J. Am. Chem. Soc. **1994,** *116,* 3609-3610 3609

Measurements of Solvent and Secondary Kinetic Isotope Effects for the Gas-Phase S_N2 Reactions of Fluoride with Methyl Halides

Richard A. J. O'Hair,[†] Gustavo E. Davico, Jale Hacaloglu,[‡]
Thuy Thanh Dang,[§] Charles H. DePuy, and
Veronica M. Bierbaum*

Department of Chemistry and Biochemistry
University of Colorado
Boulder, Colorado 80309-0215

Received August 2, 1993

Bimolecular nucleophilic substitution reactions have been the focus of extensive theoretical and experimental work in recent years due to their central importance in organic chemistry.[1,2] Nevertheless, fewer studies have addressed the role of solvation in gas-phase S_N2 reactions.[3,4] In particular, Truhlar and coworkers have noted the dearth of experimental information on solvent kinetic isotope effects.[4]

In this paper we describe our studies of the S_N2 reactions of F^-, $F^-(H_2O)$, and $F^-(D_2O)$ with CH_3X and CD_3X, where X = Cl, Br, and I, using the tandem flowing afterglow selected ion flow tube technique. In keeping with previous work,[1e,f] we observe inverse kinetic isotope effects for deuteration of methyl halide; moreover, we observe for the first time substantial *inverse* kinetic isotope effects for deuteration of the solvent.

The reactions were carried out at 302 ± 3 K in a tandem flowing afterglow selected ion flow tube[5] at a helium buffer gas pressure of 0.5 Torr and a flow of 225 STP $cm^3\ s^{-1}$. Fluoride ions were formed by electron impact on nitrogen trifluoride; hydrated fluoride ions were generated by reacting fluoride ions with a mixture of tetrahydrofuran[6] and H_2O or D_2O. Mass-selected reagent ions were allowed to react with a measured flow of methyl halide,[7] added through a manifold of reagent inlets. Reaction rate coefficients and product distributions were determined by standard methods.

The displaced halide ion X^- is the sole product in the reactions of F^- (eq 1) and the major product in the reactions of $F^-(H_2O)$ (eq 2) and $F^-(D_2O)$ (eq 3), where solvated X^- is also formed.[8]

$$F^- + CH_3X/CD_3X \rightarrow X^- + CH_3F/CD_3F \tag{1}$$

$$F^-(H_2O) + CH_3X/CD_3X \rightarrow X^- + CH_3F/CD_3F + H_2O \tag{2a}$$

$$\rightarrow X^-(H_2O) + CH_3F/CD_3F \tag{2b}$$

$$F^-(D_2O) + CH_3X/CD_3X \rightarrow X^- + CH_3F/CD_3F + D_2O \tag{3a}$$

$$\rightarrow X^-(D_2O) + CH_3F/CD_3F \tag{3b}$$

The rate coefficients,[9,10] reaction efficiencies,[11] and kinetic isotope effects for these reactions are summarized in Table 1. In keeping with earlier results, these data demonstrate that S_N2 reactivity increases as the reaction exothermicity[12] increases, i.e.,

---

[†] Current address: Department of Chemistry, Kansas State University, Manhattan, KS 66506.

[‡] Current address: Department of Chemistry, Middle East Technical University, 06531 Ankara, Turkey.

[§] Current address: College of Chemistry, University of California, Berkeley, CA 94720.

(1) For a selection of recent experimental work on gas-phase S_N2 reactions, see: (a) Riveros, J. M.; Jose, S. M.; Takashima, I. *Adv. Phys. Org. Chem.* **1985**, *21*, 197. (b) Barlow, S. E.; Van Doren, J. M.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1988**, *110*, 7240–7242. (c) DePuy, C. H.; Gronert, S.; Mullin, A.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1990**, *112*, 8650–8655. (d) Su, T.; Morris, R. A.; Viggiano, A. A.; Paulson, J. F. *J. Phys. Chem.* **1990**, *94*, 8426–8430. (e) Gronert, S.; DePuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1991**, *113*, 4009–4010. (f) Viggiano, A. A.; Paschkewitz, J. S.; Morris, R. A.; Paulson, J. F.; Gonzalez-Lafont, A.; Truhlar, D. G. *J. Am. Chem. Soc.* **1991**, *113*, 9404–9405. (g) Graul, S. T.; Bowers, M. T. *J. Am. Chem. Soc.* **1991**, *113*, 9696–9697. (h) Cyr, D. M.; Posey, L. A.; Bishea, G. A.; Han, C.-C.; Johnson, M. A. *J. Am. Chem. Soc.* **1991**, *113*, 9697–9699. (i) Wilbur, J. L.; Brauman, J. I. *J. Am. Chem. Soc.* **1991**, *113*, 9699–9701. (j) Wladkowski, B. D.; Lim, K. F.; Allen, W. D.; Brauman, J. I. *J. Am. Chem. Soc.* **1992**, *114*, 9136–9153. (k) Viggiano, A. A.; Morris, R. A.; Paschkewitz, J. S.; Paulson, J. F. *J. Am. Chem. Soc.* **1992**, *114*, 10477–10482.

(2) For a selection of recent theoretical studies of S_N2 reactions, see: (a) Mitchell, D. J.; Schlegel, H. B.; Shaik, S. S.; Wolfe, S. *Can. J. Chem.* **1985**, *63*, 1642. (b) Evanseck, J. D.; Blake, J. F.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1987**, *109*, 2349–2353. (c) Tucker, S. C.; Truhlar, D. G. *J. Phys. Chem.* **1989**, *93*, 8138–8142. (d) Tucker, S. C.; Truhlar, D. G. *J. Am. Chem. Soc.* **1990**, *112*, 3338–3347. (e) Vande Linde, S. R.; Hase, W. L. *J. Phys. Chem.* **1990**, *94*, 6148–6150. (f) Vande Linde, S. R.; Hase, W. L. *J. Chem. Phys.* **1990**, *93*, 7962–7980. (g) Cho, Y. J.; Vande Linde, S. R.; Zhu, L.; Hase, W. L. *J. Chem. Phys.* **1992**, *96*, 8275–8287. (h) Shaik, S. S.; Schlegel, H. B.; Wolfe, S. *Theoretical Aspects of Physical Organic Chemistry—The S_N2 Mechanism*; Wiley: New York, 1992.

(3) For a general review of the influence of solvation on ion reactivity in the gas phase, see: (a) Bohme, D. K. In *Ionic Processes in the Gas Phase*; Almoster Ferreira, M. A., Ed.; Reidel: Dordrecht, 1984; pp 111–134. For experimental studies of gas-phase S_N2 reactions of solvated nucleophiles, see: (b) Bohme, D. K.; Mackay, G. I. *J. Am. Chem. Soc.* **1981**, *103*, 978–979. (c) Henchman, M.; Paulson, J. F.; Hierl, P. M. *J. Am. Chem. Soc.* **1983**, *105*, 5509–5510. (d) Bohme, D. K.; Raksit, A. B. *J. Am. Chem. Soc.* **1984**, *106*, 3447–3452. (e) Bohme, D. K.; Raksit, A. B. *Can. J. Chem.* **1985**, *63*, 3007–3011. (f) Henchman, M.; Hierl, P. M.; Paulson, J. F. *J. Am. Chem. Soc.* **1985**, *107*, 2812–2814. (g) Hierl, P. M.; Ahrens, A. F.; Henchman, M.; Viggiano, A. A.; Paulson, J. F.; Clary, D. C. *J. Am. Chem. Soc.* **1986**, *108*, 3142–3143.

(4) For theoretical studies of gas-phase S_N2 reactions of solvated nucleophiles, see: (a) Zhao, X. G.; Tucker, S. C.; Truhlar, D. G. *J. Am. Chem. Soc.* **1991**, *113*, 826–832. (b) Gonzalez-Lafont, A.; Truong, T. N.; Truhlar, D. G. *J. Phys. Chem.* **1991**, *95*, 4618–4627. (c) Truhlar, D. G.; Lu, D.; Tucker, S. C.; Zhao, X. G.; Gonzalez-Lafont, A.; Truong, T. N.; Maurice, D.; Liu, Y. P.; Lynch, G. C. *ACS Symp. Ser.* **1992**, *502*, 16–36. (d) Zhao, X. G.; Lu, D. H.; Liu, Y. P.; Lynch, G. C.; Truhlar, D. G. *J. Chem. Phys.* **1992**, *97*, 6369–6383.

(5) Van Doren, J. M.; Barlow, S. E.; DePuy, C. H.; Bierbaum, V. M. *Int. J. Mass Spectrom. Ion Processes* **1987**, *81*, 85–100.

(6) Tetrahydrofuran has been found to enhance the formation of hydrated anions: (a) DePuy, C. H.; Beedle, E. C.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1982**, *104*, 6483–6488. (b) Bickelhaupt, F. M.; de Koning, L. J.; Nibbering, N. M. M. *Tetrahedron* **1993**, *49*, 2077–2092.

(7) Undeuterated methyl halides, 99.5% pure. Atom % D, CD_3Cl (99%), CD_3Br (99.5%), CD_3I (99.5%). Since the reactions of CH_3Cl/CD_3Cl are relatively slow, traces of highly reactive impurities such as HCl could produce anomalous results. However, reaction of N_3^- (PA = 344 kcal mol^{-1}) with CH_3Cl/CD_3Cl produced only a trace of Cl^- (PA = 333 kcal mol^{-1}), indicating that HCl contamination is not significant. For some samples of CH_3I, purification was required to remove trace impurities of CH_3OH and HI, which induce facile solvent exchange or proton-transfer reactions, respectively.

(8) The branching ratios and reaction exothermicities for the formation of X^- and $X^-(H_2O)$ for reaction 2 are: (i) Cl^- 0.7 ($\Delta H \approx -11$ kcal mol^{-1}); $Cl^-(H_2O)$ 0.3 ($\Delta H \approx -24$ kcal mol^{-1}); (ii) Br^- 0.9 ($\Delta H \approx -18$ kcal mol^{-1}); $Br^-(H_2O)$ 0.1 ($\Delta H \approx -31$ kcal mol^{-1}); (iii) I^- 0.9 ($\Delta H \approx -25$ kcal mol^{-1}); $I^-(H_2O)$ 0.1 ($\Delta H \approx -35$ kcal mol^{-1}). Deuteration of the methyl halide or the solvent is expected to have only a minor effect on the energetics, and deuteration caused no measurable change in the product distribution. Error bars of ±50% are estimated for the branching ratios since collisional dissociation of the weakly bound $X^-(H_2O)$ product ions in the flow tube may be occurring. The branching ratios were corrected for mass discrimination as well as for the presence of ~5% F^- in the reactions of $F^-(H_2O)$ and $F^-(D_2O)$ (arising from CID in the injection region).

(9) For the reactions of $F^-(H_2O) + CH_3Cl/CD_3Cl$, rate coefficients are corrected for the formation of $^{37}Cl^-$, which has the same nominal mass as $F^-(H_2O)$. For the reactions of $F^-(D_2O)$, the reactant ion signal may have a small contaminant of $F^-(HF)$ ions, which have the same nominal mass. At worst, the contribution of $F^-(HF)$ is 10%, and since these ions are less reactive than $F^-(D_2O)$, the overall rates of $F^-(D_2O)$ with CH_3X/CD_3X may be slightly larger. This in turn would make k_H/k_D slightly smaller than reported. For the $F^-(D_2O)$ studies, it was found that the $F^-(HF)$ contaminant can be minimized by replacing tetrahydrofuran in the source with carbon tetrachloride.

(10) Our measured rate coefficients for $F^- + CH_3X$ are in excellent agreement with recent SIFT results (ref 1d) but in poorer agreement with earlier results (Ikezoe, Y.; Matsuoka, S.; Takebe, M.; Viggiano, A. A. *Gas Phase Ion–Molecule Reaction Rate Constants Through 1986*; Maruzen: Tokyo, 1987). Our measured rate coefficients for $F^-(D_2O) + CH_3Cl$, CH_3Br are in fair agreement with earlier flowing afterglow results (ref 3e).

(11) Su, T.; Bowers, M. T. *Int. J. Mass Spectrom. Ion Phys.* **1973**, *12*, 347–356.

(12) NIST Standard Reference Database 19B: NIST Negative Ion Energetics Database Version 2.07, program written/data compilation by John E. Bartmess, Department of Chemistry, University of Tennessee, Knoxville TN 37996-1600. This compilation is based on original data from Lias, S. G.; Bartmess, J. E.; Liebman, J. F.; Holmes, J. L.; Levin, R. D.; Mallard, W. G. Gas-Phase Ion and Neutral Thermochemistry *J. Phys. Chem. Ref. Data* **1988**, *17*, Suppl. 1.

0002-7863/94/1516-3609$04.50/0

Table 1. Rate Coefficients, Reaction Efficiencies, and Kinetic Isotope Effects

reaction	k^a	$k/k_{ADO}{}^b$	$k_H/k_D{}^c$ (CH_3X/CD_3X)	$k_H/k_D{}^c$ (H_2O/D_2O)
$F^- + CH_3Cl$	14.1 ± 0.1	0.61		
$F^-(H_2O) + CH_3Cl$	0.149 ± 0.002	0.0080		
$F^-(D_2O) + CH_3Cl$	0.230 ± 0.008	0.013		0.65 ± 0.03
$F^- + CD_3Cl$	15.6 ± 0.2	0.68	0.90 ± 0.02	
$F^-(H_2O) + CD_3Cl$	0.175 ± 0.005	0.0095	0.85 ± 0.03	
$F^-(D_2O) + CD_3Cl$	0.268 ± 0.002	0.015	0.86 ± 0.03	0.65 ± 0.02
$F^- + CH_3Br$	18.8 ± 0.2	0.84		
$F^-(H_2O) + CH_3Br$	4.97 ± 0.05	0.29		
$F^-(D_2O) + CH_3Br$	5.99 ± 0.06	0.35		0.83 ± 0.02
$F^- + CD_3Br$	19.2 ± 0.4	0.86	0.98 ± 0.02	
$F^-(H_2O) + CD_3Br$	5.41 ± 0.07	0.32	0.92 ± 0.02	
$F^-(D_2O) + CD_3Br$	6.42 ± 0.07	0.38	0.93 ± 0.02	0.84 ± 0.02
$F^- + CH_3I$	19.4 ± 0.2	0.87		
$F^-(H_2O) + CH_3I$	8.64 ± 0.09	0.51		
$F^-(D_2O) + CH_3I$	9.76 ± 0.10	0.59		0.89 ± 0.05
$F^- + CD_3I$	19.7 ± 0.4	0.89	0.98 ± 0.05	
$F^-(H_2O) + CD_3I$	9.38 ± 0.10	0.56	0.92 ± 0.05	
$F^-(D_2O) + CD_3I$	10.3 ± 0.5	0.63	0.95 ± 0.05	0.91 ± 0.05

[d] Units of 10^{-10} cm^3 s^{-1}; error bars represent one standard deviation of the mean of 3 or more measurements, or ±1%, whichever is larger; absolute accuracy is ±25%. [b] Reference 11. [c] Errors bars reflect the propagation of stated errors in the rate coefficients. To obtain accurate isotope effects, the relevant rate coefficients, k_H and k_D, were measured within a period of a few days. Experimental checks indicate that over this period, the rate coefficients for CH_3Cl and CH_3Br are reproducible to better than ±5% and the isotope effects (k_H/k_D) to better than ±3%; for CH_3I these values are ±10% and ±5%, respectively.

for a given nucleophile, the rate coefficients increase in the sequence $CH_3Cl < CH_3Br < CH_3I$. Similarly, for a given methyl halide, reactivity decreases with solvation; this effect is most dramatic for CH_3Cl, where solvation lowers the rate coefficient by 2 orders of magnitude. We note that kinetic isotope effects are absent for extremely rapid reactions but become evident for slower processes, where the height of the central barrier is important. Inverse kinetic isotope effects are observed for deuteration of the methyl halide with k_H/k_D as small as 0.85 ($k[F^-(H_2O) + CH_3Cl]/k[F^-(H_2O) + CD_3Cl]$). More importantly, significant inverse kinetic isotope effects are also observed for deuteration of the solvent molecule[13] with k_H/k_D as small as 0.65 ($k[F^-(H_2O) + CD_3Cl]/k[F^-(D_2O) + CD_3Cl]$). These results are in excellent agreement with recent theoretical findings of Hu and Truhlar.[14] Their work predicts that both low- and high-frequency vibrations at the transition state make significant contributions to the inverse kinetic isotope effects.

The interplay of experiment and theory provides valuable insight into the gas-phase S_N2 reactions of solvated nucleophiles. Further studies are underway in this laboratory to explore the kinetic isotope effects in reactions of more highly hydrated nucleophiles[15] as well as nucleophiles complexed by other solvent molecules.

Acknowledgment. We are very grateful to Professor Donald Truhlar for a preprint of ref 14 and for his valuable insight and helpful discussions. We gratefully acknowledge support of this work by the National Science Foundation under Grants Nos. CHE-9121781 (V.M.B.) and CHE-9122828 (C.H.D.). J.H. acknowledges Tubitak Turkey, and G.E.D. acknowledges Consejo Nacional de Investigaciones científicas y técnicas de Argentina (CONICET) for additional financial support.

---

(13) The nucleophile–solvent bond is ~0.25 kcal mol^{-1} stronger for $F^-(H_2O)$ than for $F^-(D_2O)$. Larson, J. W.; McMahon, T. B. *J. Am. Chem. Soc.* **1988**, *110*, 1087–1093.

(14) Hu, W. P.; Truhlar, D. G. *J. Am. Chem. Soc.*, submitted.

(15) Preliminary results indicate $k = 1.2 \times 10^{-12}$ cm^3 s^{-1} for $F^-(H_2O)_2 + CH_3I$ and $k = 1.7 \times 10^{-12}$ cm^3 s^{-1} for $F^-(D_2O)_2 + CH_3I$, with $k_H/k_D = 0.7 \pm 0.15$. The error bars are large due to the low reaction efficiency and possible contribution of reagent impurities (see footnote 7).