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REACTION BRANCHING AS A MECHANISTIC ALTERNATIVE TO TUNNELING IN EXPLAINING ANOMALOUS TEMPERATURE-DEPENDENCIES OF KINETIC ISOTOPE EFFECTS

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ABSTRACT

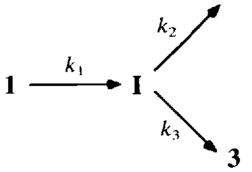
The temperature-dependence of the kinetic isotope effects for branched reactions proceeding via a common intermediate has been simulated by calculations. It is shown that, under certain conditions, anomalously small isotope effects on the Arrhenius preexponential factors, as well as unusually large observed isotope effects, may originate from the branching.

INTRODUCTION

Kinetic isotope effects significantly larger than those that can be calculated from the zero-point energies between the bonds to the heavy and light isotopes, respectively, i.e., $\Delta E_a > E_0' - E_0$, are usually attributed to a significant fraction of tunneling. Another indication for a substantial tunnel contribution is a ratio of the preexponential factors that is considerably smaller than unity ($A^H/A^D < 0{\cdot}6$). Combined, these indications have frequently been considered as conclusive evidence for tunneling.[1] However, this conclusion is not unambiguous since, as will be shown in the present paper, under certain conditions reaction branching may give rise to an unusually large isotope effect that is sometimes combined with an anomalous temperature-dependence.

RESULTS AND DISCUSSION

Under certain conditions, reaction branching can give rise to unusually large as well as unusually small isotope effects. Let us consider the following simple type of reaction branching, where I denotes a short-lived intermediate:



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The steady-state approximation yields the following relations between the phenomenological ('observed') and microscopic rate constants:

$$k_{12} = k_1\, k_2/(k_2 + k_3) \tag{2}$$

$$k_{13} = k_1\, k_3/(k_2 + k_3) \tag{3}$$

Accordingly, the following expressions for the kinetic isotope effects are obtained (heavy isotopes are denoted by primes):

$$k_{12}/k'_{12} = (k_1/k'_1)\,(k_2/k'_2)\,(k'_2 + k'_3)\,/\,(k_2 + k_3) \tag{4}$$

$$k_{13}/k'_{13} = (k_1/k'_1)\,(k_3/k'_3)\,(k'_2 + k'_3)\,/\,(k_2 + k_3) \tag{5}$$

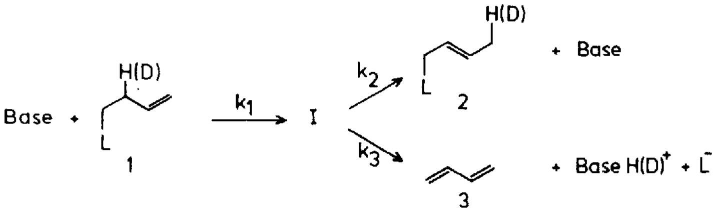
Thus, for example, the observed isotope effect on the reaction of **1** to **2** is a product of two isotope effects, k_1/k'_1 and k_2/k'_2, and a third factor. Apart from the effect of the isotopic substitution, the value of the latter depends on the relative magnitude of k_2 and k_3.

If $k_2/k'_2 > k_3/k'_3$, the following expression is valid:

$$k_{12}/k'_{12} > k_1/k'_1 > k_{13}/k'_{13} \tag{6}$$

Thus we conclude:[2] *Competition between two processes which have different kinetic isotope effects and which follow a common (rate-limiting) step sensitive to isotopic substitution results in an amplified observed isotope effect for the overall reaction, which proceeds via the competing step with the largest isotope effect. The other overall reaction will show an attenuated isotope effect. If the isotope effect on the first step is substantial, the amplification may yield an unusually large overall isotope effect.*

Extreme kinetic isotope effects caused by branching have been measured in several reaction systems.[3] For example, such a large primary kinetic isotope effect as $k^H/k^D \sim 90$ has been measured for a base-catalyzed 1,3-hydron transfer reaction competing with base-promoted elimination via a common hydrogen-bonded intermediate, baseH$^+\cdots$ carbanion (Scheme I).[4] It will be shown in the following example that the temperature-dependence of the isotope effect for a reaction of a branched system may mimic that of tunneling.



I = BaseH$^+$, tightly hydrogen-bonded carbanion

Scheme I

For a one-step reaction, the Arrhenius equation may be written as

$$k_i = A_i \exp\,(-E_i/RT) \tag{7}$$

Let us assume that $A_i^H/A_i^D = 1$ and that k_1 and k_2 of equation 1 are hydron transfer processes having, for simplicity, equal isotope effects; $k_1^H/k_1^D = k_2^H/k_2^D = 7{\cdot}740$ at 30 °C. Moreover, let us assume that k_3 is insensitive to isotopic substitution, i.e., $k_3^H/k_3^D = 1$.

Division of the Arrhenius equation for reaction with protium substrate with that with deuterium substrate at 30 °C yields

$$k_1^{\mathrm{H}}/k_1^{\mathrm{D}} = 7{\cdot}740 = \exp\left[-(E_1^{\mathrm{H}} - E_1^{\mathrm{D}})/RT\right]$$
$$\longrightarrow E_1^{\mathrm{D}} - E_1^{\mathrm{H}} = 1232{\cdot}40 \text{ cal mol}^{-1} \tag{8}$$

Application of the Arrhenius equation to equations (2) and (3):

$$k_{12} = A_1 \exp(-E_1/RT) \,/\, [1 + (A_3/A_2)\exp\{-(E_3 - E_2)/RT\}] \tag{9}$$

$$k_{13} = A_1 \exp(-E_1/RT) \,/\, [1 + (A_2/A_3)\exp\{-(E_2 - E_3)/RT\}] \tag{10}$$

These equations combined with equations (4) and (5) yield

$$\ln(k_{12}^{\mathrm{H}}/k_{12}^{\mathrm{D}}) = 1232{\cdot}40/RT + \ln[\{1 + (A_3/A_2)\exp(-(E_3 - E_2^{\mathrm{D}})/RT)\} \,/\, \{1 + (A_3/A_2)\exp(-(E_3 - E_2^{\mathrm{H}})/RT)\}] \tag{11}$$

$$\ln(k_{13}^{\mathrm{H}}/k_{13}^{\mathrm{D}}) = 1232{\cdot}40/RT + \ln[\{1 + (A_2/A_3)\exp(-(E_2^{\mathrm{D}} - E_3)/RT)\} \,/\, \{1 + (A_2/A_3)\exp(-(E_2^{\mathrm{H}} - E_3)/RT)\}] \tag{12}$$

where
$$E_3 - E_2^{\mathrm{H}} = 303{\cdot}16R\ln[(A_3/A_2)\,(k_2^{\mathrm{H}}/k_3)_{30^\circ\mathrm{C}}]$$
$$E_3 - E_2^{\mathrm{D}} = 303{\cdot}16R\ln[(A_3/A_2)\,(k_2^{\mathrm{H}}/k_3)_{30^\circ\mathrm{C}}/7{\cdot}740]$$

Equations (11) and (12) are not linear like the ordinary Arrhenius expression for a one-step reaction; the magnitude of the curvature of plots of the isotope effects versus $1/T$ is dependent on the ratio A_3/A_2. The plots of equations (11) and (12) shown in Figures 1 and 2 are based upon data calculated for three A_3/A_2 ratios at 0, 30, and 60 °C, assuming $k_2^{\mathrm{H}} = k_3$ at 30 °C. The data for these Arrhenius plots are recorded in Table 1, which also includes data calculated for other k_2^{H}/k_3 ratios. Straight lines are fair approximations of the plots shown in Figures 1 and 2. Accordingly, in experimental work, such small curvatures are easily hidden by the errors in the measured isotope effects, especially if the temperature interval is small.

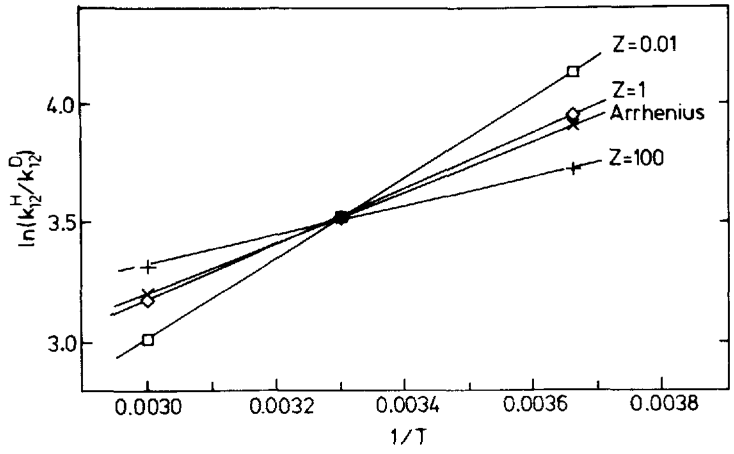


Figure 1. Plots of equation (11) for reaction **1** → **2**; $k_{12}^{\mathrm{H}}/k_{12}^{\mathrm{D}}$ is calculated assuming $k_2^{\mathrm{H}} = k_3$ at 30 °C; $z = A_3/A_2$

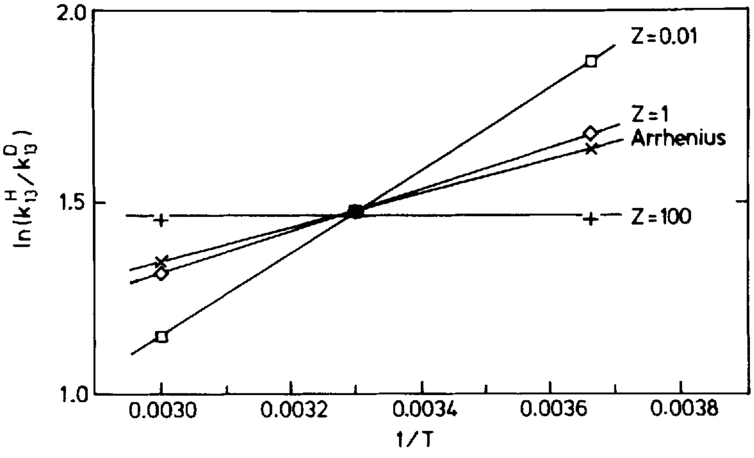


Figure 2. Plots of equation (12) for reaction **1** → **3**; k^H_{13}/k^D_{13} is calculated assuming $k_2^H = k_3$ at 30°C; $z = A_3/A_2$

Table 1 also shows the isotope effects for Arrhenius preexponential factors, A^H_{12}/A^D_{12} and A^H_{13}/A^D_{13}, which are obtained from the intercept of the regression lines of Figures 1 and 2, based upon the calculated isotope effects on the rate constants at the three temperatures. Thus, for example, $k_2^H = k_3$ at 30 °C and $A_3/A_2 = 0{\cdot}01$ correspond to such small values as $A^H_{12}/A^D_{12} = 0{\cdot}13$ and $A^H_{13}/A^D_{13} = 0{\cdot}13$.

As shown in Table 1, these parameter values correspond to $k_2^H/k_3 = 1{\cdot}51$ at 60 °C, i.e., the amount of product **2** increases from 50% at 30 °C to 60% at 60 °C, equivalent to an entropy difference of $\Delta S_2 - \Delta S_3 = 9\,\text{cal mol}^{-1}\,\text{deg}^{-1}$. On the other hand, parameter values corresponding to a decrease in k_2^H/k_3 with temperature yield a normal or large isotope effect on A_{12} (Table 1).

Obviously, a requirement for a temperature-dependency that mimics tunneling is that the rate of reaction from intermediate to product **2** (the reaction path that is sensitive to isotopic substitution) should *increase more* with temperature than the rate of reaction from intermediate to **3** (the path that is insensitive to isotopic substitution). This is consistent with $\Delta S_2^{\#} > \Delta S_3^{\#}$.

Table I also presents results from calculations with other product ratios; $k_2^H/k_3 = 10$ and 100, respectively, at 30 °C. As shown, 10% of the by-product **3** is enough for obtaining an unusually large isotope effect k^H_{12}/k^D_{12} and an abnormally small A^H_{12}/A^D_{12}.

At present, we have no experimental results that exhibit both an unusually large isotope effect on k_{12} and an anomalously small A^H_{12}/A^D_{12}. The unusually large kinetic isotope effect on the base-catalyzed 1,3-proton transfer competing with base-promoted elimination that was mentioned above (Scheme I) is not expected to exhibit an anomalously small A^H_{12}/A^D_{12}, since the rate of formation of the elimination product increases more with temperature than the formation of 1,3-proton transfer product **2**.

Solvolysis which proceeds via a carbocation or an ion pair and which yields elimination and substitution products (13) may give rise to a curved Arrhenius plot for the elimination reaction (k_{12}) combined with an anomalously small isotope effect on A_{12} and an 'enlarged', but probably not unusually large, isotope effect on k_{12}. (An unusually large isotope effect k^H_{12}/k^D_{12} requires that k_2^H/k_2^D is large. However, the deprotonation of the high-energy carbocationic

Table 1. Isotope effects on rate constants and Arrhenius parameters calculated by means of equations (11) and (12)

k_2^H/k_3	A_3/A_2	temp., °C	k_{12}^H/k_{12}^D	A_{12}^H/A_{12}^D [a]	k_{13}^H/k_{13}^D	A_{13}^H/A_{13}^D [a]
'expected' isotope effects[b,c]						
1		0	49·79	1	5·14	1
		30	33·82		4·37	
		60	24·63		3·83	
calculated isotope effects[f]						
0·6	0·01	0	62·23	0·13	6·42	0·13
1	0·01	30	33·82		4·37	
1·5	0·01	60	20·36		3·16	
1	1	0	51·80	0·71	5·35	0·71
1	1	30	33·82		4·37	
1	1	60	23·94		3·72	
1·7	100	0	41·37	4·36	4·27	4·36
1	100	30	33·82		4·37	
0·7	100	60	27·52		4·27	
'expected' isotope effects[b,d]						
10		0	16·47	1	1·70	1
		30	12·48		1·61	
		60	9·94		1·54	
Calculated isotope effects[f]						
7·8	0·01	0	19·30	0·29	1·99	0·29
10	0·01	30	12·48		1·61	
12·3	0·01	60	9·07		1·41	
9·8	0·08	0	17·52	0·60	1·81	0·60
10	0·08	30	12·48		1·61	
10·2	0·08	60	9·56		1·49	
12·9	1	0	15·76	1·47	1·63	1·47
10	1	30	12·48		1·61	
8·1	1	60	10·27		1·60	
21·4	100	0	13·46	6·86	1·39	6·86
10	100	30	12·48		1·61	
5·4	100	60	11·93		1·85	
'expected' isotope effects[b,e]						
100		0	10·41	1	1·07	1
		30	8·26		1·07	
		60	6·83		1·06	
calculated isotope effects[f]						
100	0·01	0	10·52	0·92	1·09	0·92
100	0·01	30	8·26		1·07	
100	0·01	60	6·78		1·05	
166	1	0	10·20	1·22	1·05	1·22
100	1	30	8·26		1·07	
66	1	60	6·96		1·08	
275	100	0	10·00	1·63	1·03	1·63
100	100	30	8·26		1·07	
44	100	60	7·22		1·12	

[a] Intercept of the regression line of the plot of equations (11) and (12), respectively (Figures 1 and 2).

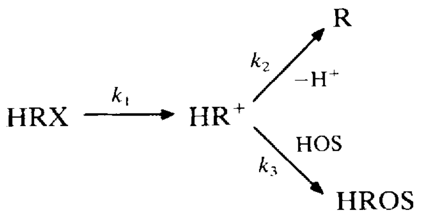
[b] According to the Arrhenius equation for a one-step reaction.

[c] Assuming $k_{12}^H/k_{12}^D = 33\cdot82$ and $k_{13}^H/k_{13}^D = 4\cdot37$, respectively, at 30°C (see text).

[d] Assuming $k_{12}^H/k_{12}^D = 12\cdot48$ and $k_{13}^H/k_{13}^D = 1\cdot61$, respectively, at 30°C.

[e] Assuming $k_{12}^H/k_{12}^D = 8\cdot26$ and $k_{13}^H/k_{13}^D = 1\cdot07$, respectively, at 30°C.

[f] Assuming $k_1^H/k_1^D = k_2^H/k_2^D = 7\cdot740$ and $k_3^H/k_3^D = 1$ at 30°C (see text).



(13)

intermediate is not expected to exhibit a large isotope effect.) The requirements are a large secondary isotope effect on the ionization step and the substitution adduct (**3**) constituting a large fraction of the products; this fraction increases with temperature. An example is the solvolysis of 9-($^2H_6$)-9-(2-chloro-2-propyl)fluorene in 25 vol% acetonitrile in water.[5] However, the temperature-dependence of the isotope effects for this system has not been investigated.

An interesting result of the calculations presented in Table 1 is an isotope effect k_{13}^{H}/k_{13}^{D} that *increases* with temperature. Experimentally, we have found k^H/k^D values for a base-promoted 1,4-elimination that are approximately constant with temperature.[6] It was concluded that the results were caused by a stepwise mechanism (14) involving a fast

$$\text{Base} + \text{HR} \rightleftarrows \text{BaseH}^+ \ldots\ldots \text{R}^- \longrightarrow \text{product} \tag{14}$$

collapse of the hydrogen-bonded carbanion back to starting material; the amount of internal return decreases with temperature. Independent results confirm this type of internal-return mechanism.[7] It was also concluded that the temperature-dependencies of the isotope effects are a much more sensitive probe for a stepwise mechanism than a simple Arrhenius plot for the protium substrate. Koch and co-workers have found similar behavior in base-promoted 1,2-elimination, i.e., a slight increase in isotope effect with temperature, that is also interpreted by a mechanism of this type.[8] Recently, another example of increase in kinetic deuterium isotope effect with temperature was reported.[9] The temperature-dependencies of the isotope effects of the internal-return mechanism have been simulated by calculations.[10]

The internal-return mechanism may be considered as a special case of the branched reaction scheme of equation (1); the expression for the observed rate constant is the same. Thus, k_2 represents collapse of intermediate back to starting material, and k_3 reaction to product. Accordingly, the calculations for the temperature-dependencies of the isotope effect on the observed rate constant k_{13} are valid for this type of reaction.

Melander and Saunders have pointed out that an anomalous value for the observed ratio of Arrhenius preexponential factors A/A' may also arise from two parallel reactions which give the same product.[11] However, no unusually large isotope effect can originate from such competing reactions.

CONCLUSIONS

The calculations clearly show that anomalous Arrhenius parameters may be obtained for branched reactions. The requirements for observation of parameters that mimic tunneling, i.e., an unusually large primary kinetic isotope effect and $A^H/A^D < 0{\cdot}6$ are:

(i) the two processes should have quite different kinetic isotope effects and follow a common rate-limiting step substantially sensitive to isotopic substitution, and

(ii) the rate of the reaction which is more sensitive to isotopic substitution should *increase more* with temperature than the competing side reaction; the latter can be an order of magnitude slower than the main reaction.

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