

# The Temperature Dependence of the Secondary Deuterium Isotope Effect in Hydrolysis

L. Hakka,<sup>1a</sup> A. Queen,<sup>1b</sup> and R. E. Robertson

Contribution No. 8294 from the Division of Pure Chemistry, National Research Council, Ottawa, Canada. Received September 24, 1964

The secondary deuterium isotope effect for the hydrolysis of *t*-butyl chloride-*d*<sub>9</sub> in water and in 50:50 ethanol-water was shown to conform closely to the approximation  $\delta_i\Delta F^* = \delta_i\Delta H^*$ . This result, while in agreement with accepted hypotheses, contrasts with the temperature dependence of  $k_H/k_D$  where there is strong interaction between the alkyl group and the solvent in the quasi-ionic or ionic state.

Zero-point energy differences are frequently considered to be the dominant factor among those determining not only primary but also secondary deuterium isotope effects.<sup>2,3</sup> This assumption implies that  $\delta_i\Delta F^* \sim \delta_i\Delta H^*$ . Accordingly it was surprising to find that the secondary  $\beta$ -deuterium isotope effects on the rates of hydrolysis of isopropyl-*d*<sub>6</sub> methanesulfonate, toluenesulfonate, and bromide showed negligible temperature dependence (i.e.,  $\delta_i\Delta F^* \cong \delta_i\Delta S^*$ ).<sup>4</sup> Subsequently the secondary  $\beta$ -deuterium isotope effect was shown to be apparently temperature independent in the solvolysis of two other secondary halides<sup>5</sup> and for the acid-base equilibria involving deuterated mono- and diethylamines.<sup>6</sup> Such temperature independence was in apparent conflict with the requirements of the zero-point hypothesis and the earlier experimental results of Shiner<sup>7</sup> and of Lewis and Boozer.<sup>8</sup>

We have accordingly examined the temperature dependence of the secondary  $\beta$ -deuterium isotope effect in *t*-butyl-*d*<sub>9</sub> chloride in 50:50 ethanol-water over a range of temperature from 5–30° at 5° intervals. At the time the work was initiated, techniques of rate determination required the study to be made in 50:50 ethanol-water, but there was no reason to expect this change of solvent would alter the mechanism (S<sub>N</sub>1) or notably change the corresponding isotope effect. This assumption has recently been supported by rate data for *t*-butyl-*d*<sub>9</sub> in water (Table III).<sup>9</sup>

Some doubt existed as to whether the mechanism of hydrolysis of the isopropyl compounds<sup>4</sup> was also S<sub>N</sub>1, but it was considered that if the nonbonded inter-

action argument of Leffek, *et al.*, applied in the case of the secondary compounds, it might equally well apply in the hydrolysis of the *t*-butyl chloride.

## Results and Discussion

Average rate data for protonated and 99% deuterated *t*-butyl-*d*<sub>9</sub> chloride determined consecutively are given in Table I for six temperatures. Assuming the

Table I. Solvolytic Data for *t*-Butyl Chloride in 50:50 Ethanol-Water<sup>a</sup>

Temp., °C.	$k_1 \times 10^4, \text{sec.}^{-1}$		$k_H/k_D$	
	H	D	Obsd.	Calcd.
5.686	0.3069 ± 0.0005	0.1207 ± 0.0005	2.542	2.543
10.550	0.6112 ± 0.0009	0.2440 ± 0.0007	2.505	2.502
15.020	1.119 ± 0.004	0.4539 ± 0.0021	2.465	2.465
20.054	2.153 ± 0.010	0.8900 ± 0.0011	2.419	2.424
24.999	4.001 ± 0.008	1.676 ± 0.002	2.387	2.379
30.014	7.310 ± 0.001	3.117 ± 0.004	2.345	2.346
55.686	...	...	...	2.086

<sup>a</sup> Shiner, *et al.*<sup>10</sup> used 60:40 v./v. ethanol-water.

indicated *d*<sub>9</sub> content to be 99%, the ratio at 25° is about 1% lower than the corresponding value recently reported by Shiner, Murr, and Heinemann.<sup>10</sup> Accordingly, with the cooperation of Mr. A. Morse of Merck Sharp and Dohme, Montreal, a new, carefully purified sample of *t*-butyl-*d*<sub>9</sub> chloride gave a ratio of 2.351 at 30.16°. The corresponding value calculated from the three-constant equation from our previous work was 2.345, well within the combined experimental error. A least-square fit to the empirical relation  $\log k_1 = A/T + B \log T + C$  using 25 individual rates gave the following values for the constants (*D*<sub>9</sub>).

	A	B	C
H <sub>9</sub> <sup>a</sup>	-6790.4175	-15.9116	58.7490
D <sub>9</sub>	-6721.4192	-14.3998	54.3994

From these constants smoothed rate ratios at the corresponding temperatures were calculated (Table I,  $k_H/k_D$  (calcd.)). Corresponding values of  $\Delta H^*$ ,  $\Delta S^*$ , and  $\Delta C_p^*$  are given in Table II.

In Table III corresponding values of  $k_H/k_D$  are given for hydrolysis in water at five temperatures. The values of  $\Delta H^*$  and  $\Delta S^*$  for the *d*<sub>9</sub> compound were calculated for 10°, the center of the experimental range. These data were not sufficiently accurate or extensive to justify calculation of a meaningful  $\Delta C_p^*$ . The value of  $k_H/k_D$  at 25° in 50:50 EtOH-H<sub>2</sub>O is the same (2.387) as the average value recently reported by Frisone and Thornton<sup>11</sup> for a series of solvents with somewhat

(10) V. J. Shiner, Jr., B. L. Murr, and G. Heinemann, *J. Am. Chem. Soc.*, **85**, 2413 (1963).

(11) G. J. Frisone and E. R. Thornton, *ibid.*, **86**, 1900 (1964).

(1) (a) Summer Research Assistant, National Research Council, 1961; (b) National Research Council of Canada Postdoctorate Fellow, 1961–1963.

(2) A. Streitwieser, Jr., R. H. Jagow, R. S. Fahey, and S. Suzuki, *J. Am. Chem. Soc.*, **80**, 2326 (1958).

(3) (a) L. Melander, "Isotope Effects on Reaction Rates," The Ronald Press Co., New York, N. Y., 1960, p. 89; (b) E. A. Halevi, "Progress in Physical Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1963, p. 127.

(4) K. T. Leffek, R. E. Robertson, and S. Sugamori, *Can. J. Chem.* **39**, 1989 (1961).

(5) K. T. Leffek, R. E. Robertson, and S. Sugamori, unpublished work.

(6) W. Van der Linde and R. E. Robertson, *J. Am. Chem. Soc.*, **86**, 4505 (1964).

(7) V. J. Shiner, Jr., *ibid.*, **76**, 1603 (1954).

(8) E. S. Lewis and C. E. Boozer, *ibid.*, **76**, 791 (1954).

(9) These rate determinations were by Mr. S. Sugamori using a method described in a recent paper: E. A. Moelwyn-Hughes, R. E. Robertson, and S. Sugamori, in press.

**Table II.** Derived Thermodynamic Parameters for the Hydrolysis of *t*-Butyl Chloride

	Cal./mole deg.		
	$\Delta H^*$	$\Delta S^*$	$\Delta C_p^*$
In 50:50 Ethanol-Water at 20°			
H <sub>9</sub>	21,220	-2.9	-34
D <sub>9</sub>	21,780	-2.7	-31
In Water at 10°			
H <sub>9</sub>	23,810	14.4	-83 <sup>a</sup>
D <sub>9</sub>	24,330	14.6	...

<sup>a</sup> See ref. 9.**Table III.** Solvolytic Rate Data for *t*-Butyl-*d*<sub>9</sub> Chloride in Water

Temp., °C.	$k_1 \times 10^{-4}$ , sec. <sup>-1</sup>		$k_H/k_D$
	H (calcd.) <sup>a</sup>	D (exptl.)	
2.070	1.003	0.3140 ± 0.0004	2.61
5.014	1.624	0.6373 ± 0.0037	2.55
10.049	3.579	1.414 ± 0.009	2.53
15.008	7.492	3.023 ± 0.014	2.48
20.014	15.21	6.199 ± 0.025	2.45

<sup>a</sup> See ref. 9.

different *Y* values.<sup>12</sup> A comparison of the  $k_H/k_D$  values in Tables I and III shows that this ratio is essentially the same in water ( $Y = 3.5$ ) and in a 50:50 ethanol-water mixture ( $Y = 1.6$ ). This result either supports the suggestion that there is no specific interaction between the solvent and the developing cation<sup>13</sup> or that it is the same in both systems. That the  $k_H/k_D$  ratio is not independent for all ranges of *Y* values is illustrated in Table IV by our results in methanol ( $Y = -1.05$ ).

**Table IV.** Secondary  $\beta$ -Deuterium Isotope Effect for the Solvolysis of *t*-Butyl Chloride in Methanol at 55.87°

$k_H \times 10^5$ , sec. <sup>-1</sup>	$k_D \times 10^5$ , sec. <sup>-1</sup>
3.922	1.715
3.902	1.717
3.902	
$k_H/k_D = 2.274$	

The corresponding rate for the protonated halide calculated from the equation of Biordi and Moelwyn-Hughes is 4.05,<sup>14</sup> in agreement with our value considering the combined sources of error. The increase in the  $\beta$ -deuterium isotope effect ( $k_H/k_D = 2.09$  in 50:50 ethanol-water but 2.27 in methanol) is in the direction required by a greater degree of charge development (or hyperconjugation) rather than giving any suggestion that reaction is less limiting in the poorer ionizing solvent.

It will be apparent from Table II that the  $\beta$ -deuterium isotope effect for solvolysis of *t*-butyl arises almost entirely from a difference in  $\Delta H^*$ , whether the medium is water ( $Y = 3.5$ ) or 50:50 ethanol-water ( $Y = 1.6$ ). Were solvation of the quasi-carbonium ion an important factor in determining  $k_H/k_D$ ,  $\delta_I \Delta S^*$  would not be expected to approximate to zero.<sup>15</sup>

(12) E. Grunwald and S. Winstein, *J. Am. Chem. Soc.*, **70**, 846 (1948).(13) R. E. Robertson, *Can. J. Chem.*, **42**, 1707 (1964).(14) J. Biordi and E. A. Moelwyn-Hughes, *J. Chem. Soc.*, 4291 (1962).

(15) E. A. Halevi, ref. 3b, Vol. 1, Chapter 4, pp. 191, 192.

A reasonable working hypothesis which will take account of the difference in the  $\beta$ -deuterium isotope effect for solvolysis of *t*-butyl chloride ( $\delta_I \Delta F^* = \delta_I \Delta H^*$ ) and the comparable reactions of secondary halides and sulfonates ( $\delta_I \Delta F^* = \delta_I \Delta S^*$ ) can be advanced in terms of probable solvation differences and the recent theoretical analysis of the effect of temperature on the latter isotope effect by Wolfsberg and Stern.<sup>16</sup> They showed that  $k_H/k_D$  could be virtually temperature independent for reasonable changes in the force constants of two compensating effects. Thus, in the SN2 mechanism, strong interaction between the nucleophilic water molecule and the  $\alpha$ -C provides an obvious means for increasing the torsional or bending frequencies of the methyl group about the C-C axis. At the same time electronic changes associated with partial bonding to O and to Cl provide for a decrease in "high" frequencies such as stretching.

In the SN1 mechanism (by which we assume the *t*-butyl chloride to react), the transition state is reached when charge development on the quasi-cation is such that the water-water interaction of the first layer of solvation shell = the cation-water interaction at the transition state; exothermic solvation of the cationic moiety is thus just beginning; the solvent molecules are not strongly oriented toward the *t*-butyl group; nearest-neighbor water molecules are more disorganized than in either the initial state or indeed the final state.

These conclusions are borne out both by the more positive entropy of activation for the tertiary than for secondary halides (where nucleophilic interaction may act as a structure maker) and the much less negative heat capacity of activation ( $\Delta C_p^*$ ) for the solvolysis of secondary halides in water (-55 cal./mole deg., average value<sup>17</sup>) compared to the values for *t*-butyl chloride (-83 cal./mole deg.<sup>9</sup>) and for *t*-pentyl chloride (93 cal./mole deg.<sup>18</sup>).

There is no evidence of nucleophilic interaction in the hydrolysis of *t*-butyl chloride, hence the above arguments leading to cancellation of temperature effects on  $k_H/k_D$  in the SN2 mechanism will not apply. Rather the source of the  $k_H/k_D$  ratio is to be found in some combination of those possible sources of internal difference: hyperconjugation, inductive effects, non-bonded interaction.

Since evidence of very considerable changes in solvent reorganization are apparent for solvolysis of *t*-butyl chloride in water and in ethanol-water (e.g.,  $\Delta C_p^* = -80$  cal./mole deg. in water but -30 in EtOH-H<sub>2</sub>O, Table II) without influencing  $k_H/k_D$ , the contribution of differential exothermic solvation to  $k_H/k_D$  arising from differences in partial molar volume or other causes, such as differential solvent shielding, appears to be negligible.<sup>19-21</sup>

These results together with those published by Leffek, *et al.*,<sup>4</sup> raise the possibility that a further mechanistic distinction between the SN1-SN2 mechanisms may be based on the distinction of whether  $\delta_I \Delta F^*$  approximates to  $\delta_I \Delta S^*$  or  $\delta_I \Delta H^*$ .

(16) M. Wolfsberg and M. J. Stern, *Pure Appl. Chem.*, **8**, 325 (1964).(17) R. E. Robertson, R. L. Heppollette, and J. M. W. Scott, *Can. J. Chem.*, **37**, 803 (1959).

(18) K. T. Leffek, R. E. Robertson, and S. Sugamori, unpublished work.

(19) V. J. Shiner, *J. Am. Chem. Soc.*, **83**, 240 (1961).(20) V. J. Shiner and C. J. Verbanic, *ibid.*, **79**, 373 (1957).(21) W. Schubert and R. J. Minton, *ibid.*, **82**, 6188 (1960).

## Experimental

**Materials.** Conductivity water was prepared by passing distilled water through a column packed with analytical grade Amberlite resin.

Ethanol was a very pure grade obtained from Consolidated Alcohol Ltd., and was used without further treatment.

Ethanol (50%) was prepared by weight and had a density of 0.9185 at 30.04°. One hundred liters of the original mixture was sealed in 10-l. containers and these in turn, on opening, sealed in 1-l. dispensers.

Absolute methanol was prepared by distillation from magnesium methoxide.

*t*-Butyl chloride was a redistilled sample of BDH "Analar" grade, b.p. 51°.

*t*-Butyl-*d*<sub>9</sub> chloride was obtained from Merck Sharp and Dohme of Canada, Ltd., Montreal, and was shown by means of mass spectrometry to contain not less than 99% deuterium content. The analysis was confirmed by integration of the proton magnetic resonance signal from a Varian DP-60 n.m.r. spectrophotometer using a weighed amount of hexamethylbenzene as an internal indicator.<sup>22</sup>

In the course of this work, it was discovered that *t*-butyl-*d*<sub>9</sub> chloride would readily exchange hydrogen with moisture from the air; hence in addition to the usual precaution of keeping purified samples cold and in the dark, it was necessary to store them under dry atmosphere and warm to room temperature before removing a sample.

**Conductance Cells.** These were essentially the same as those described by Daggett, Blair, and Kraus<sup>23</sup> apart from the incorporation of a multipaddled glass stirrer containing a sealed-in magnet. All constants were approximately 0.4. In the thermostat, the cells were held in a rack fitted with a rotating magnet. Before use the cells were cleaned with hot nitric acid, thoroughly washed with water and 50% aqueous ethanol, and thereafter kept filled with this solvent containing sufficient hydrogen chloride to give a resistance of about 20,000 ohms across the electrodes. This value remained constant for several hours indicating

(22) We are grateful to Dr. P. M. Laughton, Carleton University, for suggesting this method.

(23) H. M. Daggett, Jr., E. J. Blair, and C. A. Kraus, *J. Am. Chem. Soc.*, **73**, 799 (1951).

that there was not significant adsorption of ions in the cell. The total volume of each cell was about 100 ml.

**Calibration of Concentration-Conductance Relation.** The apparatus and procedures for obtaining an empirical relation between conductance and concentration of HCl over the concentration range of interest in these studies are detailed in a separate publication.<sup>9</sup> Briefly, small increments of HCl in 50:50 w./w. ethanol-water (~0.003 *M*), obtained by hydrolyzing the corresponding amount of *t*-butyl chloride, were introduced by an accurate titrimeter. Steady resistance readings were obtained in ~30 sec., and in this way a series of corresponding concentrations and resistances were conveniently determined and could be used to derive concentrations from resistances either graphically, or by means of a smoothed table,<sup>24</sup> or as direct reference data for use with a suitable program for machine computation based on the Guggenheim method for determining first-order rate constants. Of these methods the second is the most convenient, unless computer time is easily available. The largest potential source of error in the rate, aside from possible temperature errors, will be the linearity of the titrimeter count-volume relationship.

**Rate Measurements.** The conductance bridge, thermostats, temperature control and measurement, and methods of taking data have been described previously.<sup>25</sup> In 50:50 EtOH-H<sub>2</sub>O, prior to each run, the cells were filled with solvent containing sufficient HCl to give a resistance of about 22,000 ohms, *i.e.*, into the range of the calibration and brought to temperature equilibrium in the thermostat. Approximately 10 mg. of *t*-butyl chloride was dissolved in 1 ml. of solvent and 0.25 ml. of this added to the cell. This was sufficient to just fill the cell, which was then tightly stoppered. Because of the internal stirrer, concentration and temperature equilibrium were rapidly established. Resistance-time data yielded rates as previously described. Typical values were similar to those reported in previous papers, reproducibility being indicated by the average deviation from the mean (Table I).

(24) S. Martin, R. E. Robertson, and G. C. Benson, *J. Sci. Instr.*, **41**, 237 (1964).

(25) K. T. Leffek, J. A. Llewellyn, and R. E. Robertson, *J. Am. Chem. Soc.*, **82**, 6315 (1960).