>
<td>12b</td>
</tr>
<tr>
<td>CH₃C(O)CH=CH₂⁺</td>
<td>-230.47885</td>
<td>201.1</td>
<td>197.4 (b)</td>
<td>195</td>
<td>(c)</td>
</tr>
<tr>
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<td>188.2</td>
<td>184.1</td>
<td>182</td>
<td>13a</td>
</tr>
<tr>
<td>2-methyloxetene ion (Scheme 1)</td>
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<td>197.2</td>
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<tr>
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<td>12a</td>
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</table>

(a) E(total) in Hartrees, all other components, including the ZPE scaled by 0.99, are in kcal mol⁻¹.
(b) refers to the anti conformer; the ionic and neutral syn conformers are 0.5 kcal mol⁻¹ higher in energy; (c) ionic ΔH°₂⁹⁸ based upon IE₃ = 9.65 ± 0.02 eV and ΔH° neutral ketone = -27.4 ± 2.6 kcal mol⁻¹ as quoted in ref. 12b; (d) derived from PA ketene = 197.3 kcal mol⁻¹ [12b] and ΔH°₂⁹⁸ ketene = -11.4 ± 0.6 kcal mol⁻¹ [12a]; (e) from PA acetaldehyde = 183.7 kcal mol⁻¹ [12c] and ΔH° aldehyde = -39.6 ± 0.1 kcal mol⁻¹ [12a]; (f) refers to the “U” shaped conformer, the “S” conformer is 0.6 kcal mol⁻¹ higher in energy; (g) 2A’ state; (h) value of the lowest energy syn/anti (position hydroxyl H’s relative to CH₃ group) conformer; (i) from PA acetic acid = 187.3 kcal mol⁻¹ [12c] and ΔH°₂⁹⁸ acid = -103.3 ± 0.1 kcal mol⁻¹ [12a]; (j) lowest energy conformer; (k) upper limit: see ref. 21d for details.
In the same vein, ion $\text{EA-4}$ could undergo a [1,2]-hydroxycarbene shift [10b], leading to $\text{[CH}_3\text{C(OH)C(H)(CH}_3\text{)O]}^{++}$, a 1,5-hydrogen-shift isomer of $\text{CH}_3\text{C(=O)CH(OH)CH}_3^{++}$, ionized acetoin. This reaction does not play a role in the water elimination either, since (i) the isomerization barrier is not sufficiently low and (ii) low energy acetoin ions do not lose $\text{H}_2\text{O}$ but rather dissociate into $\text{CH}_3\text{C(H)OH}^+ + \text{CH}_3\text{C}=\text{O}^*$, via a remarkable hidden rearrangement [20]. However, as will be discussed in Section 1.5 in conjunction with the energy diagram of Fig. 4b, this rearrangement sheds light on another intriguing aspect of ethyl acetate’s ion chemistry (8). This concerns the formation of the prominent m/z 45 $\text{C}_2\text{H}_5\text{O}^+$ ions in the CID mass spectra of $\text{EA-1/2}$ shown in Fig. 2a/b.

Despite these negative answers from theory, we further pursued the idea that the water loss from $\text{EA-1/2}$ occurs via the PES of $\text{HB-1}$ and considered the distonic ion $\text{EA-3}$ to be the most likely intermediate for the conversion. This indeed proved to be the case: as shown in the calculated energy diagram of Fig. 3a, $\text{EA-3}$ can rearrange into $\text{HB-1}$ via a two-step low energy route. This finding and its implication on the interpretation of the labelling results will be discussed in Section 1.3. However, we will first deal with our
mechanistic proposal for the water elimination from HB-1, which, as we shall see, involves a [1,2]-hydroxycarbene shift [10b] as the key step of the reaction.

1.2. The water elimination from ionized 4-hydroxy-2-butanone (HB-1)

Before we discuss our mechanistic proposal for the water loss from HB-1 we will first briefly review the experimental observations. The spectrum of metastable ions HB-1 displays a single narrow peak at m/z 70, indicating that loss of H₂O represents the reaction of lowest energy requirement. The kinetic energy release derived from the m/z 70 peak at half-height, T₀.5, is only 7 meV [7] indicating that the water elimination may well occur at the thermochemical threshold. The CID mass spectrum of the resulting C₄H₆O⁺⁺ product ion, generated from metastable ions HB-1, is shown in Fig. 2d. Comparison of this spectrum with that of CH₃C(=O)CH=CH₂⁺⁺ (MVK) and other isomeric C₄H₆O⁺⁺ ions [7,13] leaves little doubt that MVK is the product ion generated from HB-1. We note in particular that the peak at m/z 69 (loss of H⁺) in the spectrum of Fig. 2d is barely visible (< 1% of the base peak at m/z 55). Since loss of H⁺ represents [7,13a] a major collision induced dissociation of the enol ion of MVK, CH₂=C(OH)CH=CH₂⁺⁺, it is unlikely that this more stable isomer (see Table 2) is co-generated from HB-1 to any significant extent.

Our CID mass spectrum of the C₄H₆O⁺⁺ ion generated from metastable ethyl acetate ions is identical with that of Fig. 2d. This reinforces the conclusion of the PI study of Baer et al. [8] that the water elimination from EA-1 yields MVK at the thermochemical threshold. Their derived ΔₜH°₂₉₈ value of 194 ± 2 kcal mol⁻¹ is close to its experimental estimate of 195 ± 3 kcal mol⁻¹, see Table 2. On the other hand, see Introduction, Holmes et al. [7] invoked the co-generation of the enol ion because the ΔₜH°₂₉₈ (C₄H₆O⁺⁺) they derived from their AE (EI) measurements, 190 kcal mol⁻¹, lies 5 kcal mol⁻¹ below the experimental estimate for MVK. We note that the AE values from the PI and EI studies are virtually the same, 10.31 ± 0.1 eV, and that the discrepancy between the derived ΔₜH°₂₉₈ values arises from differences in the thermochemical treatment of the appearance energies [8].
The ambiguities in defining appearance energies and their conversion into $\Delta H_{298}^\circ$ values of the reaction products has been a matter of considerable debate [21]. Here we note that applying the Traeger-McLoughlin correction term [21a], $\Delta H_{\text{cor}} = \Delta H_{298} \text{ (MVK} + \text{ H}_2\text{O}) - 1.48 \text{ kcal mol}^{-1}$, raises the $\Delta H_{298}^\circ (\text{C}_4\text{H}_6\text{O}^{**})$ value derived by Holmes et al. by 5.3 kcal mol$^{-1}$ to 195 kcal mol$^{-1}$ (using the $\Delta H_{298}^\circ$ values available from the CBS-QB3 calculations). Note that $\Delta H_{\text{cor}}$ is negative and this negative number is subtracted from the measured AE, thereby raising the derived $\Delta H_{298}^\circ$. This correction holds rigorously if all the available internal energy of the precursor ion is used for dissociation, that is, the products are formed at 0 K. The actual thermal content of the products is not known and hence the correction term only provides an upper limit to the derived enthalpy.

Interestingly, the same situation obtains for the water loss from HB-1. The available AE, 9.78 eV [22], leads to a $\Delta H_{298}^\circ (\text{C}_4\text{H}_6\text{O}^{**})$ value of only 190.3 kcal mol$^{-1}$; when the above correction term is applied, the number increases to 195.6 kcal mol$^{-1}$ and becomes compatible with the formation of MVK.

The above observations lead us to conclude that the water elimination from both HB-1 and EA-1 yields MVK at the thermochemical threshold. Further, the MI spectrum of the $^{18}$O labelled isotopologue CH$_3$C(=O$^{18}$)CH$_2$CH$_2$OH$^{**}$ reveals that the H$_2$O molecule lost from metastable ions HB-1 largely (~ 95%) consists of the hydroxyl $^{16}$O atom. The inset of the CID mass spectrum of Fig. 2c shows that this is also true for stable ions undergoing collision induced dissociation, although it should be noted that the larger part (~ 70 %) of the dominating peak for water loss in the CID spectrum is of metastable origin. This also applies to the m/z 70 peak in the CID mass spectrum of EA-1 but now the water loss, see inset of Fig. 2a, largely (~ 90 %) involves the keto $^{16}$O atom. For both isomers the kinetic energy release (T$_{0.5}$ value) associated with the major loss of H$_2^{16}$O from the labelled isotopomers is significantly lower than that of the minor H$_2^{18}$O loss : 8.6 vs 13.0 meV for EA-1 [7] and 5.5 vs 11.5 meV for HB-1 (this work). This observation

* Using $\Delta H_{298}^\circ$ (4-hydroxy-2-butane) = - 93 kcal mol$^{-1}$, from Benson additivity (12e) estimate ; our CBS-QB3 value is - 93.4 kcal mol$^{-1}$.

82
suggests that the $H_2^{18}O$ loss from EA-1 and HB-1 involves an oxygen equilibration reaction whose energy requirement is somewhat higher than the atom specific water loss. As we shall see, the mechanistic proposal of Fig. 3 provides a rationale for these labelling results.

Our mechanistic proposal for water loss from metastable ions HB-1 is presented in the bottom part of the energy diagram of Fig. 3. Starting from the lowest energy conformer HB-1a, a facile rotation of the CH$_2$OH moiety yields conformer HB-1b which forms the connection with the PES of ethyl acetate in the top part of the energy diagram. Ion HB-1b then rearranges into the very stable distonic ion HB-2a via a 1,4-H shift. The TS for this shift is undoubtedly not high but the calculated value is clearly too low; this point is further discussed in the Theoretical Methods section.

Ion HB-2a may undergo a facile rotation of its HCOH moiety to yield the slightly more stable conformer HB-2b, which has a planar structure. However, its HCOH and CH$_3$COH moieties can slightly move out of the plane - with a negligible energy requirement, see Table 1b - to form HB-2c which, see also Fig. 5, can be viewed as a one-electron long bonded species. Contraction of its one-electron bond was expected to initiate the isomerization of HB-2c into HB-3a, see Fig. 3b, via a [1,2]-hydroxycarbene shift [10b]. However, HB-3a does not appear to be a minimum on the PES: all attempts to optimize its geometry yielded its conformer HB-3b, in which the hydroxyl groups are bridged, in such a way that an ensuing loss of water into MVK can easily be envisaged. We were able to locate the transition state connecting HB-2c and HB-3b and it appears to lie at only 124 kcal mol$^{-1}$, well below the threshold for the water elimination. HB-3b does not directly lose water but rather it isomerizes (TS at 138 kcal mol$^{-1}$) into an ion-dipole type complex between MVK and H$_2$O, HB-4, which then dissociates into its components at the thermochemical threshold.
Fig. 3 Energy-level diagram derived from CBS-QB3 calculations describing the water elimination from metastable ethyl acetate ions (EA-1). The top part (a) describes the isomerization of EA-1 into ionized 4-hydroxy-2-butanone (HB-1); the bottom part (b) presents the mechanism by which ions HB-1 lose H₂O. The numbers refer to ΔH₂⁹⁸ values in kcal mol⁻¹.

We note that other conformers of HB-2b may also undergo a [1,2]-hydroxy carbene shift, as illustrated in Scheme 3 for HB-2a. However, the stable HB-3 conformers then generated cannot immediately lose water but must first isomerize via rotation(s) into HB-
3b. We have examined several of these pathways but they all appear to have a slightly higher energy requirement than the direct route HB-2b → HB-3b depicted in Fig. 3b.

Scheme 3

Three points deserve further comment:

(i) The minor loss of $H_2^{18}O$ from $CH_3C(=O^{18})CH_2CH_2OH^{**}$ could be ascribed to a partial equilibration of HB-3b with its 1,2-H shift isomer $CH_3C(OH)=C(OH)CH_3^{**}$ (HB-6): the associated TS (see Table 1b) lies at 139 kcal mol$^{-1}$, i.e. at the threshold for the water elimination.

(ii) The $H_2O$ molecule in HB-4 is not expected to promote enolization of the ketone moiety by proton-transport catalysis [19]. This is because the proton affinity (PA) of water (164 kcal mol$^{-1}$) is much lower than the (calculated) topical PAs at $^*CH_2$ and $C=O$ in the deprotonated ketone $^*CH_2C(=O)CH=CH_2$, 187 and 200 kcal mol$^{-1}$ respectively.

(iii) A McLafferty type rearrangement in HB-1 would yield enol ions $CH_3C(OH)=CH_2^{**}$ at m/z 58 by loss of $CH_2=O$. As seen from Table 2, the minimum energy requirement for this reaction is only 136 kcal mol$^{-1}$, i.e. lower than that for the loss of water. However, our calculations indicate that the formaldehyde loss involves a reverse barrier of 4 kcal mol$^{-1}$, see Fig. 4 and Table 1b, which makes the energy requirements for the losses of formaldehyde and water comparable. Yet, neither the MI nor the CID spectrum, see Fig. 2c, of HB-1 displays a signal at m/z 58!

Standard RRKM calculations for the formaldehyde loss from HB-5a and the water loss from HB-3b indicate that the internal energy needed for the formaldehyde loss in the metastable time frame is lower than that for the water loss. However, this model is
misleading because it does not take into account that both isomers communicate with the much more stable isomers HB-2a – HB-2c via low barriers, see Fig. 3. This leads to a rapid interconversion of the various isomeric ions involved in the competing losses of formaldehyde and water.

The extended RRKM model as described by Baer et al. [23] (see also theoretical methods Section) does account for the competition between the two dissociation channels. Calculations based on this model revealed that equilibration via the low lying distonic ions HB-2a – HB-2c leads to a much lower yield (by a factor of 140) of the m/z 58 product ion formed by loss of formaldehyde compared to the yield of m/z 70 MVK ions formed by loss of water. As a result, loss of formaldehyde from HB-1 cannot effectively compete with its water loss.

1.3. The water elimination from ionized ethyl acetate (EA-1)

As discussed in the previous section, 4-hydroxy-2-butanone ions HB-1 lose water via the mechanism presented in the bottom part of the energy diagram of Fig. 3. The top part of this diagram, Fig. 3a, shows that ionized ethyl acetate can undergo a three-step isomerization reaction into HB-1, which may then serve as the precursor for its subsequent water elimination. The first step involves the conversion of EA-1 into its stable distonic isomer EA-3 via a facile 1,5-H shift. This reaction involves ionized ethyl acetate’s conformer HB-1a and it yields the distonic ion’s conformer EA-3b. Rotation of its hydroxyl group via a low lying transition state converts EA-3b into EA-3a. Next, the O-CH₂ bond in EA-3a stretches and breaks while the methylene group moves to the hydroxyl O atom to make a new bond, yielding distonic ion EA-5. Ion EA-5, akin to the well-documented (24) distonic C₇H₆O⁺⁺ isomer H₂O⁺-CH₂-CH₂⁺, lies in a shallow potential well and requires only 4 kcal mol⁻¹ to further rearrange into ionized 4-hydroxy-2-butanone’s conformer HB-1b. This rearrangement can be viewed as a 1,3-acetyl shift.

This three-step isomerization route of EA-1 into HB-1 takes place at energies below that required for the water loss and it thus satisfies the energetic constraints imposed by experiment. It further converts the ¹⁸O labelled EA-1 isotopologue
CH$_3$C(=O)$^{18}$OC$_2$H$_5$$^\ast$ into the HB-1 isotopologue CH$_3$C(=O)$^{18}$CH$_2$CH$_2$OH$$^\ast$ which, see Fig. 3b, is expected to specifically lose H$_2^{16}$O. This, too, is in agreement with the experimental observations albeit that a small fraction of high energy metastable ions (~5%) appears to lose H$_2^{18}$O. The loss of H$_2^{18}$O from both labelled isotopologues probably results from a weakly competing oxygen equilibration reaction rather than a different dissociation pathway. Two equilibration mechanisms are feasible: (i) the equilibration of HB-3b with its 1,2-H shift isomer HB-6 mentioned in the previous Section and (ii) the route EA-3b $\rightarrow$ EA-6a depicted in Fig. 3a. The transition state energies for the two processes are very close but the first route is kinetically less attractive because the equilibration HB-3 $\leftrightarrow$ HB-6 is associated with a very large activation energy (44 kcal mol$^{-1}$ relative to HB-6) and a tight transition state. This makes it unlikely that this equilibration can effectively compete with the dissociation HB-3 $\rightarrow$ HB-4 $\rightarrow$ MVK + H$_2$O, even at elevated energies. The dynamic picture is more favourable for the second route which converts EA-3b by elongation of its O-CH$_2$ bond into the hydrogen-bridged radical cation EA-6a. As depicted in Fig. 3a, EA-6a can undergo a facile exchange of its vinyl moiety via a low-lying transition state which makes its oxygen atoms equivalent.

We further note that elongation of the O-CH$_2$ bond in other conformers of EA-3 leads to various EA-6 conformers – including EA-6b whose structure is shown in Fig. 5 – which are similar in energy and may dissociate into CH$_3$C(OH)$_2$$^\ast$ + C$_2$H$_3$$^\ast$ at elevated energies. Elongation of the O-CH$_2$ bond in EA-3 can also lead to ion-dipole complexes of ionized ethylene and acetic acid. Such species can be formed from EA-3 at fairly low internal energies, as seen in Fig. 3a where the symmetrical ion-dipole structure at 130 kcal mol$^{-1}$ represents the transition state for switching the acetic acid dipole molecule between the methylene moieties of ionized ethylene, see Section 1.5. This switching reaction makes the C and H atoms of the ethyl group in EA-1 equivalent and accounts in part for the H-D exchange reactions of D-labelled isotopologues of EA-1 as will be discussed in Section 1.5. At elevated energies the ion-dipole complexes do not dissociate into C$_2$H$_4$$^\ast$ + CH$_3$COOH. Instead, proton transfer (PT) occurs from the ionized ethylene
moiety to the acetic acid dipole which allows the energetically more favourable
dissociation into $\text{CH}_3\text{C(OH)}_2^+ + \text{C}_2\text{H}_3^*$ to take place.

In this context we note that the PI study by Baer and co-workers [8] reports an AE
of $10.67 \pm 0.08$ eV for the dissociation of $\text{EA-1}$ into $\text{CH}_3\text{C(OH)}_2^+ (m/z 61) + \text{C}_2\text{H}_3^*$. From
the experimental enthalpies of Table 2 and using $\Delta H_{\text{cor}} = 4.7$ kcal mol$^{-1}$, we derive a
thermochemical AE of 10.75 eV. These results indicate that this dissociation takes place
virtually at the thermochemical threshold, i.e. it has no reverse activation barrier. As
discussed above, loss of $\text{C}_2\text{H}_3^*$ from $\text{EA-1}$, see Fig. 3a, may be envisaged to occur from
the hydrogen-bridged ion $\text{EA-6}$ or by proton transfer from ethylene-acetic acid ion-dipole
complexes, rather than by a formal 1,3-H shift as mentioned in the Introduction.

1.4. The [1,3]-hydroxycarbene shift in the distonic ion $[\text{CH}_3\text{C(OH)OCH}_2\text{CH}_2]^*^* (\text{EA-3})$

The energy-level diagram of Fig. 4a describes the communication of ionized ethyl
acetate with its enol ($\text{EA-2}$) which will be addressed in the next Section. It also shows the
energetics associated with a [1,3]-hydroxycarbene shift in distonic ion $\text{EA-3}$. This
isomerization leads to $\text{HB-1}$ via its 1,5-hydrogen-shift isomer $\text{HB-5}$ and it could in
principle provide an alternative pathway for the loss of water. The energy requirement for
this rearrangement precludes this possibility: Fig. 4a shows that TS $\text{EA-3} \rightarrow \text{HB-5}$ lies
some 10 kcal mol$^{-1}$ above the threshold for the dissociation of the incipient $\text{HB-5}$ ions into
$\text{CH}_3\text{C(OH)=CH}_2^{**} (m/z 58) + \text{CH}_2=\text{O}$ by direct bond cleavage. The fact that this
dissociation is not observed in either the MI, the CID or the conventional mass spectrum
of $\text{EA-1}$ implies that the [1,3]-hydroxycarbene shift does not even occur. This is not
surprising considering the discussion of the previous Section where it was shown that
ions $\text{EA-3}$ are able to undergo several isomerization and dissociation reactions at energies
well below that required for the [1,3]-hydroxycarbene shift.
Fig. 4 Energy-level diagrams derived from CBS-QB3 calculations for the isomerization of ionized ethyl acetate (EA-1) into the distonic ions EA-3 (part a) and EA-4 (part b) and the subsequent [1,3]- and [1,2]-hydroxycarbene shift. The numbers refer to $\Delta H^0_{298}$ values in kcal mol$^{-1}$.

The energy diagram of Fig. 4a also shows that Yeo’s mechanism of Scheme 1 can be refuted: his proposed intermediate is not a minimum on the PES but rather corresponds to the high lying TS EA-3b $\rightarrow$ HB-5b associated with the [1,3]-hydroxycarbene shift. Interestingly, our calculations (see Table 2) indicate that the cyclic product ion structure proposed in his Scheme, ionized 2-methyloxetene, has the same heat of formation as its ring-opened isomer MVK.

Another simple mechanism for water loss from ionized ethyl acetate which complies with the finding that its keto oxygen atom is preferentially lost, would involve a double H transfer to its keto oxygen atom. This reaction would generate an ionized oxycarbene via the sequence EA-1 $\rightarrow$ EA-4 $\rightarrow$ EA-4 CH$_3$-C-O-CH=CH$_2$ $^{+} +$ H$_2$O. Ionized oxycarbenes are well documented species in the gas-phase which may be as stable as their keto or aldehyde counterparts [25]. However, CH$_3$-C-O-CH=CH$_2$ $^{+}$ appears to be much higher in energy than CH$_3$-O-CH=CH$_2$ $^{+}$, by 21 kcal mol$^{-1}$ (see Table 2) and so its formation, certainly as a product ion in the metastable time-frame, can effectively be ruled out.
The diagram of Fig. 4a also shows that the thermochemical energy requirement for the dissociation $\text{EA-1/2} \rightarrow \text{CH}_2=\text{C(OH)}_2^{+*}$ (m/z 60) + $\text{C}_2\text{H}_4$ is lower than that for the loss of $\text{H}_2\text{O}$. However, metastable ions $\text{EA-1/2}$ do not lose $\text{C}_2\text{H}_4$ indicating that the associated dissociative rearrangement, possibly a 1,3-H shift in $\text{EA-2}$, has a high activation energy. As seen in Fig. 2a/b this dissociation becomes prominent upon collisional activation. A double collision experiment confirmed that the m/z 60 ions in the CID spectra are ions $\text{CH}_2=\text{C(OH)}_2^{+*}$, not $\text{CH}_3\text{COOH}^{+*}$.

1.5. Deuterium labelling experiments: the relationship between ionized ethyl acetate (EA-1) and its enol (EA-2) and identification of the rate-determining step for the loss of $\text{H}_2\text{O}$

In Table 3 are given selected deuterium labelling results taken from references 6 and 7. Metastable ions fragmenting in the second field free region (2ffr) of the ZAB and MS902 instruments do so at the same average rate so that the data are comparable [7]. From the results of Table 3 it can be deduced that there are two $\text{H/D}$ equilibration reactions.

In the first reaction, which is so fast that it readily occurs for ions dissociating in the source, the H atoms of the ethyl chain become positionally equivalent, see the results for $\text{CD}_3\text{C(=O)OCD}_2\text{CH}_3$. A complete exchange of these H atoms would yield a $\text{H}_2\text{O} : \text{HDO} : \text{D}_2\text{O}$ ratio of 33 : 67 : 00 which is close to the observed ratio of 39 : 52 : 09. Reversible rearrangement of $\text{EA-1}$ into $\text{EA-3}$ followed by isomerization into the ion-dipole complex $\text{CH}_3\text{C(OH)=O} \cdots \text{C}_2\text{H}_4^{+*}$ as discussed in Section 1.3 accounts for this exchange reaction.
Table 3. Relative abundances for the loss of water from selected D-labeled isotopologues of ionized ethyl acetate and its enol.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Source</th>
<th>H$_2$O : HDO : D$_2$O</th>
<th>Calculated$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD$_3$C(=O)OCD$_2$CH$_3$</td>
<td>m$^*$</td>
<td>39 52 09</td>
<td>11 53 36</td>
</tr>
<tr>
<td>CH$_3$C(=O)OCD$_2$CD$_3$</td>
<td>m$^*$</td>
<td>17 58 25</td>
<td></td>
</tr>
<tr>
<td>CD$_3$C(=O)OCH$_2$CH$_3$</td>
<td>m$^*$</td>
<td>06 44 50</td>
<td></td>
</tr>
<tr>
<td>CH$_2$=C(OH)OCD$_2$CD$_3$</td>
<td>m$^*$</td>
<td>07 51 42</td>
<td></td>
</tr>
<tr>
<td>CD$_2$=C(OH)OCH$_2$CH$_3$</td>
<td>m$^*$</td>
<td>73 26 01</td>
<td></td>
</tr>
</tbody>
</table>

$^a$Assuming complete loss of positional identity; $^b$metastable ions 2ffr ZAB or MS902

In the longer lived metastable ions, the H atoms of the acetyl group also participate in the exchange reactions, almost to the statistical limit. This can be rationalized by invoking a slow but reversible isomerization of EA-3 into the enol ion EA-2. It leads to exchange of the H atoms of the acetyl group with those of the methyl H atoms of the ethyl group and together with the above fast exchange reaction, an (almost) complete equilibration of all H atoms now takes place. This would imply that metastable ethyl acetate ions consist of an (almost) equilibrated mixture of the keto, distonic and enol isomers.

Our calculations, see Fig. 4a, indicate that ions EA-2 and EA-3 are lower in energy than EA-1 and that they can be produced at energies just above the formation of EA-1. This makes it very likely that metastable ions EA-1 primarily exist as enol ions EA-2 and distonic ions EA-3. This is in good agreement with a Fourier Transform Ion Cyclotron Resonance study of Kiminkinen et al. [26] who conclude that the long-lived (time scale > 1s) radical cation of ethyl acetate exists as its enol form in the gas-phase. Their experiments further indicate, in agreement with our calculations, that the energy barriers for isomerization of EA-1 to the distonic ion EA-3 and of EA-3 to the enol ion EA-2 must be near or below the enthalpy of formation of EA-1 and that this radical cation is kinetically unstable.
As expected from the above scenario, the enol ion also shows fast H/D equilibration reactions of the ethyl side chain, see Table 3. Earlier work [7] has noted that enol ions dissociating in the source rearrange irreversibly to the distonic ion, i.e. \( \text{CH}_2=\text{C(OH)}\text{OCD}_2\text{CD}_3^{**} \rightarrow \text{CH}_2\text{DC}^*(\text{OH})\text{OCD}_2\text{CD}_2^{**} \). As discussed in Section 1.3, the latter ion can then access the ion-dipole complex \( \text{CH}_2\text{DC(OH)}=\text{O} \cdots \text{C}_2\text{D}_4^{**} \) and fall back to the distonic form leading to equilibration of the OH hydrogen and the four C\(_2\)D\(_4\) deuterium atoms. Again, in the metastable time-frame almost complete equilibration of all H and D atoms occurs.

The labelled ion \( \text{CD}_3\text{C(=O)}\text{OCH}_2\text{CH}_3^{**} \) shows a H\(_2\)O/HDO loss ratio of 1.69, while the D\(_2\)O/HDO loss ratio for the inversely labelled compound \( \text{CH}_3\text{C(=O)}\text{OCD}_2\text{CD}_3 \) is 1.25 and so an H/D isotope effect is operative. According to the energy diagram of Fig. 3b, the final step is rate-determining. This step is a H transfer and so we propose that the isotope effect can be connected with this step.

From the data in Table 3 we can calculate that for the metastable ions loss of H\(_2\)O is 36% specific for the keto ions and 41% specific for the enol ions: the final entry in Table 3, for example, can be broken down into a 41% specific H\(_2\)O loss and random H\(_2\)O, HDO and D\(_2\)O losses of 32, 26 and 1%. This small increase in specificity may well indicate that the starting enol ions fragment at a slightly higher internal energy than the keto ions. This is corroborated by the finding that the kinetic energy release (T\(_{0.5}\)) for loss of water is slightly larger for the enol ion than for the keto ion [7]. The larger T\(_{0.5}\) value cannot be taken as showing that a rate-determining isomerization precedes fragmentation of the enol ion, paralleling the behaviour of the acetamide system [27].

Baer and coworkers [8] note that the measured activation energy for loss of H\(_2\)O from ionized ethyl acetate (0.3 eV) is too small to allow the molecular ion to be metastable, unless it rearranges into a more stable form. By modelling their experimentally derived k vs E curve with standard RRKM calculations Baer and coworkers concluded that the rearranged form has a \( \Delta H^\circ_{298} \) of 110 kcal mol\(^{-1}\), which can be associated with EA-2, EA-3 or HB-2. The slow rate constant is the result of the
participation of all the low energy isomers leading to a large density of states of the
dissociating ions.

1.6. The [1,2]-hydroxycarbene shift in the distonic ion \([\text{CH}_3\text{C(OH)}\text{OCHCH}_3]^{++}\) (EA-4)

Using the energy diagram of Fig. 4b as a guide, we note that the distonic ion EA-4
is readily accessible from EA-1 via a low energy 1,4-H shift. The ion can communicate
with EA-2 via its conformer EA-4c but the TS for the associated 1,4-H shift (see Table 1a)
is c. 8 kcal \(\text{mol}^{-1}\) higher in energy than that for the enolization of its slightly less stable
distonic isomer EA-3, see Fig. 4a.

The energy diagram of Fig. 4b further shows that conformer EA-4c may serve as
the immediate precursor for a [1,2]-hydroxycarbene shift which connects EA-1 with the
PES of the acetoin radical cation, \(\text{CH}_3\text{C(=O)}\text{CH(OH)}\text{CH}_3^{++}\) (AC-1). This rearrangement,
whose transition state lies c. 6 kcal \(\text{mol}^{-1}\) above the level for the water loss, does not
contribute to the loss of water because low energy acetoin ions exclusively dissociate into
\(\text{CH}_3\text{C(H)}\text{OH}^+ + \text{CH}_3\text{C}=\text{O}^*\). This reaction involves a remarkable hidden rearrangement -
metastable ions \(\text{CH}_3\text{C(=O)}^{18}\text{CH(OH)}\text{CH}_3^{++}\) generate \(\text{CH}_3\text{C(H)}^{18}\text{OH}^+\) and \(\text{CH}_3\text{C(H)}^{16}\text{OH}^+\) in a
1:1 ratio – and a mechanism involving the hydrogen-bridged radical cation
\(\text{CH}_3\text{C(=O)}^{18}\text{H}...\text{O=C(H)}\text{CH}_3^{++}\) as the key intermediate has been proposed [20].

Metastable ions EA-1 do not dissociate into \(\text{CH}_3\text{C(H)}\text{OH}^+ + \text{CH}_3\text{C}=\text{O}^*\) but the reaction becomes important upon collisional activation, as seen from the prominent m/z
45 peak in the CID mass spectrum of Fig. 2a. From the inset of Fig. 2a it is seen that this
peak shifts almost completely to m/z 47 in the CID spectrum of \(\text{CH}_3\text{C(=O)}^{18}\text{OCH}_2\text{CH}_3\). This observation is in line with the expectation that the energy rich acetoin ions
\(\text{CH}_3\text{C(O)}\text{CH}^{18}\text{OH})\text{CH}_3^{++}\) resulting from the [1,2]-hydroxycarbene shift will not rearrange
but immediately dissociate.

Baer and co-workers [8] have reported the experimental AE for this reaction,
10.70 ± 0.1 eV. They note that this value is too high to account for the threshold
generation of the above products and suggest that the reaction may have a significant
reverse activation barrier. From the evaluated experimental enthalpies of Table 2 and
using $\Delta H_{\text{cor}} = 4.7 \text{ kcal mol}^{-1}$, we derive a thermochemical AE of 10.46 eV, implying that a reverse barrier of c. 5.5 kcal mol$^{-1}$ may indeed be present. Our calculations support this proposal: the barrier for the [1,2]-hydroxycarbene shift, see Fig. 4b, lies 5 kcal mol$^{-1}$ above the dissociation level $\text{CH}_3\text{CH}(\text{H})\text{OH}^+ + \text{CH}_3\text{C}=$O$^*$. 

As mentioned above, metastable acetoin ions do not lose water. Nevertheless, our CBS-QB3 calculations indicate that AC-1 can communicate with HB-3b of Scheme 3 at the threshold for the water loss. The barrier for the isomerization of conformer AC-1b into HB-3c lies at 139 kcal mol$^{-1}$ while TS HB-3c $\rightarrow$ 3b lies at 130 kcal mol$^{-1}$ (Table 1a/b). Thus the overall energy requirement for this rearrangement of AC-1 is very close to that of the products formed by its direct bond cleavage into $\text{CH}_3\text{C}(\text{H})\text{OH}^+$, 140 kcal mol$^{-1}$, see Table 2. However, the dynamical situation for these two reactions is very different. The rearrangement has a tight transition state, whereas the dissociation, which has no reverse activation energy, corresponds to a loose transition state. A standard RRKM calculation predicts that the excess energy needed for the rearrangement to take place in the metastable time window (10 $\mu$s) exceeds 5 kcal mol$^{-1}$. This is caused by the large activation energy associated with the rearrangement. For the direct bond cleavage reaction we have used the model derived from the statistical adiabatic channel theory [28]. Here the excess energy needed is less than 1 kcal mol$^{-1}$ because the acetyl radical lost has a large dipole moment (2.5 D at the B3LYP/CBSB7 level of theory). Therefore low energy acetoin ions AC-1 prefer the direct dissociation pathway above rearrangement into HB-3c and the subsequent loss of water. In the same vein, the rearrangement HB-3b $\rightarrow$ AC-1 $\rightarrow$ $\text{CH}_3\text{CH}(\text{H})\text{OH}^+ + \text{CH}_3\text{C}=$O$^*$ does not occur, as demonstrated by the complete shift of the m/z 45 peak to m/z 47 in the CID spectrum of $^{18}$O labelled HB-1, see the inset of Fig. 2c.
Conclusion

Our computational study, in concert with previous and present experimental work, leads to the following mechanistic proposal for the loss of water from ionized ethyl acetate in the metastable time-frame:

![Chemical structures]

The mechanism involves seven steps. These are: (1) a 1,5-hydrogen shift in ionized ethyl acetate yielding its distonic isomer \( \text{EA-3} \); (2) an ethylene shift in \( \text{EA-3} \) generating another distonic ion, \( \text{EA-5} \); (3) a 1,3-acetyl shift in \( \text{EA-5} \) yielding a conformer of ionized 4-hydroxy-2-butanone, \( \text{HB-1} \); (4) a 1,4-hydrogen shift in \( \text{HB-1} \) yielding its distonic isomer \( \text{HB-2} \); (5) a 1,2-hydroxycarbene shift in \( \text{HB-2} \). This step leads to \( \text{HB-3} \), a one-electron long bonded species whose hydroxyl groups are bridged; (6) a formal 1,4-hydrogen shift in which the bridging hydrogen moves to the adjacent hydroxyl group to form the water molecule of the ion-dipole complex \( \text{HB-4} \). This step is rate-determining and may account for the kinetic H/D isotope effect; and (7) dissociation into ionized methyl vinyl ketone and a water molecule.

Each step is a simple transformation in itself and all consecutive steps yield a transparent picture of the seemingly complex dissociation behaviour of ionized ethyl
acetate. Our mechanism satisfies the energetic constraints imposed by experiment and provides a rationale for the $^{18}$O- and D-labelling results.
References

22. From unpublished EI results of the late Dr F.P. Lossing (J.L. Holmes, personal communication 2005).
### Appendix for Chapter 4

**Table 4.** A comparison between energetic data derived from the CBS-QB3, G3B3 and G3 with experiment data for selected ions and neutrals in the ethyl acetate system of ions.

<table>
<thead>
<tr>
<th>Species</th>
<th>CBS $\Delta H^0_{298}$</th>
<th>ZPE</th>
<th>CBS $\Delta H^0_{298}$</th>
<th>ZPE</th>
<th>G3 $\Delta H^0_{298}$</th>
<th>ZPE</th>
<th>Exp. $\Delta H^0_{298}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>EA-1a</td>
<td>126.5</td>
<td>71.2</td>
<td>122.4</td>
<td>69.8</td>
<td>126.5</td>
<td>70.4</td>
<td>125</td>
</tr>
<tr>
<td>HB-1a</td>
<td>124.2</td>
<td>72.6</td>
<td>120.3</td>
<td>71.0</td>
<td>cannot optimize</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HB-1b</td>
<td>130.3</td>
<td>71.5</td>
<td>125.9</td>
<td>69.8</td>
<td>130.7</td>
<td>69.9</td>
<td></td>
</tr>
<tr>
<td>HB-2a</td>
<td>114.5</td>
<td>72.1</td>
<td>110.4</td>
<td>70.2</td>
<td>optimizes to HB-2b</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TS HB-1b/2a</td>
<td>125.9</td>
<td>70.1</td>
<td>121.8</td>
<td>68.1</td>
<td>cannot find this TS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH$_3$C(=O)CH=CH$_2$</td>
<td>-25.8</td>
<td>55.3</td>
<td>-29.8</td>
<td>54.1</td>
<td>-26.4</td>
<td>54.0</td>
<td>-27.4</td>
</tr>
<tr>
<td>CH$_3$C(=O)CH=CH$_2^+$</td>
<td>197.4</td>
<td>54.2</td>
<td>193.2</td>
<td>53.1</td>
<td>197.0</td>
<td>53.2</td>
<td>195</td>
</tr>
<tr>
<td>CH$_3$C(H)OH$^+$</td>
<td>142.2</td>
<td>45.5</td>
<td>140.7</td>
<td>41.4</td>
<td>142.7</td>
<td>41.3</td>
<td>142.4</td>
</tr>
<tr>
<td>CH$_3$OH$^+$</td>
<td>-6.1</td>
<td>40.4</td>
<td>-7.9</td>
<td>38.9</td>
<td>-5.6</td>
<td>39.0</td>
<td>-7</td>
</tr>
<tr>
<td>CH$_3$CH$_2$O$^+$</td>
<td>-3.5</td>
<td>39.8</td>
<td>-6.2</td>
<td>38.9</td>
<td>-3.2</td>
<td>39.3</td>
<td>-3.6</td>
</tr>
<tr>
<td>CH$_3$=O$^+$</td>
<td>158.0</td>
<td>27.6</td>
<td>155.4</td>
<td>27.0</td>
<td>157.8</td>
<td>27.0</td>
<td>157</td>
</tr>
<tr>
<td>CH$_3$=O$^+$</td>
<td>-2.5</td>
<td>26.7</td>
<td>-4.5</td>
<td>26.2</td>
<td>-2.5</td>
<td>26.1</td>
<td>-2.4</td>
</tr>
<tr>
<td>CH$_3$COOH$^+$</td>
<td>74.3</td>
<td>46.0</td>
<td>72.0</td>
<td>44.8</td>
<td>74.9</td>
<td>44.8</td>
<td>75</td>
</tr>
<tr>
<td>CH$_2$=CH$^+$</td>
<td>-104.3</td>
<td>38.3</td>
<td>-106.3</td>
<td>37.4</td>
<td>-106.8</td>
<td>37.5</td>
<td>-103.3</td>
</tr>
<tr>
<td>CH$_3$=C(OH)=CH$_2^+$</td>
<td>71.7</td>
<td>22.6</td>
<td>69.2</td>
<td>22.1</td>
<td>70.6</td>
<td>21.7</td>
<td>71.6</td>
</tr>
<tr>
<td>CH$_3$O$^+$</td>
<td>163.0</td>
<td>51.6</td>
<td>161.3</td>
<td>50.4</td>
<td>163.4</td>
<td>50.2</td>
<td>163.4</td>
</tr>
<tr>
<td>CH$_2$=O</td>
<td>-27.3</td>
<td>16.5</td>
<td>-28.3</td>
<td>16.2</td>
<td>-26.6</td>
<td>16.4</td>
<td>-26.0</td>
</tr>
</tbody>
</table>
Fig. 5. The CBS-QB3 optimized geometries for ionized 4-hydroxy-2-butanone, HB-1, and ethyl acetate, EA-1, isomers and selected transition states.
Fig. 5. ctd. (1)

TS HB-1a to HB-5a

TS HB-2d to HB-3c

HB-6

EA-1a

EA-1b

EA-2a

EA-2b

EA-2c

EA-3a

EA-3b

EA-3c

EA-4a

EA-4b

EA-4c

EA-5
The research presented in this thesis is focused on an integrated computational chemistry and mass spectrometric approach to solve complex dissociation mechanisms of radical cations in the gas-phase.

In Chapter 2a, it is shown that computational chemistry and tandem mass spectrometry based experiments allow for the study of proton-transport catalysis in the formaldehyde elimination of low energy 1,3-dihydroxyacetone radical cations. Theory predicts that solitary ketene-water ions, CH₂⁻C(=O)OH⁺, and CH₂⁻C(OH)₂⁺ are separated by a high energy barrier so that their unassisted interconversion does not occur. A mechanistic analysis using the CBS-QB3 model chemistry showed that metastable 1,3-dihydroxyacetone radical cations rearranged into the HBRC [CH₂C(=O)O(H)-H•••OCH₂]⁺, where the CH₂⁻O catalyzed the transformation of CH₂⁻C(=O)OH⁻ into CH₂⁻C(OH)₂⁺.

Chapter 2b described the dissociation of metastable pyruvic acid radical cations, CH₃C(=O)COOH⁺, into m/z 44 ions, C₂H₄O⁺, via decarboxylation, in competition with the formation of CH₃C=O⁺ + COOH⁻ by direct bond cleavage. Metastable ion spectrum of ionized pyruvic acid indicated that generation of CH₃C=O⁺ is preferred. The collision-induced dissociation experiments suggest that m/z 44 ions have structure connectivity of oxycarbene ions CH₃COH⁺ but they also suggest the more stable isomer CH₃C(H)=O⁺ may be co-generated. Computational results predicted that the oxycarbene ion should be equally likely to be generated as CH₃C=O⁺ further kinetic analysis is required.

In chapter 3, the isomeric ions CH₃O-P=S⁺⁺ and CH₃S-P=O⁺⁺ were characterized and differentiated by tandem mass spectrometry. Metastable ion spectra of CH₃O-P=S⁺⁺ and CH₃S-P=O⁺⁺ ions show that water elimination is the most prominent reaction to yield m/z 74 cyclic product ion [-S-CH=]P⁺⁺. The CBS-QB3 derived mechanism showed that these two isomers communicate via a common intermediate, the distonic ion CH₂S-P-OH⁺⁺, prior to the loss of water.

Finally, in Chapter 4, it was shown that computational chemistry played an integral role in the elucidation of the mechanism for the water elimination from
metastable ethyl acetate ions. Metastable ethyl acetate ions yield ionized methyl vinyl ketone and water. Theory suggests that prior to the water loss, ethyl acetate radical cations rearranges into ionized 4-hydroxy-2-butanone, where it proceeds to lose water.