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Secondary kinetic deuterium isotope effects. The CC cleavage of labeled tetramethylethylenediamine radical cations—Who gets to keep the electron?

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Dedicated to the memory of Nico M. M. Nibbering, for many years an important figure in European mass spectrometry research.

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ABSTRACT

The simple cleavage of the C–C bond in tetramethylethylenediamine molecular ions yields two fragments that are identical but for the positions of the charge and radical; nonetheless, the reactions of deuterium labeled analogs are accompanied by substantial secondary kinetic isotope effects. The underlying transition state zero-point vibrational energy differences depend particularly on the properties of the incipient radicals rather than on those of the charge-retaining products. The α-secondary effects arise primarily from vibrations related to deformation of the product –CH_2N– and –CD_2N– groups when the reactant is labeled at the central C–C bond, whereas CH/CD stretching vibrations are the origin of the γ-secondary effects observed for reactants with labeled methyl groups. These zero-point energy differences are mainly due to hyperconjugative interactions (Bohlmann shifts) and do not reflect bonding changes in the transition state; the secondary isotope effects on the dissociation of protonated amine dimers have a similar origin.

1. Introduction

Isotope labeling is often used to examine reactions and reaction mechanisms when ions react in mass spectrometers, to provide structural information and to study dynamical aspects of the processes. Kinetic isotope effects arise when the isotopic substitution influences the rate of reactions; the effects are called ‘primary’ when bonds to the isotopic atom are formed or broken during the reaction, ‘secondary’ otherwise.

Kinetic isotope effects on unimolecular gas-phase reactions of ions are generally examined in intramolecular experiments, in studies of symmetrical (apart from the isotopic substitution) reactants [1]. The first systematic results in this area were reported by Neeter and Nibbering [2], who described the secondary kinetic isotope effects that accompany the loss of CH_3 and CD_3 radicals from the molecular ions of deuterium labeled *tert*-butylbenzene and *tert*-butylpyridine (Scheme 1a).

Most reported studies of secondary isotope effects examine the rate of cleavage of two different bonds, but for certain bifunctional molecules the competition involves cleavage of only one bond. One example is the fragmentation of the tetramethylethylenediamine (TMEDA) molecular ion (Scheme 2), where cleavage of the central C–C bond produces two fragments that are identical except for the location of the charge and radical. The cleavage of deuterium labeled TMEDA molecular ions exhibit remarkable secondary kinetic isotope effects (Fig. 1A–C).

2. Methods

2.1. Instrumental and computational methods

The spontaneous fragmentation reactions of metastable TMEDA molecular ions formed by 70 eV electron ionization were studied with mass analyzed ion kinetic energy (MIKE) spectrometry [4]. The MIKE spectra were recorded on a JEOL HX110/HX110A four-sector mass spectrometer (EBEB) operated in three-sector mode; the reactions examined take place in front of the second E-sector.

The Gaussian 09 suite of programs [8] was used to determine structure and harmonic vibrational frequencies with several wave-function and density functional theory methods, employing

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a variety of basis sets. They all yield qualitatively the same results; typical values in Tables 1–3 . Calculations examining the stretching of the TMEDA radical cation CC bond (from 1.5 to 4.0 Å in 0.05 Å increments) were performed with UMP2/6-311+G(d,p).

2.2. Labeled compounds

The deuterium labeled tetramethylethylenediamines were prepared by unexceptional methods, as shown in Scheme 3. Identity and purity of the products was ascertained by ^{13}C NMR spectroscopy and GC–MS. The deuterium incorporation was better than 97% in all three instances.

3. Results and discussion

3.1. Secondary kinetic isotope effects

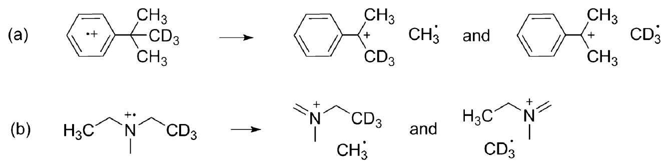
The secondary kinetic isotope effect is defined as the ratio of the rate constants of two near-identical reactions that differ only with regard to isotopic substitution. The origin is nearly always the difference between the transition state zero-point vibrational energies (zpve). The isotope effect is labeled 'normal' if the pathway least likely to be influenced by the isotopic substitution is preferrred.

The reactions shown in Scheme 1 are influenced by 'normal' isotope effects; loss of $CH_{3.}$ is in both cases favored over loss of CD_3. The relative yield of the competing reactions is determined by two effects, the zpve-consequences of releasing $CH_{3.}$ or $CD_{3.}$, and the zpve-consequences of forming a labeled or unlabeled cation. The deuterium substitution gives rise to an α-secondary isotope effect on the amine fragmentation where the properties of the incipient methyl radical in particular influence the transition state zero-point vibrational energy. The fragmentation of the *tert*-butylbenzene ions involves the combination of an α-secondary effect (on the loss of methyl) and a β-secondary effect (on the formation of the benzyl ion).

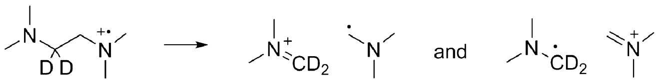
Isotope effects that give rise to peaks of unequal size in 70 eV electron ionization mass spectra are in most cases difficult to interpret. The ion-source fragmentation involves reactions with rate constants that span five orders of magnitude, and the internal energy of the reacting ions can be correspondingly different. However, field ionization kinetics studies illustrate that statistical weight effects in addition to zpve-differences can influence picosecond simple cleavage reactions of amine radical cations with deuterium at remote positions [3].

The reactions of metastable ions, on the other hand, involve reactants with a relatively narrowly delimited internal energy distribution. In particular, the metastable molecular ions that react by straight-forward simple cleavage are those with insufficient internal energy to react rapidly (in the ion source), yet enough to react at all. The metastable ion energy distribution, the 'metastable window', depends on the critical energy of the prominent ion source cleavage reactions.

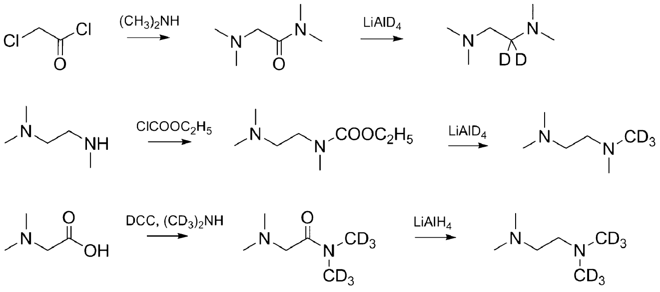
The metastable peaks that reflect reactions influenced by kinetic isotope effects are conveniently examined with mass analyzed ion kinetic energy spectroscopy (the MIKE technique) [4]. The ratio of these peaks (heights or areas) represents the ratio of rate constants of the two near-identical reactions, averaged over the internal energy distibution of the reacting ions, under the assumption that the two rate constants rise equally with increasing internal energy, that the two $k(E)$ curves are parallel.



Scheme 1. Typical simple cleavage reactions that are influenced by normal secondary kinetic deuterium isotope effects.



Scheme 2. The cleavage of tetramethylethylenediamine-d$_2$ molecular ions.



Scheme 3. Preparation of deuterium labeled tetramethylethylenediamines.

3.1.1. Variations

As the ratio of energy-dependent rate constants, the magnitude of the kinetic isotope effect depends on the internal energy of the reacting ions [5] and on the difference between the critical energies of the two reaction channels, that is, on the difference between the transition state zero-point vibrational energies. The isotope effect is further influenced by factors that modify the excess energy of the reacting ions.

The influence of isotopic substitution on the relative rates of simple cleavage reactions with no energy barrier other than the reaction endothermicity can be accounted for with simple RRKM considerations, particularly when comparing isotope effects on the reactions of related metastable ions, or describing the variation of isotope effects with changed reaction conditions. Secondary isotope effects are particularly prominent for low-energy reactants. The consequences of small differences between the critical energies of competing reactions become relatively less important if the internal energy increases, and the isotope effect diminishes accordingly.

Among the metastable ions, the higher-energy segment makes the more important contribution to the observed isotope effect because the reaction probability [6] is a function of internal energy. The higher-energy reactants will show the lower isotope effect, and the isotope effect observed should therefore increase if there is selective depletion of the higher-energy metastable reactant ions. This will be the case in the presence of a third, competing, reaction, which will increase the difference between the yield of the isotopically different reactions (a competitive shift [7]). The apparent isotope effect then changes (increases), but the rate constants of the two competing reactions do not.

Reactions with higher critical energy should exhibit lower isotope effects, because the kinetic shift [7] will allow an increased proportion of higher-energy molecular ions to survive long enough to appear as metastable ions. Likewise, the reactions of larger reactant ions should exhibit decreased isotope effects, because an increased number of degrees of freedom will also result in a kinetic shift and allow more higher-energy molecular ions to reach the mass spectrometer field-free regions. Conversely, the reactions of heavier reactant ions should exhibit an increased isotope effect, as these ions will be older when they reach the field-free regions, as