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Use of Kinetic Isotope Effects in Mechanism Studies. Anomalous Arrhenius Parameters in the Study of Elimination Reactions

Sir:

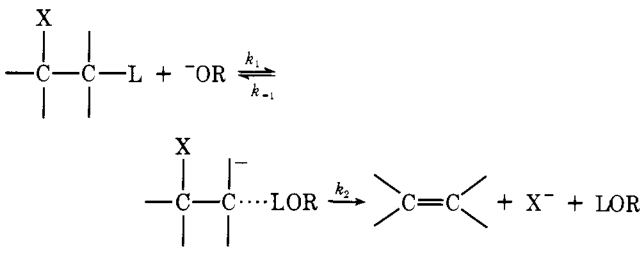
We have recently reported kinetic evidence that suggested the formation of carbanion intermediates during the ethanolic ethoxide dehydrohalogenation of $C_6H_5CHClCF_2Cl$ (III-*h*) even though the benzylic proton does not exchange with bulk solvent prior to elimination.[1] A kinetic study of the three isotopes of hydrogen was undertaken to find out if the low primary kinetic isotope effect, $k^H/k^D = 3.00$ at 0°, resulted from an internal return mechanism.[2] During the course of our studies we encountered anomalous Arrhenius parameters and we wish to report these unusual results at this time.

Primary kinetic isotope effects should arise from differences in zero point energies between C–L bonds in the ground state and transition state. In normal situations one would therefore expect rate differences between isotopically labeled compounds to come from differences in activation energies and that the ratio of Arrhenius preexponential factors, A^H/A^D, be 1.0 ± 0.4.[3] Bell has reviewed recent advances in the study of kinetic hydrogen isotope effects and lists anomalous effects on Arrhenius parameters.[4] Most cases cited gave values of A^H/A^D less than unity, and this has been interpreted as evidence for proton tunneling. In such cases $E_A{}^D - E_A{}^H$ is larger than $E_0{}^D - E_0{}^H$ and k^H/k^D is usually larger than predicted. For our systems, we find exactly the reverse situation (Tables I and II). The methanolic sodium methoxide dehydrohalogenation of $C_6H_5CLBrCF_2Br$ (II), III, *p*-$ClC_6H_4CLClCF_2Cl$ (IV), and $C_6H_5CLBrCH_2Br$ (V) shows anomalous behavior since $E_A{}^D \simeq E_A{}^H$ and $A^H/A^D > 2$. Compound III exhibits similar behavior in ethanolic sodium ethoxide. *p*-$ClC_6H_4CLBrCF_2Br$ (I) shows more normal behavior with $E_A{}^D - E_A{}^H = 0.5$ kcal mol^{-1} and the A^H/A^D value of 1.5 is just outside the limits of normal behavior. In all systems studied the k^H/k^D values are within the range of 2-5 at 25°.

Compound I is the most reactive and may mark the start of normal behavior, while V is the least reactive and still gives anomalous Arrhenius parameters. Included in Tables I and II are literature data for the ethanolic sodium ethoxide dehydrobromination of $C_6H_5CL_2CH_2Br$ (VII)[5] and $C_6H_5CL(CH_3)CH_2Br$ (VI).[6] These two compounds are less reactive than our systems and, although they also give anomalous Arrhenius parameters, they are of the usual type cited by Bell.

A major reason for the study of primary kinetic isotope effects is to gain insight into reaction pathways and to attempt to describe the nature of the transition state(s) during that reaction. There has been a renewed interest in mechanisms of elimination reactions,[7] and along with other investigators,[8,9] we are currently trying to find if there is a smooth transition between the concerted E2 and the two-step E1cb mechanisms. We feel that our isotope effect data are inconsistent with both the E2 pathway or with an E1cb mechanism where either the first or second step is clearly rate limiting. The anomalous Arrhenius parameters indicate that in our systems the E1cb mechanism may have a fine balance where neither step is clearly rate determining and that internal return (k_{-1}) can compete favorably with the forward reaction (k_2) in Scheme I. Additional evidence has been obtained for II and III to suggest that an intermediate carbanion is present along the reaction pathway. Hammett ρ values of 3.6 and 3.9 were calculated for substituted derivatives of II and III, respectively.[10] Sodium methoxide concentrations were varied from 0.2 to 2.1 N and the log of the corresponding pseudo-first-order rate constants were plotted against Streitwieser's H_M values,[11] to give good linear plots with slopes of 0.99 ± 0.03 (II) and 1.02 ± 0.02 (III).

Scheme I



Streitwieser[2] has shown that one of the simplest experimental methods of detecting internal return, when k_{-1} and k_2 are of comparable size, is to make use of the Swain-Schaad equation:[12]

$$k^H/k^T = (k^D/k^T)^y$$

For a simple proton transfer process, which is not complicated by internal return, $y = 3.26$[12] or 3.344,[2] depending on assumptions made in the derivation. Ethoxide dehydrochlorination of III and methoxide dehydrobromination of II require y values of 3.14 and 3.39 which suggest negligible internal return. Methoxide dehydrochlorination of III requires $y = 2.94$ which results in $a_H \sim 0.5$, $a_D \sim 0.1$, and a_T

Table I. Activation Parameters and Rate Constants (25°) for Alcoholic Sodium Alkoxide Dehydrohalogenation Reactions

Compound[a]	Solvent	$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, eu	10^2k, M^{-1} s^{-1}	No. of points	Temp range (°C)
I-*h*	MeOH	16.3 ± 0.1	−1.3 ± 0.6	672.0	8	−50 to −10
I-*d*	MeOH	16.8 ± 0.1	−0.9 ± 0.4	180.0	6	−40 to −5
II-*h*	MeOH	17.1 ± 0.2	−1.5 ± 0.8	90.9	6	−40 to 6
II-*d*	MeOH	17.2 ± 0.1	−3.7 ± 0.6	22.7	6	−30 to 20
II-*t*	MeOH	17.2 ± 0.1	−4.9 ± 0.4	12.7	9	−30 to 25
III-*h*	EtOH	19.5 ± 0.2	3.8 ± 0.6	23.3	6	−10 to 30
III-*d*	EtOH	19.2 ± 0.1	0.7 ± 0.3	7.62	5	−20 to 20
III-*t*	EtOH	18.7 ± 0.2	−2.1 ± 0.7	4.52	5	−10 to 30
IV-*h*	MeOH	19.0 ± 0.2	1.1 ± 0.7	12.2	7	−10 to 25
IV-*d*	MeOH	19.1 ± 0.1	−0.4 ± 0.5	5.52	8	−20 to 30
III-*h*	MeOH	20.6 ± 0.1	2.5 ± 0.4	1.76	8	0 to 50
III-*d*	MeOH	20.6 ± 0.1	0.7 ± 0.2	0.749	8	10 to 50
III-*t*	MeOH	19.6 ± 0.1	−3.5 ± 0.3	0.482	7	0 to 45
III-*t*	MeOD	19.5 ± 0.3	−1.6 ± 0.9	1.33	6	−5 to 45
V-*h*	MeOH	20.2 ± 0.1	−1.9 ± 0.3	0.367	5	10 to 50
V-*d*	MeOH	20.2 ± 0.1	−4.8 ± 0.3	0.0846	5	20 to 60
VI-*h*[b]	EtOH	20.1 ± 0.1	−5.5 ± 0.3	0.0782	6	5 to 55
VI-*d*[b]	EtOH	21.8 ± 0.2	−3.5 ± 0.5	0.0104	6	5 to 55
VII-*h*[c]	EtOH	20.4 ± 0.6	−6.6 ± 1.9	0.0232	3	30 to 50
VII-*d*[c]	EtOH	22.0 ± 0.4	−5.3 ± 1.4	0.00309	3	30 to 50

[a] I = *p*-$ClC_6H_4CLBrCF_2Br$, II = $C_6H_5CLBrCF_2Br$, III = $C_6H_5CLClCF_2Cl$, IV = *p*-$ClC_6H_4CLClCF_2Cl$, V = $C_6H_5CLBrCH_2Br$, VI = $C_6H_5CL(CH_3)$-CH_2Br, VII = $C_6H_5CL_2CH_2Br$. [b] Data from ref 6. [c] Data from ref 5.

Table II. Kinetic Isotope Effects (25°), A^H/A^D Ratios and Swain–Schaad Exponents (y at 25°)

Compound	k^H/k^D	A^H/A^D	y
I	3.73[b]	1.5	—
II	4.00[b]	3.0	3.39
III	3.06[a]	4.8	3.14
III	2.35[b]	2.4	2.94
IV	2.21[b]	2.1	—
V	4.34[b]	4.3	—
VI	7.52[a]	0.4	3.08
VII	7.51[a]	0.5	—

[a] EtONa–EtOH. [b] MeONa–MeOH.

~ 0.07 (where $a_L = k_{-1}{}^L/k_2$). This latter calculation assumes $k_2{}^H = k_2{}^D = k_2{}^T$.[2]

We assume that CF_2X groups (X = Br, Cl, F) have about the same effect on C–H acidities or carbanion stabilities.[13] This, however, leads to an inconsistency when considering all the data in Table I. If II and III have similar C–H acidities,[14] $E_A{}^{II}$ should be the barrier for the proton transfer step for reaction of III. Why then is there so little calculated internal return when $E_A{}^{III} - E_A{}^{II}$ is over 3 kcal mol^{-1}? The validity of the Swain-Schaad equation has been demonstrated even when extensive tunneling leads to usual type anomalous Arrhenius parameters.[16] The Streitwieser equation has been applied to data from lithium cyclohexylamide catalyzed isotope exchange of triphenylmethane, which from the large isotope effect (k^H/k^D = 6.88 at 25°)[17] would seem to preclude thinking of an internal return mechanism. However, that reaction requires a y = 2.88 which results in $a_H \sim 0.9$, $a_D \sim 0.06$, and $a_T \sim 0.02$. When interpreting our data, we do not imply a breakdown of either the Swain-Schaad relationship or the Streitwieser extension applied to internal return mechanisms. We do feel that they cannot be used in interpreting our data since the isotope effects appear to arise from entropy rather than enthalpy terms and caution that care should be taken when interpreting single temperature primary kinetic isotope effects.

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