

# Transition State Looseness and $\alpha$ -Secondary Kinetic Isotope Effects

Sanne Schröder Glad and Frank Jensen\*

Contribution from the Department of Chemistry, Odense University,  
Campusvej 55, DK-5230 Odense M, Denmark

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**Abstract:** The correlation between hydrogen/deuterium  $\alpha$ -secondary kinetic isotope effects and transition state looseness has been investigated by MP2/6-31++G(d,p) calculations on three identity  $X^- + CH_3X$   $S_N2$  reactions. By varying the C–X distances in these systems it is shown that the secondary kinetic isotope effect increases with increasing transition structure looseness. Furthermore, it is shown that looseness is best defined as a  $\Delta$ -elongation of the C–X bond lengths, where the reference state can be either the isolated reactants or the ion–dipole complex. The variation of kinetic isotope effects is shown by factor analysis to be determined by C–H bending vibrations. The contributions from C–H stretching vibrations are important for the absolute values of the kinetic isotope effects, and are partly due to C–H bond length changes. The variation of the secondary kinetic isotope effect from the stretching vibrations with looseness is in the opposite direction as the bending contribution, causing a level-off in the total kinetic isotope effect for tight transition structures.

## Introduction

Kinetic isotope effects (KIEs) are ratios of rate constants for reactions differing only in isotopic substitution.  $\alpha$ -Secondary kinetic isotope effects (SKIEs), where the isotope is at the reacting center but where no covalent bonding changes occur, have been widely used to estimate  $S_N2$  transition structures (TSs).<sup>1</sup> A “normal” KIE is a ratio greater than unity while an “inverse” effect is a ratio less than unity. Below, an increasing (decreasing) SKIE means increasing (decreasing) value of the secondary kinetic isotope effect.

Kinetic isotope effects are determined primarily by changes in vibrational frequencies along the reaction coordinate. An increase in force constants increases the zero-point energy differences between the isotopically different transition states leading to a smaller absolute value of the KIE, and vice versa. It has been generally accepted that hybridization and “crowding” effects determine the  $\alpha$ -SKIE, primarily through changes in the  $C_\alpha$ –H(D) out-of-plane bending vibrations.<sup>1,2</sup> Factor analyses of the frequencies, however, have shown that both bending and stretching vibrations are important in determining the absolute value of the SKIE.<sup>3–6</sup> The stretching vibrations contribute inversely to the secondary kinetic isotope effect, while the bending vibrations result in normal SKIEs. Nevertheless, the

conclusions regarding the importance of the different contributions are contradictory.

For  $S_N2$  reactions, the focus has primarily been on correlations between SKIEs and transition state “looseness”,<sup>7</sup> where looseness refers to the geometry around the  $\alpha$ -hydrogens. Different measures of looseness, however, have resulted in opposite conclusions.<sup>1,3–5,8</sup> The interpretations are further complicated by the fact that the SKIE can be calculated with reference to either isolated reactants or to the initially formed ion–dipole complex. The main question addressed in this paper is how transition state looseness should be defined, based on results for  $X^- + CH_3X$  identity  $S_N2$  reactions, where X is either F, Cl, or Br.

## Background

The simplest definition of transition state looseness is using the breaking/forming bond lengths directly, that is

$$R^\ddagger = R_{\text{CNu}}^\ddagger + R_{\text{CL}}^\ddagger \quad (1)$$

where the nucleophile and the leaving group are labeled Nu and L, respectively, and the symbol  $\ddagger$  refers to the transition structure. Poirier et al.<sup>3</sup> have argued that  $R^\ddagger$  indicates the space available for the out-of-plane bending vibrations in the transition state, since it measures the distance between the nucleophile and the leaving group.

This measure does not, however, distinguish between different nucleophiles and leaving groups. Although a transition structure C–Br bond length is longer than a C–F bond length, Br is also larger than F, and it is not clear that the available space is given directly by the bond lengths. It would therefore seem reasonable that the size of the entering/leaving groups should be taken into account when discussing TS looseness. One

(7) See for example: (a) Westaway, K. C. *Can. J. Chem.* **1978**, *56*, 2691–2699. (b) Westaway, K. C.; Ali, S. F. *Can. J. Chem.* **1979**, *57*, 1089–1097. (c) Westaway, K. C.; Ali, S. F. *Can. J. Chem.* **1979**, *57*, 1354–1367. (d) Westaway, K. C.; Waszczylo, Z. *Can. J. Chem.* **1982**, *60*, 2500–2520. (e) Fang, Y.; Westaway, K. C. *Can. J. Chem.* **1991**, *69*, 1017–1021. (f) Westaway, K. C. *Can. J. Chem.* **1993**, *71*, 2084–2094.

(8) (a) Lee, I. *Adv. Phys. Org. Chem.* **1992**, *27*, 57–117. (b) Lee, I. *Chem. Soc. Rev.* **1995**, 223–229.

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(1) Shaik, S. S.; Schlegel, H. B.; Wolfe, S. *Theoretical Aspects of Physical Organic Chemistry. The  $S_N2$  Mechanism*; Wiley: New York, 1992.

(2) (a) Streitwieser, A., Jr.; Jagow, R. H.; Fahey, R. C.; Suzuki, S. *J. Am. Chem. Soc.* **1958**, *80*, 2326–2332. (b) McLennan, D. J. In *Isotopes in organic chemistry*; Buncl, E., Lee, C. C., Eds.; Elsevier: New York, 1987; Vol. 7, Chapter 6.

(3) Poirier, R. A.; Wang, Y.; Westaway, K. C. *J. Am. Chem. Soc.* **1994**, *116*, 2526–2533.

(4) (a) Wolfe, S.; Kim, C.-H. *J. Am. Chem. Soc.* **1991**, *113*, 8056–8061.

(b) Boyd, R. J.; Kim, C.-H.; Shi, Z.; Weinberg, N.; Wolfe, S. *J. Am. Chem. Soc.* **1993**, *115*, 10147–10152.

(5) Barnes, J. A.; Williams, I. H. *J. Chem. Soc., Chem. Commun.* **1993**, 1286–1287.

(6) (a) Llewellyn, J. A.; Robertson, R. E.; Scott, J. M. W. *Can. J. Chem.* **1960**, *38*, 222–232. (b) Leffek, K. T.; Llewellyn, J. A.; Robertson, R. E. *Can. J. Chem.* **1960**, *38*, 1505–1510. (c) Bron, J. *Can. J. Chem.* **1974**, *52*, 903–909. (d) Williams, I. H. *J. Am. Chem. Soc.* **1984**, *106*, 7206–7212. (e) Zhao, X. G.; Tucker, S. C.; Truhlar, D. G. *J. Am. Chem. Soc.* **1991**, *113*, 826–832. (f) Hu, W.-P.; Truhlar, D. G. *J. Am. Chem. Soc.* **1995**, *117*, 10726–10734.

possibility is to subtract the equilibrium bond length and define a  $\Delta$ -elongation as

$$\begin{aligned}\Delta R_{CX}^\ddagger &= R_{CX}^\ddagger - R_{CX}^0 \\ \Delta R^\ddagger &= \Delta R_{\text{CNu}}^\ddagger + \Delta R_{\text{CL}}^\ddagger\end{aligned}\quad (2)$$

where superscript zero refers to the reactant or product bond length and X is either nucleophile or leaving group. Equivalently to this is the usage of bond orders,<sup>9</sup> an exponential transformation of  $\Delta R_{CX}^\ddagger$ :

$$\begin{aligned}n_{CX}^\ddagger &= \exp\left(\frac{-\Delta R_{CX}^\ddagger}{a}\right) \\ n^\ddagger &= n_{\text{CNu}}^\ddagger + n_{\text{CL}}^\ddagger\end{aligned}\quad (3)$$

The constant  $a$  has traditionally been set to 0.3 Å, but a value of 0.6 Å for breaking or forming single bonds has been shown to be more appropriate.<sup>10</sup>

None of these measures take into account that a longer bond in general is also a weaker bond, i.e., the energy cost of stretching a long bond is smaller than stretching a short bond by the same amount. This can be accounted for by using a constant in the bond order equation that depends on the nature of the nucleophile or leaving group. By comparing a Morse function<sup>11</sup> with the bond order equation (eq 3), a constant can be defined from the dissociation energy ( $D$ ) and force constant ( $f$ ) of the specific bond as

$$a_{\text{Morse}} = \sqrt{\frac{2D}{f}}\quad (4)$$

The resulting bond order (labeled  $n_{\text{Morse}}^\ddagger$ ) can be interpreted as an energy bond order, reflecting a percentage of the energy necessary to break the bond.

An alternative way of accounting for the short bond/strong bond correlation is to measure the C–Nu and C–L elongations relative to the equilibrium values ( $\Delta_{\text{rel}}R_{CX}^\ddagger$ ). The looseness of the transition state is then defined as the sum of the relative elongations (often taken as percentages) for the two bonds:

$$\begin{aligned}\Delta_{\text{rel}}R_{CX}^\ddagger &= (R_{CX}^\ddagger - R_{CX}^0)/R_{CX}^0 \\ L^\ddagger &= \% \Delta_{\text{rel}}R_{\text{CNu}}^\ddagger + \% \Delta_{\text{rel}}R_{\text{CL}}^\ddagger\end{aligned}\quad (5)$$

Bond orders are restrained to be in the range 0 to 1, whereas the  $R^\ddagger$ ,  $\Delta R^\ddagger$ , and  $\Delta_{\text{rel}}R^\ddagger(L^\ddagger)$  parameters in principle can have any value between 0 and infinity.

Unfortunately, different measures of looseness can lead to different conclusions regarding the variation of secondary kinetic isotope effects with transition state looseness. Wolfe et al.<sup>14</sup> define TS looseness as  $L^\ddagger$  (eq 5) and find that the secondary kinetic isotope effect decreases as the TS looseness increases. Poirier et al.<sup>3</sup> and Barnes et al.<sup>5</sup> use the bond lengths directly (eq 1) and find that the secondary kinetic isotope effect increases with increasing looseness. Lee<sup>8</sup> uses a cross-interaction constant,<sup>12</sup> which is inversely related to  $R^\ddagger$ , and also finds an increasing SKIE with increasing TS looseness.

An additional difference between the investigations is whether the KIEs are calculated with respect to isolated reactants or to

ion–dipole complexes. In solution, the  $S_N2$  reaction proceeds directly from isolated reactants, whereas in the gas phase, the reaction profile includes ion–dipole complexes in both the reactant and the product channel. Comparison of theoretical with experimental numbers is facilitated by using isolated reactants as reference, as most experiments are performed in solution. On the other hand, theoretical calculations correspond to gas-phase reactions, justifying the choice of ion–dipole complexes as reference state.

The aim of the present investigation is to establish whether the secondary kinetic isotope effect increases or decreases as a function of transition state looseness in systems where looseness is unambiguously defined. Transition structures for identity  $S_N2$  reactions of the type  $X^- + \text{CH}_3\text{X}$  have  $D_{3h}$  symmetry, and the high symmetry allows a detailed dissection of the KIE into individual frequency contributions. Specifically, we will investigate how the KIE changes as the TS is made tighter or looser by varying the C–X bond lengths. All of the above measures will agree that an elongation of both C–X bonds will make the TS looser. A comparison of the three systems with  $X = \text{F}, \text{Cl},$  and  $\text{Br}$ , however, allows an analysis of which measure is the best indicator for the transition state looseness.

### Computational Details

Calculations have been done at the MP2/6-31++G(d,p) level with the Gaussian-94 program package.<sup>13</sup> For bromine the Binning and Curtis' contraction<sup>14</sup> of the (14s,11p,5d) primitive basis<sup>15</sup> has been used. This level of theory has been found to provide reactant geometries, transition structures, and kinetic isotope effects in close agreement with higher level calculations for E2 reactions.<sup>16</sup> Kinetic isotope effects ( $k_H/k_D$ ) corresponding to substitution of all three hydrogens are calculated from standard statistical mechanics using harmonic vibrational frequencies.

$$\begin{aligned}k_H/k_D &= \exp((\Delta G_D - \Delta G_H)/RT) \\ \Delta G &= G^\ddagger - G^r\end{aligned}\quad (6)$$

A uniform frequency scaling changes the absolute values of the isotope effects, but does not necessarily improve the agreement with higher level methods,<sup>16</sup> and scaling has not been employed. The effect of tunneling and variational optimization has been shown to be negligible for the systems studied.<sup>6d,17</sup> The reported kinetic isotope effects refer to a temperature of 298.15 K; we have checked that the conclusions remain valid for temperatures in the range 0 to 1000 K.

Kinetic isotope effects can be broken down into contributions from translations, rotations, and vibrations, as  $\text{KIE}_{\text{tot}} = \text{KIE}_{\text{trans}} \times \text{KIE}_{\text{rot}} \times \text{KIE}_{\text{vib}}$ . The vibrational part may similarly be broken down into products of contributions from individual frequencies.<sup>6c</sup>

(12) The cross-interaction constant is an experimentally determined parameter (related to the Hammett and Brønsted parameters) reflecting the effect of a substituent in one reactant on a selectivity parameter for another reactant. The magnitude of these interaction constants represents the intensity of interaction between two substituents through the two reaction centers in the TS, and is inversely proportional to the distance between them.

(13) *Gaussian 94*, Revision B.2/Revision C.3; Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M.W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. Gaussian, Inc.: Pittsburgh, PA, 1995.

(14) (a) Binning, R. C., Jr.; Curtiss, L. A. *J. Comp. Chem.* **1990**, *11*, 1206–1216. (b) Curtiss, L. A.; McGrath, M. P.; Bladeau, J.-P.; Davis, N. E.; Binning, R. C., Jr.; Radom, L. *J. Chem. Phys.* **1995**, *103*, 6104–6113.

(15) Dunning, T. H., Jr. *J. Chem. Phys.* **1977**, *66*, 1382–1383.

(16) Glad, S. S.; Jensen, F. *J. Phys. Chem.* **1996**, *100*, 16892–16898.

(17) Tucker, S. C.; Truhlar, D. G. *J. Am. Chem. Soc.* **1990**, *112*, 3338–3347.

(9) Pauling, L. *J. Am. Chem. Soc.* **1947**, *69*, 542–553.

(10) (a) Houk, K. N.; Gustavson, S. M.; Black, K. A. *J. Am. Chem. Soc.* **1992**, *114*, 8565–8572. (b) Glad, S. S.; Jensen, F. *J. Am. Chem. Soc.* **1994**, *116*, 9302–9310.

(11) Hirst, D. M. *A Computational Approach to Chemistry*; Blackwell: Oxford, London, 1990.

**Table 1.** Calculated Geometry Parameters for Minimum and Transition Structures<sup>a</sup>

X	$R_{CX}^0$	$R_{CH}^0$	$\theta_{HCX}$	$R_{CX}^\ddagger$	$R_{CH}^\ddagger$
F	1.405 (1.383)	1.087 (1.086)	108.2 (108.8)	1.832	1.071
Cl	1.778 (1.776)	1.085 (1.085)	108.9 (108.6)	2.310	1.069
Br	1.950 (1.934)	1.084 (1.082)	107.7 (107.7)	2.432	1.069

<sup>a</sup> Bond lengths are in angstroms, angles in degrees. Experimental values in parentheses.<sup>18</sup>

**Table 2.** Calculated Geometry Parameters of Ion–Dipole Complexes<sup>a</sup>

X	$R_{CX}^0$	$R_{C-X}^0$	$R_{CH}^0$	$\theta_{HCX}$
F	1.453	2.501	1.080	108.8
Cl	1.808	3.080	1.081	108.9
Br	1.980	3.074	1.079	107.5

<sup>a</sup> Bond lengths are in angstroms, angles in degrees.

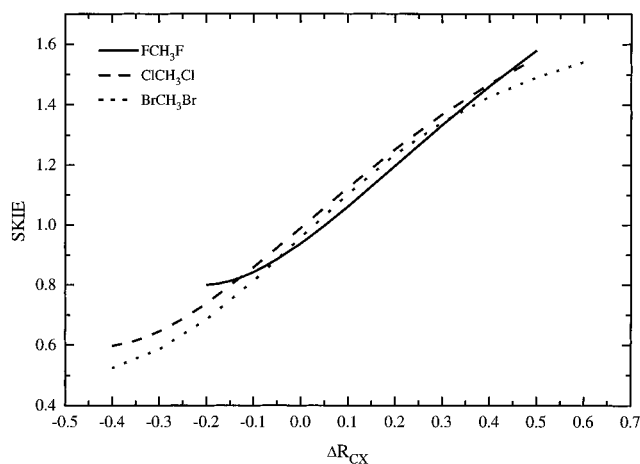
## Results and Discussion

Table 1 shows reactant and TS geometries for the three identity  $S_N2$  reactions with X being F, Cl, and Br. The reactant bond lengths are in reasonable agreement with experimental values,<sup>18</sup> the largest difference being 0.02 Å for the C–F bond length. All calculated values are very close to earlier published values obtained at comparable theoretical levels.<sup>19</sup> Table 2 gives corresponding geometries calculated for the three ion–dipole complexes.

The calculated KIEs with respect to either the isolated reactants (SKIE) or ion–dipole complexes (SKIE<sup>C</sup>) are given in Table 3, along with the corresponding translational, rotational, and vibrational contributions. The SKIEs with respect to ion–dipole complexes are exclusively determined by the vibrational contribution, whereas the absolute magnitude of the SKIE with respect to isolated reactants has a strong rotational component. In both cases the variation in SKIE<sub>tot</sub> among the three systems is determined by the vibrational contribution.

The TSs have  $D_{3h}$  symmetry and a total of seven different vibrational frequencies (four are degenerate). Their symmetries, approximate descriptions, and contributions to the KIE with respect to both isolated reactants and ion–dipole complexes are given in Table 4. The  $1a_1'$  vibration (symmetric X–C–X stretch) of the transition state is essentially independent of the hydrogens. This is also the case for the isolated reactants, and the vibration consequently does not contribute to the SKIE. There is a small isotopic dependence of the vibration in the ion–dipole complexes, however, and accordingly a small contribution to the SKIE<sup>C</sup>.

The symmetric X–C–X stretch is the motion associated with the TS looseness. We may therefore form a series of increasingly looser or tighter geometries by elongating or decreasing both C–X bonds. Such geometries do not correspond to stationary points on the energy surface; however, by allowing the C–H bond distance to relax the only non-zero gradient components will be along the C–X bonds. Projecting the gradient out from the force constant matrix prior to diagonal-



**Figure 1.** Secondary kinetic isotope effect as a function of TS C–X bond elongation for three transition structures. Bond lengths are in angstroms.

ization allows calculation of a set of generalized frequencies.<sup>20</sup> The frequency associated with the gradient direction becomes zero with this procedure, and we cannot calculate the corresponding KIE contribution. The associated normal coordinate, however, is exactly the  $1a_1'$  mode at the TS, and the frequency removed by projection accordingly makes no or little contribution to the KIE. This is mainly a consequence of the high symmetry of the TS. We are therefore able to calculate *directly* the KIE as a function of the TS looseness.

For each of the three reactions, the  $R_{CX}$  distances were fixed at specific lengths while allowing the  $R_{CH}$  distances to relax. Although this leads to comparison of geometries with slightly different C–H bond lengths, which influences the KIE, the factor analysis reported below shows that this effect is negligible. The C–X bond lengths were continuously shortened or lengthened until there was either zero or more than one imaginary frequency. With this constraint, the  $R_{CF}$  bond length could be varied from  $-0.2$  to  $0.5$  Å with respect to the optimized TS bond length, the  $R_{CCl}$  from  $-0.4$  to  $0.5$  Å, and the  $R_{CBr}$  bond length from  $-0.4$  to  $0.6$  Å. Secondary kinetic isotope effects were calculated at all geometries with respect to isolated reactants. The resulting plots of the SKIEs as functions of  $\Delta R_{CX}$  are shown as Figure 1, and it clearly shows that the secondary kinetic isotope effect for the  $S_N2$  reaction *increases* with increasing transition state looseness. Furthermore, it can be seen that the slopes for positive  $\Delta R_{CX}$  are almost identical.

Having established that TS looseness implies a large SKIE, we can use this to evaluate the different geometry-derived parameters described in the Background section; Table 5. The secondary kinetic isotope effects are all inverse and increase from 0.937 for FCH<sub>3</sub>F, to 0.957 for BrCH<sub>3</sub>Br, and to 0.989 for ClCH<sub>3</sub>Cl. A looseness parameter should accordingly reflect this order. The results show that the two parameters used by Wolfe<sup>4</sup> and Poirier,<sup>3</sup> the relative elongation and the absolute bond length, give an opposite ordering of the three TSs, and none of them reflects the order of increasing SKIEs. Neither parameter seems like a good estimate of the TS looseness. However, an almost linear correlation exists between  $\Delta R^\ddagger$  and the SKIE. Employing bond orders with a constant  $a$  parameter provides the same correlation, as this is just an exponential transformation of  $\Delta R^\ddagger$ . The bond order with  $a$  being dependent on the entering/leaving groups reflects not only the fact that the groups have different sizes but also that a long bond should be easier to stretch than

(18) (a) Jensen, P.; Brodersen, S.; Guelachvili, G. *J. Mol. Spectrosc.* **1981**, *88*, 378–393. (b) Graner, G. *J. Mol. Spectrosc.* **1981**, *90*, 394–438. (c) Egawa, T.; Yamamoto, S.; Nakata, M.; Kuchitsu, K. *J. Mol. Struct.* **1987**, *156*, 213–228.

(19) (a) Tucker, S. C.; Truhlar, D. G. *J. Phys. Chem.* **1989**, *93*, 8138–8142. (b) Vetter, R.; Zülicke, L. *J. Am. Chem. Soc.* **1990**, *112*, 5136–5142. (c) Shi, Z.; Boyd, R. J. *J. Am. Chem. Soc.* **1990**, *112*, 6789–6796. (d) Jensen, F. *Chem. Phys. Lett.* **1992**, *196*, 368–376. (e) Deng, L.; Branchadell, V.; Ziegler, T. *J. Am. Chem. Soc.* **1994**, *116*, 10645–10656. (f) Glukhovtsev, M.; Pross, A.; Radom, L. *J. Am. Chem. Soc.* **1995**, *117*, 2024–2032.

(20) (a) Miller, W. H.; Handy, N. C.; Adams, J. E. *J. Chem. Phys.* **1980**, *72*, 99–112. (b) Lu, D.-h.; Truhlar, D. G. *J. Chem. Phys.* **1993**, *99*, 2723–2738.

**Table 3.** Factor Analysis of Secondary Kinetic Isotope Effect<sup>a</sup>

X	SKIE <sub>tot</sub>	SKIE <sub>trans</sub>	SKIE <sub>rot</sub>	SKIE <sub>vib</sub>	SKIE <sub>tot</sub> <sup>C</sup>	SKIE <sub>trans</sub> <sup>C</sup>	SKIE <sub>rot</sub> <sup>C</sup>	SKIE <sub>vib</sub> <sup>C</sup>
F	0.937	1.045	1.229	0.730	0.906	1.000	0.997	0.909
Br	0.957	1.022	1.239	0.757	0.978	1.000	1.000	0.979
Cl	0.989	1.036	1.223	0.781	0.986	1.000	0.999	0.987

<sup>a</sup> The last four columns refer to ion–dipole complexes. TSs are listed in order of increasing SKIE<sub>tot</sub>.

**Table 4.** Contributions of Individual Frequencies to the Secondary Kinetic Isotope Effect<sup>a</sup>

vib	F	Cl	Br	F <sup>C</sup>	Cl <sup>C</sup>	Br <sup>C</sup>	description
$\nu_i(1a_2'')$ <sup>b</sup>	1.143	1.105	1.105	1.047	1.074	1.076	reaction coordinate
$\nu_1(1e')$	0.916	0.921	0.912	1.039	1.032	1.026	X–C–X bend
$\nu_2(1a_1')$	1.000	1.000	1.000	1.014	1.012	1.007	symmetric X–C–X stretch
$\nu_3(1e'')$	0.910	0.962	0.945	0.876	0.944	0.933	out-of-plane C–H bend
$\nu_4(2a_2'')$	1.003	1.102	1.091	1.032	1.103	1.091	out-of-plane C–H umbrella
$\nu_5(2e')$	1.114	1.084	1.080	1.082	1.063	1.061	in-plane C–H bend
$\nu_6(2a_1')$	0.876	0.856	0.871	0.924	0.886	0.903	C–H stretch
$\nu_7(3e')$	0.918	0.900	0.912	0.962	0.931	0.943	C–H stretch
all	0.730	0.781	0.757	0.909	0.986	0.979	

<sup>a</sup> The last three columns refer to ion–dipole complexes. Vibrational modes are numbered in order of increasing frequencies at the FCH<sub>3</sub>F TS.

<sup>b</sup> The symmetry refers to the imaginary vibration; the contribution to the secondary kinetic isotope effect is from the corresponding vibration in the reactant.

**Table 5.** Different Geometry-Derived Parameters and the Secondary Kinetic Isotope Effect Referring to Isolated Reactants (See Text for Details)

X	$R_{CX}^{\ddagger}$	$\Delta R_{CX}^{\ddagger}$	$\Delta_{rel}R_{CX}^{\ddagger}$	$1 - n^{\ddagger}$	$1 - n_{Morse}^{\ddagger}$	SKIE
F	1.832	0.427	0.304	0.509	0.557	0.937
Br	2.432	0.482	0.247	0.553	0.577	0.957
Cl	2.310	0.532	0.299	0.588	0.625	0.989

**Table 6.** Different Geometry-Derived Parameters and the Secondary Kinetic Isotope Effect Referring to Ion–Dipole Complexes (See Text for Details)

X	$R_{CX}^0$	$\Delta R_{CX}^{\ddagger}$	$\Delta_{rel}R_{CX}^{\ddagger}$	$1 - n_{CX}^{\ddagger}$	SKIE
F	1.453	0.379	0.261	0.468	0.906
Br	1.980	0.452	0.228	0.529	0.978
Cl	1.808	0.502	0.278	0.567	0.986

a short bond. Employing experimental dissociation energies<sup>21</sup> and calculated force constants yields (eq 4)  $a$  parameters of 0.525, 0.542, and 0.561 for F, Cl, and Br, respectively. These are almost constant and close to the fixed value of 0.6, and the energy bond order also correlates nicely with the SKIEs. Employing either constant types indicates approximately half-formed bonds. The current results therefore indicate that transition state looseness is best measured by a  $\Delta$ -elongation or by bond order.

The above conclusions are based on isotope effects calculated with respect to isolated reactants; corresponding correlations when calculated relative to the ion–dipole complexes are given in Table 6. It has been speculated<sup>8</sup> that the contradictory results of Wolfe<sup>4</sup> and Poirier<sup>3</sup> might originate from the use of ion–dipole complexes and isolated reactants, respectively. Table 6 shows that this is not the case. Both the  $\Delta$ -elongation for the C–X bond and the corresponding bond orders correlate with the secondary kinetic isotope effects, while neither the absolute  $R_{CX}$  nor the relative elongation  $\Delta_{rel}R_{CX}$  are good measures of transition state looseness.

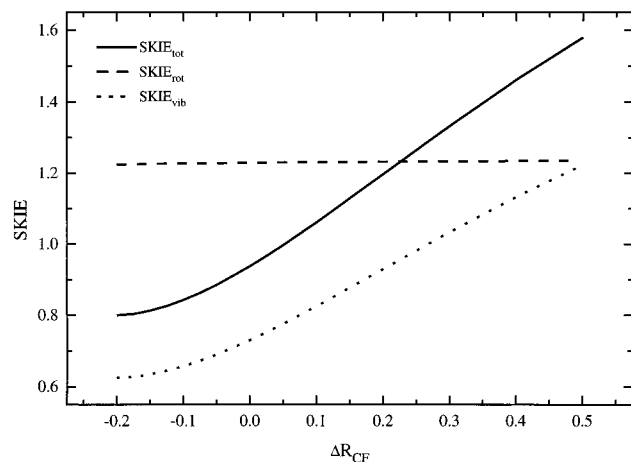
From Figure 1, it is possible to estimate the kinetic isotope effect for the three reactions having the same  $R_{CX}^{\ddagger}$  distance. If looseness was given directly by absolute bond lengths in the transition states, the kinetic isotope effects should be very similar for the three reactions when required to have the same bond length. The corresponding three SKIEs for a C–X distance of

the ClCH<sub>3</sub>Cl TS (2.310 Å) are 0.78 for Br, 0.99 for Cl, and 1.55 for F. These numbers clearly show that for a constant C–X distance, a TS with F as entering/leaving group is more loose than a corresponding TS with X = Cl, which again is more loose than with X = Br. This just reflects the fact that the atom size increases in the order F < Cl < Br. It also suggests that it might be possible to correct for different entering/leaving groups by subtracting an atomic radius instead of using the equilibrium bond length in the reactant/product. We have tried using either van der Waals radii, atomic radii, or ionic radii, but none of these results in parameters correlating with the increasing SKIE. The correction by subtracting the reactant/product bond length in the  $\Delta$ -elongation may therefore be seen not only as correcting for different sizes but also as correcting for different force constants of the TS bonds. As the secondary kinetic isotope effects are determined by force constant changes, the correlation with  $\Delta R_{CX}^{\ddagger}$  seems reasonable.

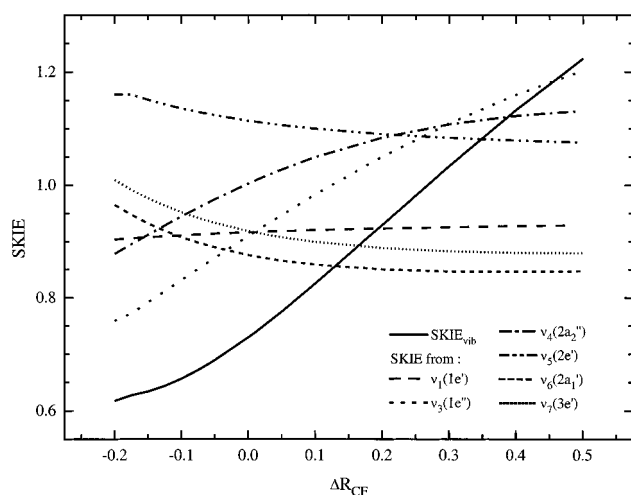
**Factor Analyses of the Frequencies.** In order to analyze further why there is a correlation between TS looseness and SKIEs, the KIE may be broken down into contributions from translations, rotations, and vibrations, and the latter further divided into contributions from individual frequencies. The results of such factor analyses for the three reactions are very similar, and only the results for the F<sup>−</sup> + CH<sub>3</sub>F reaction are presented. Tables containing results for the other reactions are available as Supporting Information.

The translational contribution to the SKIE as a function of the  $R_{CX}$  distance is constant, as the masses do not change. SKIE<sub>tot</sub> and the SKIEs from rotations and vibrations (SKIE<sub>rot</sub> and SKIE<sub>vib</sub>) as functions of  $\Delta R_{CF}$  are shown in Figure 2, and the variation of SKIE<sub>tot</sub> with transition state looseness is clearly governed by the vibrational contribution. The SKIE<sub>vib</sub> may be further factored into contributions from individual frequencies, shown in Figure 3. The F–C–F symmetric stretch, as already mentioned, gives no contribution to the KIE, and the F–C–F bend makes an essentially constant contribution independent of the looseness. The variation of SKIE<sub>vib</sub> is clearly determined by the 1e'' and 2a<sub>2</sub>'' C–H out-of-plane bending frequencies. The KIE of the 2e' in-plane C–H bending and the 2a<sub>1</sub>' and 3e' C–H stretching vibrations decreases as the TS becomes looser; however, the effect is much smaller than the out-of-plane bendings. Note, however, that the stretching vibrations (and the F–C–F bending) give inverse contributions to SKIE<sub>vib</sub>, i.e., the *absolute* value is strongly dependent on the stretching

(21) *CRC Handbook of Chemistry and Physics*; 74th ed.; Lide, P. R., Ed.; CRC Press: Boca Raton, FL, 1993.



**Figure 2.** Secondary kinetic isotope effect for  $\text{FCH}_3\text{F}$ ,  $\text{SKIE}_{\text{tot}}$ , and the rotational and vibrational contribution,  $\text{SKIE}_{\text{rot}}$  and  $\text{SKIE}_{\text{vib}}$ , as a function of TS C–X bond elongation. Bond lengths are in angstroms.

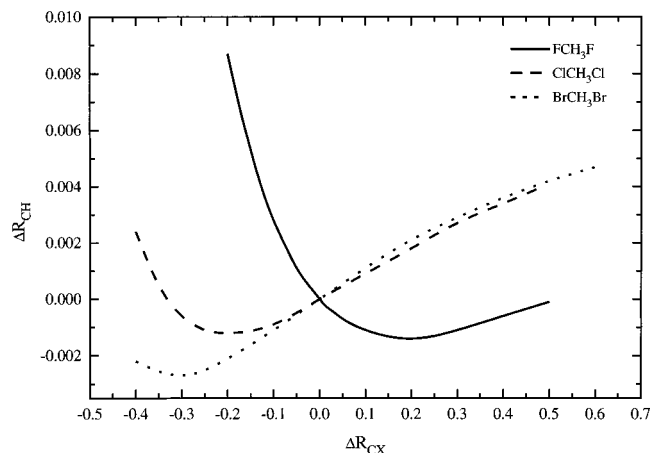


**Figure 3.** Contribution of individual frequencies to the secondary kinetic isotope effect for  $\text{FCH}_3\text{F}$  as a function of TS C–X bond elongation. Bond lengths are in angstroms.

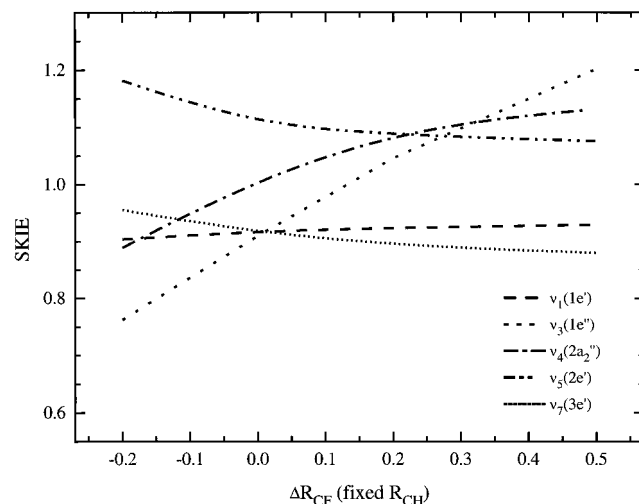
vibrations, whereas the *variation* is almost exclusively determined by the bending frequencies. The factor analysis thus confirms that the variation of SKIE with TS looseness stems from changes in the  $\text{C}_\alpha\text{--H(D)}$  out-of-plane and the umbrella bending vibrations, in agreement with the traditional interpretation.

The corresponding correlations of SKIEs from individual frequencies calculated with respect to ion–dipole complexes in essence give the same conclusions. The most important difference is that the  $1e'$  contributes with a normal SKIE ( $>1$ ), resulting in significantly higher absolute values of the  $\text{SKIE}_{\text{vib}}$ . Tables containing the respective values can be found as Supporting Information.

The results above are for transition structures constrained in the C–X bond lengths, but with  $R_{\text{CH}}$  allowed to relax. The changes in the C–H bond length as a function of  $\Delta R_{\text{CX}}$  for the three reactions are shown in Figure 4. As the C–F distance is varied, the C–H bond length initially decreases and passes through a minimum, whereas an increase in  $R_{\text{CBr}}$  is followed almost exclusively by an increase in  $R_{\text{CH}}$ . For  $X = \text{Cl}$  there is a clear minimum at a tight transition structure. A change in C–X bond lengths is thus accompanied by a variation in the C–H bond lengths that might have an influence on the SKIE variation. To test how a change in the C–X bond length alone influences the SKIE, we have performed a series of frequency calculations with no prior geometry optimization. That is,  $R_{\text{CH}}$



**Figure 4.** Variation of transition state C–H bond length as a function of constrained TS C–X bond lengths, for three transition structures. Bond lengths are in angstroms.



**Figure 5.** Contribution of individual frequencies to the secondary kinetic isotope effect for  $\text{FCH}_3\text{F}$  as a function of TS C–X bond elongation at fixed  $R_{\text{CH}}$ . Bond lengths are in angstroms.

is kept at its TS length while  $R_{\text{CX}}$  is varied. The corresponding geometries have non-zero gradients along both the C–F and C–H bonds. Projection of the force constant matrix to remove the gradient direction results in changes in the  $2a_1'$  vibration (symmetric C–H stretch), and disappearance of the  $1a_1'$  vibration. All other vibrations belong to irreducible representations that are not totally symmetric, and they are unaffected by the projection. The contributions from the  $a_2''$ ,  $e'$ , and  $e''$  vibrations at different C–X bond lengths can accordingly be calculated straightforwardly. The disappearance of the  $1a_1'$  vibration by the projection is inconsequential as this vibration makes no contribution to the KIE. From Figure 3 it can be seen that the variation of the  $2a_1'$  contribution is practically identical to the variation of the  $3e'$  contribution. This is reasonable since both are linear combinations of the same three C–H stretching motions. The  $2a_1'$  contribution to the SKIE may therefore be estimated from the corresponding  $3e'$ . However, we do not calculate a total secondary kinetic isotope effect, but concentrate on the variation of individual contributions.

The variation of the SKIE for fixed C–H bond lengths was calculated for  $X = \text{F}$ , and the results are shown in Figure 5. The only difference between Figures 3 and 5 is that the C–H bond distance is optimized in the former. A comparison of the two figures shows that the variations in SKIE from the individual vibrations are practically identical, except for the  $3e'$  C–H stretching vibration. In Figure 3, the KIE contribution from

**Table 7.** Frequencies for the Two Out-of-Plane Bending Vibrations Most Important for the Variation of the Secondary Kinetic Isotope Effect with Transition State Looseness

X		TS(H)	TS(D)	R(H)	R(D)	SKIE
1e''	F	1121	798	1212	925	0.910
	Br	942	667	998	742	0.945
	Cl	952	675	1072	805	0.962
2a <sub>2</sub> ''	F	1279	932	1525	1175	1.003
	Br	1035	738	1393	1053	1.091
	Cl	1097	790	1459	1106	1.102

this stretching vibration (and for the symmetric 2a<sub>1</sub>') decreases and levels out as the C–F bond lengths are increased. For fixed R<sub>CH</sub>, however, the SKIE of 3e' is only slightly decreasing. For negative ΔR<sub>CF</sub>, the SKIE variation of 3e' is therefore primarily a result of the decrease in C–H bond length with increasing C–F bond length.

As shown in Figure 4, the correlation between the C–X and C–H bond lengths is parabolic for all three reactions, but whereas X = F is dominated by an initial decrease in R<sub>CH</sub>, the C–H bond lengths primarily increase for X = Cl and Br. This difference is reflected in the stretching contributions to the SKIE, as the negative slope for tight transition structures is much more prominent for X = F than for X = Br. Similar to the analysis of R<sub>CX</sub> with fixed R<sub>CH</sub>, the effect of varying the C–H bond distances alone was also analyzed. This was done for all three reactions with essentially identical results; tables are provided as Supporting Information. The bending contributions decrease slightly as the C–H bonds are elongated, while the 3e' stretching contribution increases and is almost linearly correlated with the C–H bond distance. For all three reactions, a decrease in R<sub>CH</sub> should accordingly result in a decreasing stretching contribution. The different slopes of the stretching contributions at tight transition structures for the three reactions can therefore be explained by the different behavior of R<sub>CH</sub> as a function of R<sub>CX</sub> for negative ΔR<sub>CX</sub>. For positive ΔR<sub>CX</sub>, however, the 3e' contribution does not depend on R<sub>CH</sub> and all three reactions show a decreasing stretching contribution as a function of ΔR<sub>CX</sub>.

In summary, the variation of the secondary kinetic isotope effect as a function of transition state looseness is determined primarily by changes in the 2a<sub>2</sub>'' and 1e'' bending vibrations, and these are due to variations in R<sub>CX</sub> and not in R<sub>CH</sub>. The secondary kinetic isotope effects from the stretching vibrations decrease as transition state looseness increases, most significant for tight structures. This variation in SKIE is attributable to changes in R<sub>CH</sub> as R<sub>CX</sub> is varied, whereas the overall decrease with increasing transition state looseness can only be explained by the C–X, and not by the C–H, distance.

The two most important bending vibrations (2a<sub>2</sub>'' and 1'') can alone explain the ordering of the total secondary kinetic isotope effects for the three reactions; frequencies are given in Table 7. The ordering of both individual SKIE contributions is the same as SKIE<sub>tot</sub>. Looking at the actual frequencies in the hydrogenated and deuterated reactants and transition states shows that the variation cannot be explained by changes in either

the reactant or the transition state as a result of deuteration, but only by differences in the changes. The correlation between the secondary kinetic isotope effect and transition state looseness is therefore not due to properties of the TS alone, but to differences in the effect of H/D substitution in the reactant and TS. This further indicates that the Δ-elongation and bond order parameters are the most appropriate for measuring transition structure looseness.

## Conclusions

We have performed MP2/6-31++G(d,p) ab initio calculations on three identity S<sub>N</sub>2 reactions of the type X<sup>−</sup> + CH<sub>3</sub>X, for X = F, Cl, and Br, with the purpose of investigating the correlation of secondary hydrogen/deuterium kinetic isotope effects and transition state looseness.

Due to the high symmetry of these transition structures it is possible explicitly to demonstrate that the absolute value of the α-secondary kinetic isotope effect *increases* with increasing TS looseness. A comparison of the three reactions indicates that transition state looseness is best described by a Δ-elongation, where the reactant bond length is subtracted from the TS bond length or, equivalently, by bond orders. There is no correlation between uncorrected TS bond lengths or relative bond length elongation and the SKIEs. Subtraction of experimental measures of atom sizes, such as van der Waals, atomic, or ionic radii, does not result in useful looseness parameters either. This suggests that the reactant bond length correction corresponds to a force constant correction rather than to a size-correction. As kinetic isotope effects are determined by changes in the force constants between reactants and TS, a correlation between SKIEs and ΔR<sub>CX</sub> seems reasonable.

The variation of SKIEs with TS looseness is shown to be due to the vibrational contribution, and it is primarily determined by the two C<sub>α</sub>–H(D) out-of-plane bending modes. The secondary kinetic isotope effects increase with increasing transition state looseness as a result of increased space around the C<sub>α</sub>-hydrogens, decreasing the force constants of the out-of-plane bendings. The contributions from stretching vibrations are important in determining the absolute values of the SKIEs and are the direct source of a level-off in SKIE at tight transition structures. The variation in the stretching contributions is for large R<sub>CX</sub> caused by the C–X distances but for small R<sub>CX</sub> by an indirect effect where differences in the looseness influence the C–H bond distance, which in turn affects the stretching frequencies. This indirect effect gives only a very small contribution to the out-of-plane vibrations.

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**Supporting Information Available:** Listing of total and vibrational secondary kinetic isotope effects and individual frequency contributions (6 pages). See any current masthead page for ordering and Internet access instructions.

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