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Solvent-Promoted E2 Reaction Competing with S_N2 Reaction and Stepwise Solvolytic Elimination and Substitution Reactions

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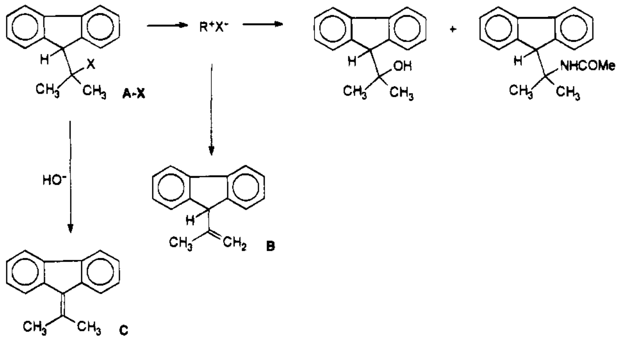
Abstract: Solvolysis of 9-(1-X-ethyl)fluorene (**1**-X, X = I, Br, Cl, OTs, or OBs) in 25 vol % acetonitrile in water gives the elimination products 9-(1-ethylidene)fluorene (**3**) and 9-vinylfluorene (**2**) and the substitution products 9-(1-hydroxyethyl)fluorene (**1**-OH) and 9-(1-acetamidoethyl)fluorene (**1**-NHCOMe). The iodide (**1**-I) and the bromide (**1**-Br) yield **3** as the main product by a solvent-promoted concerted E2 reaction (*J. Am. Chem. Soc.* **1995**, *117*, 1839), but the tosylate (**1**-OTs) and the brosylate (**1**-OBs) do not undergo any significant concerted reaction with the solvent. Added strong nucleophiles open up a competing bimolecular substitution pathway (S_N2). The importance of this route is leaving-group-dependent; this "synergism" between nucleophile and leaving group favors S_N2 reaction with $I^- > Br^- > Cl^- > OTs^-, OBs^-$ leaving groups. A similar trend in leaving-group effects is observed for solvent- and base-promoted E2 reaction; e.g., **1**-I, **1**-Br, and **1**-OBs yield 95%, 69%, and 0% solvent-promoted E2 reaction, respectively. The S_N2/E2 ratio with thiocyanate as nucleophile/base increases in the series **1**-I, **1**-Br, and **1**-OBs; the ratios were measured as 0.2, 0.7, and 3.2, respectively. The S_N2 reactions with thiocyanate ion in methanol–water mixtures show small sensitivity to solvent "ionizing power"; e.g., with the deuteriated analogue (9-^{2}H)-9-(1-bromoethyl)fluorene (*d*-**1**-Br) a value of $m = 0.20$ was measured which can be compared with the value of $m = 0.59$ obtained for solvolysis through the ion pair.

Introduction

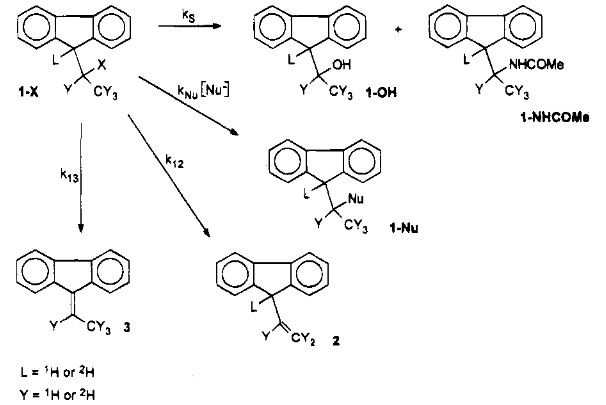
Solvolysis of substrates having a β-hydron usually provides elimination as well as substitution products. Frequently, the elimination and substitution reactions are carbocationic processes having a common carbocation or ion-pair intermediate.[1] Such a system, involving very short-lived carbocations in highly aqueous media, has been studied recently by employing the tertiary system 9-(2-X-propyl)fluorene (**A**-X, X = Br, Cl, OAc, $PhOH^+$).[2-4] It was shown by the measured kinetic isotope effects that reaction of **A**-X involves irreversible ionization to an ion pair or ion–molecule pair, and that this species is a common intermediate for the elimination and substitution reactions (Scheme 1). Only a trace of the more stable alkene **C** is formed in the solvolysis reaction. The preferential formation of the terminal alkene **B** was concluded to be due to a large hyperconjugative stabilization of the rate-limiting formation of the short-lived carbocationic intermediate, which reacts to form products with a rate constant of about 1×10^{11} s^{-1}. Accordingly, the results were rationalized in terms of preassociation mechanisms. The formation of the alkene **B** from the ion pair is catalyzed by general bases, $\beta = 0.05$.[2]

Addition of strong bases is required to afford any significant amount of alkene **C**. This reaction occurs by a parallel E2 reaction by abstraction of the relatively acidic 9-hydron of the fluorene moiety.[2,5]

Scheme 1



Scheme 2



In the present study we have employed the corresponding secondary system (Scheme 2) which is expected to react even more slowly, and to give a potential ion pair with an even shorter lifetime. Recent results show that the slower ionization of this secondary system makes it possible for concerted solvent-promoted E2 reaction to compete successfully.[6] It was reported that the E2 reaction is the predominant reaction with both the bromide **1**-Br and the iodide **1**-I, even in highly aqueous media. Thus, changing the substrate structure from tertiary (**A**-Br) to

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[1] Thibblin, A. *Chem. Soc. Rev.* **1993**, *22*, 427–433.

[2] Thibblin, A. *J. Am. Chem. Soc.* **1987**, *109*, 2071–2076.

[3] Thibblin, A.; Sidhu, H. *J. Chem. Soc., Perkin Trans. 2* **1994**, 1423–1428.

[4] Sidhu, H.; Thibblin, A. *J. Phys. Org. Chem.* **1994**, *7*, 578–584.

[5] Thibblin, A. *J. Am. Chem. Soc.* **1988**, *110*, 4582–4586.

[6] Meng, Q.; Thibblin, A. *J. Am. Chem. Soc.* **1995**, *117*, 1839–1840.

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Table 1. Rate Constants for the Reactions of **1**-X in 25 vol % Acetonitrile in Water

substrate[a]	temp, °C	salt	10^6k_{obs},[c] s^{-1}	$10^6k'_{Nu}$, s^{-1}	10^6k_S, s^{-1}	10^6k_{12}, s^{-1}	10^6k_{13}, s^{-1}
1-I[b]	70	none	136		7.2	0.1	129
d-**1**-I	70	0.75 M NaSCN	83.8	29.2	7.4		47.2
1-Br[b]	70	none	33.6		10.3	0.2	23.3
1-Br	70	0.75 M NaSCN	68.1	16.4	10.0		41.7
d-**1**-Br	70	0.75 M NaSCN	35.3	16.0	10.0	0.3	9.0
d_4-**1**-Br	70	0.75 M NaSCN	64.4	16.6	8.9		39.0
1-Cl[b]	70	none	0.9		0.5		0.3
1-Cl	70	0.75 M NaSCN	1.7	0.4	0.5		0.8
1-OTs	55	none	191		182	2.1	6.8
1-OTs	55	0.75 M NaN_3[d]	298	85.8	150		61.4
1-OTs	55	0.75 M NaSCN	245	46.8	179	2.4	16.4
1-OTs	55	0.75 M NaBr[d]	182	15.3	149		18.3
1-OBs	35	none	55.2		51.1	0.7	3.4
1-OBs	35	0.75 M $NaClO_4$	59.2		56.1	0.8	2.4
1-OBs	35	0.75 M NaN_3[d]	126	47.0	49.1		30.2
1-OBs	35	0.75 M NaSCN	71.8	14.8	49.0	0.8	7.2
1-OBs	35	0.75 M NaBr[d]	61.4	5.5	47.5	1.0	7.5
1-OBs	35	0.50 M NaCl[d]	61.4	2.6	51.8	0.9	6.0
1-OBs	35	0.75 M NaI[d]	76.1	11.8	54.9		9.5
1-OBs	35	0.50 M NaOAc[e]	40.0	0.5	32.7	0.4	6.4

[a] Substrate concentration 0.2 mM. [b] pH 2.8. [c] $k_{obs} = k_S + k_{12} + k_{13} + k'_{Nu}$, where $k'_{Nu} = k_{Nu}[Nu^-]$; see Scheme 2. [d] pH 6.5. [e] $[AcO^-]/[HOAc] = 100$.

Table 2. Relative Rates and Product Compositions for Reactions of **1**-X in 25 vol % Acetonitrile in Water[a] at 70 °C

substrate[b]	k_{obs}[c]	k_S	k_{13}	[**3**]/[all products]	k_{MeCN}/k_{HOH}[d]
1-I	4.0	0.7	5.5	0.95	0.41
1-Br	1	1	1	0.70	0.39
1-Cl	0.026	0.051	0.014	0.38	(0.28)[e]
1-OTs	25	76	1.3	0.038	0.40
1-OBs	83	250	6.2	0.052	0.40

[a] pH 2.8. [b] Substrate concentration 0.2 mM. [c] $k_{obs} = k_S + k_{12} + k_{13}$, defined in Scheme 2. [d] Measured with the 9-deuteriated substrate *d*-**1**-X. [e] Measured after 1 week.

Table 3. Kinetic Deuterium Isotope Effects for the Solvolytic Reactions of **1**-X[a]

substrate	temp, °C	$k_{obs}H/k_{obs}D$	k_SH/k_SD	$k_{12}H/k_{12}D$	$k_{13}H/k_{13}D$	$k_{SCN}H/k_{SCN}D$
1-I	70	3.8[b]	0.9[c]		4.7[b]	
1-Br	70	2.0[c] (1.2)[c]	0.9[c] (1.2)[c]		4.3[b] (1.2)[c]	1.03[d] (1.04)[d]
1-OTs	55	1.08[d]	1.06[d]	0.88[e]	2.7[c]	
1-OBs	35	1.01[d]	0.97[d]	0.98[e]	2.8[c]	

[a] The values within parentheses refer to reactions of 9-(1-bromo(1,2,2,2-$^2H_4$)ethyl)fluorene (d_4-**1**-Br). [b] Estimated maximum error ±0.2. [c] Estimated maximum error ±0.1. [d] Estimated maximum error ±0.05. [e] Estimated maximum error ±0.08.

Table 4. Rate Constants and Kinetic Deuterium Isotope Effects for the Reactions of **1**-X with Hydroxide and Acetate Anions

substrate[a]	base	temp, °C	10^6k_{13}, M^{-1} s^{-1}	$k_{13}H/k_{13}D$	$k_{13}H/k_{13}D4$
1-I	HO^- [b]	25	1.86×10^6	6.3[d]	
1-I	AcO^- [c]	70	10.7×10^3	5.3[e]	
1-Br	HO^- [b]	25	6.76×10^5	7.5[d]	1.3[f]
1-Br	AcO^- [c]	70	1851	5.1[e]	1.3[f]
1-Cl	HO^- [b]	25	8.08×10^4	7.1[d]	
1-OTs	HO^- [b]	25	5.69×10^4	5.5[d]	
1-OBs	HO^- [b]	25	1.33×10^5	6.6[d]	

[a] Substrate concentration 0.2 mM. [b] Base concentration 1−100 mM. [c] Base concentration 1−100 mM. [d] Estimated maximum error ±0.3. [e] Estimated maximum error ±0.5. [f] Estimated maximum error ±0.1.

secondary (**1**-Br), which means a decreased reactivity to ionization, causes a shift in the major reaction path from stepwise solvolysis to concerted solvent-promoted E2 reaction. A full account of these results is now presented, also including data for other leaving groups.

Efficient nucleophiles give rise to concerted S_N2 reactions. The appearance of concerted displacement reactions is concluded to be due to absence of a significant lifetime of the ion pair in the presence of an efficient nucleophile. Strong assistance is observed in reactions with good leaving groups. Borderline mechanisms for the elimination and substitution reactions are discussed, in addition to the possibility of concerted substitution with the solvent acting as the nucleophile.

Results

The solvolysis of 9-(1-X-ethyl)fluorene (**1**-X, X = I, Br, Cl, OTs, or OBs) in 25 vol % acetonitrile in water provides the alkenes 9-vinylfluorene (**2**) and 9-(1-ethylidene)fluorene (**3**) and the substitution products 9-(1-hydroxyethyl)fluorene (**1**-OH) and 9-(1-acetamidoethyl)fluorene (**1**-NHCOMe) (Scheme 2). Solvolysis in mixtures of water with methanol affords 9-(1-methoxyethyl)fluorene (**1**-OMe) instead of the amide. The kinetics of the reactions were studied by a sampling-quench high-performance liquid chromatography procedure, or by following the increase in absorbance at 312 nm by UV spectrophotometry. The product compositions are strongly dependent on the nature of the leaving group. The measured rate constants and reaction conditions are shown in Table 1. Relative rates for different leaving groups are shown in Table 2. The deuteriated substrates (9-^{2}H)-9-(1-X-ethyl)fluorene (*d*-**1**-X) yield smaller fractions of alkene **3**. The measured kinetic deuterium isotope effects for solvolysis of these deuteriated substrates and for solvolysis of 9-(1-bromo(1,2,2,2-$^2H_4$)ethyl)fluorene (d_4-**1**-Br) are given in Table 3.

Addition of bases increases the fraction of alkene **3**. Only a low concentration of hydroxide ion is required to obtain **3** as the sole product. The rate constants and kinetic deuterium isotope effects are presented in Table 4. The formation of **3** is general base catalyzed.

A representative plot showing the effect of buffer base on the rate constants k_{13} and k_S for **1**-Br (defined in Scheme 2) is presented in Figure 1. The second-order rate constants of the elimination reaction, obtained from the slopes of plots of the type shown in Figure 1, are reported in Table 5. As seen in Figure 1, the substitution reaction rate to give **1**-OH and **1**-NHCOMe decreases at constant ionic strength with increasing trifluoroacetate concentration. This is attributable to a special salt effect on the rate-limiting ionization step (see Discussion).

Perchlorate anion has a small rate-enhancing effect on the solvolysis reaction of **1**-OBs which mainly reacts through the

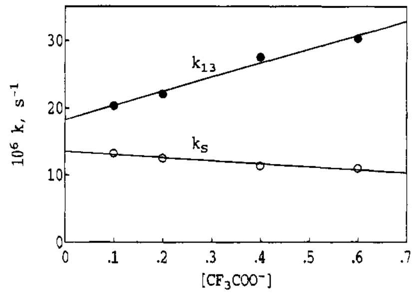

Figure 1. Rate constants k_{13} (●) and k_S (○) for **1**-Br (Scheme 2) as a function of trifluoroacetate anion concentration in 25 vol % acetonitrile in water at 70 °C. The ionic strength was maintained constant (0.75 M) with sodium perchlorate.

Table 5. Second-Order Rate Constants for Reaction of **1**-X with Bases

substrate^a	base	pK_a^{b}	10^6k_{13}, M^{-1} s^{-1}	base concn, M
1-I^c	HO^-	15.74	20×10^{6} ^{j}	0.0025
1-I^c	AcO^- ^{e}	4.76	10.7×10^3	0.02–0.08
1-I^c	$MeOCH_2COO^-$	3.53	3063	0.020–0.100
1-I^c	$NCCH_2COO^-$	2.43	1436	0.10–0.25
1-I^c	SCN^-	0.85	(36.0)^f	0.25–0.75
1-I^c	CF_3COO^-	0.23	148	0.25–0.75
1-I^c	HOH	−1.74	3.1	
1-Br^c	HO^-	15.74	5.2×10^6 ^{j}	0.0050
1-Br^c	HMTA^h	5.13	2.52×10^4	0.017–0.067
1-Br^c	AcO^- ^{e}	4.76	1851	0.02–0.08
1-Br^c	$NCCH_2COO^-$	2.43	279	0.25–0.75
1-Br^c	SCN^-	0.85	32.8	0.25–0.75
1-Br^c	CF_3COO^-	0.23	20.9	0.10–0.60
1-Br^c	HOH	−1.74	0.56	
1-OTs^d	HO^-	15.74	0.19×10^6 ^{j}	0.075
1-OTs^d	$(CF_3)_2CHO^-$ ^{k}	9.3	22042	0.001–0.005
1-OTs^d	AcO^- ^{i}	4.76	23.2	0.10–0.30
1-OTs^d	N_3^-	4.72	75.4	0.25–0.75
1-OTs^d	$MeOCH_2COO^-$	3.53	11.2	0.10–0.30
1-OTs^d	$NCCH_2COO^-$	2.43	2.50	0.10–0.30
1-OTs^d	SCN^-	0.85	13.1	0.25–0.75
1-OTs^d	HOH	−1.74	0.163	
1-OBs^g	AcO^- ^{i}	4.76	7.7	0.10–0.50
1-OBs^g	SCN^-	0.85	6.2	0.25–0.75
1-OBs^g	HOH	−1.74	0.082	

[a] Substrate concentration 0.2 mM. [b] In water: Jencks, W. P.; Regenstein, J. In *Handbook of Biochemistry and Molecular Biology*, 3rd ed.; Fasman, G. D., Ed.; CRC Press: Cleveland, 1976. [c] At 70 °C. [d] At 55 °C. [e] [AcO^-]/[HOAc] = 4. [f] With *d*-**1**-I. [g] At 35 °C. [h] Hexamethylenetetramine, [base]/[acid] = 2. [i] [AcO^-]/[HOAc] = 100. [j] Extrapolated from lower temperatures by means of the Arrhenius equation. [k] [HA]/[A^-] = 9.

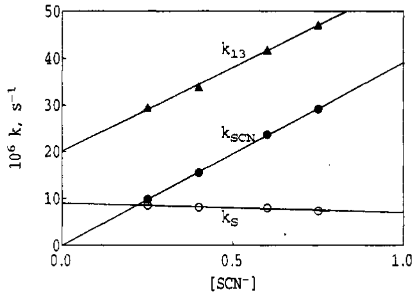

Figure 2. Rate constants k_{SCN} (●), k_S (○), and k_{13} (▲) for *d*-**1**-I (Scheme 2) as a function of thiocyanate concentration in 25 vol % acetonitrile in water at 70 °C. The ionic strength was maintained constant (0.75 M) with sodium perchlorate.

ion pair. Addition of more efficient nucleophiles (Nu^-) significantly increases the overall reaction rate by opening up a bimolecular reaction route to substitution product **1**-Nu (Scheme 2) as shown for *d*-**1**-I with thiocyanate ion in Figure 2. Thiocyanate also functions as a general base which catalyzes elimination.

The rate increase caused by nucleophilic reaction with thiocyanate ion is largest for iodide as the leaving group. The measured second-order rate constants (k_{Nu}) obtained from slopes of plots of the observed rate constants for the formation of the product **1**-Nu versus the nucleophile concentration are shown in Table 6. Some of these rate constants were measured using the deuteriated substrate *d*-**1**-X in order to suppress the competing E2 elimination reaction, making the bimolecular nucleophilic substitution more easy to study. A few of the second-order rate constants with nucleophiles (k_{Nu}, Table 6) were obtained by dividing the pseudo-first-order rate constant (k'_{Nu}), obtained at high concentration of nucleophile, by [Nu^-].

The nucleophilic substitution reactions with SCN^- give rise to two products owing to the ambident character of the nucleophile. The amount of **1**-NCS relative to **1**-SCN increases in the series I < Br < OTs ≈ OBs (Table 6). Azide ion is a relatively basic nucleophile and gives rise to a large amount of alkene **3** with **1**-Br and even greater quantities with **1**-I. Accordingly, only small amounts of **1**-N_3 are formed in the reactions of these two substrates.

The observed product ratio of **1**-Nu to **1**-OH is a measure of the competition between nucleophile (Nu^-) and water for reaction with substrate and/or ion pair. The nucleophilic selectivities were calculated from treating the substitution reaction with solvent water as a second-order reaction. Some of the nucleophilic selectivities were calculated from the measured product ratios by using eq 1; others were obtained

$$k_{Nu}/k_{HOH} = ([\mathbf{1}-Nu]/[\mathbf{1}-OH])([H_2O]/[Nu^-]) \qquad (1)$$

by dividing the second-order rate constant k_{Nu} by k_{HOH}, which is the pseudo-first-order reaction rate constant for formation of **1**-OH divided by the water concentration (41.7 M). The parameters k_{Nu}/k_{HOH} and k_{MeOH}/k_{HOH} are thus dimensionless ratios of second-order rate constants. Some nucleophilic discrimination ratios are given in Table 7. The rate-constant ratio k_{MeOH}/k_{HOH} for formation of ether **1**-OMe and alcohol **1**-OH is not constant. There is a small but significant decrease with leaving group in the series I > Br > OTs ≈ OBs (Table 7).

Grunwald–Winstein plots for the reactions of *d*-**1**-Br and **1**-OBs in methanol–water mixtures are shown in Figures 3 and 4. The deuteriated substrate *d*-**1**-Br was used since **1**-Br in the presence of SCN^- yields mostly **3**, which makes the *m* values for the substitution reactions difficult to measure. The measured *m* values for these and some other reactions are given in Table 8. The *m* values for reaction to alkene **2** are not reported since they are difficult to measure owing to the small amount of **2** that is formed.

Swain–Scott plots for the reactions of *d*-**1**-I and **1**-OBs are presented in Figure 5. The *n* values are based upon nucleophilic reactivity toward methyl iodide in methanol.[7] Brønsted plots for the general-base-catalyzed formation of alkene **3** from **1**-I and **1**-Br, which have been reported previously,[6] and from **1**-OTs are shown in Figure 6. The plots are based upon the data of Table 5.

Discussion

Stepwise Elimination and Substitution. There are strong indications of a carbocationic reaction path for the solvolysis. (i) The formation of the substitution product **1**-NHCOMe as well as the formation of the terminal alkene **2** cannot be categorized reasonably as S_N2 and E2 reactions, respectively, but should be the result of ionization of the substrate to an ion

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(7) Pearson, R. G.; Sobel, H.; Songstad, J. *J. Am. Chem. Soc.* **1968**, *90*, 319–326. The nucleophilicity of water has been estimated as $n = -0.27$: Dietze, P. E.; Jencks, W. P. *J. Am. Chem. Soc.* **1986**, *108*, 4549–4555.

Table 6. Second-Order Rate Constants for the Reactions of **1**-X with Nucleophiles

substrate[a]	temp, °C	$10^6k_{N_3}$, $M^{-1}\,s^{-1}$	10^6k_{SCN}, $M^{-1}\,s^{-1}$	[**1**-SCN]/[**1**-NCS]	10^6k_I, $M^{-1}\,s^{-1}$	10^6k_{Br}, $M^{-1}\,s^{-1}$	10^6k_{Cl}, $M^{-1}\,s^{-1}$	10^6k_{OAc}, $M^{-1}\,s^{-1}$
d-**1**-I	70		39.1	56				
1-Br	70		22.2	40				
d-**1**-Br	70		21.6	40				
d_4-**1**-Br	70		21.4					
1-OTs	55	112.0	61.1	4.5		21.1		
1-OBs	35	60.0	20.0	5.4[c]	16	7.1	5.2[b]	1.0[b]

[a] Substrate concentration 0.2 mM. [b] Obtained by dividing the pseudo-first-order rate constant (k'_{Nu}), obtained at high concentration of nucleophile, by [Nu$^-$]; the other rate constants were calculated from the slope of k'_{Nu} versus [Nu$^-$]. [c] Deuteriated substrate *d*-**1**-OBs.

Table 7. Nucleophilic Selectivities Expressed as Ratios of Second-Order Rate Constants

substrate[a]	temp, °C	k_{MeOH}/k_{HOH}[b]	k_{N_3}/k_{HOH}[c]	k_{SCN}/k_{HOH}[c]	k_I/k_{HOH}[c]	k_{Br}/k_{HOH}[c]	k_{Cl}/k_{HOH}	k_F/k_{HOH}	k_{AcO}/k_{HOH}
d-**1**-I	70	1.16	~1538[e]	194		30[f]	17[f]		
1-Br	70	1.00		75					
d-**1**-Br	70	1.02	~450[e]	69					
1-Cl	70			52[g]					
1-OTs	55	0.98[d]	23	14		4.9			
1-OBs	35	1.00[d]	46	16	12	5.7	4.5[h]	0.66[i]	1.4[j]

[a] Substrate concentration 0.2 mM. [b] Solvent: 50 vol % methanol in water. [c] Based upon the data of Table 6. [d] Measured with the 9-deuteriated substrate *d*-**1**-X. [e] From product data using 0.614 M NaN_3 ([N_3^-]/[HN_3] = 10, eq 1). [f] From product data using 0.70 M sodium salt (eq 1). [g] From product data using 0.75 M NaSCN (eq 1). [h] From product data using 0.50 M NaCl (eq 1). [i] From product data using 0.375 M NaF (eq 1). [j] From product data using 0.50 M NaOAc ([AcO$^-$]/[HOAc] = 100, eq 1).

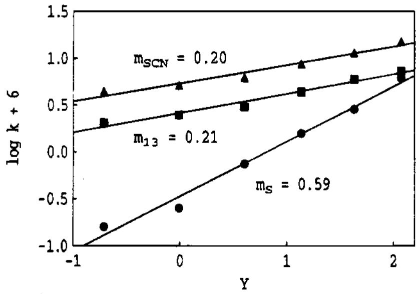

Figure 3. Grunwald–Winstein plots for the elimination (k_{13} (■)) and substitution reactions (k_S (●) and k_{SCN} (▲)) of *d*-**1**-Br in methanol–water mixtures at 70 °C in the presence of 1.00 M NaSCN. The *Y* values are based upon solvolysis of *tert*-butyl chloride.[29]

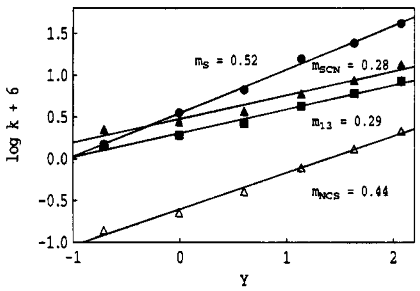

Figure 4. Grunwald–Winstein plots for the elimination (k_{13} (■)) and substitution reactions (k_S (●), k_{SCN} (▲), and k_{NCS} (△)) of **1**-OBs in methanol–water mixtures at 35 °C in the presence of 1.00 M NaSCN. The *Y* values are based upon solvolysis of *tert*-butyl chloride.[29]

Table 8. Grunwald–Winstein Parameters Measured in Methanol–Water Mixtures

substrate	temp, °C	m_S	m_{13}	m_{SCN}	m_{NCS}
1-I	70	0.57	0.26		
d-**1**-I	70	0.55	0.27		
1-Br	70	0.63	0.36		
d-**1**-Br[a]	70	0.59	0.21	0.20	
1-OBs	35	0.65	0.20		
1-OBs[a]	35	0.52	0.29	0.28	0.44

[a] 1 M NaSCN.

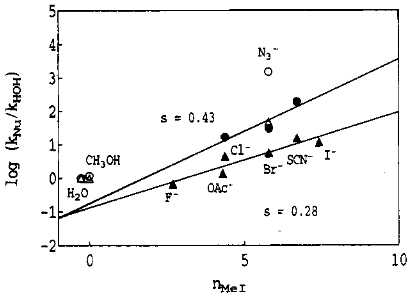

Figure 5. Swain–Scott plots of nucleophilic selectivities against the *n* value of the nucleophile[7] for the substitution reactions of *d*-**1**-I (circles) and **1**-OBs (triangles) in 25 vol % acetonitrile in water (μ = 0.75 M, maintained with $NaClO_4$) at 70 and 35 °C, respectively.

pair followed by competing substitution and elimination. Such a mechanism has been proposed for the solvolysis of the closely related tertiary substrate 9-(2-X-propyl)fluorene (**A**-X, Scheme 1). Experimental support for this type of branched mechanism was the measured extreme kinetic deuterium isotope effects and Brønsted parameters, and the anomalously small nucleophilic selectivities.[2-4] (ii) The reactivity order for the stepwise reactions of **1**-X of OBs > OTs >> Br ≈ I > Cl (k_S, Table 2) is what is expected for such a mechanism. (iii) A logarithmic plot of the relative ionization rates of **1**-X versus the relative rates of typical stepwise solvolytic reactions is shown in Figure 7. The observed good correlation supports the conclusion that the alcohol **1**-OH and the amide **1**-NHCOMe are formed by a stepwise mechanism through rate-limiting ionization to a carbocationic intermediate. The slope of 0.6 (Figure 7) indicates that the stepwise reactions of **1**-X are less sensitive to a change in the leaving group than the reference reactions.

The rate-enhancing effect of the poorly nucleophilic perchlorate ion on the rate-limiting ionization step of, e.g., **1**-OBs, is small in 25 vol % acetonitrile in water (Table 1). Acetate anion has a rate-depressing effect on the substitution reaction for **1**-X. For example, the rate constant k_S for reaction of **1**-OBs decreases 42% for an increase in acetate ion concentration from 0 to 0.50 M at a constant ionic strength of 0.75 M, maintained with sodium perchlorate. Similar specific salt effects, which may be confused with a decline in k_S as other channels for the ion pair become important, have been observed previously for solvolysis reactions in water–acetonitrile[2,8,9] as well in other

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(8) Richard, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 1383–1396.

(9) Thibblin, A. *J. Am. Chem. Soc.* **1989**, *111*, 5412–5416.

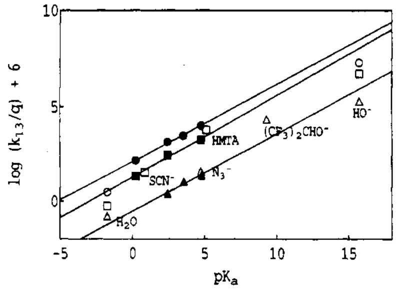

Figure 6. Brønsted plots for the solvolyses of **1-I** (circles) and **1-Br** (squares) at 70 °C and **1-OTs** (triangles) at 55 °C in 25 vol % acetonitrile in water. The ionic strength (0.75 M) was maintained with sodium perchlorate. The data are recorded in Table 5. The slopes β = 0.41, β = 0.43, and β = 0.41, from top to bottom, are based upon the data for the substituted acetate anions (filled symbols; see Table 5). The pK_a values refer to water. The rate constants for hydroxide ion are extrapolated from lower temperatures. The rate constants for HMTA (=hexamethylenetetramine) and N_3^- have been statistically corrected.

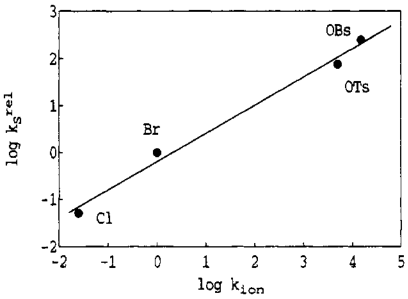

Figure 7. Logarithmic plot of relative rate constants of solvolytic substitution with the solvent (k_S, Table 2) versus relative rate constants of some typical S_N1 reactions.[30]

aqueous solvent mixtures.[10] For example, a positive salt effect of sodium perchlorate was also measured for **A-Cl** in the same solvent as well as negative effects of some other salts.[2] Acetate anion (0.75 M), which showed the largest effect, decreases the rate relative to solvolysis in 0.75 M perchlorate ion by a factor of 2.5, and the same concentration of chloride ion has a rate-depressing effect of 50%.[2] The observed increases in the pseudo-first-order rate constants k'_{Nu} and k_{13} with efficient nucleophiles/bases are much larger than the decrease in k_S (Table 1 and Figure 2). These are attributable to bimolecular reactions (*vide infra*).

The ionization of **1-X** shows a relatively low sensitivity to the Grunwald–Winstein "ionization power" of the solvent (Table 8). The *m* value for the ionization, which can be approximated by the value for substitution by the solvent, m_S, decreases in the series OBs > Br > I which indicates a decrease in transition state polarity and agrees with theoretical results of *tert*-butyl halide solvolysis.[11] The *m* values are smaller than those for the corresponding tertiary chloride and bromide, which were measured as 0.82 and 0.70, respectively.[3] The secondary substrates ionize much more slowly than the tertiary substrates **A-X**. For example, **1-Br** is about 1.5 × 10^5 times less reactive than **A-Br**.[12] This reactivity ratio corresponds to a difference of about 7 kcal/mol in the free energy of activation. The methyl groups of the tertiary carbocation A^+ have been concluded to provide significant hyperconjugative stabilization.[2–4]

The fraction of elimination product **2** increases with a decrease in the ionizing power of the solvent which corresponds to a difference in *m* values for this elimination reaction and for the reaction to the substitution products **1-OH** and **1-NHCOMe**.

The dehydronation of the ion pairs should be catalyzed by general bases. The Brønsted β parameters are expected to be very small, smaller than the value of β = 0.05 measured for the tertiary chloride.[2] However, it has not been possible to measure any catalysis by general bases on the reaction to terminal alkene **2** since E2 reaction, which yields alkene **3**, is very dominant, even with catalysts of very low basicity, and only a trace of **2** is formed.

Also the leaving group may act as the hydron acceptor. A more basic leaving group is expected to favor elimination relative to substitution through the ion pair. The results of this work (Table 1) show an approximately constant k_{12}/k_S ratio with decreasing basicity of the leaving group in the series OBs^- > Br^- > I^- which may suggest that the solvent is the dominant hydron abstractor in this system. An increasing elimination-to-substitution ratio is expected for solvent-promoted E2 reaction which is manifested as a very large change in k_{13}/k_S with leaving group (Table 1).

The selectivity of the carbocationic intermediate toward different nucleophiles should be very low. The corresponding tertiary chloride and bromide show selectivities of k_{N_3}/k_{HOH} = 4–5 and k_{MeOH}/k_{HOH} = 0.6–0.7 (ratios of second-order rate constants).[2,3] Comparable or smaller selectivities are expected for the carbocationic intermediates formed from **1-X**. The k_{MeOH}/k_{HOH} ratio is approximately constant at different compositions of methanol–water mixtures for **1-OTs** and **1-OBs** but are in fact *larger*, not smaller as would have been expected (Table 7). These changes in selectivity could be due to contributing S_N2 reactions with the methanol component of the solvent or to the change in steric hindrance at the carbocation center. As discussed below, all substrates show bimolecular kinetics with efficient nucleophiles.

The nucleophilic selectivity between water and acetonitrile is approximately the same for all substrates, k_{MeCN}/k_{HOH} = 0.4 at 70 °C (Table 2). The reaction with the very poorly nucleophilic acetonitrile should occur by a stepwise carbocationic route to give the amide product **1-NHCOMe**, since it could not be formed reasonably by an S_N2 reaction.

It has been found previously that amide formation from the analogous tertiary system is favored by acid. A substantial amount of the amide is produced by acid-catalyzed solvolysis of the phenyl ether as well as by solvolysis of the bromide under acidic conditions.[4] Only traces of amide were found to be produced under neutral conditions. However, owing to the lower stability of the ion-pair intermediate formed from **1-X**, a smaller selectivity, i.e., a much larger k_{MeCN}/k_{HOH} ratio is observed. The mechanism of amide formation has been discussed previously.[4] The initial product of the nucleophilic attack of acetonitrile on the carbocation should be the nitrilium ion which in subsequent steps is hydrolyzed. More stable carbocations do not react with acetonitrile under neutral conditions in aqueous solvent mixtures.

The ion pairs are expected to be extremely short-lived. The ion pairs formed from the tertiary analogs (**A-X**, Scheme 1) react with solvent water to give terminal alkene and alcohol with estimated rate constants of (~7–10) × 10^{10} and ~4 × 10^{10} s^{-1}.[2–4] Thus, it has been concluded that the tertiary ion pairs have such high reactivities that the reactions would occur within a pool of solvent molecules and added reactants that are present when the carbocationic intermediate is born. The rotational correlation time of water, which has been estimated

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[10] Grunwald, E.; Butler, A. F. *J. Am. Chem. Soc.* **1960**, *82*, 5647–5654. Duynstee, E. F. J.; Grunwald, E.;Kaplan, M. L. *J. Am. Chem. Soc.* **1960**, *82*, 5654–5660.

[11] Mathis, J. R.; Kim, H. J.; Hynes, J. T. *J. Am. Chem. Soc.* **1993**, *115*, 8248–8262.

[12] The estimated reactivity ratio is based upon the ionization rate of 14 × 10^{-6} s^{-1} measured for **1-OBS** at 25 °C, a rate ratio of 250 for **1-OBs** and **1-Br** (at 70 °C, Table 2), and an extrapolated rate of ~8560 × 10^{-6} s^{-1} for **A-Br** at 25 °C (ref 3).

as $\tau \approx 10^{-11}$ s,[13] may be used as a rough estimate of the time required for reorientation of a solvent molecule. Faster processes occur by preassociation mechanisms in which the reactant, a water molecule or a methanol molecule, is in reaction position before the intermediate is formed. We have suggested that the unexpectedly high reactivity of acetonitrile with the carbocationic intermediate formed from the tertiary substrate reflects the high dipole moment of acetonitrile (11.8 compared to 5.9 for water). Accordingly, charge–dipole interactions between the carbocation and acetonitrile are assumed to be of importance in stabilizing the ion–molecule pair.[4]

A very rough estimate of the reactivity of the secondary carbocation could be obtained by multiplying the rate constant of the tertiary carbocation ($\sim 1 \times 10^{11}$ s^{-1}) by a factor of 10, which yields a rate constant for reaction of the carbocation intermediate of $\sim 1 \times 10^{12}$ s^{-1}. The factor of 10 is based upon an estimation of the reactivity ratio of 6 proposed for the carbocations $PhC(Me)_2^+$ and $PhCH(Me)^+$ in 50 vol % 2,2,2-trifluoroethanol in water,[14] and the assumption that a methyl group should have a somewhat larger effect on the fluorenyl-destabilized carbocations.

Bimolecular Reactions. Appearance of S_N2 Reactions. Efficient nucleophiles open up a bimolecular route to substitution products. An example, the reaction of *d*-**1**-I with thiocyanate ion, is shown in Figure 2. Second-order reactions are progressively more important for the leaving groups $BsO^- \approx TsO^- < Cl^- < Br^- < I^-$ (Table 6). Thus, for **1**-OBs with 0.75 M SCN^- only about 20% of the substitution products consist of **1**-SCN and **1**-NCS, but the corresponding fraction for *d*-**1**-I is about 80%. This is an example of "synergism" between the leaving group and nucleophile which has been seen previously in nucleophilic displacement reactions.[8] It is likely caused by a favorable interaction between polarizable entering and leaving groups in the "coupled" S_N2 transition state.

Also, bimolecular elimination relative to bimolecular substitution, expressed by the ratio k_{13}/k_{Nu}, increases in the same series, e.g., from <0.5 for reaction of SCN^- with **1**-OBs up to ~4 with **1**-I.

The S_N2 transition state becomes less polar when the nucleophile provides more assistance since the data in Table 8 show that the Grunwald–Winstein parameter for the S_N2 reaction with thiocyanate decreases with increasing assistance. The *m* values are small and indicate that the transition states have little carbocation character and do not have properties that closely resemble those of a carbocation. Reactions of the S_N2 type usually exhibit *m* values in the range of 0.25–0.35,[15] but such a large *m* value as 0.8 has been measured.[8] The large assistance provided by efficient nucleophiles (Figure 2 and Table 7) is in strong contrast to the anomalously small nucleophilic discriminations which were observed for the corresponding tertiary substrates. For example, the tertiary bromide **A**-Br reacts to give substitution product only about 3 times more rapidly with a thiocyanate anion than with a solvent water molecule.[3] The latter reactions, owing to the very short lifetime of the ion-pair intermediate, occur through stepwise preassociation mechanisms.

There are some indications, but not conclusive evidence, that concerted S_N2 reaction with the methanol component of the solvent competes with stepwise reaction through the ion pair. Thus, the nucleophilic selectivity ratio k_{MeOH}/k_{HOH} is larger for more efficient leaving groups; it increases in the series OBs ≈ OTs < Br < I (Table 7). Moreover, the ratios for all leaving groups are larger than the constant selectivity ratio of $k_{MeOH}/k_{HOH} = 0.6–0.7$ which was measured for the tertiary bromide and chloride.[2,3]

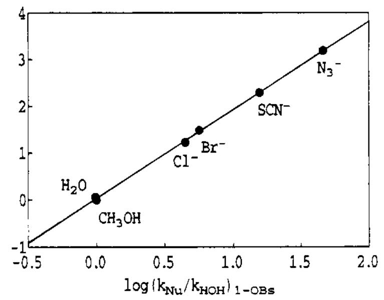

Figure 8. Comparision of nucleophilic selectivities toward *d*-**1**-I and **1**-OBs in 25 vol % acetonitrile in water ($\mu = 0.75$ M, maintained with $NaClO_4$) at 70 and 35 °C, respectively.

Water and methanol show positive deviations from Swain–Scott correlations of nucleophilic reactivity toward *d*-**1**-I and **1**-OBs (Figure 5). This is consistent with, but does not require, nucleophilic assistance from the solvent. There are positive deviations of 8-fold and 28-fold for reaction of azide ion with **1**-OBs and *d*-**1**-I, respectively, consistent with S_N2 transition states possessing some carbocationic character.

Thiocyanate ion, owing to its ambident character, gives rise to two products. There is a change in reactivity of the S and N parts of the nucleophile with a change in the leaving group of the substrate. The more polarizable ("soft") the leaving group is, the more of **1**-SCN relative to **1**-NCS is formed. This is in accord with the concept of synergism between the leaving group and nucleophile which reflects favorable interaction between polarizable entering and leaving groups in the coupled, concerted transition state since sulfur is more easily polarized than nitrogen. Consistently, m_{NCS} is significantly greater than m_{SCN} for reaction of **1**-OBs (Table 8), which shows that the transition state with the N atom as nucleophile is more polar than the transition state with the S atom.

There is a linear correlation of the values of $\log(k_{Nu}/k_{HOH})$ for the reactions with *d*-**1**-I and **1**-OBs (with a slope of 1.9, Figure 8). The rate constants for reactions with azide ion, water, and methanol, which show large deviations from Swain–Scott correlations (Figure 5), fit this linear correlation. Thus, the factors which cause the enhanced reactivity of these nucleophiles are probably the same for the reactions of these two substrates, but the degree of the enhanced reactivity is leaving-group-dependent. This supports a coupled concerted mechanism.

Concurrent stepwise reaction of added efficient nucleophiles with the ion-pair intermediate by trapping must, of course, also exist but is too slow to be detected in the presence of the fast reaction with solvent and S_N2 reaction with the nucleophile. This also applies to the reaction of the carbocationic intermediate with the strongly nucleophilic azide and thiocyanate anions, which are assumed to be diffusion-controlled since there should be no barrier for reaction of the highly unstable ion pair with these anions.[8]

Bimolecular Reactions. Appearance of Solvent- and Base-Promoted E2 Reactions. Recently we reported briefly that solvolytic elimination reactions of **1**-I and **1**-Br to give alkene **3** are the dominant reactions of these substrates in 25 vol % acetonitrile in water (Table 1).[6] It was concluded that these reactions are mechanistically of the solvent-promoted E2 type. The evidence for this type of one-step mechanism is as follows.

(i) The large isotope effects of $k_{obs}^H/k_{obs}^D = 3.8$ and $k_{obs}^H/k_{obs}^D = 2.0$ for the reaction of **1**-I and **1**-Br, respectively, without added base at 70 °C (Table 3) show that the reaction to give alkene **3** does not have an irreversibly formed carbocationic

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[13] Chiang, Y; Kresge, A. J. *J. Am. Chem. Soc.* **1985**, *107*, 6363–6367.

[14] Amyes, T. L.; Richard, J. P., and Novak, M. *J. Am. Chem. Soc.* **1992**, *114*, 8032–8041.

[15] Reichardt, C. In *Solvents and Solvent Effects in Organic Chemistry*, 2nd ed.; VCH: Weinheim, Germany, 1988.

intermediate in common with the other reactions, since an isotope effect of $k^H/k^D \leq 1.15$ at 25 °C is expected for such a mechanism.[16] A reversibly formed intermediate which undergoes rate-limiting hydron transfer can be ruled out since it is unreasonable that such a short-lived ion pair would react exclusively to yield **3** at low concentration of hydroxide anion. Accordingly, the results strongly indicate a separate reaction to alkene **3**. The isotope effects on this solvent-promoted E2 reaction of the iodide and the bromide are $k_{13}{}^H/k_{13}{}^D = 4.7$ and $k_{13}{}^H/k_{13}{}^D = 4.3$, respectively (Table 3).

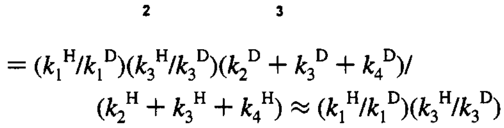
(ii) Another independent, strong indication of a one-step mechanism for the elimination reactions of **1-I** and **1-Br** is the measured Brønsted parameters of $\beta = 0.41$ and $\beta = 0.43$,[17] respectively (Figure 6). Very small β values are expected for a mechanism in which a reversibly formed, very unstable carbocationic intermediate is dehydronated in the rate-limiting step. Accordingly, these large values exclude reactions through ion pairs, either coupled with the substitution reactions or as separate reactions. However, they indicate irreversible carbanion reactions ($E1cB_{irrev}$) or one-step concerted reactions (E2).

(iii) The sensitivity to solvent "ionizing power" is small; the Grunwald–Winstein parameters for the solvent-promoted eliminations in methanol–water mixtures are $m_{13} = 0.26$ (**1-I**) and $m_{13} = 0.36$ (**1-Br**) (Table 8).

The corresponding tertiary substrates **A-Br** and **A-Cl** only exhibit E2 reaction in the presence of strong bases (Scheme 1).[2,5] The shift in the major reaction pathway, from stepwise solvolysis to solvent-promoted E2 reaction, is caused by the decreased reactivity of the substrate to ionization. Thus, the appearance of solvent-promoted reactions with **1–I** and **1-Br** is due to slower ionization providing more unstable ion pairs, making the solvent-promoted E2 reaction path competitive.

The fact that the fraction of elimination to give alkene **3** is larger for **1-I** than for **1-Br**, the opposite of what is expected for a stepwise carbocationic mechanism in which the leaving group of the ion pair acts as the hydron acceptor, is further support for the E2 mechanism. Thus, the tertiary substrates, which have been concluded to react through the ion pairs, provide more terminal alkene **2** from the chloride than from the bromide.[2]

The sulfonyl esters **1-OTs** and **1-OBs** yield much smaller fractions of alkene **3** than the halides, only 3–5% (Table 2). The kinetic isotope effects on the observed rate of disappearance of the substrates are accordingly smaller, $k_{obs}{}^H/k_{obs}{}^D = 1.1$ and 1.0, respectively. Moreover, the isotope effects on the solvolytic eliminations are relatively small, $k_{13}{}^H/k_{13}{}^D = 2.7$ and 2.8 for **1-OTs** and **1-OBs**, respectively (Table 3), which correspond to $k_{13}{}^H/k_{13}{}^D \approx 2.9$ at 25 °C. These isotope effects are consistent with reaction through an ion pair (eq 2). The corresponding expression for the isotope effect of the reaction to give alkene **3** is given in eq 3.

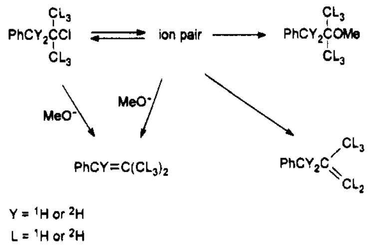


(2)

$$k_{13}{}^H/k_{13}{}^D = (k_1{}^H/k_1{}^D)(k_3{}^H/k_3{}^D)(k_2{}^D + k_3{}^D + k_4{}^D)/(k_2{}^H + k_3{}^H + k_4{}^H) \approx (k_1{}^H/k_1{}^D)(k_3{}^H/k_3{}^D) \quad (3)$$

Thus, owing to the reaction branching, the magnitude of this isotope effect is a product of the ionization isotope effect, which is equal to $k_{obs}{}^H/k_{obs}{}^D$ if no parallel E2 reaction occurs, and the isotope effect on the elimination step. The latter isotope effect should be relatively small since it involves dehydronation of a very short-lived ion-pair intermediate. An isotope effect of less than 3 seems reasonable. Branching as the cause of extreme kinetic isotope effects in solvolytic reactions[1] and in general[18] has been discussed previously.

Scheme 3



Reaction through the ion pair should explain why water shows a positive deviation in the Brønsted plot for **1-OTs** (Figure 6). The normal behavior of water as a catalyst is shown in the Brønsted plots for **1-Br** and **1-I**. The catalytic constants for water as a base fall below the Brønsted lines for the acetate anions (Figure 6) by factors of 6–8. Negative deviations of the catalytic constant for water are well-known for hydron transfer to and from carbon.[19–21] The low catalytic activity of water probably reflects some kind of solvation effect.

It is plausible that some solvent-promoted E2 reaction accompanies the stepwise elimination to alkene **3** from the esters. However, it has to be very slow, and it does not seem possible to confirm this reaction path for **1-OTs** and **1-OBs** experimentally. For example, it is not possible to substantially increase the fraction of E2 reaction by decreasing the polarity of the solvent. In 98 vol % acetonitrile in water, **1-OBs** reacts to give more than 90% alkene **3** (some of it is produced by rearrangement of alkene **2**) but the isotope effect is small, $k_{13}{}^H/k_{13}{}^D \approx 2.4$. Similar results were obtained in methanol and ethanol. Only the terminal, less stable alkene is formed from the ion pair in reactions of the corresponding tertiary substrates.[2,3,4]

The primary kinetic deuterium isotope effects $k_{13}{}^H/k_{13}{}^D$ for the iodide and bromide are large and normal (Table 3). They correspond to isotope effects at 25 °C of 5.9 and 5.4 for **1-I** and **1-Br**, respectively, which are somewhat lower than the isotope effects measured with hydroxide as base (Table 4). Conceivably, the relatively moderate size of the isotope effect $k_{13}{}^H/k_{13}{}^D$ for the bromide is caused by competing E2 reaction to alkene **3**, with an isotope effect of about 7, and some stepwise reaction through the ion pair, with an isotope effect of about 2.9 (all at 25 °C). Competing methoxide-promoted E2 reaction and elimination *via* a reversibly formed ion pair with methoxide ion and solvent as hydron abstractors occurs with 2-chloro-2-methyl-1-phenylpropane in methanol, providing the elimination product 2-methyl-1-phenyl-1-propene (Scheme 3).[9] The other alkene was found to be formed only from the ion pair, and no catalysis from methoxide was detected. Thus, there are similarities with the reactions of **1-X**; both systems undergo E2 reaction by abstraction of the more acidic hydron only, but a strong base is required for the less acidic 1-phenylpropyl system. Also, the same product is formed by a parallel hydron abstraction from the ion pair by the same base, i.e., water and methoxide ion, respectively.

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(16) Westaway, K. C. In *Isotopes in Organic Chemistry;* Buncel, E., Lee, C. C., Eds.; Elsevier: Amsterdam, 1987; Vol 7, Chapter 5.

(17) Corrigendum: There are two printing errors in ref 6: the β value for **1-Br** should be 0.43, third paragraph under the table, p 1839, and figure text, p 1840.

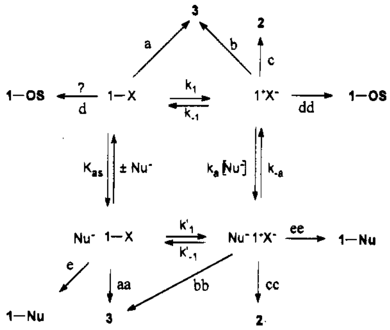
(18) Thibblin, A.; Ahlberg, P. *Chem. Soc. Rev.* **1989**, *18*, 209–224.

(19) Thibblin, A.; Jencks, W. P. *J. Am. Chem. Soc.* **1979**, *101*, 4963–4973.

(20) Kresge, A. J.; Chiang, Y. *J. Am. Chem. Soc.* **1973**, *95*, 803–806.

(21) Hupe, D. J.; Wu, D. *J. Am. Chem. Soc.* **1977**, *99*, 7653–7659.

Scheme 4



The assignment of the E2 mechanism, and not the irreversible E1cB mechanism, to the solvent- and base-promoted eliminations of **1**-X is based upon comparison with the base-promoted elimination of 9-(2-chloromethyl)fluorene, which has been concluded to be of the E2 type.[5] The latter assignment was based upon analysis of Brønsted β as a function of substrate acidity, leaving group, and α-substituents. A small decrease in β for a change in the leaving group from Br^- to I^- is predicted by the variable E2 transition-state theory.[5,22]

Mechanistic Borderlines. The substitution and elimination reactions of **1**-X can be summarized mechanistically as shown in Scheme 4. The results of this investigation show that one-step solvent-promoted elimination to provide alkene **3** (path a) is the major reaction for the iodide and bromide substrates. Addition of efficient bases/nucleophiles gives rise to concerted E2 and S_N2 reactions (paths aa and e, respectively) with all of the substrates.

The competition between these E2 and S_N2 reactions with added nucleophile (Nu^-) are of course dependent on the basicity and nucleophilicity of Nu^-. Thus, hydroxide ion gives no S_N2 reaction. Thiocyanate ion, which is a much weaker base ($pK_a = 0.85$) but a very good nucleophile, exhibits S_N2/E2 ratios of 0.2, 0.7, and 3.2 for **1**-I, **1**-Br, and **1**-OBs, respectively. Azide ion is more basic ($pK_a = 4.72$) and gives almost exclusively elimination with **1**-I but both reactions with the other leaving groups. This demonstrates that the nature of the leaving group is of great importance for the S_N2/E2 product ratio.

The data also show that stepwise reactions occur with all the studied substrates. Thus, the alcohol and the amide are formed from the ion pairs (path dd). The results with the sulfonyl esters show that alkenes **3** and **2** are formed from the ion pairs (paths b and c); there is no significant E2 reaction with the solvent. The trace of **2** that is formed from the halides should also come from the ion pair. Presumably the substitution reaction of the iodide with the methanol component of the solvent is concerted (path d).

A change from a stepwise to a one-step reaction mechanism for the studied elimination and substitution reactions, respectively, could occur in two principally different manners.[8]

(i) The same reaction product is formed by two parallel, competing reaction paths with different transition-state structures. A change in experimental conditions or structure of the reactants changes the relative energies of the rate-limiting transition states, which may induce a shift in the major reaction path. At the borderline, the transition states of the parallel reactions are of equal energy. Owing to a large difference in free energy of activation, one of the mechanisms frequently dominates and is the only mechanism observed. Apparently, this type of borderline does not correspond to merging of transition-state structures.[9,23]

(ii) A transformation of the stepwise to the one-step mechanism occurs when the intermediate ceases to exist in the presence of a given reactant, e.g., a base/nucleophile. Thus, only one mechanism could exist. The borderline represents merging of transition-state structures.

A shift in mechanism from stepwise elimination (path b, Scheme 4) to solvent-promoted concerted elimination (path a) obviously occurs by a change in the leaving group from tosylate or brosylate to bromide or iodide. This mechanistic change should be caused by two factors. Firstly, ionization occurs more easily with TsO^- and BsO^- as leaving groups. Secondly, the halide leaving groups give more assistance to the concerted elimination, most likely by providing more stabilization to the partially developed double bond. Thus, the mechanistic change is caused by a change in relative energy of the ionization transition state and the solvent-promoted E2 transition state. Apparently, this borderline does not correspond to merging of the transition-state structures,[9,23] but is of type i above.

An analogous change from stepwise to concerted substitution reaction with the solvent by a change in the leaving group does not seem to occur in water—acetonitrile mixtures but presumably occurs with the more nucleophilic methanol in methanol—water solvent mixtures. Accordingly, we suggest that the substitution reaction of **1**-OBs with methanol is stepwise but the corresponding reaction with **1**-I is concerted. This change in mechanism corresponds to merging of transition-state structures; i.e., it is of type ii.

Reactions through the triple-ion complex $Nu^-{-}\mathbf{1}^+{-}X^-$ (Scheme 4), which, if they occur *via* the association complex, represent stepwise preassociation mechanisms, are not likely significant for **1**-I and **1**-Br owing to the large assistance provided by Nu^-. Furthermore, the triple-ion complex formed from **1**-OTs or **1**-OBs should not have a significant lifetime in the presence of a good nucleophile/base. However, reactions of the brosylate and the tosylate with weak nucleophiles/bases may proceed to some extent through stepwise preassociation mechanisms. Such an elimination mechanism has been found to be significant for the formation of the terminal alkene **B** in the solvolysis of the tertiary substrate **A**-Cl (Scheme 1) in which the elimination (path cc, Scheme 4) was found to be catalyzed by general bases.[2]

One more α-methyl group in the substrate increases the ionization rate considerably ($\sim 1.5 \times 10^5$ times, *vide supra*) and also provides some steric hindrance to direct attack of a nucleophile/base on the substrate. Accordingly, S_N2 and E2 reactions with the solvent, added nucleophiles, or weak bases do not occur with the substrate **A**-X, but stepwise preassociation mechanisms giving terminal alkene (path cc) and substitution product (path ee) are significant.[2-4]

We conclude that the above-discussed change in solvolytic elimination mechanism for the reactions of **1**-X and **A**-X is of type i. Thus, a change from stepwise to concerted solvent-promoted elimination can be induced by either a change in the leaving group X in **1**-X or a change in structure from tertiary to secondary (e.g., from **A**-Br to **1**-Br).

The change in substitution mechanism from stepwise to concerted, on the other hand, is likely caused by the absence of a significant lifetime of the ion pair in the presence of an efficient nucleophile. This borderline is of type ii, i.e., represents

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(22) Saunders, W. H., Jr.; Cockerill, A. F. *Mechanisms of Elimination Reactions;* Wiley-Interscience: New York, 1973.

(23) (a) More O'Ferrall, R. A. *Structure and Dynamics in Chemistry,* Proceedings from Symposium held at Uppsala, 1977; Ahlberg, P., Sundelöf, L.-O., Eds.; Almqvist and Wicksell International: Stockholm, 1978. (b) Jencks, W. P. *Chem. Soc. Rev.* **1981**, *10*, 345–375.

merging of transition-state structures. This type of mechanistic change has been discussed in detail for the 1-phenylethyl system.[8]

Experimental Section

General Procedures. The ^{1}H-NMR analyses were performed with a Varian XL 300 spectrometer. The high-performance liquid chromatography (HPLC) analyses were carried out with a Hewlett-Packard 1090 liquid chromatograph equipped with a diode-array detector on a C18 (5 μm, 3 × 200 mm) reversed-phase column. The mobile phase was a solution of acetonitrile or methanol in water. The reactions were studied at constant temperature in a HETO 01 PT 623 thermostat bath. The semipreparative HPLC separations were carried out with a Hewlett-Packard 1084B HPLC apparatus using a semipreparative C8 column (7 μm, 8 × 250 mm) with methanol–water as the mobile phase. The UV spectrophotometry was performed with a Kontron Uvicon 930 spectrophotometer equipped with an automatic cell changer kept at constant temperature with water from the thermostat bath. The pH was measured using a Radiometer PHM82 pH meter with an Ingold micro glass electrode.

Materials. Acetonitrile (Riedel de Haen or J. T. Baker) and methanol (J. T. Baker or Merck) were of HPLC grade and were used without further purification. All other chemicals were of reagent grade and were used without further purification.

(9,9-^{2}H$_2$)Fluorene.[24] Fluorene (8.5 g) was dissolved in 75 mL of dimethoxyethane dried over molecular sieves. This solution was refluxed with potassium *tert*-butoxide (2.91 g) and 50 mL of ^{2}H$_2$O (99.8 atom % ^{2}H) for 2 days. The reaction mixture was then poured into a mixture of acetic acid and ice, filtered, and washed with ice–water. The entire procedure was repeated once and the product recrystallized from ethanol. No trace of protium in the 9-position was detected by ^{1}H NMR; thus, the ^{2}H content was estimated to be >99.5 atom %.

9-(1-Hydroxyethyl)fluorene (1-OH) was prepared from fluorene and acetaldehyde by a procedure which has been used previously to prepare the corresponding tertiary alcohol;[2] mp 101–102 °C (same as reported previously).[25]

(9-^{2}H)-9-(1-Hydroxyethyl)fluorene (*d*-1-OH) and 9-(1-Hydroxy-(1,2,2,2-^{2}H$_4$)ethyl)fluorene (*d*$_4$-1-OH) were prepared from (9,9-^{2}H$_2$)-fluorene and acetaldehyde and from fluorene and (1,2,2,2-^{2}H$_4$)-acetaldehyde (>99 atom % ^{2}H, Cambridge Isotope Laboratories, Inc.), respectively, as above. The ^{2}H content of *d*-1-OH was measured as >98.8 atom % in the 9-position.

9-(1-Bromoethyl)fluorene (1-Br) was prepared from the alcohol **1**-OH, ZnBr$_2$, and concentrated hydrobromic acid in chloroform.[2] Recrystallization from pentane gave pure material: mp 66–67 °C (lit.[26] mp 58 °C); ^{1}H NMR (CDCl$_3$) δ 7.30–8.05 (8 H, m), 4.93 (1 H, m), 4.49 (1 H, d), 1.25 (3 H, d).

(9-^{2}H)-9-(1-Bromoethyl)fluorene (*d*-1-Br) and 9-(1-bromo(1,2,2,2-^{2}H$_4$)ethyl)fluorene (*d*$_4$-1-Br) were prepared from the corresponding alcohol by the method described above. The deuterium content of *d*-**1**-Br was measured by ^{1}H NMR to be >98.5 atom % in the 9-position, and *d*$_4$-**1**-Br has >99.3 and >99.3 atom % ^{2}H in the 1- and 2-postitions, respectively.

9-(1-Iodoethyl)fluorene (1-I) was synthesized from the alcohol **1**-OH by reaction with ZnI$_2$ and HI in chloroform, analogous to the method for the preparation of the bromide. Recrystallization from pentane followed by washing of the crystals with methanol gave pure material: mp 94–95 °C; ^{1}H NMR (CDCl$_3$) δ 7.30–8.05 (8 H, m), 4.90 (1 H, m), 4.18 (1 H, d), 1.60 (3 H, d).

(9-^{2}H)-9-(1-Iodoethyl)fluorene (*d*-1-I) was prepared from *d*-**1**-OH by the same method as above.

9-(1-Chloroethyl)fluorene (1-Cl)[27] was prepared from the alcohol **1**-OH, ZnCl$_2$, and concentrated hydrochloric acid in chloroform,[2] and purified by distillation.

(9-^{2}H)-9-(1-Chloroethyl)fluorene (*d*-1-Cl) was prepared from *d*-**1**-OH by the same method as above.

9-[1-[(4′-Methylbenzyl)sulfonyl]ethyl]fluorene (1-OTs). Alcohol **1**-OH (1 g) was dissolved in dry dichloromethane (20 mL), and dry pyridine (10 mL) and *p*-toluenesulfonyl chloride (2 g) were added. The mixture was stirred at room temperature for 2 days, poured into excess cold dilute hydrochloric acid, and extracted with chloroform. After washing with water and brine, the solvent was evaporated and the residue recrystallized from ethanol–chloroform–heptane (1:2:5) in the refrigerator: mp 126–127 °C; ^{1}H NMR (CDCl$_3$) δ 7.26–7.90 (12 H, m), 5.38 (1 H, m), 4.25 (1 H, d), 2.46 (3 H, s), 0.68 (3H, d).

(9-^{2}H)-9-[1-[(4′-Methylbenzyl)sulfonyl]ethyl]fluorene (*d*-1-OTs) was prepared as above from *d*-**1**-OH.

9-[1-[(4′-Bromobenzyl)sulfonyl]ethyl]fluorene (1-OBs) was synthesized by stirring a mixture of **1**-OH (0.5 g), dry dichloromethane (10 mL), dry pyridine (5 mL), and *p*-bromobenzenesulfonyl chloride (1.5 g) at room temperature for 1 day. The product was isolated as above and recrystallized from ethanol–chloroform–heptane (3:1:1): mp 93–94 °C; ^{1}H NMR (CDCl$_3$) δ 7.26–7.90 (12 H, m), 5.40 (1 H, m), 4.30 (1 H, d), 0.78 (3 H, d).

(9-^{2}H)-9-[1-[(4′-Bromobenzyl)sulfonyl]ethyl]fluorene (d-1-OBs) was prepared as above from *d*-**1**-OH.

9-(1-Acetamidoethyl)fluorene (1-NHCOMe) and 9-vinylfluorene (2) were made from **1**-OBs by the following method. The brosylate **1**-OBs (1.4 g) dissolved in a mixture of acetic acid (4 mL) and acetonitrile (16 mL) was refluxed for 1 day. The products were worked-up by adding 20 mL of 1 M sodium acetate, extraction with ether, and washing with water and brine followed by evaporation. Recrystallization from a mixture of dichloromethane–pentane (1:2) gave pure **1**-NHCOMe: mp 151–152 °C; ^{1}H NMR (CDCl$_3$) δ 7.26–7.85 (8 H, m), 5.38 (1 H, d), 4.85 (1 H, m), 4.37 (1 H, d), 1.97 (3H, s), 0.83 (3H,d).

The alkene **2** was obtained from the mother liquid by flash column chromatography on silica gel with pentane–ethyl acetate (97:3) followed by recrystallization from pentane; mp 39.5–40.5 °C (lit.[28] mp 35–36 °C).

Kinetics and Product Studies. The reaction solutions were prepared by mixing acetonitrile or methanol with water at room temperature, *ca.* 22 °C. The reaction vessel was a 2-mL HPLC flask, sealed with a gas-tight PTFE septum, which was placed in an aluminum block in the water thermostat bath. The reactions were initiated by fast addition of a few microliters of the substrate dissolved in acetonitrile by means of a syringe. The concentration of the substrate in the reaction solution was usually about 0.2 mM. At appropriate intervals, samples were analyzed using the HPLC apparatus. The rate constants for the disappearance of the substrates were calculated from plots of substrate peak area versus time by means of a nonlinear regression computer program. Very good pseudo-first-order behavior was seen for all of the reactions studied. The separate rate constants for the elimination and substitution reactions were calculated by combination of product composition data, obtained from the peak areas and the relative response factors determined in separate experiments, with the observed rate constants.

The relative response factors were measured for **1**-Br, **1**-OH, **2**, and **3**. The response factors for all other compounds were assumed to be the same as that of **1**-OH.

In the presence of strong base at 25 °C, the reactions were followed for at least 10 half-lives by monitoring the increase in absorbance at 312 nm by using thermostated 3-mL quartz cells as reaction vessels. Analysis by HPLC showed that alkene **3** is the sole product.

The estimated errors are considered as maximum errors derived from maximum systematic errors and random errors.

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(24) Ek, M. *Abstracts Uppsala Dissertations from the Faculty of Sciences*, 692, Acta Universitatis Upsaliensis, 1983.

(25) More O'Ferrall, R. A.; Larkin, F.; Walsh, P. *J. Chem. Soc., Perkin Trans. 2* **1982**, 1573–1579.

(26) Greenhow, E. J.; McNeil, D. *J. Chem. Soc.* **1956**, 3204–3209.

(27) Greenhow, E. J.; Harris, A. S.; White, E. N. *J. Chem. Soc.* **1954**, 3116–3121.

(28) Ipaktschi, J. *Chem. Ber.* **1972**, *105*, 1989–1995.

(29) Fainberg, A. H.; Winstein, S. *J. Am. Chem. Soc.* **1956**, *78*, 2770–2777.

(30) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*; Harper International Edition: New York, 1987; p 374.