Mechanistic Inferences from Deuterium Isotope Effects on Competing Metastable Decompositions of Organic Ions

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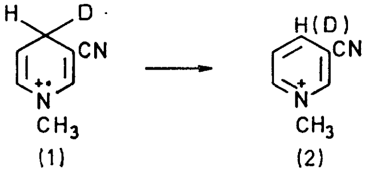
Substantial changes in relative abundances of competing metastable transitions from organic ions in the mass spectrometer are shown to occur in certain cases on partial or complete deuteriation. In the case of benzene, primary isotope effects occur upon the loss of H and H_2 from the molecular ion. The occurrence of a primary isotope effect on the loss of Cl from the molecular ion of *p*-chloroethylbenzene is demonstrated by this method and this isotope effect strongly implicates a rearrangement (probably to a 7-membered-ring isomer) before loss of Cl. A quasi-equilibrium theory calculation is carried out to illustrate that a change in relative metastable abundance by a factor of 2·4 is consistent with a primary isotope effect upon one of the reactions. A rearrangement is also inferred from isotope-effect data for the elimination of Br from *p*-bromoethylbenzene.

DEUTERIUM kinetic isotope effects have found wide use in the elucidation of organic reaction mechanisms.[1] Their simplest use lies in deciding whether a bond to hydrogen is broken in the rate-determining step of the reaction. In this way, mechanistic information can be constructed.

In organic mass spectrometry, although isotope effects on unimolecular reaction rates have been recognised qualitatively, few quantitative assessments have been attempted.[2-5] An effective way to determine an isotope effect in the conventional mass spectrometer has been to measure relative ion yields of reactions from a specifically deuteriated ion. For example, the $[M^+ - H]:[M^+ - D]$ ratio in the spectrum of (1) readily yields information on the intramolecular primary deuterium isotope effect for the reaction (1) ⟶ (2).[2] Consistent with theory, the largest isotope effects have been found in lowest-energy ions,[2-5] *e.g.*, in metastable transitions.[5]



(1) (2)

A serious drawback to this method of isotope effect measurement in many cases is the occurrence of H–D scrambling between the reaction site and the rest of the ion. Even if scrambling does occur, it may be possible to determine isotope effects in some cases. For example, scrambling is not a problem in $CH_3{\cdot}CD_3$ since H and D occupy equivalent positions [3] and in the molecular ion of toluene (singly and doubly charged) isotope effects have been measured, despite extensive scrambling, by use of several different deuteriated samples.[5-7]

Quantitative measurements have concentrated on loss of H or H_2 from molecular ions and occurrence of isotope effects in such cases is not surprising. However, it is possible to investigate isotope effects on reactions not involving elimination of a hydrogen-containing neutral molecule by use of a competing reference reaction from the organic ion under study. For example, an isotope effect on loss of CO from the molecular ion of *p*-bromophenol, $p\text{-Br}{\cdot}C_6H_4{\cdot}OH$, has been detected by measurement of competing metastable ion abundances for CO and Br loss in the undeuteriated compound and in $p\text{-Br}{\cdot}C_6H_4{\cdot}OD$.[8] Similarly, a deuterium isotope effect has been shown to operate on HCN loss from *p*-chloroaniline.[9]

This paper reports the effect of partial or complete deuteriation on relative abundances of competing metastable reactions and shows how valuable mechanistic information, concerning ring expansions and stepwise rearrangements, can be gleaned from the data.

RESULTS AND DISCUSSION

Benzene.—A suitable molecular ion for illustration of the effects of perdeuteriation on competing metastable ion abundances is that of benzene. Five reactions accompanied by appropriate metastable peaks have previously been observed from the benzene molecular ion and the metastable transitions from molecular ions containing ^2H and/or ^{13}C have indicated extensive hydrogen and carbon scrambling.[10-12]

Consider the relative metastable ion abundances for the five reactions from the molecular ions of benzene and $[^2H_6]$benzene (Table 1).

It is evident that the abundances of the metastable ions formed by loss of CH_3, C_2H_2, and C_3H_3 increase on perdeuteriation relative to those involving loss of H and

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[1] See, for example, (*a*) L. Melander, ' Isotope Effects on Reaction Rates,' Ronald Press, New York, 1960; (*b*) K. B. Wiberg, ' Physical Organic Chemistry,' Wiley, New York, 1966, p. 351.

[2] B. J.-S. Wang and E. R. Thornton, *J. Amer. Chem. Soc.*, 1968, **90**, 1216.

[3] U. Löhle and Ch. Ottinger, *J. Chem. Phys.*, 1969, **51**, 3097.

[4] M. Vestal and J. H. Futrell, *J. Chem. Phys.*, 1970, **52**, 978.

[5] I. Howe and F. W. McLafferty, *J. Amer. Chem. Soc.*, 1971, **93**, 99.

[6] J. H. Beynon, J. E. Corn, W. E. Baitinger, R. M. Caprioli, and R. A. Benkeser, *Org. Mass Spectrometry*, 1970, **3**, 1371.

[7] T. Ast, J. H. Beynon, and R. G. Cooks, *J. Amer. Chem. Soc.*, 1972, **94**, 1834.

[8] I. Howe and D. H. Williams, *Chem. Comm.*, 1971, 1195.

[9] N. A. Uccella, I. Howe, and D. H. Williams, *Org. Mass Spectrometry*, 1972, **6**, 229.

[10] K. R. Jennings, *Z. Naturforsch.*, 1967, **22a**, 454.

[11] I. Horman, A. N. H. Yeo, and D. H. Williams, *J. Amer. Chem. Soc.*, 1970, **92**, 2131.

[12] R. J. Dickinson and D. H. Williams, *J. Chem. Soc.* (*B*), 1971, 249.

H_2. The explanation is that loss of H and H_2 involve C–H bond rupture in the rate-determining step. Hence in the $C_6D_6^{+\cdot}$ molecular ion, the rate of loss of D and D_2 is suppressed relative to loss of CD_3, C_2D_2, and C_3D_3 owing to a primary isotope effect on the first two reactions. The inference is that the other three reactions do not involve a carbon–hydrogen rupture in the rate-determining step, a situation which is wholly feasible. A qualitative interpretation of these results in terms of the quasi-equilibrium theory of mass spectra[13] may be found in the rate–energy curves for benzene.[14] In $C_6D_6^{+\cdot}$, the activation energies for D and D_2 loss are elevated by up to 0·1 eV relative to the $C_6H_6^{+\cdot}$ case, thus allowing the other three reactions to compete more effectively at energies yielding metastable ions. Benzene has been cited as a case for which isolated states should be considered because of the wide range of appearance potentials for the five reactions,[15] but the results in Table 1 support the validity of the quasi-equilibrium theory in the benzene molecular ion.[14] The effect of deuteriation on plots of k against E will be considered in more detail below, with reference to *p*-chloroethylbenzene.

TABLE 1

Relative metastable abundances * for reactions from the molecular ions of benzene and [$^2H_6$]benzene

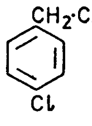
$C_6H_6^{+\cdot}$ Neutral fragment eliminated	Relative abundance	$C_6D_6^{+\cdot}$ Neutral fragment eliminated	Relative abundance
H	1000	D	1000
H_2	170 ± 10	D_2	190 ± 5
CH_3	2·3 ± 0·1	CD_3	5·3 ± 0·1
C_2H_2	140 ± 10	C_2D_2	330 ± 5
C_3H_3	41 ± 2	C_3D_3	98 ± 2

* First drift region (refocussed mode), A.E.I. MS9 mass spectrometer.

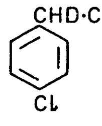
Concerning the structure of the decomposing benzene ions which undergo the five reactions, it is only *necessary* to suggest a rearranged structure in the case of loss of CH_3. Considerable internal rearrangement is possible in the benzene ion before the metastable transitions, since the internal energy is in excess of 4 eV.

p-*Chloroethylbenzene*.—The rearrangement of ions containing benzylic groups to seven-membered ring isomers before decomposition in the mass spectrometer has been a vexing question, but in certain cases deuterium isotope effects on competing metastable transitions provide a means of confirming or refuting the rearrangement.

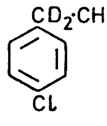
p-Chloroethylbenzene (3) provides a suitable model for study, since the molecular ion eliminates chlorine and methyl radicals in competing reactions in the first drift region. Specific deuteriation of the benzylic position (4) and (5) was undertaken to investigate the possibility that a benzylic carbon–hydrogen bond might be broken in the rate-determining step of either of these reactions. Accordingly the metastable peak intensity ratio $m^*[M^+ - Cl] : m^*[M^+ - CH_3]$ was measured for each of the compounds (3)—(5) (see Table 2).



(3)



(4)



(5)

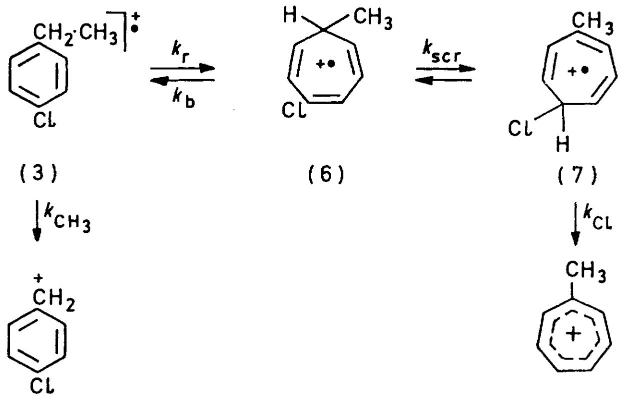
There is no H–D scrambling between the α- and β-positions of the molecular ion. Therefore no complications arise over the $M^+ \longrightarrow M^+ - CH_3$ reaction in compounds (4) and (5) and the reaction is uniquely defined by one metastable peak.

TABLE 2

Metastable peak intensity ratios (first drift region) from some aromatic compounds, illustrating deuterium isotope effects

No.	Compound	Ratio measured	Value
(3)	*p*-Cl·C_6H_4·CH_2·CH_3	$[M^+ - Cl] : [M^+ - CH_3]$	3·71 ± 0·20
(4)	*p*-Cl·C_6H_4·CHD·CH_3	$[M^+ - Cl] : [M^+ - CH_3]$	1·83 ± 0·06
(5)	*p*-Cl·C_6H_4·CD_2·CH_3	$[M^+ - Cl] : [M^+ - CH_3]$	1·37 ± 0·05
(8)	*p*-Br·C_6H_4·CH_2·CH_3	$[M^+ - Br] : [M^+ - CH_3]$	4·23 ± 0·03
(9)	*p*-Br·C_6H_4·CD_2·CH_3	$[M^+ - Br] : [M^+ - CH_3]$	1·92 ± 0·20

The results show that the rate of Cl loss in the metastable drift region is suppressed relative to CH_3 loss in compounds (4) and (5) compared with compound (3). The considerable change in the metastable peak intensity ratio [a factor of 2·7 between compounds (3) and (5)] is consistent with a primary isotope effect on the rate of Cl loss (see calculation below), with no isotope effect on the rate of CH_3 loss. These data are interpreted as shown in the Scheme.



SCHEME

Competition occurs in the molecular ion between

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[13] H. M. Rosenstock, M. B. Wallenstein, A. L. Wahrhaftig, and H. Eyring, *Proc. Nat. Acad. Sci.*, 1952, **38**, 667.

[14] M. L. Vestal, in 'Fundamental Processes in Radiation Chemistry,' ed. P. Ausloos, Wiley–Interscience, New York, 1968.

[15] H. M. Rosenstock and M. Krauss, in 'Mass Spectrometry of Organic Ions,' ed. F. W. McLafferty, chap. 1, p. 36.

direct loss of methyl and a rearrangement to the 7-membered ring (6). This rearranged isomer then scrambles hydrogen and deuterium atoms to a configuration (7) favourable to eliminate chlorine. The rate of loss of chlorine is fast compared with reversion to the benzylic structure (3) (*i.e.*, $k_{\mathrm{Cl}} > k_{\mathrm{b}}$). The importance of the isotope effect is found in the reactions of the unrearranged molecular ion. There is a primary kinetic isotope effect on the rearrangement (which involves a hydrogen transfer) but not on the direct loss of methyl. If it is assumed that these two reactions are in direct competition, and since k_{r} decreases relative to $k_{\mathrm{CH_3}}$ on deuteriation, there will be a corresponding decrease in the metastable yield of $M^{+} - \mathrm{Cl}$ compared with $M^{+} - \mathrm{CH_3}$ (see quasi-equilibrium theory calculation below).

There is another test which can be applied to competing reactions to determine whether one of the reactions might be a rearrangement. It has been pointed out[16] that rearrangements (which often have low activation energies and tight transition states) become more prevalent relative to direct cleavages (higher activation energies and loose transition states) at low electron energy. The variation of $[M^{+} - \mathrm{Cl}] : [M^{+} - \mathrm{CH_3}]$ with electron energy is shown in Table 3. It is evident that the $M^{+} \longrightarrow M^{+} - \mathrm{Cl}$ reaction becomes more prevalent at low molecular ion energies [see also the metastable peak intensity ratio for compound (3) in Table 2]. Hence this reaction has the properties of a rearrangement.

TABLE 3

Daughter-ion intensities as a function of electron energy (nominal)

No.	Compound	Ratio	Energy/eV 70	30	20	16	12	10	8
(3)	p-Cl·C_6H_4·C_2H_5	$\frac{[M^{+} - \mathrm{Cl}]}{[M^{+} - \mathrm{CH_3}]}$	0·50	0·50	0·55	0·56	0·57	0·60	0·64
(8)	p-Br·C_6H_4·C_2H_5	$\frac{[M^{+} - \mathrm{Br}]}{[M^{+} - \mathrm{CH_3}]}$	0·68	0·69	0·70	0·73	0·74	0·74	0·87

Quasi-equilibrium Theory Calculation.—In neutral chemistry, experience has shown that the primary kinetic isotope effect $k_{\mathrm{H}}/k_{\mathrm{D}}$ commonly lies in the range 5—8 at 25 °C, although isotope effects for reactions having non-linear activated complexes may be somewhat smaller.[1b] In order to evaluate the change in metastable peak intensity ratios that might be expected by a primary isotope effect on one of the reactions, we have carried out a quasi-equilibrium theory calculation on p-chloroethylbenzene.

The curves of k against E for the rearrangement and for the loss of methyl were computed by use of the improved form of the quasi-equilibrium theory with the formula of Vestal *et al.*[14,17] for estimating the density of state functions for a collection of harmonic oscillators. A tight transition state was assumed for the rearrangement reaction (k_{r}) and a loose transition state for the loss of methyl ($k_{\mathrm{CH_3}}$) by direct cleavage. The activation energies for the two reactions were estimated by measuring the respective appearance potentials and adjusting the activation energy E_0 until the particular rate constant acquired a value of 10^5 s^{-1} at the appearance potential.

The relevant curves of k against E are shown in the Figure. It is evident that for the direct cleavage (loss of CH_3) it rises more steeply than that for the rearrangement which controls Cl loss. The two curves cross at $k = 1{\cdot}5 \times 10^7$ s^{-1}.

Metastable abundance ratios are calculated from these curves by employing the formula[18] (1) where $E_{\mathrm{max.}}$

$$\frac{m_{\mathrm{A}}^*}{m_{\mathrm{B}}^*} = \frac{\displaystyle\int_{E_0}^{E_{\mathrm{max.}}} k_{\mathrm{A}}/(k_{\mathrm{A}} + k_{\mathrm{B}}) \,.\, P(E)\, [\exp\,(k_{\mathrm{A}} + k_{\mathrm{B}})t_1 - \exp\,(k_{\mathrm{A}} + k_{\mathrm{B}})t_2]}{\displaystyle\int_{E_0}^{E_{\mathrm{max.}}} k_{\mathrm{B}}/(k_{\mathrm{A}} + k_{\mathrm{B}}) \,.\, P(E)\, [\exp\,(k_{\mathrm{A}} + k_{\mathrm{B}})t_1 - \exp\,(k_{\mathrm{A}} + k_{\mathrm{B}})t_2]} \qquad (1)$$

is the maximum internal energy of the molecular ion, $P(E)\mathrm{d}E$ is the fraction of molecular ions with energy between E and $E + \mathrm{d}E$, and t_1 and t_2 are the times taken respectively for ions to reach the beginning and end of the first drift region. t_1 Was taken as 5×10^{-6} s and t_2 as 10^{-5} s. $P(E)$ Was taken to be effectively constant over the narrow 'metastable energy range'. Ions having a rate constant greater than $10^{6{\cdot}5}$ s^{-1} make little contribution to the metastable abundance and integration above the corresponding energy is not necessary.

A metastable peak intensity ratio ($m^*\mathrm{Cl} : m^*\mathrm{CH_3}$) for compound (3) of **3·6** is computed and the Figure shows that a metastable ratio of this order is predicted, since the relative k values of the two reactions differ by about $\frac{1}{2}$ log unit in the $k = 10^5$ s^{-1} region.

It is emphasised that errors in determination of ionisation potentials and appearance potentials and the uncertainty in some of the parameters may cause an absolute error in a given k–E profile. However, the curves of k against E having been determined and found to give good agreement between the observed and calculated metastable peak intensity ratios, the effect of deuteriation on these curves, and hence on the metastable ratio, can be predicted with confidence.

Curves of k against E were therefore computed for the deuteriated compound (5). In the case of the rearrangement reaction there is a primary isotope effect on the

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[16] D. H. Williams and R. G. Cooks, *Chem. Comm.*, 1968, 663.

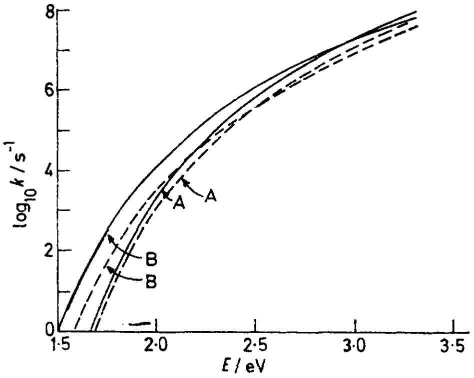
[17] M. Vestal, A. L. Wahrhaftig, and W. H. Johnston, *J. Chem. Phys.*, 1962, **37**, 1276.

[18] A. N. H. Yeo and D. H. Williams, *J. Amer. Chem. Soc.*, 1971, **93**, 395.

reaction rate which produces a rise of 0·05 eV in E_0 (see Appendix). The E_0 value for the loss of CH_3 is not altered by deuteriation.

The overall consequence of deuteriation, therefore, is to shift the k–E curve for the rearrangement to lower k values for a given E (as shown in the Figure). The k–E profile for the loss of CH_3 is changed by a relatively small amount. As a result, the loss of CH_3 competes more effectively with the rearrangement in the region of $k = 10^5$ s^{-1}, thus lowering the computed metastable peak intensity ratio to 1·5. The two curves cross at a k value of 7×10^5 s^{-1} in the deuteriated compound (5).

A change in the metastable peak intensity ratio of a factor of 2·4 is therefore predicted by an assumption of a primary isotope effect on the rearrangement followed by loss of Cl. This isotope effect agrees closely with that found in practice (see Table 2). If the reaction proceeded *via* direct Cl loss the curve of k against E would be little different in compound (5) compared with compound (3) and the predicted secondary isotope effect is small. This calculation therefore supports the rearrangement mechanism to the seven-membered-ring isomer presented in the Scheme.



Plots of k against E for loss of A, CH_3 and B, Cl from the molecular ions of *p*-chloroethylbenzene (solid lines) and p-$Cl{\cdot}C_6H_4{\cdot}CD_2{\cdot}CH_3$ (broken lines)

p-*Bromoethylbenzene*.—Table 2 shows that the situation for *p*-bromoethylbenzene (8) is analogous to that for *p*-chloroethylbenzene. On substitution of two deuterium atoms for hydrogens in the benzylic position, the metastable ratio ($[M^+ - Br] : [M^+ - CH_3]$) is lowered from 4·23 to 1·92 owing to a primary deuterium isotope effect on the elimination of Br. These data (and those in Table 3) again support a rearrangement to a seven-membered ring before loss of bromine, as suggested for *p*-chloroethylbenzene in Scheme 1.

The earlier conclusion[19] that *p*-bromotoluene does not undergo ring expansion before loss of bromine may well be true for higher-energy ions. The earlier data[19] establish that the activation energies for loss of bromine from bromobenzene and from *p*-bromotoluene are similar (AP — IP 2·5 eV). The present isotope-effect work indicates that the ring expansion is faster than direct loss of bromine at energies near threshold. In ions of higher internal energy, the direct loss of bromine (single-bond cleavage) may well become faster than ring expansion (rearrangement).

EXPERIMENTAL

Compounds (5) and (9) were prepared from the corresponding *p*-halogenoacetophenone toluene-*p*-sulphonylhydrazones by reduction with $LiAlD_4$ followed by D_2O addition.[20] Synthesis of compound (4) required only H_2O addition.

All compounds were pure by g.l.c. and were introduced into an AEI MS9 mass spectrometer *via* the heated inlet at a source temperature of 150 °C. The electron beam energy was 70 eV. The calculations were performed on a PDP-8 computer.

APPENDIX

The quasi-equilibrium theory rate expression used for calculation of curves of k against E may be written as (2)[14]

$$k(E) = \frac{S}{h}\,\frac{W^{\ddagger}(E - E_0)}{\rho(E)} \qquad (2)$$

where S is the symmetry factor, h is Planck's constant, $W^{\ddagger}(E - E_0)$ is the number of states of the activated complex configuration with energy $\leqslant E - E_0$, and $\rho(E)\mathrm{d}E$ is the number of states of the molecular ion with energy between E and $E + \mathrm{d}E$.

The formula of Vestal *et al.*[17] was used to evaluate $W^{\ddagger}(E - E_0)$ and $\rho(E)$. Normal vibrational frequencies for the molecular ion were assumed to be the same as those for the neutral molecule, which in turn were constructed from those of chlorobenzene[21] and ethylbenzene.[22] The two internal free rotations were taken as low-frequency vibrations ($\nu = 200$ cm^{-1}).[22] The normal vibrational frequencies for compounds (3) and (5) are shown in Table 4. In the activated complex for the rearrangement from (3), a C–H bending mode (1200 cm^{-1}) was taken as the reaction coordinate, the corresponding C–H stretch (3000 cm^{-1}) was reduced by a factor of 2.[14] The symmetry factor (S) is 2.

TABLE 4

Normal vibrational frequencies of the molecular ion used in quasi-equilibrium theory calculations

No.	Compound	Frequencies/cm^{-1}
(3)	p-$Cl{\cdot}C_6H_4{\cdot}C_2H_5$	3100 (2), 3000 (7), 1600(2), 1500 (2), 1400 (4), 1300 (2), 1200 (6), 1100 (2), 1000 (5), 900 (6), 700 (4), 600, 500, 400 (3), 300 (2), 200 (3), 150
(5)	p-$Cl{\cdot}C_6H_4{\cdot}CD_2{\cdot}CH_3$	3100 (2), 3000 (5), 2100 (2), 1600 (2), 1500 (2), 1400 (3), 1300 (2), 1200 (4), 1100 (2), 1000 (7), 900 (2), 700 (4), 600, 500, 400 (3), 300 (2), 200 (3), 150

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[19] A. N. H. Yeo and D. H. Williams, *Chem. Comm.*, 1970, 886.

[20] (*a*) L. Caglioti and M. Magi, *Tetrahedron*, 1963, **19**, 1127; (*b*) M. Fischer, Z. Pelah, D. H. Williams, and C. Djerassi, *Chem. Ber.*, 1965, **98**, 3236.

[21] D. H. Whiffen, *J. Chem. Soc.*, 1956, 1350.

[22] F. G. Brickwedde, M. Moskow, and R. B. Scott, *J. Chem. Phys.*, 1945, **13**, 547.

For CH_3 loss, the reaction co-ordinate of the activated complex was taken as a C–C stretch (1400 cm^{-1}), the CH_3 deformation frequencies were reduced by a factor of 4 to 350 cm^{-1} (2), and the C–C–C– bend by a factor of 4 to 100 cm^{-1}.[14] Two C–H bending frequencies (1500 and 1200 cm^{-1}) were also reduced to 1000 cm^{-1} (2).[23]

The changes in activation energy on deuteration were calculated from the formula[4] (3). The main difference

$$E_{\mathrm{D}} = E_{\mathrm{H}} + \tfrac{1}{2}h\Big[\sum_i(\nu_i\mathrm{H} - \nu_i\mathrm{D}) - \sum_i(\nu_i^{\ddagger}\mathrm{H} - \nu_i^{\ddagger}\mathrm{D})\Big] \qquad (3)$$

between curves of k against E calculated from the improved[14] and simplified[13] rate equation lies in the steeper rise of k with E near threshold. The improved rate expression has previously been used for relatively large organic molecules[24] and internal free rotors were included in the model.

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