Temperature Dependence of Bromine Kinetic Isotope Effects for Reactions of *n*-Butyl and *tert*-Butyl Bromides[1]

John F. Willey and James W. Taylor*

Contribution from the Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706. *Received July 26, 1979*

Abstract: Techniques for the measurement of bromine leaving group kinetic isotope effects (KIE) are described. Experimental values at 20 °C for the solvolysis of *tert*-butyl bromide (0.045 M) in methanol with 0.3 M 2,6-lutidine and for the reaction of *n*-butyl bromide (0.047 M) with thiophenoxide anion (0.052 M) in 0.25 M lithium methoxide/methanol solvent are 1.003 10 (±0.000 04) and 1.001 69 (±0.000 03), respectively. The natural logarithm of the KIE was found to vary linearly with $1/T$ from 0 to 40 °C for *tert*-butyl bromide, slope = 0.472 (±0.080) deg^{-1}, and from −10 to 40 °C for *n*-butyl bromide, slope = 0.531 (±0.029) deg^{-1}. The significance of the KIE temperature dependencies is discussed.

Introduction

Heavy atom kinetic isotope effects (KIE) have shown great utility in the study of organic reaction mechanisms[2,3] and as a probe of transition-state structure.[4-7] When the isotopically substituted species is a nonbonded product of the reaction (e.g., chloride ion), the KIE have been found to behave qualitatively according to simple theoretical predictions and chemical intuition.[8-10]

In like manner, the temperature dependencies have been shown to yield information of importance in characterizing the transition state. Among these studies are the central carbon effects reported by Bron and Stothers,[11,12] the theoretical calculations of Stern and co-workers,[13] and the use of the temperature variation in chlorine KIE to "tune" the transition-state models calculated by Williams and Taylor[5] and by Julian and Taylor.[6]

Turnquist, Taylor, Grimsrud, and Williams[10] have studied the temperature dependence of chlorine KIE for the S_N1 solvolysis of *tert*-butyl chloride in 0.25 M lithium methoxide and the S_N2 reaction of *n*-butyl chloride with thiophenoxide anion in the same solvent. Simplified theoretical calculations predicted that the slope of the line obtained by plotting ln KIE vs. $1/T$ should be 1.94 cm^{-1} for the *tert*-butyl reaction and 1.55 cm^{-1} for the *n*-butyl reaction. The experimental values gave slopes of 1.76 and 1.77 cm^{-1}, respectively, and it was not known at that time if the agreement between the two experimental values for the slope had theoretical significance.

This paper reports the development of techniques for measuring the leaving group KIE for bromine, and reports bromine KIE at several temperatures for the solvolysis of *tert*-butyl bromide in methanol and the reaction of *n*-butyl bromide with thiophenoxide anion in 0.25 M lithium methoxide. The decision to study the bromine analogues of the reactions studied previously[10] was predicated on the assumption that the reactions of the bromide and chloride would be mechanistically similar. If so, this would allow evaluation of the effect of the leaving-group mass (and the attendant vibrational frequency and isotopic shift differences) on the observed KIE and the temperature dependencies of these heavy atom KIE.

Experimental Section

Materials. Laboratory **distilled water** was further purified by distillation from alkaline permanganate and then from sulfuric acid solution. The ***n*-butyl** and ***tert*-butyl bromides** (Eastman) were distilled under nitrogen prior to each kinetic run. The 0.3 M **lithium methoxide** solvent was prepared by adding 2.08 g of freshly cut lithium rod (Alfa Inorganics) to reagent grade methanol under an argon atmosphere and diluting to 1 L with methanol. Lithium nitrate/2,6-lutidine/methanol solvent was prepared by dissolving approximately 10.32 g of lithium nitrate (Fisher certified) in methanol, adding 16.1 g of 2,6-lutidine (Aldrich) which had been distilled under nitrogen, and diluting to 500 mL with methanol. All solvents were sparged with methanol-saturated nitrogen gas. For reactions with thiophenoxide ion, freshly vacuum distilled thiophenol (Aldrich) was added to the 0.3 M lithium methoxide solvent shortly before the addition of the bromide.

Kinetic Procedures. All kinetic runs were carried out in 250-mL low actinic flat-bottom flasks with ground-glass stoppers at the temperature stated ±0.01 °C for reactions above 0 °C and ±0.02 °C for reactions at 0 °C and below. At timed intervals, 25-mL aliquots of the reaction mixture were transferred to a separatory funnel and extracted between a 25-mL aqueous layer and 250 mL of heptane; the heptane layer was washed with 5–8 mL of water and the combined aqueous layers were extracted with 150 mL of heptane, which was also washed with 5–7 mL of water. For the reactions involving thiophenoxide anion, the initial 25-mL aqueous layer was 1.5 M in nitric acid. This stopped the reaction by protonating the thiophenoxide. For reactions of *tert*-butyl bromide the reaction was quenched by using heptane which had been chilled in a dry ice/methanol bath. For the reactions of *tert*-butyl bromide in 0.3 M lithium methoxide, the extracted aqueous layer was acidified by the dropwise addition of 1.5 M nitric acid, 10 drops past the phenolphthalein end point. For reactions in lutidine solvent the acidification was done by the addition of 10 mL of concentrated nitric acid. The aqueous solutions were then brought to high ionic strength by the addition of 4 g of potassium nitrate and titrated with 0.01 M silver nitrate. During the titrations, the silver ion concentration was measured using a silver wire electrode referenced to a saturated calomel electrode which was connected to the solution through an agar/potassium nitrate salt bridge. The potential difference between the electrodes was monitored using a Radiometer potentiometer. After determination of the end point, a 20–25% excess of titrant was added to ensure that all of the bromide ion was removed from solution. The silver bromide precipitates were allowed to age overnight, washed with dilute (1:250) nitric acid, and dried at 105 °C for 12–24 h. All titrations and subsequent steps involving silver bromide were carried out under photographic safelights (Kodak Type OC filter).

The reference bromide samples, representing 100% reaction, were prepared by refluxing the alkyl bromide in 0.3 M lithium methoxide under nitrogen. For *n*-butyl bromide the reflux mixture also contained a twofold excess of thiophenoxide.

Conversion of Silver Bromide to Methyl Bromide. The dried silver bromide was converted to methyl bromide using a procedure similar to that used previously for chloride samples[14] except that the conversion vessel was a two-piece stopcock-sealed vessel with the two halves joined by a 14/35 ground-glass joint and held together with steel springs. Both the vacuum stopcock and the ground-glass joint were lubricated with Apiezon H high-temperature vacuum grease (James G. Biddle and Co.), and the stopcock was clamped with a no. 28 joint clamp which had been filed slightly to fit. A threefold mole excess of methyl iodide was used and the reaction was carried out at 120 °C for 64–72 h.

After separation from the excess methyl iodide via gas chromatography, the methyl bromide was found to contain trace amounts of methanol and water. Both caused mass spectrometer instability problems. A two-step vacuum distillation at dry ice/methanol temperature was employed to remove these contaminants.

Isotopic Analysis of Methyl Bromide. The relative isotopic com-

0002-7863/80/1502-2387$01.00/0

position of the methyl bromide gases was determined using a Nuclide Model 6-60 RMS isotope ratio mass spectrometer modified to allow capacitive integration of the ion beam currents.[15] The measured values were corrected for proton fragmentation using the method described by Taylor and Grimsrud[14] and for valve mixing according to the procedure of Deines.[16]

A series of sodium bromide solutions of known enrichment were prepared by the addition of highly enriched $Na^{79}Br$ or $Na^{81}Br$ (Oak Ridge National Laboratories) to a solution of reagent grade sodium bromide (J. T. Baker) which was assumed to be near natural abundance. Aliquots of these solutions were converted to methyl bromide and analyzed on the mass spectrometer. The experimentally determined δ values were compared to the δ values calculated from the known enrichment factors. (δ is the relative difference between the measured ion beam ratios for the sample and standard gases in parts per thousand and is calculated by $\delta = [1 - (R\text{ sample}/R\text{ standard})] \times 1000$). A linear least-squares regression of δ measured on δ calculated yielded a slope of 1.0036 (standard deviation = 0.061) indicating that the measured values do accurately reflect the calculated enrichments and that the two instrumental correction factors are reasonably correct. (It should be noted that these data were taken prior to modifications of the mass spectrometer to improve the precision with which isotope ratio measurements could be made. Therefore, the scatter in the measured δ values does not reflect the sample to sample variation currently experienced[15] in this laboratory.)

To test both the sample to sample variation of the chemical conversion of bromide ion to methyl bromide and the run to run variation of the mass spectrometer, three separate conversions were carried out on aliquots of the same solution, and the resulting methyl bromide gases were analyzed on the mass spectrometer on each of three different days. A two-way analysis of variance with the data grouped according to sample number and day run indicated no difference significant at the 0.05 level of confidence. The standard deviation of the nine values was 0.0072.

Calculation of Isotope Effects. The bromine KIE values were calculated from the measured isotopic enrichment of the samples with respect to the starting materials and the measured fraction of reaction (from the titration values) at which the sample was taken using an equation derived by Bigeleisen and Wolfsberg:[17]

$$\mathrm{KIE} = \frac{k_{79}}{k_{81}} = 1 + \frac{\log\left[1 + \left(\dfrac{R_0 - R}{R_0}\right)\left(\dfrac{f(1 + R_0)/(1 + R)}{1 - f(1 + R_0)/(1 + R)}\right)\right]}{\log\,[1 - f(1 + R_0)/(1 + R)]} \tag{1}$$

where f is the fraction of reaction, R_0 is the ratio of $^{81}Br/^{79}Br$ in the starting material (assumed to be 0.9786, the natural abundance of bromine isotopes[18]), and R is the same ratio for the bromide product from the reaction.

For the *tert*-butyl bromide solvolysis in 0.3 M lithium methoxide, the measured values of the KIE were found to be low at very low fractions. After about 15% of the reactant had reacted, the values were invariant with fraction of reaction to within experimental error. The source of this variation is believed to be a small bromide blank (ca. 0.5%) in the reactant bromide. The data reported for the reactions of *tert*-butyl bromide with methoxide are only those values obtained after 15% reaction. For the reactions where lutidine was added, the bromide reactant was distilled from potassium carbonate prior to use and the measured KIE values do not show this effect.

Product Analysis of *tert*-Butyl Bromide Reactions. The product analysis was done on an F&M Scientific Corp. Model 720 programmed temperature gas chromatograph with a Model 1609 flame ionization attachment. The column was 6.35 mm o.d. by 2.18 m stainless steel packed with 15% (w/w) ethylene glycol isophthalate (Wilkins Instrumentation, Inc.) on HMDS-treated Chromosorb P (Johns-Manville), 60/80 mesh. The reaction samples were placed in glass capillary melting point tubes, frozen with liquid nitrogen, and sealed with an oxyacetylene torch. Each tube was then wrapped in aluminum foil to exclude light and placed back into the temperature bath. At timed intervals, a tube was removed from the bath, unwrapped, and crushed in the injection port of the GC using a capillary crusher sampler. At ambient temperature (ca. 22 °C) and a helium flow rate of 28 cm^3/min, the retention time (uncorrected) of 1-butene was 72 s, that of butyl bromide was 180 s, and that of butyl methyl ether was 230 s. After the emergence of the ether, the column temperature was raised to 90 °C until the solvent peak had completely emerged.

Statistical Treatment of Data. The error limits for the reaction rate constants reported in this paper are the standard deviation of the slope of the least-squares line fit to the appropriate kinetic equation for first- or second-order reactions. These then estimate the within run precision of the rate constants and are not estimates of the run to run uncertainty.

Because the KIE values reported here are based on four or five values at each temperature, the simplified statistics for small numbers of observations described by Dean and Dixon[19] have been used. The reported value is the median value while the error limits are the 95% confidence limits of the median estimated from the range.

Results and Discussion

Before comparison of the chlorine KIE values of Turnquist et al.[10] with the bromine values, it became of interest to determine whether the *tert*-butyl bromide reaction conditions were clearly S_N1-E1 or were complicated by E2 elimination. In the alkaline medium of 0.3 M lithium methoxide in methanol, it is possible that a significant contribution to the overall reaction comes from base-induced E2 elimination.[20] The S_N1 and E1 processes are expected to exhibit the same KIE because they both proceed through the carbonium ion intermediate, and the KIE is determined in the rate-limiting formation of the carbonium ion. The E2 mechanism, however, would be expected to have a lower KIE, and, if the reaction in 0.3 M lithium methoxide contains a significant E2 contribution, the measured KIE value would be lower than the value indicative of a pure S_N1-E1 reaction. A comparison of the relative amount of olefin produced in methanol containing 0.3 M $LiNO_3$ and 0.3 M 2,6-lutidine should indicate if the methoxide is causing E2 elimination. This determination was possible using gas chromatography as described in the Experimental Section. In 0.3 M lithium methoxide, the ratio of the 1-butene peak area to that of the *tert*-butyl methyl ether was 0.49 and was constant throughout the complete course of the reaction. In the presence of 0.3 M 2,6-lutidine and 0.3 M $LiNO_3$, the ratio was 0.22 and was again constant through the complete reaction. (Lutidine was used to preclude the possibility of the addition of HBr to the olefin product by preventing the buildup of hydrogen ion concentration.) To verify that the lutidine itself was not promoting E2 elimination, a product analysis of a reaction run with 0.3 M $LiNO_3$ and 0.15 M 2,6-lutidine in methanol was run. The ratio of the 1-butene peak area to the *tert*-butyl methyl ether peak area was again found to be 0.22. From these data, it appeared that the reaction in 0.3 M lithium methoxide does include E2 elimination, and the KIE value in that solvent would, therefore, probably be lower than the value representative of the purely S_N1-E1 process.

The solvolysis of *tert*-butyl bromide (0.04–0.05 M) was run both in 0.3 M lithium methoxide/methanol and in 0.3 M lithium nitrate/0.3 M 2,6-lutidine/methanol at 20.0 °C. In the methoxide-containing solvent, the first-order rate constant, which was calculated as the slope of the least-squares fit to the equation $-\ln(1 - f) = k_1T$, was $1.72\ (\pm 0.01) \times 10^{-5}\ s^{-1}$. The KIE value was 1.002 95 (±0.000 04). In the lutidine-containing solvent, the values were $k_1 = 2.27\ (\pm 0.01) \times 10^{-5}\ s^{-1}$ and KIE = 1.003 10 (±0.000 04). The larger value of the KIE measured in the lutidine-containing solvent is consistent with the hypothesis that the value obtained in the methoxide solvent reflects a contribution from the E2 process.

The increase in reaction rate observed in going from the methoxide/methanol solvent to the nitrate/lutidine/methanol solvent system probably can be interpreted as a normal salt effect. The possiblity of nucleophilic attack by nitrate is unlikely because tertiary alkyl halides are reported to react via S_N1 mechanisms in polar solvents even when in the presence of large concentrations of nucleophiles,[21] and because a large contribution from an S_N2 process would have led to a decrease

Table I. Rate Constants and KIE Values for *tert*-Butyl Bromide Solvolysis

0.0 °C		20.0 °C		40.0 °C	
$[t\text{-BuBr}]_0 = 0.046$ M		$[t\text{-BuBr}]_0 = 0.045$ M		$[t\text{-BuBr}]_0 = 0.048$ M	
$k = 1.10\ (\pm 0.01) \times 10^{-6}\ \mathrm{s^{-1}}$		$k = 2.27\ (\pm 0.01) \times 10^{-5}\ \mathrm{s^{-1}}$		$k = 2.93\ (\pm 0.01) \times 10^{-4}\ \mathrm{s^{-1}}$	
f	KIE	f	KIE	f	KIE
0.19	1.003 27	0.19	1.003 12	0.11	1.003 06
0.20	1.003 28	0.27	1.003 11	0.20	1.003 03
0.21	1.003 24	0.30	1.003 06	0.24	1.003 02
0.22	1.003 23	0.34	1.003 08	0.29	1.003 04
				0.36	1.002 95
median	= 1.003 25	median	= 1.003 10	median	= 1.003 03
	± 0.000 04		± 0.000 04		± 0.000 06

Table II. Rate Constants for KIE Values for the Reaction of *n*-Butyl Bromide with Thiophenoxide Anion

−10.0 °C		0.0 °C		20.0 °C		40.0 °C	
$[n\text{-BuBr}]_0 = 0.049$ M		$[n\text{-BuBr}]_0 = 0.046$ M		$[n\text{-BuBr}]_0 = 0.047$ M		$[n\text{-BuBr}]_0 = 0.048$ M	
$[\mathrm{PhS^-}]_0 = 0.050$ M		$[\mathrm{PhS^-}]_0 = 0.049$ M		$[\mathrm{PhS^-}]_0 = 0.052$ M		$[\mathrm{PhS^-}]_0 = 0.047$ M	
$k = 8.35\ (\pm 0.02) \times 10^{-5}$ L/mol·s		$k = 2.79\ (\pm 0.004) \times 10^{-4}$ L/mol·s		$k = 2.58\ (\pm 0.004) \times 10^{-3}$ L/mol·s		$k = 1.78\ (\pm 0.02) \times 10^{-2}$ L/mol·s	
f	KIE	f	KIE	f	KIE	f	KIE
0.16	1.001 89	0.16	1.001 84	0.19	1.001 69	0.14	1.001 59
0.21	1.001 95	0.20	1.001 81	0.25	1.001 71	0.17	1.001 55
0.24	1.001 91	0.24	1.001 81	0.28	1.001 69	0.21	1.001 56
0.27	1.001 97	0.28	1.001 79	0.33	1.001 71	0.30	1.001 62
0.30	1.001 89	0.32	1.001 75	0.36	1.001 66		
median	1.001 91	median	1.001 81	median	1.001 69	median	1.001 58
	± 0.000 04		± 0.000 05		± 0.000 03		± 0.000 04

in the measured KIE value rather than the observed increase.

The kinetic isotope effects at various temperatures in the range of −10 to 40 °C were determined for the solvolysis of *tert*-butyl bromide in lithium nitrate/lutidine/methanol solvent and for the reaction of *n*-butyl bromide with thiophenoxide anion in lithium methoxide/methanol solvent. The results are summarized in Tables I and II. At each temperature, the measured KIE value for the *n*-butyl bromide reaction was lower than the value for *tert*-butyl bromide. This is consistent with previous results for the corresponding chloride compounds[10] and agrees with other results[8] which indicate that S_N2 reactions exhibit lower leaving group KIE values than S_N1 reactions.

Theoretical calculations of KIE are usually based on a general case equation which is then modified for elements heavier than hydrogen.[17] This modified equation, which applies for intermediate temperatures, consists of a temperature-independent factor (TIF) and a temperature-dependent factor (TDF). Direct evaluation of the KIE using this general case equation would require knowledge of all the normal modes of vibration of both the reactant and transition state. Because vibrational frequency data on the transition state are not available, it has been necessary to make simplifying assumptions to allow values to be estimated from available data.

A method for calculating the TIF from experimental values of KIE at several temperatures is the $\bar{\gamma}$ equation:

$$\ln \mathrm{KIE} = \ln \mathrm{TIF} + (\bar{\gamma}/24)\left[\sum^{3N-6} (u_{1i}{}^2 - u_{2i}{}^2) - \sum^{3N-7} (u_{1i}{}^{\ddagger 2} - u_{2i}{}^{\ddagger 2})\right] \tag{2}$$

where the u_i's are the same as for the general case equation.[17] The values of $\bar{\gamma}$ may be calculated using the procedure prescribed by Monse, Spindel, and Stern,[22] and are shown here as eq 3, where only a few frequencies are actually required for the calculation.

$$\bar{\gamma} = \Sigma\gamma_i\Delta(\nu_i{}^2)/\Sigma\Delta(\nu_i)^2 \tag{3}$$

where

$$\Delta(\nu_i{}^2) = \nu_{1i}{}^2 - \nu_{2i}{}^2$$

and

$$\gamma_i = 12G(u_i)/u_i$$

Using the spectral data of Julian and Taylor[6] and of Julian,[23,24] shown here in Tables III and IV, values of $\bar{\gamma}$ were calculated for the *n*-butyl and *tert*-butyl chlorides and bromides. A linear least-squares regression of ln KIE on $\bar{\gamma}/T^2$ was then carried out using the KIE values of Turnquist et al.[10] for the chlorides and the values from the present study for the bromides. The coefficient of regression for the worst case was 0.988, and for the best was 0.999. The $T = \infty$ intercepts of the regressions were taken to be ln TIF according to eq 2. The TIF values thus determined are shown in Table V. Also shown in this table are the corresponding KIE values at 20 °C and the TIF values calculated by Williams and Taylor[5] and by Julian and Taylor[6] using the complete Bigeleisen KIE equation.[17] The excellent agreement between these latter values and the values obtained from the $\bar{\gamma}$ method indicates that the $\bar{\gamma}$ method may be used to obtain values which are consistent with those produced through much more laborious computer calculations.

The TIF values for the *n*-butyl and *tert*-butyl halides differ on the same order of magnitude as the differences in the KIE values (0.001 84 vs. 0.001 63 for the chlorides; 0.001 65 vs. 0.001 43 for the bromides). This suggests that the major source of the differences in the leaving group KIE for S_N1 and S_N2 reactions lies in the ratio of the decomposition frequencies in the transition state. This conclusion also requires that the TDF for these two types of reactions be roughly equivalent, which is in agreement with the results of Turnquist et al.[10] and provides a reason for obtaining the temperature dependences of the bromine values as will be discussed subsequently.

If the TIF values for *tert*-butyl chloride and bromide determined from the $\bar{\gamma}$ method are used in Bigeleisen and Wolfsberg's[17] molecular fragment mass equation, the calculated values for the effective mass of the *tert*-butyl group (M_A) are 8.8 for the chloride and 16.8 for the bromide. Because both reactions would be expected to have product-like transition states, it would be expected that the effective mass of the

Table III. Vibrational Frequencies and Isotopic Shifts of *n*-Butyl Chloride[a] and *n*-Butyl Bromide[b]

		$CH_3CH_2CH_2CH_2{}^{35}Cl$		$CH_3CH_2CH_2CH_2{}^{79}Br$	
ν	approximate description	frequency, cm^{-1} [c]	isotopic shift, cm^{-1} [c]	frequency, cm^{-1} [c]	isotopic shift, cm^{-1} [c]
ν_1	sym C–H stretch	2965.3		2969.0	
ν_2	CH_2 wag	1453.5	0.3	1445.4	0.3
ν_3	CH_2 scissor	1318.2		1300.0	
ν_4	C–C stretch	1021.8[d]	0.4[d]	1002.7	0.5
ν_5	C–X stretch (trans)	749.680[e]	4.702[e]	659.756[e]	0.549[e]
$\nu_{5'}$	C–X stretch (gauche)	670.451[e]	4.307[e]	578.425[e]	0.507[e]
ν_6	C–C–X bend	333.0[d]	1.4[d]	294.2[d]	0.4[d]
ν_7	asym C–H stretch	2998.8		3012.7	
ν_8	CH_2 twist	1243.8	0.5	1219.9	0.3
ν_9	CH_2 rock	876.3	0.3	867.8	0.4

[a] From ref 6 except as otherwise noted. [b] From ref 23 except as otherwise noted. [c] Estimated uncertainty ±0.1 cm^{-1} except as otherwise noted. [d] Estimated uncertainty ±0.2 cm^{-1}. [e] From ref 24; estimated uncertainty ±0.003.

Table IV. Vibrational Frequencies and Isotopic Shifts of *tert*-Butyl Chloride[a] and *tert*-Butyl Bromide[b]

		t-BuCl		*t*-BuBr	
ν	approximate description	frequency, cm^{-1} [c]	isotopic shift, cm^{-1} [c]	frequency, cm^{-1} [c]	isotopic shift, cm^{-1} [c]
ν_1	sym CH_3 stretch	818.0	0.6	808.4	0.2[d]
ν_2	C–X stretch	586.4	2.4	524.0	1.0
ν_3	sym C–C–C-def	376.3[d]	2.4[d]	308.9	0.3[d]
ν_4	asym CH_3 stretch	1240.8	0.5[d]	1237.9	0.5
ν_5	asym C–C–C–def	411.8	0.2[d]	406.3[d]	
ν_6	C–C–X def	309.4	1.1[d]	284.6[d]	0.4[d]

[a] From ref 6. [b] From ref 23. [c] Estimated uncertainties ±0.1 cm^{-1} except as otherwise noted. [d] Estimated uncertainties ±0.2 cm^{-1}.

Table V. Calculated Values of TIF and Experimental KIE (20 °C) for the Solvolysis of *tert*-Butyl Chloride and Bromide and for the Reaction of Thiophenoxide Anion with *n*-Butyl Chloride and Bromide

species	TIF[a]	TIF[b]	KIE (20 °C)
n-BuCl	1.003 61	1.00 36	1.008 95
t-BuCl	1.005 45	1.00 52	1.010 58
n-BuBr	1.000 52		1.001 67
t-BuBr	1.002 17		1.003 10

[a] Calculated by $\bar{\gamma}$ method. [b] Calculated by complete expression, ref 5 and 6.

tert-butyl group should be roughly the same for these two reactions.

One possible reason that the anticipated agreement in the M_A values is not found could involve the contribution of solvent. Significant bonding to the negatively charged leaving group could cause the effective mass of this group to be larger than the atomic mass. To account for this effect, a variable M_S may be included in the molecular mass equation, which leads to the equation

$$\mathrm{TIF} = \left[\left(\frac{1}{M_A} + \frac{1}{M_{B1} + M_S}\right)\left(\frac{1}{M_A} + \frac{1}{M_{B2} + M_S}\right)\right]^{1/2} \quad (4)$$

where M_S is the effective mass contributed by the solvent, and the other terms are as defined in ref 17.

For the *tert*-butyl halide system, we may obtain a crude estimate of the magnitude of M_A and M_S if we assume that neither changes significantly in going from *tert*-butyl chloride to *tert*-butyl bromide. This assumption is not expected to be strictly valid because of the different basicity, polarizability, and hydrogen bonding for Cl^- and Br^- ions. The use does allow us to make an approximate calculation from the atomic masses of the halogen atoms and the TIF values from the $\bar{\gamma}$ method to solve eq 4 for the values of M_A and M_S which are common to the two systems. Numerical solution under these assumptions leads to a value of M_A between 31 and 32 amu and an M_S value between 26 and 27 amu. While it is difficult to comment on the reliability of these values because no other values exist with which to compare them, they appear to be reasonable in magnitude. The value for M_A is between the atomic mass of carbon and the full mass of the *tert*-butyl group as previously anticipated.[25] The value of M_S would indicate a significant contribution from solvent. This is consistent with the theoretical calculation of Burton et al.[7] and with conclusions of Grimsrud[26] based on solvent-dependent variations of chlorine KIE. This points out that further studies into the effect of solvent interactions on the magnitude of KIE values are needed.

In their study of the temperature dependence of the chlorine KIE of *n*-butyl and *tert*-butyl chlorides, Turnquist et al.[10] estimated the value of the TDF for *n*-butyl chloride by assuming that the carbon-chlorine stretching frequency became negligible and imaginary in the transition state while all other frequencies and isotopic splittings remained unchanged between the ground and transition states. Under this assumption, and accounting for the various conformers, a value called TDF_I was calculated. For *tert*-butyl chloride, these authors argued that there were two vibrational modes which exhibited large isotopic splittings—the carbon-chlorine stretch and the symmetric bending frequency between the central carbon atom and the three methyl groups. This was defined as a type II situation and a value, TDF_{II}, was calculated where it was assumed that both frequencies effectively cancel in the transition state so that the $-G(u^{\ddagger})\Delta u^{\ddagger}$ terms do not enter into the calculation. Turnquist et al.[10] expected that the TDF_{II} values calculated would be too high by the magnitude of the $G(u^{\ddagger})\cdot\Delta u^{\ddagger}$ terms.

If we assume that the TIF values from the $\bar{\gamma}$ method may serve to allow an estimate of the TDF according to the relationship KIE = TIF·TDF, it becomes possible to generate a list of calculated values of TDF_I, TDF_{II}, and $TDF_{\bar{\gamma}}$ (from the experimental KIE and $TIF_{\bar{\gamma}}$ values) for *n*-butyl and *tert*-butyl chlorides and bromides at various temperatures. (In these calculations the values for the *n*-butyl halides were obtained using a weighting of 0.7 for the trans C–X stretch and 0.3 for the gauche C–X stretch because Rao[27] reports that 70% of the 1,2-dichloroethane is in the gauche conformer. The resulting TDF values are, however, relatively insensitive to the weightings of the trans and gauche conformers.) For *n*-butyl bromide, the isotopic splitting of the C–C stretch (ν_4 in Table III) is as large as the splittings for the C–Br stretch. It therefore seemed appropriate to use TDF_{II} rather than TDF_I as was used for the chloride. For purposes of comparison, however, the values of TDF_I were also calculated. For *tert*-butyl bromide, the isotopic splitting for the symmetric C–C–C deformation is only 0.3 cm^{-1} compared to 1.0 cm^{-1} for the C–Br stretch. The appropriate choice for this molecule would therefore seem to be $\mathrm{TDF_I}$. Again, the values of $\mathrm{TDF_{II}}$ were also calculated for comparison with *tert*-butyl chloride.

A convenient means of comparing the relationship between these calculated values and the experimentally observed temperature dependence of the KIE is to compare the slope of a plot of ln TDF vs. $1/T$ with that of a plot of ln KIE vs. $1/T$. Over a limited temperature range, such plots are nearly linear. The slopes obtained from linear regressions of ln TDF and ln KIE on $1/T$ are listed in Table VI. (The excellent agreement between the slopes predicted from the $\mathrm{TDF}_{\bar{\gamma}}$ values and the experimental slopes is, of course, the result of the fact that the $\mathrm{TDF}_{\bar{\gamma}}$ values were calculated from the experimental KIE by division by a constant.)

For both the chlorides and bromides, the slopes of plots of the experimental KIE values for the *tert*-butyl and *n*-butyl reactions are very close. This is consistent with the results of the $\mathrm{TIF}_{\bar{\gamma}}$ calculations which indicated that the major source of the difference in KIE values for these systems is situated in the TIF (vide supra). For *n*-butyl bromide, the agreement between the slopes of the KIE values (0.531) and the $\mathrm{TDF_{II}}$ values (0.636) is much better than with the $\mathrm{TDF_I}$ values (0.301).

Comparison of the $\mathrm{TDF}_{\bar{\gamma}}$ values with the appropriate $\mathrm{TDF_I}$ or $\mathrm{TDF_{II}}$ values shows that for all but the *tert*-butyl chloride reaction the agreement with $\mathrm{TDF_I}$ is quite good. This agreement is quite encouraging because the $\mathrm{TDF_I}$ and $\mathrm{TDF_{II}}$ values are calculated solely from spectroscopic data while the $\mathrm{TDF}_{\bar{\gamma}}$ values are calculated from the experimental KIE values in conjunction with the $\bar{\gamma}$ values calculated from the spectroscopic data.

The lesser degree of agreement for the *tert*-butyl chloride system may indicate a true limitation of the methods. Indeed, even this degree of agreement might be the result of an experimental complication in the *tert*-butyl chloride reaction. For the *tert*-butyl bromide reaction, it was demonstrated that the amount of olefin formation was higher in 0.3 M lithium methoxide/methanol than in 0.3 M 2,6-lutidine/0.3 M lithium nitrate/methanol and that the KIE value was lower in the more basic solvent. This was attributed to the occurrence of an E2 elimination process and was the reason that the lutidine-containing solvent was chosen for the temperature-dependence study. If the *tert*-butyl chloride reaction, which was studied in 0.25 M lithium methoxide, is complicated by an E2 elimination, then the KIE values used in the calculation of $\mathrm{TDF}_{\bar{\gamma}}$ may not be indicative of an uncomplicated $\mathrm{S_N1}$ reaction. This would mean that the $\mathrm{TDF}_{\bar{\gamma}}$ values generated from the observed KIE should be slightly higher, in which case the agreement with $\mathrm{TDF_{II}}$ values will be somewhat worse than indicated.

In conclusion, this work shows that reliable techniques for the measurement of bromine leaving group kinetic isotope effects have been developed and that the temperature dependence of the bromine KIE for nucleophilic substitution reactions of *n*-butyl and *tert*-butyl bromide are in accord with theoretical predictions. The comparisons of bromine KIE values with chlorine KIE values from analogous reactions have suggested the relative importance of various factors in determining the magnitude of the KIE, and, in particular, agree with the previous work[7] which suggests that solvation of the atomic leaving group must be considered in understanding the details of the mechanisms. These data also suggest a way to evaluate the magnitude of that effect. Additionally, the results of this work and that of previous work[10] indicate that the use of the $\bar{\gamma}$ method and the $\mathrm{TDF_I}$ and $\mathrm{TDF_{II}}$ equations provide simple and convenient methods of obtaining reasonable estimates for the values of TIF and TDF for atomic leaving group KIE.

Table VI. Slopes[a] of ln TDF vs. $1/T$ and ln KIE vs. $1/T$ for *n*-Butyl and *tert*-Butyl Chlorides and Bromides

	calcd slope			obsd slope
	$\mathrm{TDF_I}$	$\mathrm{TDF_{II}}$	$\mathrm{TDF}_{\bar{\gamma}}$	KIE
n-BuCl	2.73		2.56	2.56
t-BuCl		2.21	2.55	2.55
n-BuBr	0.301	0.636[b]	0.531	0.531
t-BuBr	0.498[b]	0.597	0.473	0.472

[a] All slopes are in deg^{-1}. [b] Assumed to be a more representative calculation from spectral data; see text.

References and Notes

(1) This research was supported by the National Science Foundation under Grant MPS75-21059. Purchase of the mass spectrometer and digital voltmeter was made possible through funds from the Wisconsin Alumni Research Foundation and the Department of Chemistry. Taken in part from the Ph.D. Dissertation of John F. Willey, Dec 1978.

(2) Fry, A. In "Isotope Effects in Chemical Reactions", Collins, C. J., Bowman, N. S., Eds.; Van Nostrand-Reinhold: Princeton, N.J., 1970.

(3) Saunders, W. H., Jr. *Surv. Prog. Chem.* **1966**, *3*, 109–146.

(4) Sims, L. B.; Fry, A., Netherton, L. T.; Wilson, J. C.; Reppond, K. D.; Crook, S. W. *J. Am. Chem. Soc.* **1972**, *94*, 1364–1365.

(5) Williams, R. C.; Taylor, J. W. *J. Am. Chem. Soc.* **1974**, *96*, 3721–3727.

(6) Julian, R. L.; Taylor, J. W. *J. Am. Chem. Soc.* **1976**, *98*, 5238–5248.

(7) Burton, G. W.; Sims, L. B.; Wilson, J. C.; Fry, A. *J. Am. Chem. Soc.* **1977**, *99*, 3371–3379.

(8) Hill, J. W.; Fry, A. *J. Am. Chem. Soc.* **1962**, *84*, 2763–2769.

(9) Grimsrud, E. P.; Taylor, J. W. *J. Am. Chem. Soc.* **1970**, *92*, 739–741.

(10) Turnquist, C. R.; Taylor, J. W.; Grimsrud, E. P.; Williams, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 4133–4138.

(11) Bron, J.; Stothers, J. B. *Can. J. Chem.* **1968**, *46*, 1435–1439.

(12) Bron, J.; Stothers, J. B. *Can. J. Chem.* **1968**, *46*, 1825–1829.

(13) Stern, M. J.; Spindel, W.; Monse, E. U. *J. Phys. Chem.* **1968**, *48*, 2908–2919.

(14) Taylor, J. W.; Grimsrud, E. P. *Anal. Chem.* **1969**, *41*, 805–810.

(15) Willey, J. F.; Taylor, J. W. *Anal. Chem.* **1978**, *50*, 1930–1933.

(16) Deines, P. *Int. J. Mass Spectrom. Ion Phys.* **1970**, *4*, 283–295.

(17) Bigeleisen, J.; Wolfsberg, M. *Adv. Chem. Phys.* **1958**, *1*, 15–76.

(18) Weast, R. C., Ed. "Handbook of Chemistry and Physics", 53rd ed.; Chemical Rubber Publishing Co.: Cleveland, Ohio, 1972.

(19) Dean, R. B.; Dixon, W. J. *Anal. Chem.* **1951**, *23*, 636–638.

(20) Dhar, M. L.; Hughes, E. D.; Ingold, C. K. *J. Chem. Soc.* **1948**, 2065–2072.

(21) Thornton, E. R. "Solvolysis Mechanisms"; Ronald Press: New York, 1964; p 84.

(22) Monse, E. U.; Spindel, W.; Stern, M. J. *Adv. Chem. Ser.* **1969**, *89*, 148.

(23) Julian, R. L. "Evaluation of Transition State Models Using Chlorine Kinetic Isotope Effects and High Resolution Vibrational Measurements", Ph.D. Dissertation, University of Wisconsin—Madison, 1976.

(24) Julian, R. L., unpublished results, Nicolet Instrument Corp., Madison, Wis., 1978.

(25) Turnquist, C. R. "Temperature and Solvent Dependencies of Chlorine Kinetic Isotope Effects", Ph.D. Dissertation, University of Wisconsin—Madison, 1972.

(26) Grimsrud, E. P. "Chlorine Kinetic Isotope Effects in Nucleophilic Displacement Reactions", Ph.D. Dissertation, University of Wisconsin—Madison, 1970.

(27) Rao, C. N. R. "Chemical Applications of Infrared Spectroscopy"; Academic Press: New York, 1963.