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A STEREOCHEMICAL BRIDGE BETWEEN MASS SPECTROMETRY AND FREE RADICAL CHEMISTRY

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INTRODUCTION

Two years before the first commercial mass spectrometer was delivered by Consolidated Engineering Corporation to the Atlantic Refining Company in 1942,[1] Walker Bleakney and his student Charles Cummings reported on the electron impact induced mass spectrometric behavior of methanol and ethanol.[2] Working at Princeton's Palmer Laboratory, Bleakney and his co-workers had constructed a mass spectrometer capable of obtaining data at an unusually high vacuum for the time. This advance allowed the careful measurement of the electron beam energy necessary for the appearance of the molecular ion and some of the fragments derived from it. The so-derived ionization and appearance potentials could be arithmetically manipulated to yield bond energies. In this manner Bleakney discovered[2] that removal of an H atom from methanol required much less energy than the bond strength of H- bound to either C or O. This fact in combination with Mulliken's view[3] that oxygen in methanol has two nonbonding orbitals essentially free from mixing and of low ionization potential led Bleakney and Cummings to propose[2] that the molecule ion produced by electron impact ionization of methanol could be best represented as a species of localized charge on oxygen. It would follow from this hypothesis that adjacent bonds could then be broken so as to complete the bonding to oxygen, making up the octet which was disrupted by the electron beam. Thus the low appearance potential for loss of an H atom would arise because the energy necessary to break the bond would be substantially returned by making a new multiple bond to oxygen (Fig. 1).

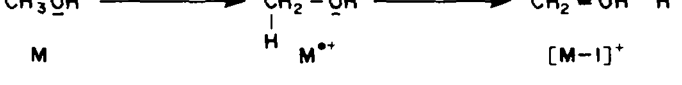


Fig. 1.

The $[M-1]^+$ ion produced from methanol by electron bombardment is now in fact known to involve loss of the carbon bound hydrogen and detailed analysis of the thermochemistry[2,4] and comparison to the behavior of higher alcohols leaves no question that these Princeton workers[2] had the correct idea.[5,6] In modern terms the molecular ion proposed (Fig. 1, $M^{\cdot+}$) would be designated a protonated alkoxy radical and would be a proper subject for study by free radical chemists.[7] In analogy to well investigated neutral alkoxy radicals a species $R\dot{O}H^+$ might be expected to show two general modes of reactivity: (1) α-cleavage; (2) inter- or intramolecular homolytic substitution at hydrogen (abstraction).[7] In a mass spectrometer of the type under discussion here the molecular ion mean free path precludes intermolecular encounters so that only the intramolecular variety of path 2 (above) could be expected. As exhibited in Fig. 2, 2-hexyloxyradical, a free radical of well understood solution phase behavior,[7,8] shows both pathways.

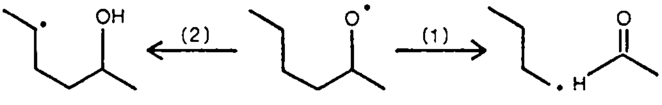


Fig. 2.

It is interesting to note that the intramolecular abstraction step (2) is regiospecific for γ-carbon bound hydrogen. Let us now return to mass spectrometry. Electron impact ionized alcohols, such as for one example, the molecular ion formed from 2-hexanol, exhibit easy loss of water.[9] This expelled water molecule arises largely from the OH group plus a single carbon bound hydrogen. For many years there was great confusion about the source of the itinerant hydrogen. This was finally resolved in 1964 when two independent groups[10] showed that greater than 90% of the loss of water involved γ-carbon bound hydrogen. This is exhibited in Fig. 3 together with the other major pathway of fragmentation: α-cleavage.

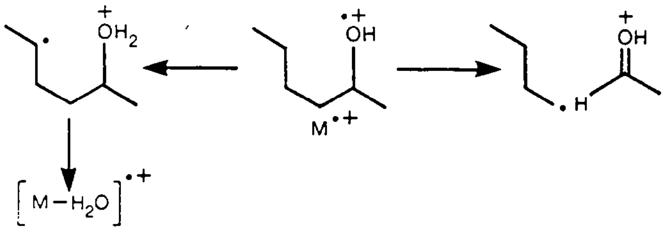


Fig. 3.

The alcohol molecular ions in the mass spectrometer are produced by a Franck–Condon ionization taking approx. 10^{-16} followed by subsequent decomposition along various reaction channels with rates varying from a single vibration to 10^{-6} sec. As mentioned above the decomposition (fragmentation) happens in the absence of all intermolecular contact because the mean free path at the pressures employed is very long compared to the size of the reaction container.[13] The chemistry of the alkoxy free radicals occurs in solution, under conditions of thermal equilibrium and these radicals may be produced by a variety of mechanisms varying from thermolysis to metal oxidation.[7] Yet as seen in the juxtaposition of Fig. 2 and 3 there is a clear, broad correspondence in the means by which these species manifest their instability.

In this report, the detail of this picture of correspondence between free radical chemistry and mass spectrometry is painted in; its theoretical basis is pointed to; its boundaries are explored and its range is shown to be well beyond the tip of the iceberg which Bleakney and Cummings[2] took note of forty years ago.

DISCUSSION

Stereochemistry

Stereochemistry has often demonstrated its power for mechanistic insight[14] and therefore was chosen to amplify the details associated with the correspondence suggested by Figs. 2 and 3.

Following from the chirality of 2-hexanol, the geminal hydrogens on C-5 are related diastereotopically[15] and therefore may be kinetically distinguished in their transfer to the oxygen radical site (Fig. 2 and 3). In order to accomplish this closer look at the hydrogen abstraction step each hydrogen must be replaced in turn by deuterium for a single configuration at the oxygen bearing carbon. This was accomplished via the synthetic procedure outlined in Fig. 4.[16]

That nervous night stands out in memory when after 6 months of synthetic work (Fig. 4)we observed the electron impact induced relative loss of light water to monodeuterowater from each diastereomer (**1A** vs **1B**). The ratios were different and a simple kinetic analysis which isolated the isotope effect (to be discussed below) revealed that the deuterium in **1A** was preferred for transfer and subsequent loss as water over **1B** by 1.10/1.00. We had moreover also prepared the analogous stereoisomers of 5-cyclohexyl-5-deutero-2-pentanol (**2A** and **2B**)[18] and there also the deuterium in **2A** was preferred for transfer over **2B** but in this case by 1.20/1.00. Conversion of the two sets of diastereomers to the derivative alkoxy radicals by $Pb(OAc)_4$ and Ag_2O/Br_2 in turn and measurement of the relative formation of deuterated to undeuterated 2,5 dimethyltetrahydrofurans revealed that these solution phase radicals

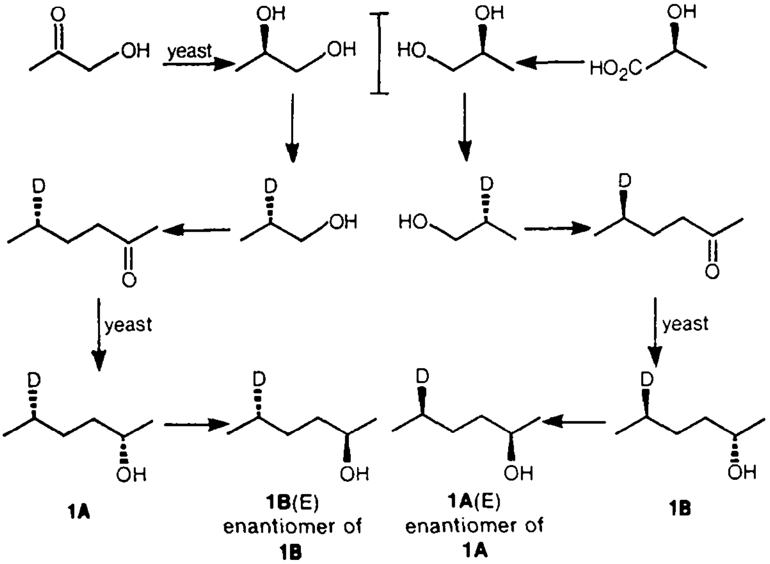
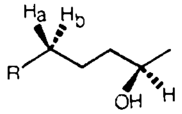


Fig. 4.

showed the same preference for deuterium transfer from **1A** and **2A** over **1B** and **2B** respectively.[16,19] The exact numbers are exhibited in Table 1.

Table 1.[a,b]



	ka/kb		
R	$M-H_2O$ 70 ev	$Pb(OAc)_4$	Ag_2O/Br_2
Methyl	1.10	1.23	1.19
Cyclohexyl	1.20	1.32	1.29

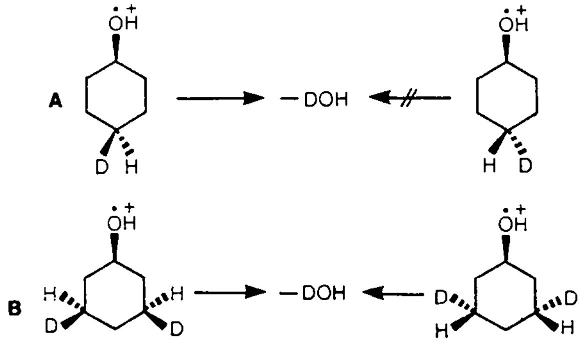
[a] Error limit is ±0.03 in each case. See ref. 16–19.

[b] $M-H_2O$ observed in an MS-902 mass spectrometer. The lead and silver initiated processes took place in hydrocarbon solvent at moderate temperatures.

Whatever may be the theoretical basis for the remarkable correspondence encountered in Table 1, it is clear that there must exist a considerable degree of structural and energetic similarity, including all the conformational factors pertinent to the C-5 hydrogen discrimination, among the various intermediates and transition states. Moreover the unfailing preference for Ha (Table 1) makes conformational sense[20] if the transition state for the hydrogen transfer resembles a 6-membered chair conformation. When Ha is transferred the R group and Me groups are both equatorial whereas for Hb transfer, one of these groups must reside axial.[21]

The elimination of water from the electron impact induced ions of cyclohexanol is not regiospecific for γ-hydrogen[22] and thereby is an apparent exception to the alkoxy radical analogy. The lost molecule of water consists with equal probability of the OH group plus a single hydrogen from either C-4(γ) or C-3(5). Stereospecific deuterium labelling reveals that the two modes of water elimination fundamentally differ. The γ-hydrogen (1,4) process is stereospecific for the hydrogen *cis* to the OH group while the 1,3 process allows access to ***both*** the *cis* and *trans* hydrogens (Fig. 5).[23]

The 1,4 hydrogen abstraction for water elimination from cyclohexanol radical cation (Fig. 5A) may be seen as a sensible extension of the acyclic situation (Fig. 3). The ring may flip into the boat form and present the *cis* C-4 hydrogen for transfer.[24,25] On the contrary the observation of abstraction of hydrogen in cyclohexyloxy radical is very slight. The ring predominately undergoes α-cleavage. The latter event in the cyclohexanol cation radical would adequately explain the nonstereospecific 1,3 process (Fig. 5B).

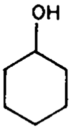
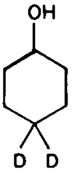
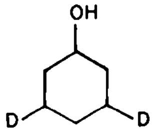


[a] See Ref. 23. In each case loss of light water is also observed.

Fig. 5.[a]

Ring opening would epimerize the C-3(5) deuterated centers. Although a molecule of water could then still find a way to form and be lost it might involve complex steps of molecular ion reorganization which we are not privy to. Such a process of α-cleavage pre-emptive to 1,3 abstraction attractively explains the absence of 1,3 water loss in the acyclic molecular ions of alcohols since the molecular ion falls into two pieces: the molecular ion no longer exists. It would follow that such a bond breaking event prior to 1,3 water loss (Fig. 5B) should raise the energy over that necessary for the straightforward 1,4 elimination (Fig. 5A). This is precisely what is observed (Table 2).[26] As seen from the appearance potential data (Table 2) the loss of DOH requires more energy when located on C-3(5). Thus we see the alkoxy radical competitive themes of hydrogen abstraction and α-cleavage are again likely played in these cyclic molecules in the mass spectrometer. We should not gloss over the fact that 1,4 hydrogen abstraction is more readily observed in cyclohexanol cation radical than in cyclohexyloxyradical. The analogy cannot be taken too far since the solution phase species discussed so far are neutral and those in the mass spectrometer are charged. Before we address this discrepancy (see Isotope Effects below) let us look into an analytical opportunity presented by these results (Fig. 5A).

Table 2. Appearance potential (eV)

	[M-HOH]$^{\cdot+}$	[M-DOH]$^{\cdot+}$
	10.4 ± 0.05	–
	11.1 ± 0.04	10.5 ± 0.06
	10.5 ± 0.10	11.3 ± 0.10

Adolph von Baeyer showed the way for stereochemical assignment of configuration to diastereomers when he utilized the stereospecific elimination of water attendant to anhydride formation only in the *cis* isomer of hexahydroterephthalic acid.[27] The analogy is clear. If elimination of water in the mass spectrometry of cyclic alcohols is stereospecific, why not follow von Baeyer and utilize this for diastereomeric assignment? This possibility appears reasonable when one looks into the details of the mass spectra of the *cis* and *trans* stereoisomers of 4-isopropylcyclohexanol. Although both diastereomers on electron impact eliminate the elements of water, stereospecific deuterium labelling for the C-4 and C-5 tertiary hydrogens reveals that the hydrogen transferred is heavily dependent on molecular geometry.[28] These results are summarized in Fig. 6.

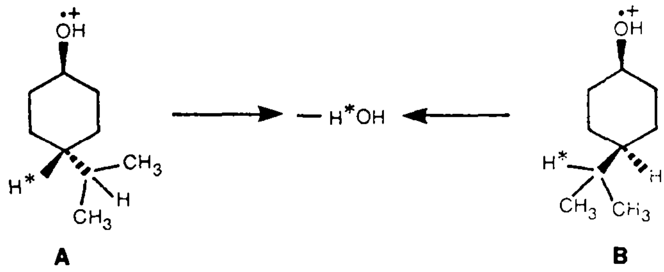


Fig. 6.[28]

Again, here as in cyclohexanol the boat conformation of the intact ring in the molecular ion of the *trans* isomer (Fig. 6A) presents the C-4 hydrogen for abstraction while the boat conformation from the *cis* isomer (Fig. 6B) allows capture of the tertiary hydrogen on the pendant isopropyl group. This geometric dependence for elimination manifests itself in more complex molecular situations. For one excellent example, Klein and Djerassi[29] observed that in the mass spectrometer the 3α-alcohol of 5β-cholane eliminates water far more readily than its 3β-hydroxy epimer. Inspection of these molecules reveals that in the 3α-alcohol the C-9 tertiary hydrogen and the OH group are related precisely as they are in *cis*-4-isopropyl cyclohexanol. Deuterium labelling confirmed the suspicion which follows this observation. This is summarized in Fig. 7.

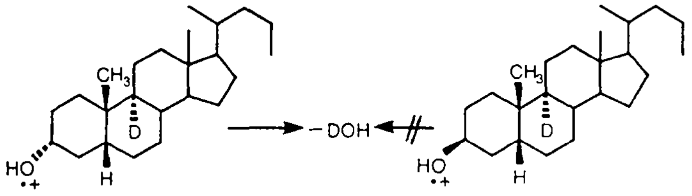


Fig. 7.[29]

Apparently, therefore, certain mass spectrometric fragmentations do offer the opportunity to follow von Baeyer's method of diastereomeric assignment.[27] One pretty utilization comes from the work of MacLeod and Wells.[30] When faced with assignment of configuration to the carbinol epimeric center pictured in Fig. 8, the Canberra group[30] added deuterium to the *exo* face of the double bond and on electron impact observed only the loss of light water. They knew from model observations that if the OH group had faced the deuterated bridge DOH would have been lost. The OH group therefore must face away from the site of deuterium and therefore also away from the site of unsaturation in the molecule which was in hand and in question.

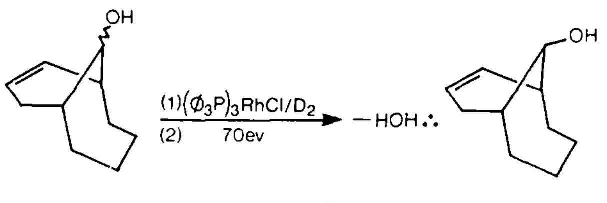


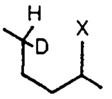
Fig. 8.[30]

This general idea and the body of observed stereochemically dependent mass spectrometric observations on which it rests now form a large literature.[31]

Isotope effects

The rosy picture of correspondence painted above is sullied by a comparison of the hydrogen deuterium kinetic isotope effects for the intramolecular rearrangements in the alkoxy radicals and their mass spectrometric counterparts. These numbers which become available by the same kinetic analysis which yields the stereoselectivities (ka/kb, Table 1)[16–19] are exhibited in Table 3. This large difference in the ability to discriminate hydrogen from deuterium in the electron impact and solution phase reactions can be seen in earlier results in the parallel behavior of the McLafferty rearrangement[32] and the photochemical Norrish Type II reaction[33] of 2-hexanone. Although both fragmentations[32,33] follow the same specific pathway[34] the kinetic isotope effect is nearly six for the photochemically reactive triplet state[35] and nearly one for the cation radical produced in the mass spectrometer.[36]

Table 3.



R	X	kH/kD		
		$\dot{O}H^+$(70 eV)[a]	O·(Pb(OAc))$_4$[b]	O (Ag$_2$O/Br$_2$)[b]
Methyl		1.1	4.6	4.8
Cyclohexyl		1.2	3.8	3.6

[a] Accuracy ±0.2.

[b] Accuracy ±0.5. Precision is much higher. See Ref. 16–19. Temperature for the solution reactions was 81°.

Because isotope effects may be reduced in magnitude by increasing the internal energy of the reacting molecules, as by raising the temperature,[37] the reduced isotope effects in the cation radicals discussed above and in Table 3 could be assigned to a high internal energy residue left by the electron impact ionization process. The immediate conflict is the high stereosensitivity (Table 1) which suggests reactive species which are not excessively energetic compared to their solution counterparts. Moreover theory predicts that rearrangement reactions of the type under discussion here should be constrained to arise from molecular cation radicals of low internal energy.[38,39]

An alternative explanation would relate the low isotope effects (Table 3) to the earlier transition state demands of the cation radical compared to the neutral radicals. Such reasoning would then be related to the long known difference in isotope effect between a Cl atom and Br atom undergoing homolytic substitution at hydrogen or deuterium on the Me group of toluene: kH/kD is nearly one for Cl atom and nearly five for Br atom under the same conditions.[40]

This idea can be tested experimentally because it demands that a γ-hydrogen abstracting thermal cation radical (e.g. in solution) should exhibit the same low isotope effect encountered in the mass spectrometer. One long known free radical reaction[44] and one newly discovered electrochemical reaction[42] presented us with the experimental opportunities to test our notion. Figure 9 exhibits the two reactions.[41,42]

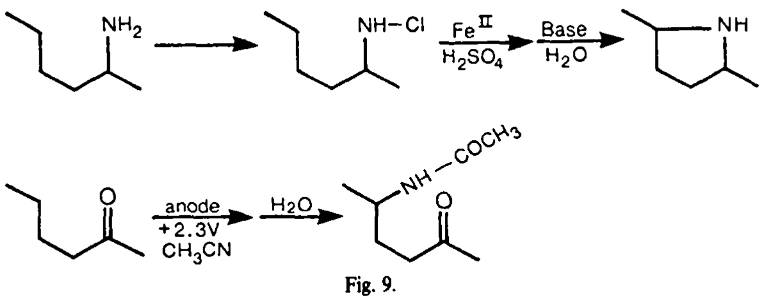


Fig. 9.

In both reactions pictured in Fig. 9 there is strong evidence that the rate determining steps are the intramolecular H atom transfers to the heteroatomic radical sites pictured in Fig. 10.[42,43] The resulting γ-carbon radicals go on to yield the products exhibited in Fig. 9. The processes pictured in Fig. 10A and

B are respectively the mechanistic analogs of the electron impact induced loss of water from alcohols and the McLafferty fragmentation of ketones.[23,32]

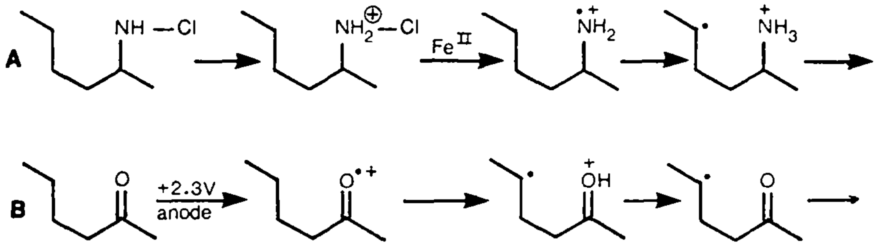
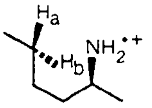


Fig. 10.

Both solution phase reactions allowed measurement of hydrogen deuterium kinetic isotope effects by measurement of the ratio of deuterium to hydrogen in the 2,5 dimethyl pyrollidine and γ-acetamido-2-hexanone derived from the monodeuterated amine and ketone precursors, respectively (Fig. 9). Moreover the chirality of the 2-aminohexane allows revelation of the stereoselectivity of the γ-hydrogen abstraction (analogously to the results in Table 1). These data are exhibited for the Hofmann–Loeffler–Freitag reaction in Table 4.[44] The isotope effect results for the anodic reaction are shown in Table 5. We also remeasured[36] the isotope effect for the electron impact induced McLafferty rearrangement of 2-hexanone and these data appear in Table 6.[45]

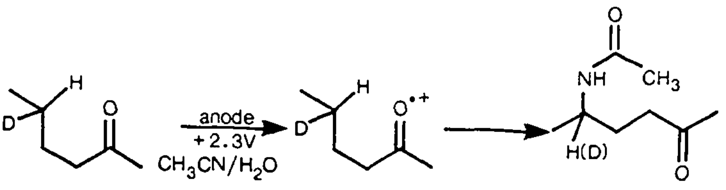
Table 4.[a]



ka/kb	kH/kD
1.5 ± 0.1	1.2 ± 0.1

[a] See Ref. 44 for the details. Conducted in H_2SO_4 at 25°.

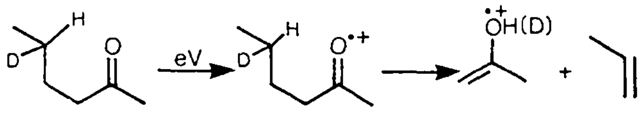
Table 5.[a]



	kH/kD
0°	1.3 ± 0.1
20°	1.5 ± 0.1
40°	1.4 ± 0.2

[a] Conducted in an H-cell at +2.3V following Miller[42] except that $LiBF_4$ was supporting electrolyte.[45] The deuterium incorporation in the product γ-acetamido-2-hexanone was determined by analysis of the molecular ion in the mass spectrometer.

Table 6.[a]



	kH/kD		
temp./eV	50°	75°	125°
10 eV	1.4 ± 0.2	1.4 ± 0.2	1.5 ± 0.2
70 eV	1.6 ± 0.1	—	1.6 ± 0.1

[a] Measured on a DuPont 21-490 mass spectrometer with source temperature specified and ambient inlet. eV uncalibrated and *m/e* 58 to *m/e* 59 ratio corrected for ^{13}C isotope.[45]

Before addressing the isotope effect results note that the amine cation radical shows the same stereochemical preference for Ha (Table 4) as the other γ-hydrogen abstracting radicals in the oxygen series (Table 1). This strongly suggests that the same conformational factors are attendant to all these processes.[21] Moreover the fact that ka/kb is not unity demands that the γ-hydrogen abstraction steps are rate determining and therefore that the low observed isotope effects in the cation radicals (Tables 3 and 4) are related to the nature of the transition state for the γ-hydrogen transfer. Whatever may be the nature of this transition state (see below) it is clear that electron impact is not a necessary prerequisite for the near unity values of kH/kD ($\overset{+}{\mathrm{O}}\mathrm{H}$ in Tables 3 and 4).

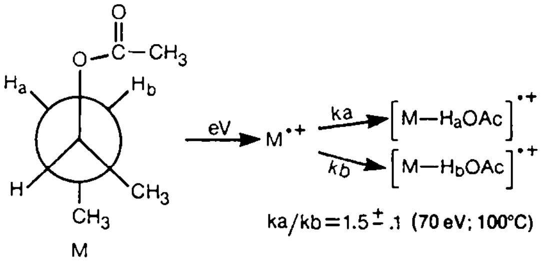
These conclusions are reinforced by the data in Tables 5 and 6. Within experimental precision the hydrogen deuterium kinetic isotope effects for the γ-hydrogen abstraction initiated by electron impact in high vacuum or by anodic voltage at platinum in acetonitrile are the same.[45,46] The cleanest and simplest explanation for these results (Tables 4–6) is that the cation radicals in the mass spectrometer and their thermal counterparts in the dissolved state are of comparable structure and that the low isotope effects are related to the early transition state demands[40] of these reactive charged radicals.[44,45] The bridge spanning mass spectrometry and free radical chemistry is now firmly in place but will be strengthened further below.

A theoretical approach

The results presented above demand some explanation. Enormous energies are utilized in the ionization process in the mass spectrometer and yet we are observing stereosensitivities and chemical behavior comparable to free radicals in the dissolved state at near ambient temperatures. This apparent conundrum yields to a simple argument centered around the quasiequilibrium theory of mass spectrometry.[38] As noted above[39] rearrangement reactions are predicted to occur from molecular ions of the lowest internal energies. Photoelectron spectroscopy demonstrates that in molecules with nonbonding electrons these lowest internal energy ions are produced by removal of an electron from these nonbonding orbitals and furthermore such ionization often gives rise to discrete and narrow bonds separated by an energy space from the broader bonds involving higher energy ionization of bonding electrons.[47] Turner[48] has pointed out that such promotion of nonbonding electrons will produce an ionized state which within reasonable approximation will have the same bonding parameters as the neutral precursor. This is a key point with regard to our inquiry because it follows from the Franck–Condon principle that such a circumstance of equivalent potential surfaces for the ion and its neutral precursor will lead to producing the ionized molecule with the same vibrational and rotational energy as the neutral.[48] Simply put, the "temperature" of the ion[49] produced by removal of a nonbonding electron, within the limits of the above approximations, would be the same as the temperature of the neutral from which it is formed.

Can the limits of the above approximations be gauged? The argument made above is true only when the rearrangement reaction arises from an energy band of infinitesimal breadth. This is so because the energy of the molecular ion in focus here will be the convolution of the thermal energy of the neutral and the ionization energy band from which the fragmentation takes place. A noninfinitesimal band will contribute to the convolution and the vibrational energy of the molecular ion will be greater than for the neutral from which it arose:[50] its "temperature" will be higher. It is never the case that the nonbonding early ionization band in the photoelectron spectrum is infinitesimal in energy breadth although it can be quite narrow.[47] There may be changes on ionization in the local geometry at the heteroatom or the nonbonding electrons may not be entirely unmixed with bonding orbitals. These factors[51] will broaden the band and this is observed.[47,48] Moreover the rearrangement reaction in focus may not be discrete in choosing only the early narrow band as its energy source.

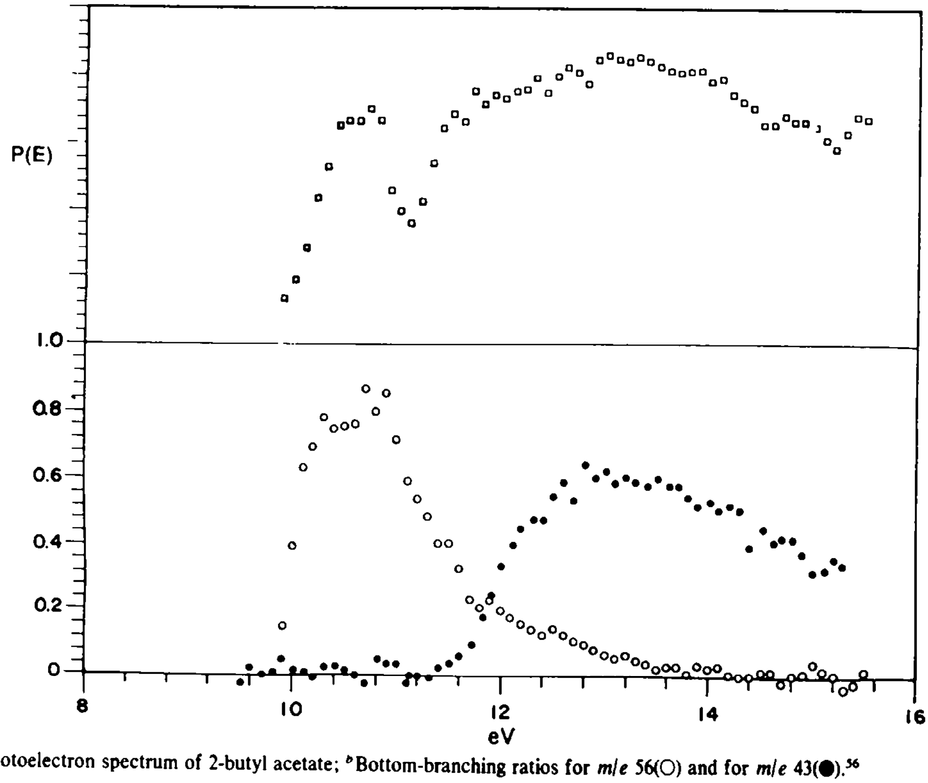
Let's follow these ideas in one particular case. Early observations on the electron impact induced elimination of acetic acid from diastereotopically deuterium labelled 2-butylacetate showed the reaction to be regio and stereoselective[52] as exhibited in Fig. 11.



[a] See Ref. 52.

Fig. 11.[a]

The observation which had been made[53] that the branching ratio ka/kb (Fig. 11) was dependent on the temperature of the neutral and independent of the electron beam energy to near threshold eV is key with respect to our current theoretical inquiries because that is precisely what would be expected following the ideas discussed above. Photoelectron photoion coincidence spectrometry[54] offers a quantitative experimental approach to the source of this phenomenon.[53] The coincidence experiment couples a photoelectron and a mass spectrometer so that the energy of an electron emitted on ionization can be determined in coincidence with the measurement of the mass of the ionic product(s) of that ionization event.[54] Thus that energy section of the photoelectron spectrum responsible for producing any ion fragment becomes known. Because the energy distribution produced by 70 volt electron bombardment and by photonionization are similar,[55] it follows that the photoelectron spectrum of 2-butylacetate and the branching ratios for *m*/*e* 56



[a] Top-photoelectron spectrum of 2-butyl acetate; [b] Bottom-branching ratios for *m*/*e* 56(○) and for *m*/*e* 43(●).[56]

Fig. 12.[a,b]

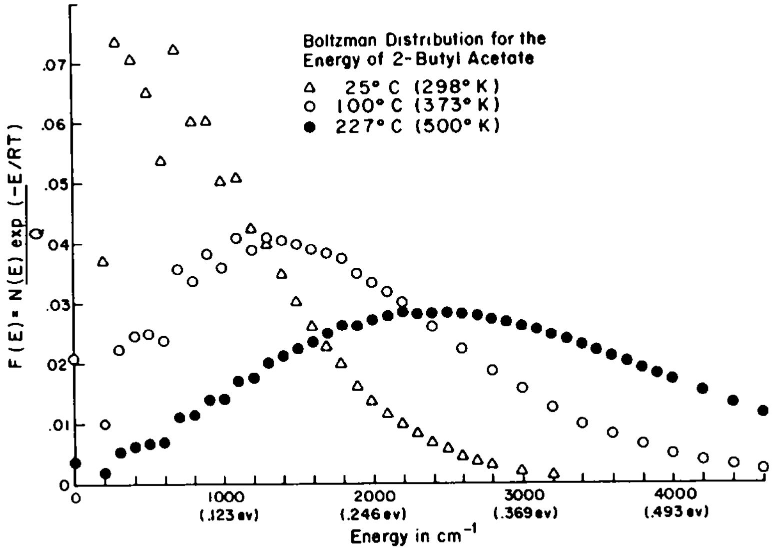
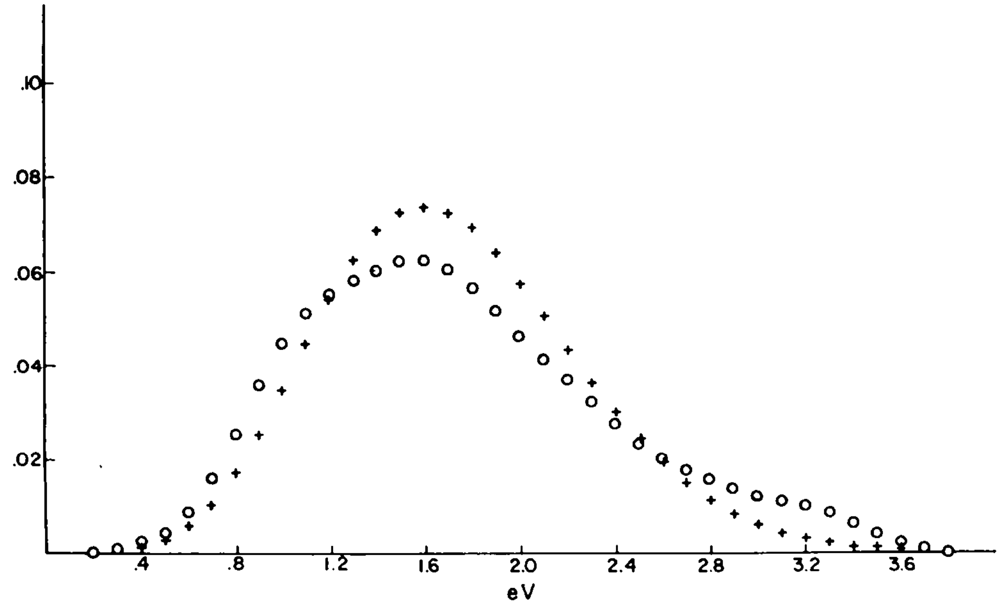


Fig. 13.

(M-HO_2CCH_3) and *m/e* 43 (Fig. 12) are relevant to our mass spectrometric inquiries.[53,56] The observations (Fig. 12) are clearly consistent with the insensitivity of the *m/e* 56 stereoselectivity to beam energy between 70 and 15 eV[53] and as well with a large body of experimental evidence and theoretical prediction: rearrangement (i.e. *m/e* 56) and cleavage (i.e. *m/e* 43) reaction channels should arise from low and high energy molecular cation radicals respectively.[39,57]

As discussed above[50] the Boltzmann distributions of thermal energies for neutral 2-butylacetate at the various temperatures of the ion source need to be fold into the ionization energy deposition to yield the overall energy distribution of the molecular ions for each ion source temperature. These calculated thermal distributions for various temperatures of the precursor neutral molecule are presented in Fig. 13.[58] For the molecular ions fragmenting to expel acetic acid and form *m/e* 56 the overall energy distribution is presented for ion source temperature 500°K in Fig. 14. The approximately overlapping curve has the same average energy and corresponds to a Boltzman thermal distribution of energies for 2-butylacetate at 1096°K. The results strongly suggest that the observed stereosensitivity to ion source temperature[53] reflects the orderly increment



[a](+) thermal distribution for 1096°K; (O) Convolution distribution (see text).

Fig. 14.[a]

of precursor neutral thermal energy to the ionization energy: an approximately thermal distribution is still maintained (Fig. 14). Indeed the molecular ion energy distribution so described (Fig. 14), although not exactly Boltzmann in form, will be maintained by ionization events which are very rapid compared to kinetic events just as rapid collisions in condensed phase maintain the statistical thermal Boltzmann distribution. One could say that the 2-butylacetate molecular ions which yield *m/e* 56 and are formed by electron bombardment in an ion chamber of 500°K have a quasi-temperature of approximately 1100°K.

The experimental and theoretical approach outlined above for the 2-butylacetate system helps to place this unimolecular fragmentation observed in mass spectrometers on energetic grounds more familiar to condensed phase chemistry.[25,52,53]

Strengthening the ties which bind mass spectrometry and free radical chemistry

In discussing future directions for research in free radical chemistry, Walling has pointed out that there is much to be learned in the chemistry of radical ions.[59] The molecular ions encountered in routinely taken mass spectra are precisely such species and strong support for Walling's view is found in the observation of the fragmentation of the molecular ion of 1-hexylchloride in an electron impact mass spectrometer. McLafferty first noted the apparently inexplicable loss of Et radical leaving the even electron ion, $C_4H_8Cl^+$. The first suggestion[60] that the process involved homolytic attack of the halogen radical orbital at the C_4–C_5 bond to form a cyclic halonium ion is exhibited in Fig. 15, and has found strong experimental support in further work from McLafferty's group.[61,62] Deuterium labelling demonstrates that the terminal Et group is expelled and moreover that $C\alpha$ and $C\gamma$ occupy equivalent positions in the product ion.[61] Although formally a simple bond breaking fragmentation the process exhibits the kinetic characteristics of a rearrangement process of low energy of activation,[62] consistent with the mechanism portrayed (Fig. 15).[60] The addition of the fact that the photoelectron spectra of these aliphatic halides show an intense and narrow low ionization band for the nonbonding electrons on halogen identifies the reacting species and crowns this process[60] as the long sought[63] free radical analog of nucleophilic substitution at saturated carbon.[64]

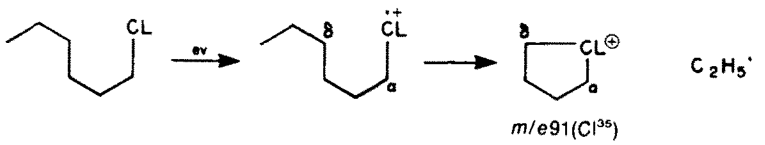


Fig. 15.

In discussing the numerous failures to observe homolytic displacement at carbon either of the inter (SH_2) or intramolecular variety (SHi), Ingold and Roberts suggested that a proper thermochemically designed attempt would be successful.[63] Although no one cleverly took them up on this suggestion[65] the mass spectrometer, as seen below, offered the opportunity serendipitously by involving radical ions in place of radicals. Consider the following competition.[64] Neutral bromine radical approaches a hydrocarbon where two modes of reaction are possible: SH_2 at carbon or at hydrogen. The competitive products are an alkylbromide and hydrogen bromide respectively and the 18 kcal mole^{-1} difference in bond strength favoring hydrogen bromide, if reflected in the transition state, will powerfully direct substitution to hydrogen as is invariably observed.[63] On the contrary, SH_2 reaction by alkylated bromine radical ($RBr^{\cdot +}$) on carbon or hydrogen will produce the competitors dialkylbromonium ion and hydridoalkylbromonium ion respectively. Kinetic evidence[66] and analogy to cabenium ion stabilities suggest that the dialkylhalonium ion is considerably more stable than the hydridoalkylhalonium ion thus favoring SH_2 reaction at carbon as is observed.[67]

CONCLUSION

Mass spectrometers offer opportunities to further our understanding of the nature of free radicals encountered in solution and one can therefore justify reactions occurring in mass spectrometers as proper subjects for study by free radical chemists.[68] One important outcome of such research will be in the area of charged radicals. Such intermediates, in crossing our research boundaries, will act to meld the areas in which they participate.

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