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PROTONATED PROPYLENE OXIDE IS STABLE TOWARDS ISOMERIZATION IN THE GAS PHASE

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The relative stabilities of gaseous protonated propylene oxide and its isomers, protonated propanal, oxetane and acetone, were reinvestigated in a Fourier transform ion cyclotron resonance mass spectrometer by using multiple-stage tandem mass spectrometric experiments. The dependence of ion structure on internal energy was examined by generating the ions in proton transfer reactions with different exothermicities and then probing their structures by using energy-resolved mass spectrometry (collision-activated dissociation as a function of collision energy). In contrast to results obtained in several recent investigations, protonated propylene oxide was found to be distinct from its more stable isomers when generated with only a small amount of internal energy. When the exothermicity of the proton transfer reaction was higher than 6 kcal mol^{-1} (1 kcal = 4·184 kJ) or when the epoxide ion was subjected to multiple activating collisions, rapid isomerization to protonated propanal occurred. The energy required for opening of the epoxide ring estimated to be similar to that measured earlier for protonated cyclohexene oxide (5–10 kcal mol^{-1}).

INTRODUCTION

The intrinsic stability of protonated epoxides is of wide interest, in part because of the great importance of acid-catalyzed reactions involving opening of an epoxide ring in organic synthesis and in various biological reactions, such as the metabolic activation of many known or suspected carcinogens.[1–3] The mechanisms proposed for acid-catalyzed ring opening of epoxides range from the attack of a nucleophile on the protonated epoxide with concomitant ring opening in a single kinetic step (a limiting A2 mechanism), to spontaneous cleavage of a C—O bond of the protonated epoxide to give a hydroxycarbenium ion intermediate (a limiting A1 mechanism) which then reacts with a nucleophile.[4–7] Rearrangement of the protonated epoxide to yield a carbonyl compound represents a minor product channel in solution. In sharp contrast, it was suggested recently that protonation of propylene oxide in the gas phase results in rapid isomerization to protonated propanal.[8–10] Indeed, protonated propylene oxide has been depicted to exist in a very shallow potential energy well (3–5 kcal mol^{-1} deep; 1 kcal = 4·184 kJ).[11]

We report here a reinvestigation of the relative stabilities of protonated propylene oxide and its isomers in the gas phase. The isomeric ions were formed in a Fourier transform ion cyclotron resonance mass spectrometer with different amounts of internal energy through the use of a series of reagent ions with various gas-phase acidities. These experiments allowed, for the first time, the generation of stable, protonated propylene oxide in the gas phase. It was demonstrated that although the barrier for opening of the protonated epoxide ring is low (5–10 kcal mol^{-1}), the epoxide ion can be distinguished from its more stable isomers on the basis of energy-resolved collision-activated dissociation.[12–14]

EXPERIMENTAL

All the experiments were carried out on a Fourier transform ion cyclotron resonance (FT-ICR) instrument, a prototype dual-cell Extrel FTMS-2001 mass spectrometer.[15] This instrument has a differentially pumped dual cell (pumped with two Balzers TPU 330 turbomolecular pumps). The dual cell is aligned colinearly with a magnetic field of 3·0 T produced by a superconducting magnet. The two approximately 2 in cubic cells share a common trapping plate which functions as the conductance limit for the differentially pumped system. When ions were transferred from one cell into another through the conductance limit aperture (diameter 2 mm), the conductance limit plate was grounded for about 200 μs. At all other times, a trapping potential of 2 V was applied to all the three trapping plates. All the data shown are averages of at least

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30 spectra acquired at a digitizer rate of 5·3 MHz, and using an excitation sweep with band width 2·7 MHz, sweep rate 3·2 kHz μs^{-1} and amplitude 105 V. The spectra were recorded as 32K data points subjected to one zero fill before Fourier transformation.

The base pressure in each side of the dual cell is less than 1×10^{-9} Torr (1 Torr = 133·3 Pa) (as read by two Bayard–Albert ionization gauges). The ionization gauges were calibrated using common procedures based on the measurement of the rate constants for several well characterized reactions.[16] Sample introduction was accomplished through a Granville–Phillips leak valve, a Varian leak valve or a prototype heated batch inlet equipped with a leak valve. All the compounds used were commercially available and were used as received. Their identification and purity were checked mass spectrometrically. A nominal pressure of 3×10^{-8}–5×10^{-8} Torr was used for each sample and $1{\cdot}5 \times 10^{-7}$–7×10^{-7} Torr for the chemical ionization reagent.

The sequence of voltage pulses used in the FT-ICR experiments is shown in Figure 1. Electron impact ionization (17–50 eV) was used to generate the primary ions from the chemical ionization reagent gas; these ions were used to protonate the reagent gas molecules during the reaction period following the electron beam. After the reaction period, the desired product ions were isolated by ejecting all the unwanted ions from the cell through a combination of radiofrequency voltage pulses and radiofrequency sweeps applied to the cell plates, and transferred into the other side of the dual cell. A 1 s time delay was allowed immediately after ion transfer in order to relax collisionally the ions into the center of the cell in the direction of the magnetic field. Collision-activated dissociation experiments were carried out using argon as the collision target at a nominal pressure of about 1×10^{-7} Torr. An excitation pulse with a fixed amplitude (0·08) V_{p-p}) and a variable duration ($\leqslant 1$ ms) was used to accelerate the mass-selected ions to different final kinetic energies. This was followed by a fixed reaction time (100 ms, unless specified otherwise). Since the ion kinetic energy computed from the infinite electrode approximation is overstated by about 92% for a cubic cell ICR,[17] the computed collision energy was divided by two to obtain the estimated laboratory collision energies reported here. The number of activating collisions that an ion experiences depends mainly on the mass to charge ratio of the ion, its kinetic energy, the pressure of the target gas and the time allowed for collisions. On the basis of the kinetic theory of gases, an ion of m/z 59 with laboratory kinetic energies of 5–100 eV activated by collisions with argon at a nominal pressure of 1×10^{-7} Torr is calculated to undergo an average of 4–20 elastic collisions during 100 ms in the instrument used for this work (four collisions for 5 eV kinetic energy). By increasing the argon pressure to 8×10^{-7} Torr, the average number of elastic collisions is calculated to be 30–140 for the same kinetic energy range; the number of activating (inelastic) collisions, however, is significantly smaller, and difficult to estimate. The number of collisions was varied in this study by varying the argon pressure and by varying the reaction time.

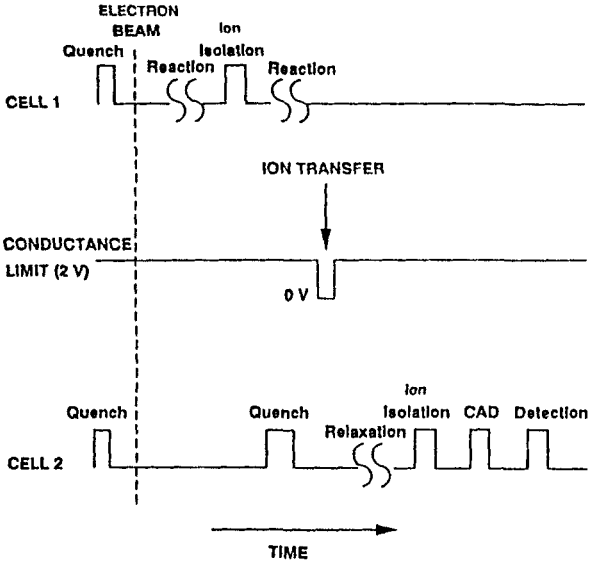

Figure 1. The sequence of voltage pulses used to carry out the experiment shown in Figure 2. Quench refers to removal of all ions from one or both sides of the dual cell through application of an attractive potential on one or several of the trapping plates. In most instances, ion isolation involved more than just one radiofrequency voltage pulse, as illustrated for simplicity. CAD refers to collision-activated dissociation

RESULTS AND DISCUSSION

Isomer distinction

Protonated propylene oxide and protonated propanal were generated in the gas phase by using thermoneutral or near-thermoneutral proton transfer reactions. The acids used in these reactions were formed in the FT-ICR mass spectrometer by self-chemical ionization [Figure 2(a)], i.e. the fragment ions obtained by electron impact ionization-induced dissociation of each reagent gas were used to protonate the neutral reagent molecules. The proton affinities (binding energy to a free proton) of the molecules[18] studied are listed in Table 1. The protonated reagent molecules were isolated by ejecting all the unwanted ions from the cell, and allowed to react with propylene oxide and its isomers [Figure 2(b)]. The ions obtained by protonating propylene oxide [Figure 2(c)], acetone, oxetane and propanal were transferred into the other

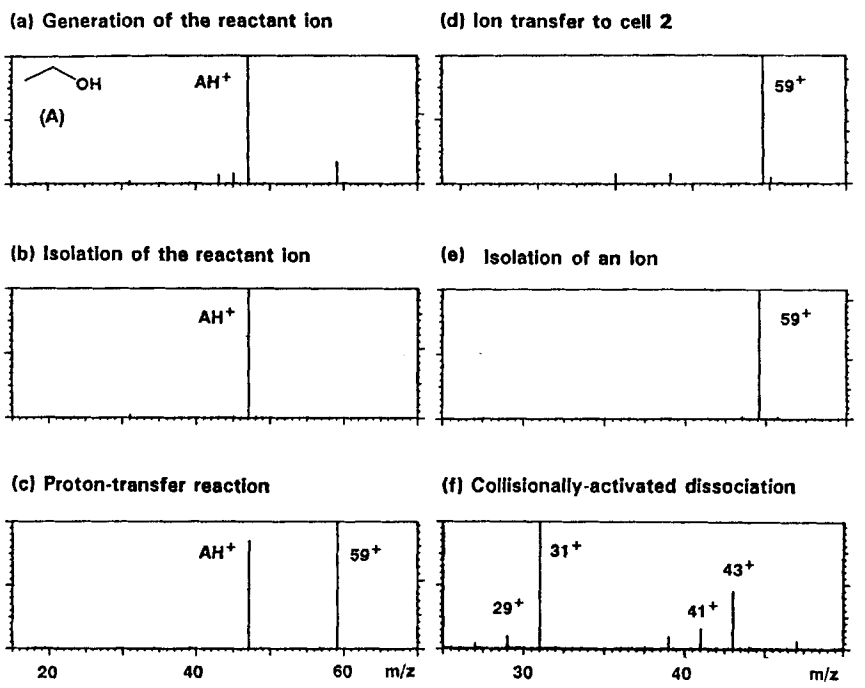

Figure 2. Mass spectra measured at different stages of the multiple-stage mass spectrometry experiment carried out to generate protonated propylene oxide, propanal, oxetane and acetone by using a mass-selected reactant ion (AH^+; parts a–c), and to study the structures of the generated ions m/z 59 by using collision-activated dissociation (parts d–f). The spectra shown are for propylene oxide. (a) Protonated ethanol was generated by self-chemical ionization of ethanol (nominal pressure $1{\cdot}5 \times 10^{-7}$ Torr) for 200 ms, (b) isolated from interfering ions, and (c) used to protonate propylene oxide (nominal pressure $1{\cdot}4 \times 10^{-8}$ Torr) for 1 s. (d) Protonated propylene oxide was transferred into the other cell, (e) isolated and (f) subjected to collision-activated dissociation at a laboratory ion kinetic energy of 100 eV with argon (nominal pressure 1×10^{-7} Torr)

side of the dual-cell reaction chamber [Figure 2(d)], all the unwanted ions were again ejected from the cell [Figure 2(e)] and the ion structures were investigated by collision-activated dissociation as a function of collision energy (energy-resolved mass spectrometry).[12–14] This method allows one to examine the effects of ion internal energy on its fragmentation patterns, and therefore permits the differentiation of many isomeric ions that produce similar dissociation products with different energy requirements.

The energy-resolved mass spectra obtained for protonated propylene oxide generated in a thermoneutral proton transfer reaction are presented in Figure 3(a). These data differ both quantitatively and qualitatively from those measured for protonated propanal [Figure 3(f)]. Most notably, the ion of m/z 43

Table 1. Proton affinities (PA) of the compounds used in this work

Compound	PA (kcal mol^{-1})[a]	Chemical ionization reagent	PA (kcal mol^{-1})[a]
Propylene oxide	194·7	Butane-2,3-dione	194·8
Propanal	189·6	Acetic acid	190·2
Acetone	196·7		
		Ethanol	188·3
Oxetane	196·9	Acetaldehyde	186·6
		Methanol	181·9

[a] All proton affinities are from Ref. 18.

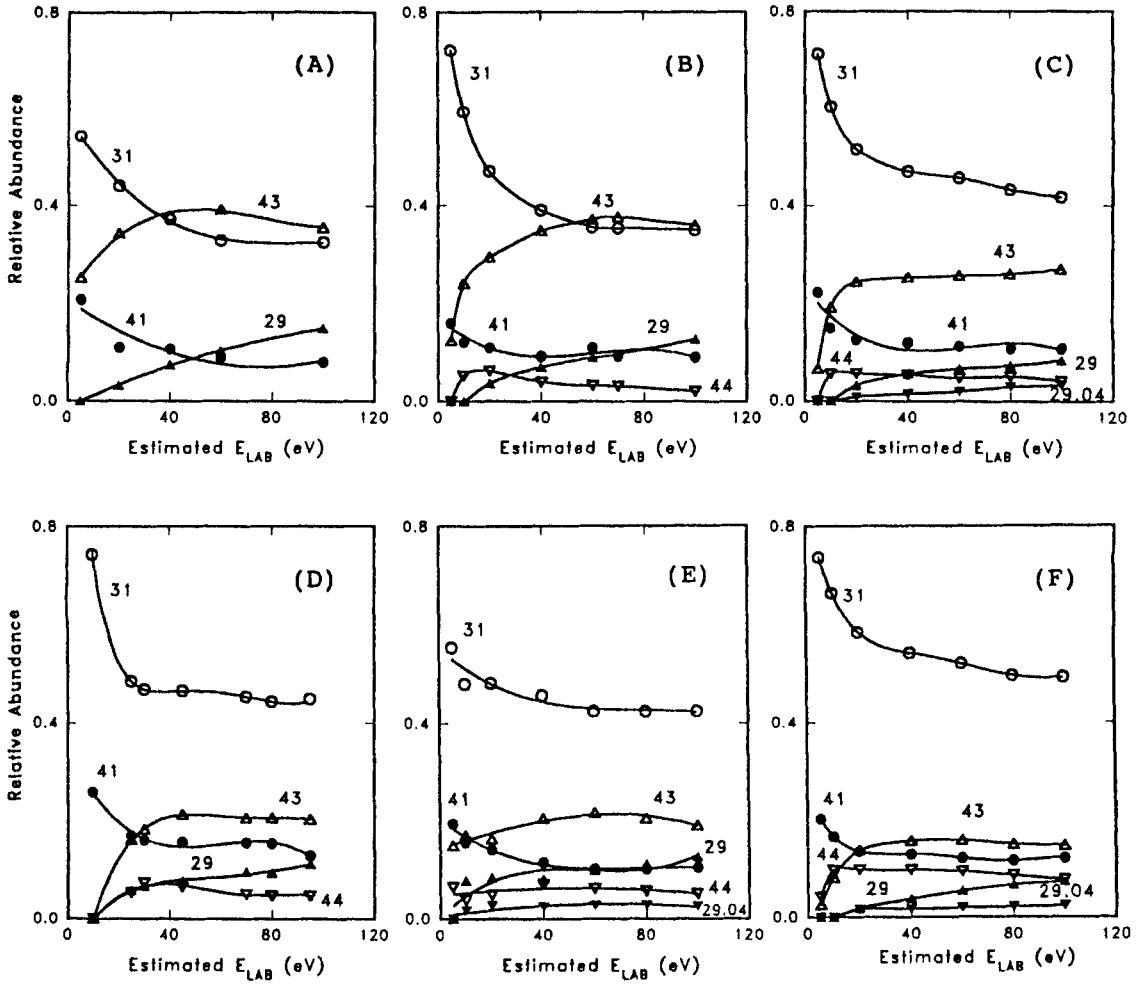

Figure 3. Energy-resolved mass spectra obtained for protonated propylene oxide generated (a) using a thermoneutral proton transfer reaction, (b) a proton transfer reaction with exothermicity of 4·5 kcal mol^{-1}, (c) 6·4 kcal mol^{-1}, (d) 8·1 kcal mol^{-1} and (e) 12·8 kcal mol^{-1}. (f) Energy-resolved mass spectra obtained for protonated propanal generated using a proton transfer reaction with exothermicity of 2 kcal mol^{-1}. A nominal pressure of 1×10^{-7} Torr of argon collision gas and a reaction time of 100 ms were used in all the experiments

($C_2H_3O^+$) formed by loss of methane dominates the dissociation product distribution of protonated propylene oxide at higher collision energies; protonated propanal, however, predominantly generates an ion of *m/z* 31 by loss of ethylene.[19] The qualitative differences between the data sets obtained for the protonated epoxide and for protonated propanal reflect the preference of the protonated epoxide to break a C—O bond rather than a C—C bond. For example, only protonated propanal generates a fragment ion $C_2H_4O^{+\cdot}$ (*m/z* 44) from loss of $CH_3^{\cdot}$. Further, the high mass resolution inherent to the FT-ICR technique allows the identification of two isobaric ions, $C_2H_5^+$ (*m/z* 29·04) and CHO^+ (*m/z* 19·00), for protonated propanal; only the ion CHO^+ is observed for protonated propylene oxide (Figure 4).

The data obtained for protonated propylene oxide are distinctly different from those reported earlier for this ion.[9] The spectra of protonated propanal and protonated oxetane (Figure 5), however, agree well with the earlier data.[9] The fragment ion of *m/z* 15 (CH_3^+), observed in the earlier experiments using a triple quadrupole mass spectrometer,[9] is not detectable in the FT-ICR used in this work because of the limited ability to detect low-mass ions (*m/z* > 16).

Protonated acetone dissociates in a similar manner to

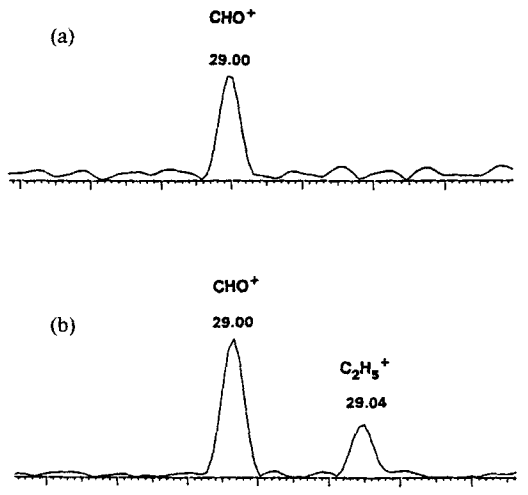

Figure 4. Expansion of the mass region around m/z 29 in the collision-activated dissociation spectrum of (a) protonated propylene oxide and (b) protonated propanal at an estimated laboratory collision energy of 60 eV. Other experimental conditions as in Figures 3(a) and (f)

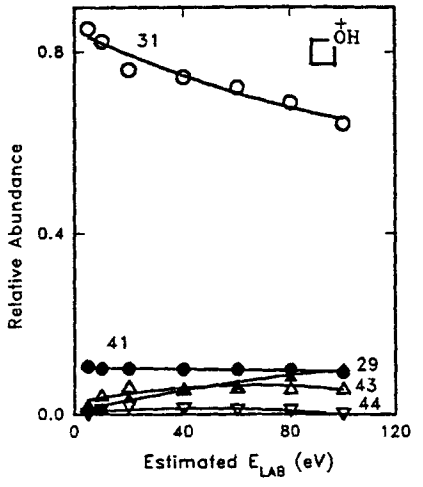

Figure 5. Energy-resolved mass spectra of protonated oxetane generated using protonated methanol

protonated propylene oxide when a small number of activating collisions is employed for both ions (Figure 6); the only difference between these two data sets is the absence of the fragment ion of m/z 44 (from loss of $CH_3^{\cdot}$) for protonated propylene oxide. When a larger number of activating collisions is employed (Figure 7), the dissociation product distributions obtained for these two isomeric ions show more differences. Interestingly, the spectra of protonated propylene oxide obtained under multiple collision conditions

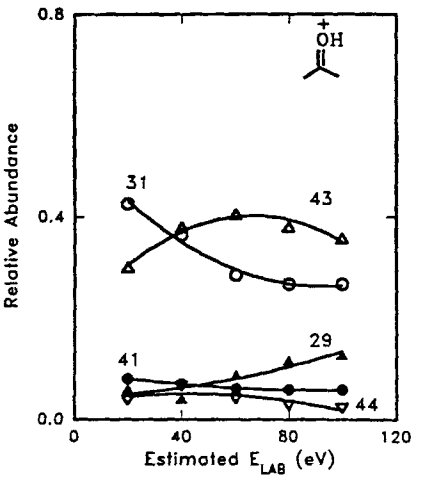

Figure 6. Energy-resolved mass spectra of protonated acetone generated using protonated ethanol

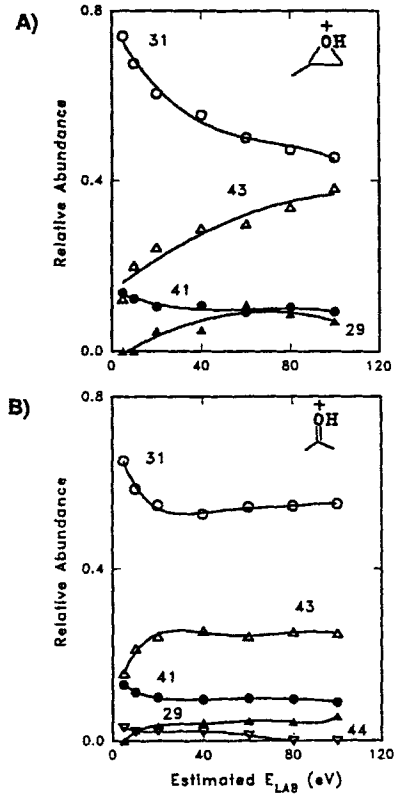

Figure 7. Energy-resolved mass spectra of (a) protonated propylene oxide generated using protonated butane-2,3-dione and (b) protonated acetone generated using protonated ethanol. The spectra were obtained at a nominal argon pressure of 4×10^{-7} Torr and using a reaction time of 200 ms. These conditions result in a large number of activating collisions (see Experimental for details)

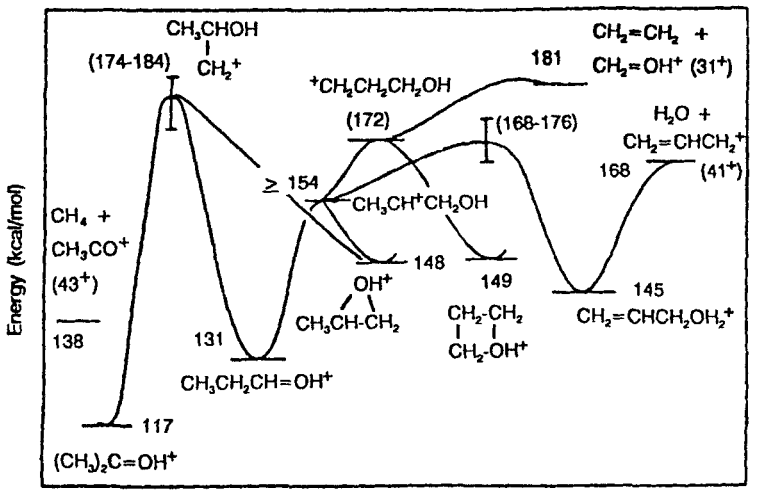

Figure 8. Potential energy surface for the isomerization and dissociation of the ions $C_3H_7O^+$ (adapted from Refs 9, 18 and 20–22, and modified on the basis of the results obtained in this study). Two different mechanisms have been proposed for the formation of the fragment ion of *m/z* 31 (Ref. 11; see also Ref. 19); for simplicity, only one is shown here. Recent *ab initio* molecular orbital calculations[23] are in good agreement with the relative energies shown for protonated propylene oxide and its isomers

resemble more the spectra measured for protonated propanal than those obtained in the experiments where the epoxide ions undergo only a few activating collisions. This finding suggests that collision-induced isomerization occurs for the kinetically excited, protonated epoxide under multiple collision conditions in the gas phase.

The similarities between the dissociation products of protonated propylene oxide and protonated acetone strongly suggest that the protonated, activated propylene oxide ions can undergo ring opening in two different ways: in addition to the energetically favored formation of the secondary carbenium ion intermediate $CH_3CHCH_2OH^+$, a high-energy, primary carbenium ion intermediate $CH_3CH(OH)CH_2^+$ can be generated. The latter intermediate is common with protonated acetone (Figure 8), [20–23] and it is likely to yield the fragment ion of *m/z* 43 (through loss of CH_4), generated in great abundance from protonated propylene oxide and from protonated acetone but not from the other isomers.[11] The ion of *m/z* 43 is assigned the structure CH_3CO^+, as opposed to the other conceivable structure, $CH_2{=}C{=}OH^+$, on the basis of the observation that the ion of *m/z* 43 formed on collision-activated dissociation of protonated acetone cannot be deprotonated by methanol (the proton affinity of methanol is 182 kcal mol^{-1}; that of $CH_2{=}C{=}O$ is 198 kcal mol^{-1} at carbon and 162 kcal mol^{-1} at oxygen).[18]

Isomerization of protonated propylene oxide

In order to obtain information concerning the energy required for isomerization of the epoxide ion, and also to explore the reasons behind the earlier difficulty[8–10] in distinguishing protonated propylene oxide from protonated propanal, the epoxide ion was generated with different amounts of internal energy by using proton transfer reactions with differing exothermicities (0–13 kcal mol^{-1}; Table 1). An earlier study[11] indicated that for the systems of interest, a large fraction (approaching 100%) of the energy released in the protonation reaction is deposited in the product ion. However, the exothermicity of the proton transfer reaction should only be considered as an upper limit for the amount of internal energy gained by the ion.

The ions generated in the proton transfer reactions were collisionally cooled with argon prior to collision-activated dissociation in order to avoid differences in reactivity due to different amounts of internal energy. If the amount of energy deposited in the epoxide on protonation is lower than the activation energy for ring opening, the ion is expected to relax to the ground state of the protonated epoxide structure. However, if the amount of energy deposited is higher than the barrier for ring opening, the internally excited protonated epoxide is likely to isomerize by irreversible ring opening followed by hydride transfer (1,2-hydride transfers are known to be facile in gaseous carbenium ions).[24] During the following collisional cooling period, this ion will relax to the ground state of protonated propanal. It should be noted that the energy of the intermediate for ring opening, $CH_3CH^+CH_2OH$, is likely to be conformation dependent.[25] In fact, it is conceivable that $CH_3CH^+CH_2OH$ formed by ring opening of protonated propylene oxide does not have the lowest-

energy conformation: the C—OH bond is likely to be in-plane with the vacant p-orbital in this conformation, causing hyperconjugative destabilization of the cation.[25] This could cause the barrier for isomerization to be above the heat of formation of $CH_3CH^+CH_2OH$.

The energy-resolved mass spectra measured for protonated propylene oxide are strongly dependent on the exothermicity of the proton transfer reaction [Figures 3(a)–(e)], whereas the data obtained for protonated propanal and for the other isomers do not show a similar sensitivity. The data shown in Figure 3 indicate that most of the epoxide ions retain their original structure when the exothermicity of the proton transfer reaction is $\leqslant 5$ kcal mol^{-1}. However, a significant fraction of the ions generated in reactions with exothermicities from 6 to 13 kcal mol^{-1} have a different structure, most likely that of protonated propanal. It is concluded that the energy required for opening of the protonated epoxide ring must be near 6 kcal mol^{-1}.

CONCLUSIONS

This study concludes a long-standing controversy[8–11] concerning the stability of gaseous protonated propylene oxide towards isomerization. In contrast to earlier results,[8–10] it is conclusively demonstrated that protonated propylene oxide is not just thermodynamically but also kinetically stable towards ring opening in the gas phase. However, isomerization of the epoxide ion to protonated propanal is readily induced if the ion is generated by a proton transfer reaction with exothermicity over 6 kcal mol^{-1}, or if the ion is subjected to multiple activating collisions. These findings may explain the earlier difficulty in distinguishing gaseous protonated propylene oxide from protonated propanal.

Thus far, four protonated epoxides have been demonstrated to be stable in the gas phase. These include the thoroughly studied protonated ethylene oxide (a 25 kcal mol^{-1} energy barrier separates this ion from the intermediate carbenium ion),[26,27] protonated cyclohexene oxide (ring opening requires about 10 kcal mol^{-1}),[28] protonated pent-2-ene oxide,[29] and now also protonated propylene oxide. It is concluded that protonated, unsubstituted epoxides that generate a primary or a secondary carbenium ion intermediate on ring opening are intrinsically stable. This conclusion is in agreement with the general observation that rearrangement of a protonated epoxide is a minor reaction channel in solution.[4–7]

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