J. Am. Chem. Soc. **1987**, *109*, 2071–2076 2071

Deprotonation of Ion Pairs in Aqueous Solvent. Competing Bimolecular and Solvolytic Elimination Reactions

Alf Thibblin

Contribution from the Institute of Chemistry. University of Uppsala, P.O. Box 531, S-751 21 Uppsala, Sweden. *Received August 5, 1986*

Abstract: Solvolysis of 9-(2-chloro-2-propyl)fluorene (**h-1-Cl**) or 9-(2-bromo-2-propyl)fluorene (**h-1-Br**) in 25 vol % acetonitrile in water at 25 °C produces 9-(2-propenyl)fluorene (**h-4**), 9-(2-hydroxy-2-propyl)fluorene (**h-2**), and a trace of 9-isopropylidenefluorene (**h-3**). The corresponding acetate 9-(2-acetoxy-2-propyl)fluorene (**h-1-OAc**) yields the same products but comparable amounts of **3** and **4**. The presence of base as well as chloride or bromide ions increases the fraction of elimination products but does not increase $k_{12} + k_{14}$. The Brønsted parameter for deprotonation of the carbocationic intermediate with substituted acetate anions is small, $\beta = 0.05$. The deuteriated analogue 9-(1,1,1,3,3,3-$^2H_6$)-9-(2-chloro-2-propyl)fluorene (***d*$_6$-1-Cl**) reacts slower than h-**1**-Cl. Thus, the overall kinetic isotope effect was measured without base as $(k_{12}{}^{H} + k_{13}{}^{H} + k_{14}{}^{H})/(k_{12}{}^{d6} + k_{13}{}^{d6} + k_{14}{}^{d6}) = 2.2 \pm 0.1$, which is composed of the isotope effect $k_{12}{}^{H}/k_{12}{}^{d6} = 1.4 \pm 0.1$ for formation of the substitution product **2** and $k_{14}{}^{H}/k_{14}{}^{d6} = 3.7 \pm 0.3$ for production of the olefin **4**. The results indicate a branched mechanism involving rate-limiting formation of a common contact ion pair (with a secondary isotope effect of 2.2) which either undergoes nucleophilic attack by water (isotope effect 1.0) or is deprotonated by water (isotope effect 2.8) or other general base (including chloride and bromide anions). Direct elimination from the ion pairs is indicated by the observation that the fraction of elimination increases with rising basicity of the leaving group. The intermediate shows very small discrimination between the nucleophiles azide anion, methanol, and water. The presence of strong base in the reaction solution opens up a parallel bimolecular elimination route (E1cB or E2) for **1**-Cl. Thus 0.16 M sodium hydroxide yields mainly **3** but the rates of formation of the solvolysis products **2** and **4** are decreased only slightly. The (9-^{2}H) analogue **d-1**-Cl, which solvolyzes 3% slower than **h-1**-Cl, undergoes hydroxide-promoted elimination with an isotope effect $k_{13}{}^{H}/k_{13}{}^{D}$ of 8.1.

The present work is part of an investigation of the role of ion pairs in water and highly aqueous media. Jencks points out that a substantial reaction of the contact or solvent-separated ion pair with a dilute reactant (<1 M) in solvents of this type is not likely since the lifetime of the ion pair should be in short to allow it to encounter and react with other reactants than those that are already close to the ion pair when it is formed.[1] Accordingly, a substantial k_p/k_{-d} ratio (eq 1) seems to require a preassociation mechanism whereby the dilute reactant C gets into reaction position before the R–X bond is ruptured, or reaction with the solvent.

$$\begin{tikzcd} \mathrm{RX} \arrow[r] & \text{ion pairs} \arrow[r, shift left, "k_{-d}"] \arrow[d, "C"', "k_p"] & \mathrm{R}^+ \arrow[l, shift left, "k_d"] \arrow[r] & \text{products} \\ & \text{products} & & \end{tikzcd} \qquad (1)$$

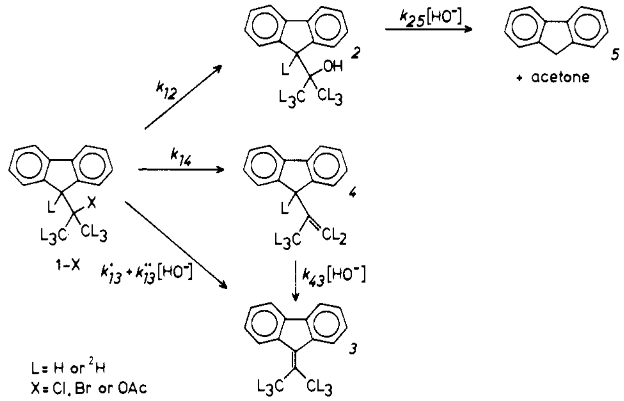
Jencks's reasoning is based upon the fact that the eqilibrium constant ($K_{as} = k_d/k_{-d}$) for formation of ion pairs from singly charged ions in water is generally <1 M^{-1}.[2] However, if there is a specific interaction between the carbocation and the leaving group that increases the barrier for separation of the two parts of the contact ion pair, the prediction breaks down.

It was found in the present work that not only ordinary bases ($pK_a > 0$) catalyze the formation of elimination products in the studied solvolysis reactions; halide ions show the same effect. Thus, there are resemblances with elimination reactions classified as E2C.[3] The results are discussed in terms of short-lived contact and solvent-separated ion pairs.

Results

The solvolysis of 9-(2-chloro-2-propyl)fluorene (**h-1**-Cl) in 25 vol % (10.3 mol %) acetonitrile in water at 25 °C or 100 °C provides 9-(2-propenyl) fluorene (**h-4**), 9-(2-hydroxy-2-propyl)fluorene (**h-2**), and a trace of 9-isopropylidenefluorene (**h-3**) (Scheme I). The kinetics of the reactions were studied at 25 °C by a sampling high-performance liquid-chromatography procedure. The measured rate constants and reaction conditions are shown in Table I. Addition of salt to the reaction solution affects reaction rates and product compositions. When the ionic strength is maintained constant, 0.75 M with sodium perchlorate, a linear correlation is a good approximation of the effect of salt concentration on the observed rate of reaction. Examples of this are shown in Figure 1.

Scheme I



Sodium azide (0.75 M) has a small negative effect on the reaction rate; only about 3% of the azide adduct **1**-N$_3$ is formed, compared with ca. 33% of the alcohol **2**. Solvolysis of **1-Cl** in 25 vol % methanol in water ($\mu = 0$) yields 4% of the methyl ether and 47% of **2**. From these results, the discrimination between water and the other two nucleophiles for the reaction with the carbocationic intermediate can be calculated as $k_{N_3}/k_{H_2O} \sim 5$ and $k_{MeOH}/k_{H_2O} \sim 0.6$ (ratio of second-order rate constants).

As shown in the last column of Table I, the more basic of the salts have the largest effect on the product ratio. The effects for AcO$^-$ and Cl$^-$ are illustrated in Figure 2. These effects of the anion concentrations, as expressed by the slope of plots of the elimination/substitution ratio, are plotted against the pK_a of the respective anion in Figure 3. The shown regression line is based upon the three acetate anions. Assuming that the substitution reaction is not sensitive to the pK_a of the acetate anion but that the elimination is,[4,5] the slope represents the Brønsted β parameter.

---

[1] Jencks, W. P. *Chem. Soc. Rev.* **1981**, *10*, 345–375.

[2] Davies, C. W. *Ion Association*; Butterworths: London, 1962; pp 77 and 168.

[3] Saunders, W. H., Jr.; Cockerill, A. F. *Mechanisms of Elimination Reactions*; Wiley-Interscience: New York, 1973.

0002-7863/87/1509-2071$01.50/0

Table I. Rate Constants for the Reactions of **1-Cl** and **1-Br** in 25 vol % Acetonitrile in Water at 25.00 ± 0.03 °C

substrate[a]	salt[b]	$10^6(k_{12}+k_{13}+k_{14})$,[g] s^{-1}	10^6k_{12}, s^{-1}	10^6k_{13}, s^{-1}	10^6k_{14}, s^{-1}	$(k_{13}+k_{14})/k_{12}$
h-1-Cl	none	142	50	1	90	1.81
	none	2.4[c]	0.26[c]	0.03[c]	2.10[c]	8[c]
	$NaClO_4$	184	69	1	115	1.67
	$NaClO_4$					2.2[d]
	NaCl	119				1.93
	NaBr	137				1.82
	NaN_3	149				
	NaOAc	73.6				2.38
	NaO_2CCH_2CN					2.23
	NaO_2CCF_3					2.09
	NaOH[e]	470	55	312	103	
h-1-Br	none					1.37
	$NaClO_4$					1.33
	NaCl					1.62
	NaBr					1.50
	NaOAc					2.00
	NaO_2CCH_2CN					1.82
	NaO_2CCF_3					1.71
***d*-1-Cl**	$NaClO_4$	180	67	<1	113	
	NaOH	184	52[f]	38[f]	94	
***d*$_6$-1-Cl**	none	0.98[c]	0.22[c]	0.01[c]	0.75[c]	
	$NaClO_4$	82.7	51.0	0.8	30.9	
	NaOAc	30.6				
	NaOH[e]	295	40	228	27	

[a] 0.02 mM. [b] 0.75 M. [c] 70.6 vol % acetonitrile in water. [d] 100 °C. [e] 0.16 M; μ = 0.75 M maintained with sodium perchlorate. [f] Based upon the assumption that $k_{43}{}^{H}/k_{43}{}^{D} \approx 8$ (see text). [g] Estimated error: ±2%.

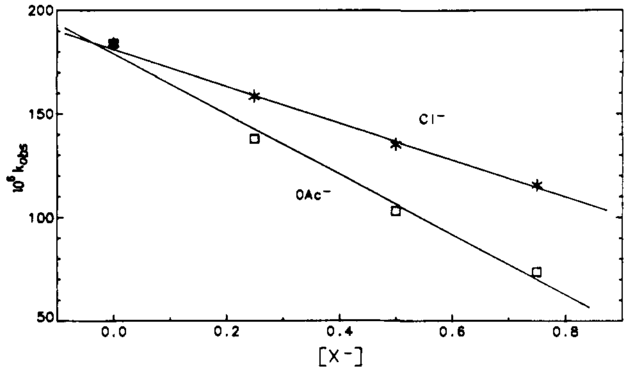


Figure 1. The decrease in the observed rate constant for the reaction of **1-Cl** with increasing concentration of Cl^- and OAc^- in 25 vol % acetonitrile in water; ionic strength 0.75 M maintained with sodium perchlorate.

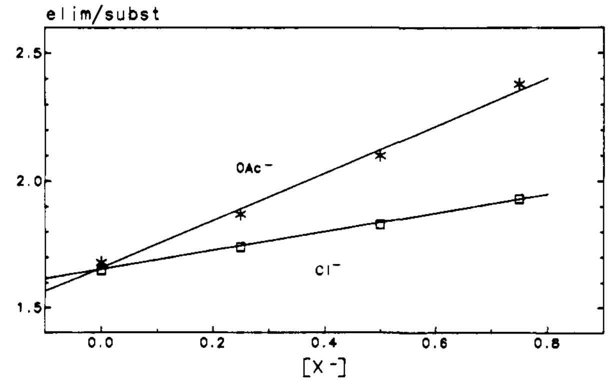


Figure 2. The increase in the elimination/substitution ratio for the reaction of **1-Cl** with increasing concentration of Cl^- and OAc^- in 25 vol % acetonitrile in water; ionic strength 0.75 M maintained with sodium perchlorate.

The low value (β = 0.05) indicates a very small amount of proton transfer from the carbocationic intermediate to the base in the elimination transition state.

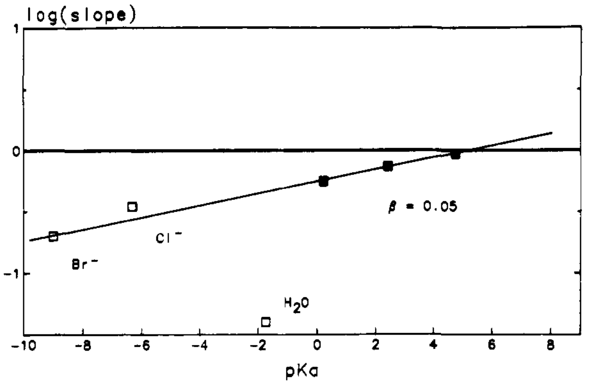


Figure 3. Brønsted plot for the deprotonation of the ion-pair intermediate formed from **1-Cl** in 25 vol % acetonitrile in water; ionic strength 0.75 M maintained with sodium perchlorate. The pK_a values refer to water.[6]

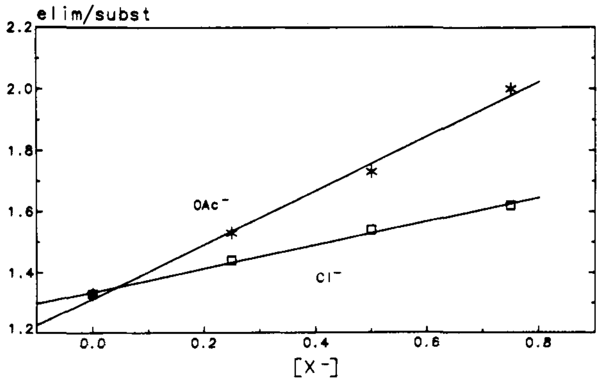


Figure 4. The increase in the elimination/substitution ratio for the reaction of **1-Br** with increasing concentration of Cl^- and OAc^- in 25 vol % acetonitrile in water; ionic strength 0.75 M maintained with sodium perchlorate.

The data for bromide anion, employing a pK_a value for HBr of −9.0,[6] correlate well with the data for the acetate anions (Figure

---

(4) Richard, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 1373–1383.
(5) Thibblin, A. *J. Chem. Soc., Perkin Trans. 2* **1986**, 313–319.
(6) Jencks, W. P.; Regenstein, J. *Handbook of Biochemistry and Molecular Biology*, 3rd ed.; Fasman, G. D., Ed.; CRC Press: Cleveland, 1976. Albert, A.; Serjeant, E. P. *Ionization Constants of Acids and Bases*; Methuen and Co.: London, 1962.

Table II. Isotope Effects on the Rate Constants for **1-Cl** of Table I

salt^a	$(k_{12}+k_{13}+k_{14})^H/(k_{12}+k_{13}+k_{14})^{d_6}$	k_{12}^H/k_{12}^D	$k_{12}^H/k_{12}^{d_6}$	k_{13}^H/k_{13}^D	$k_{13}^H/k_{13}^{d_6}$	k_{14}^H/k_{14}^D	$k_{14}^H/k_{14}^{d_6}$	$(k_{12}+k_{14})^H/(k_{12}+k_{14})^{d_6}$
none	2.4^b		1.18^b				2.8^b	
$NaClO_4$	2.2	1.03	1.4			1.02	3.7	2.2
NaOAc	2.4							
NaOH^c	1.6	1.07	1.4	8.1	1.4	1.10	3.7	2.4

^{a}0.75 M. ^{b}70.6 vol % acetonitrile in water. ^{c}0.16 M; μ = 0.75 M maintained with sodium perchlorate.

Table III. Rate Constants and Isotope Effects for the Reactions of **1-OAc** in 25 vol % Acetonitrile in Water at 100 °C^a

substrate^b	$10^6(k_{12}+k_{13}+k_{14})$, s^{-1}		10^6k_{12}, s^{-1}		10^6k_{13},^{c} s^{-1}		10^6k_{14},^{c} s^{-1}		$(k_{13}+k_{14})/k_{12}$
h-1-OAc	3.99	1.36 (1.47)^d	0.93	1.03 (1.04)^d	1.29	1.0	1.77	2.2 (2.7)^d	3.3
***d*$_6$-1-OAc**	2.93		0.90		1.24		0.79		

^{a}Ionic strength, μ = 0.75 M, maintained with sodium perchlorate. ^{b}0.02 mM. ^{c}Computer-simulated rate constants based upon a rearrangement rate constant $k_{43} = 5.8 \times 10^{-6}$ s^{-1} (see Experimental Section). ^{d}Isotope effects recalculated to 25 °C.

3). The deviation is larger for Cl^-.

The solvolysis of the corresponding bromo analogue 9-(2-bromo-2-propyl)fluorene (**h-1-Br**) is much faster. Accordingly, it was not possible to study the kinetics by the same experimental technique since some solvolysis occurs during the HPLC analysis. Only product data are therefore reported (Table I); less elimination is obtained. As exemplified in Figure 4, the effect of salts on the product compositions is very similar to that observed with **1-Cl**. The data for the three acetate anions also yield a value, 0.05, for β (Figure 5).

The presence of strong base, such as hydroxide anion, in the reaction solution opens up a new reaction route, a bimolecular elimination that provides **3** (Scheme I). The rate of disappearance of **1-Cl** varies linearly with hydroxide ion concentration (plot not shown); the slope was found to be $k_{13}'' = 17 \times 10^{-4}$ M^{-1} s^{-1}. The evaluation of the phenomenological rate constants is complicated by two other reactions, namely, a base-catalyzed 1,3-proton transfer that converts **4** to **3** and a base-promoted cleavage of the alcohol **2** that gives fluorene (**5**) and acetone. These reactions require strong base, and not even a trace of fluorene is observed in the reactions with the acetate anions. The rate constant for isomerization of **4** to **3** was measured in a separate experiment with 0.16 M sodium hydroxide (μ = 0.75 M) as 55×10^{-6} s^{-1} (= 344×10^{-6} M^{-1} s^{-1}). Another experiment with pure **4** in 0.75 M sodium acetate solution showed no trace of **3** after several days.

The reactions follow the rate laws (Scheme I)

$$\mathrm{d}[\mathbf{1}]/\mathrm{d}t = -(k_{12} + k_{13} + k_{14})[\mathbf{1}] = -(k_{12} + k_{13}' + k_{14})[\mathbf{1}] - k_{13}''[\mathrm{HO}^-][\mathbf{1}] \quad (2)$$

$$\mathrm{d}[\mathbf{2}]/\mathrm{d}t = k_{12}[\mathbf{1}] - k_{25}[\mathrm{HO}^-][\mathbf{2}] \quad (3)$$

$$\mathrm{d}[\mathbf{3}]/\mathrm{d}t = (k_{13}' + k_{13}''[\mathrm{HO}^-])[\mathbf{1}] + k_{43}[\mathrm{HO}^-][\mathbf{4}] \quad (4)$$

$$\mathrm{d}[\mathbf{4}]/\mathrm{d}t = k_{14}[\mathbf{1}] - k_{43}[\mathrm{HO}^-][\mathbf{4}] \quad (5)$$

$$\mathrm{d}[\mathbf{5}]/\mathrm{d}t = k_{25}[\mathrm{HO}^-][\mathbf{2}] \quad (6)$$

The rate constants k_{12}, k_{13}', and k_{14} are not real constants but vary with concentration of base (salt) according to the following equations (Scheme II):

$$k_{12} = k_1k_{-2}/(k_{-2} + k_{-3}' + k_{-3}''[\mathrm{base}] + k_{-4}' + k_{-4}''[\mathrm{base}]) \quad (7)$$

$$k_{13}' = k_1(k_{-3}' + k_{-3}''[\mathrm{base}])/(k_{-2} + k_{-3}' + k_{-3}''[\mathrm{base}] + k_{-4}' + k_{-4}''[\mathrm{base}]) \quad (8)$$

$$k_{14} = k_1(k_{-4}' + k_{-4}''[\mathrm{base}])/(k_{-2} + k_{-3}' + k_{-3}''[\mathrm{base}] + k_{-4}' + k_{-4}''[\mathrm{base}]) \quad (9)$$

To obtain accurate values for k_{13} and k_{14} in the reactions with hydroxide, it was necessary to compensate for the rearrangement of **4** to **3**. This was done by a computer simulation based upon the integrated rate expressions (see Experimental Section).

Relative to **h-1-Cl**, the corresponding (9-^{2}H) and 9-(1,3-$^2H_6$) analogues ***d*-1-Cl** and ***d*$_6$-1-Cl** react more slowly and give smaller amounts of the elimination products **3** and **4**, respectively (Table I). The isotope effects are collected in Table II.

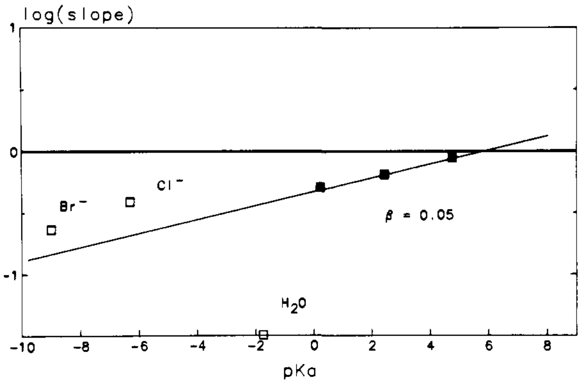
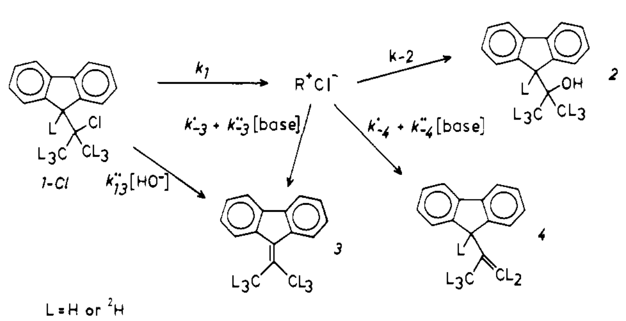


Figure 5. Brønsted plot for the deprotonation of the ion-pair intermediate formed from **1-Br** in 25 vol % acetonitrile in water; ionic strength 0.75 M maintained with sodium perchlorate. The pK_a values refer to water.[6]

Scheme II



The alcohol **2** solvolyzes very slowly in acidic solution. Thus no trace of reaction products was detected after 1 week in 0.75 M perchloric acid (25 vol % acetonitrile) at 25 °C.

The solvolysis of the acetoxy derivative 9-(2-acetoxy-2-propyl)fluorene (**1-OAc**) and its 9-(1,3-$^2H_6$) analogue ***d*$_6$-1-OAc** has been studied at 100 °C. At this high temperature, the two side reactions, isomerization of **4** to **3** and cleavage of **2** to fluorene (**5**), requiring strong base at lower temperature, accompany the solvolysis reactions. Accordingly, a simulation procedure, similar to that used for the solvolysis of **1-Cl** in the presence of hydroxide, was employed to evaluate the rate constants k_{13} and k_{14}.[7] The reaction conditions, rate constants, and isotope effects are reported in Table III. Recalculation of the measured isotope effects to 25 °C with the Arrhenius equation gives the values shown in parentheses. A much larger proportion of the olefinic products in the solvolysis of **1-OAc** consists of **3** (Table III) than that formed from **1-Cl** at 100 °C, which yields only a trace of **3**. Moreover, the elimination/substitution ratio is larger for **1-OAc** than for **1-Cl**.

---

(7) Some of the product **2** could be derived by attack on the carbonyl group of the ester. However, the analysis is not based upon any assumption about the mechanism.

Discussion

The ionization step in the reaction of **1-Cl** is not very sensitive to the ionic strength of the reaction solution (Table I), but a large effect is produced by the ionization power of the solvent. Thus, the reaction is 60 times more rapid in 25 vol % acetonitrile than in 70.6 vol % acetonitrile. The reaction is somewhat slower in the presence of chloride than perchlorate anion, which could be interpreted as a common ion effect or an induced common ion effect that regenerates the starting material. However, since there is also a depression effect by other anions, even by azide ion and especially large by acetate anion, a more reasonable interpretation is that the rate depression is caused by a specific salt effect. Similar effects have been found previously for solvolysis reactions in water–acetonitrile[8] and in other mixtures of water and organic solvents.[9]

The carbocationic intermediate shows very little selectivity toward different nucleophiles. Thus, azide anion is only about five times more reactive than a water molecule and added methanol is not more reactive than water toward the carbocation intermediate. The selectivity is so low that it may represent reaction within a pool of solvent molecules that are present at the time of formation of the carbocation.[4,5] The time required for reorientation of a solvent water molecule should be in the order of the rotational correlation time of water ($\tau = 10^{-11}$ s).[10] Processes that are faster than this occur by a preassociation mechanism in which the water molecule is in reaction position before the intermediate is formed. The rate constant for the reaction of the intermediate with water to form the alcohol **2** is estimated at $\sim 4 \times 10^{10}$ s^{-1} based upon a diffusion-controlled reaction with azide anion with $k_d = 5 \times 10^9$ M^{-1} s^{-1}.[4,5] Accordingly, the rate constant for deprotonation of the intermediate by solvent water is $\sim 7 \times 10^{10}$ s^{-1}. The employed value of k_d corresponds to $k_{-d} = 2.5 \times 10^{10}$ s^{-1} if the association constant (K_{as}) for ion pair formation from the free ions is $K_{as} = 0.2$ M^{-1}.[11] Thus, both the nucleophilic substitution and the deprotonation of the intermediate are processes that most likely occur mainly at the ion pair state before the ion pair undergoes diffusional separation (Scheme II). It has been assumed that the solvolysis of 1-(4-fluorophenyl)ethyl chloride in 50% trifluoroethanol–water yields the products directly from the ion pair; k_p (eq 1) was estimated at 2×10^{10} s^{-1}.[4]

The fraction of elimination products is increased by a decrease in ionization power of the solvent. Thus, a decrease in water content from 75 to 29.4 vol % increases the elimination-to-substitution ratio five times (Table I). The following is a plausible explanation. The decrease in ionization power corresponds to a decrease in the amount of contact ion pairs that goes on to solvent-separated ion pairs which are presumably intermediates on the reaction path from contact ion pair to the alcohol.[5] The elimination products, on the other hand, are expected to be formed mainly from the contact ion pair by a one-step process.

The deprotonation of the ion pairs is catalyzed to a small extent by general bases (Figures 2 and 4). The catalysis is smaller for the bromide ion pair which probably is thermodynamically less stable than the chloride ion pair. The small Brønsted β of 0.05 measured with substituted acetate anions indicates a very small amount of proton transfer in the transition state. The rate constant with acetate anion is 2.3×10^{10} M^{-1} s^{-1} (3.9×10^9 M^{-1} s^{-1} per proton), i.e., an acetate anion is about 23 times more efficient than a water molecule in abstracting one of the six methyl protons from the chloride ion pair. The Brønsted plots (Figures 3 and 5) indicate that water is a less efficient proton acceptor even after correction for the pK_a difference. The large rate constant with acetate anion as well as with substituted acetate anions indicates that the activation barrier for proton abstraction is very small and may suggest that the anion comes into reaction position before the intermediate is formed. Possibly, the anion does not have to be placed next to a methyl proton of the ion pair; the deprotonation may occur by a proton-jump mechanism via one (or two) water molecule.[12] However, results with hydrogen cyanide suggest that proton transfer to and from carbon does not occur through water.[13]

Chloride and bromide ions also promote deprotonation relative to formation of the alcohol (Table I). This salt effect on the fractionation of the ion pairs may arise from sensitivity of the proton-transfer transition state and/or sensitivity of the "substitution" transition state[14] toward the nature of the added salt. If it is assumed that the fractionation only reflects effects on the deprotonation step, the reason may be that they act as weak bases and deprotonate the ion pair in a similar way as the acetate anions. Bunton and co-workers have found that chloride ion speeds proton abstraction from the relatively stable 1-ferrocenylalkyl cations in 50% aqueous acetonitrile.[15,16] If added chloride ion catalyzes the deprotonation, the leaving group of the ion pair may also act as a proton acceptor. The leaving chloride ion should be an efficient "catalyst" owing to its proximity to the protons of the carbocation and also owing to the small degree of solvation reorganization of the anion that is required. Bromide ion is less basic and **1-Br** is therefore expected to give less elimination product. This is in accord with the experimental results. Furthermore, **1-OAc** yields much more of elimination products than **1-Cl**. Catalysis by the leaving group has been found previously.[4,5,17] The larger amount of **3** that is produced from **1-OAc** may be the result of the bifunctional nature of the leaving acetate anion. Another factor partly responsible for the smaller amount of elimination from the bromide ion pair may be a lower stability toward dissociation to solvent-separated ion pair.[14]

The measured secondary β-deuterium isotope effect on the solvolysis of **1-Cl** of $k^{\mathrm{H}}/k^{d_6} = 2.2$–$2.4$ (Table II) shows that the bonds to the hydrons are weakened considerably in the ionization step. The value of 2.2 for six deuteriums corresponds to a value of 1.14 per deuterium. The secondary β-deuterium isotope effect of $k^{\mathrm{H}}/k^{\mathrm{D}} = 1.03$ (Table II) measured for the 9-^{2}H substituted compound indicates a much lower hyperconjugative weakening of the bond to the 9-hydron. This large difference in carbon–hydrogen bond weakening that must be present also in the high-energy contact ion-pair intermediate is reflected in the observed large elimination product ratio **4**/**3** that cannot be explained solely by a statistical effect. The 9-proton of the substrate is much more acidic than the methyl protons (pK_a for fluorene is about 22),[18] and the thermodynamic stability of the olefin product **3** is greater than that of **4**. However, these parameters are apparently of minor importance, compared with the relatively large weakening of the bonds to the methyl protons in the ion pair which should be the cause of their greater kinetic acidity.

Large secondary isotope effects in solvolysis reactions have been found previously. For example, the solvolysis of 2-(2-cyanopropyl) triflate in trifluoroethanol and the reaction of 2-propyl tosylate, in trifluoroacetic acid, involve rate-limiting ionization; k^{H}/k^{d_6} was measured as 2.19 and 2.12, respectively.[19,20]

---

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

(9) Grunwald, E.; Butler, A. F. *J. Am. Chem. Soc.* **1960**, *82*, 5647–5654. Duynstee, E. F. J.; Grunwald, E.; Kaplan, M. L. *Ibid.* **1960**, *82*, 5654–5660.

(10) Chiang, Y.; Kresge, A. J. *J. Am. Chem. Soc.* **1985**, *107*, 6363–6367.

(11) Prue, J. E. *J. Chem. Soc.* **1965**, 7534–7535.

(12) Grunwald, E.; Eustace, D. (Chapter 4); Crooks, J. E. (Chapter 6) *Proton-Transfer Reactions*; Caldin, E., Gold, V., Eds.; Chapman and Hall: London, 1975.

(13) Bednar, R. A.; Jencks, W. P. *J. Am. Chem. Soc.* **1985**, *107*, 7126–7134.

(14) The reaction route, contact ion pair to substitution product (the alcohol **2**), may involve several steps, e.g., the solvent-separated ion pair is initially formed by insertion of a water molecule and subsequently collapses to the alcohol.

(15) Bunton, C. A.; Carrasco, N.; Cully, N.; Watts, W. E. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1859–1867.

(16) Bunton, C. A.; Carrasco, N.; Davoudzadeh, F.; Watts, W. E. *J. Chem. Soc., Perkin Trans. 2* **1981**, 924–930.

(17) (a) Seib, R. C.; Shiner, V. J., Jr.; Sendijarevic', V.; Humski, K. *J. Am. Chem. Soc.* **1978**, *100*, 8133–8137. (b) Cram, D. J.; Sahyun, M. R. V. *Ibid.* **1963**, *85*, 1257–1263. (c) Dannenberg, J. J.; Goldberg, B. J.; Barton, J. K.; Dill, K.; Weinwurzel, D. H.; Longas M. O. *Ibid.* **1982**, *103*, 7764–7768. (d) Thibblin, A. *J. Chem. Soc., Perkin Trans. 2* **1986**, 320–326. (e) Cocivera, M.; Shiner, V. J., Jr. *J. Am. Chem. Soc.* **1963**, *85*, 1702–1703.

(18) Bordwell, F. G. *Pure Appl. Chem.* **1977**, *49*, 963–968.

(19) Gassman, P. G.; Talley, J. J. *J. Am. Chem. Soc.* **1980**, *102*, 1214–1216.

The observed kinetic isotope effect on substitution and elimination for the solvolysis of **1-Cl** are $k_{12}^{H}/k_{12}^{d_6} = 1.4$ and $k_{14}^{H}/k_{14}^{d_6} = 3.7$ (Table II). These effects are quite different since the rate-limiting step is followed by branching; the competing elimination and substitution paths show differences in sensitivity to isotopic substitution. Owing to this competition, the isotope effects on k_{12} and k_{14} are attenuated and enlarged, respectively, compared with the isotope effects that would be observed if the reactions were not coupled via a common intermediate. Competition as the cause of attenuation and enlargement of isotope effects has been discussed previously[17d,21] and generalized.[22] The mechanistic scheme (eq 10) corresponds to the following expressions for the observed rate constants and rate constant ratios:

$$\begin{tikzcd} & & 2 \\ 1\text{-Cl} \arrow[r, "k_1"] & 1^{+}\text{Cl}^{-} \arrow[ur, "k_{-2}"] \arrow[dr, "k_{-4}"'] & & (10) \\ & & 4 \end{tikzcd}$$

$$k_{12} = k_1 k_{-2}/(k_{-2} + k_{-4}) \qquad (11)$$

$$k_{14} = k_1 k_{-4}/(k_{-2} + k_{-4}) \qquad (12)$$

$$k_{12}^{H}/k_{12}^{d_6} = (k_1^{H}/k_1^{d_6})(k_{-2}^{H}/k_{-2}^{d_6})(k_{-2}^{d_6} + k_{-4}^{d_6})/(k_{-2}^{H} + k_{-4}^{H}) \qquad (13)$$

$$k_{14}^{H}/k_{14}^{d_6} = (k_1^{H}/k_1^{d_6})(k_{-4}^{H}/k_{-4}^{d_6})(k_{-2}^{d_6} + k_{-4}^{d_6})/(k_{-2}^{H} + k_{-4}^{H}) \qquad (14)$$

An isotope effect of 1.0 on k_{-2} and 2.8 on k_{-4} is consistent with the experimental data and the above mechanistic model (eq 10). The secondary kinetic isotope effect on the elimination step (k_{-4}) is expected to be larger than unity, but the value is presumably small since a large hyperconjugative effect has already been operating in the first step ($k_1^{H}/k_1^{d_6} \sim 2.2$). A value of <1.4 is likely, i.e., <1.07 per deuterium. Accordingly, the primary isotope effect on k_{-4} should be ca. 2, a value consistent with the small β of 0.05 that is measured. The degree of hydron transfer to the base is small owing to the very short lived character of the intermediate (that corresponds to an early transition state) and, less importantly, to the fact that the carbon–hydrogen bond is already broken to a small extent by the hyperconjugation in the ion pair.

The branched mechanistic model (eq 10) predicts that a large fraction of elimination corresponds to smaller isotope effects for the elimination and substitution reactions. Accordingly, $k_{14}^{H}/k_{14}^{d_6}$ and $k_{12}^{H}/k_{12}^{d_6}$ were found to be 2.8 and 1.2, respectively, at 70.6 vol % acetonitrile (Table II). This indicates that the reactions are coupled via a common intermediate, most likely of contact ion-pair type as discussed above. The conclusion is supported by the fact that $k_{12} + k_{14}$ does not increase with an increase in base concentration.

The consistency of the measured isotope effects with eq 10 both at low and high water concentration indicates that internal return from the ion pairs is not significant. Reversible ionization is not expected to give these changes in isotope effects. Moreover, the isotope effects measured by **1-OAc** are very similar to those measured with **1-Cl**.

There are some reports in the literature on isotope effects on the elimination step in solvolysis reactions. Smith and Goon,[21a] for example, have studied the ethanolysis of (1,1,1-$^{2}H_3$)-2-chloro-2-phenylpropane that gives some elimination product along with the ether. The product ratio $PhC(CD_3){=}CH_2/PhC(CH_3){=}CD_2$ was used as a measure of the isotope effect for the deprotonation of the carbocationic intermediate. The result, $k^{H}/k^{d_3} = 3.15$ at 25 °C, is somewhat larger than the isotope effect measured in this work. Surprisingly, the isotope effect was found to be dependent on the leaving group; the thiobenzoate analogue showed an isotope effect of 1.7 at 50 °C. A small isotope effect (1.9) has also been measured by Tidwell and co-workers.[21c] The more stable allylic carbocation intermediate formed from (1,1-$^{2}H_2$)-3-(2-chloro-2-propyl)indene was found to eliminate in 25 vol % acetonitrile in water with a Brønsted β of 0.14 and 0.16, respectively, and $k^{H}/k^{D} = 3.0 \pm 0.4$ (35 °C).[17d]

The presence of strong base, such as hydroxide anion, opens up a new route to the elimination product **3**. The large amount of **3** that is formed from **1-Cl**, e.g., at a base concentration of 0.16 M, cannot be derived from the ion pair since, despite the fact that a very large part of the products consists of **3**, there is just a minor decrease in the rate constants k_{12} and k_{14}. Moreover, the large isotope effect k_{13}^{H}/k_{13}^{D} of 8.1 also indicates a separate hydroxide-promoted reaction. This reaction is either an E2 or an irreversible E1cB reaction. It has been concluded previously that base-promoted elimination of hydrogen chloride may employ such a stepwise carbanionic elimination mechanism.[22,23]

Experimental Section

General. The ^{1}H NMR analyses were performed with a JEOL FX 100 spectrometer equipped with a 5-mm dual probe (^{1}H, ^{13}C) or a 5-mm ^{1}H probe. The high-performance liquid-chromatography (HPLC) analyses were carried out with a Hewlett-Packard 1084B liquid chromatograph equipped with a variable-wavelength detector on a C8 reversed-phase column (3.0 × 200 mm). The mobile phase was a solution of methanol in water. The reactions were studied at constant temperature in a HETO 01 PT 623 thermostat.

Materials. Acetonitrile (Fluka for UV spectroscopy) was used as a solvent without further purification. Methanol used for preparation of reaction solutions was of spectroscopic quality, otherwise of HPLC grade. All other chemicals were of reagent grade and were used without further purification. A stock solution of sodium perchlorate was prepared from perchloric acid and sodium hydroxide solution. The pH values of the stock solutions of the acetate anions were adjusted to ca. 7.

9-(2-Hydroxy-2-propyl)fluorene (2)[24,25] was prepared from fluorene and acetone by a procedure that has been used for the corresponding indene substrate.[26] The only modification was that the fluorenyllithium was prepared at room temperature.

9-(^{2}H)-9-(2-Hydroxy-2-propyl)fluorene was prepared from 9,9-($^{2}H_2$)-fluorene according to the method above.

9-(1,1,1,3,3,3-$^{2}H_6$)-9-(2-Hydroxy-2-propyl)fluorene was synthesized from fluorene and 1,3-($^{2}H_6$)-acetone as above.

9-(2-Chloro-2-propyl)fluorene (h-1-Cl)[24] was prepared by treatment of the alcohol **2** with $ZnCl_2$–HCl in chloroform according to the method described for the corresponding indenyl chloride.[23a] A longer reaction time was required (1 h).

9-(^{2}H)-9-(2-Chloro-2-propyl)fluorene (*d*-1-Cl) and 9-(1,1,1,3,3,3-$^{2}H_6$)-9-(2-chloro-2-propyl)fluorene (d_6-1-Cl) were prepared from the corresponding deuterated alcohols by the method above. The deuterium contents were >99.0 atom % and 99.2 ± 1.0 atom % in the 9 position and methyl groups, respectively (^{1}H NMR).

9-(2-Bromo-2-propyl)fluorene (h-1-Br).[24] The method used for preparation of the bromide has been used previously for the corresponding indene compound;[23b] the reaction time was 2 h.

9-(2-Acetoxy-2-propyl)fluorene (h-1-OAc) was prepared by $ZnCl_2$-catalyzed acetylation of the alcohol **2** with acetic acid anhydride (3 h). The method has been described previously for the synthesis of the corresponding indenyl acetate.[27]

9-(^{2}H)-9-(2-Acetoxy-2-propyl)fluorene (*d*-1-OAc) and 9-(1,1,1,3,3,3-$^{2}H_6$)-9-(2-acetoxy-2-propyl)fluorene (d_6-1-OAc) were prepared from the corresponding deuteriated alcohols by the method above. The deuterium contents were >99.0 and 99.3 ± 1.0 atom % in the 9 position and the methyl group, respectively.

9-Isopropylidenefluorene (h-3)[24,25] was not isolated. Rearrangement of **h-4** with sodium hydroxide gave a single product. The recorded UV

---

[20] Streitwieser, A., Jr.; Dafforn, G. A. *Tetrahedron Lett.* **1969**, 1263–1266.

[21] (a) Smith, S. G.; Goon, D. J. W. *J. Org. Chem.* **1969**, 3127–3131. (b) Fry, A. *Chem. Soc. Rev.* **1972**, *1*, 163–210. (c) Jansen, M. P.; Koshy, M. K.; Mangru, N. N.; Tidwell, T. T. *J. Am. Chem. Soc.* **1981**, *103*, 3863–3867.

[22] Olwegard, M.; McEwen, I.; Thibblin, A.; Ahlberg, P. *J. Am. Chem. Soc.* **1985**, *107*, 7494–7499 and references therein. Ahlberg, P.; Thibblin, A. *Synthesis and Applications of Isotopically Labeled Compounds 1985*; Proceedings of the Second International Symposium, Kansas City, MO, USA; Elsevier Science Publishers B.V.: Amsterdam, 1986; pp 89–94.

[23] (a) Thibblin, A.; Ahlberg, P. *J. Am. Chem. Soc.* **1977**, *99*, 7926–7930. (b) Thibblin, A. *Chem. Scr.* **1980**, *15*, 121–127.

[24] Maitland, P.; Tucker, S. M. *J. Chem. Soc.* **1929**, 2559–2567.

[25] Kice, J. L. *J. Am. Chem. Soc.* **1958**, *80*, 348–352.

[26] Ahlberg, P. *Chem. Scr.* **1973**, *3*, 183–189.

[27] Ahlberg, P. *Chem. Scr.* **1973**, *4*, 33–39.

spectrum of the product was in accord with the expected spectrum for **h-3**.

9-(2-Propenyl)fluorene (h-4) was prepared in a small amount by the following procedure. About 50 mg of **h-1-Cl** was dissolved in acetonitrile–water (5:3). The solution was placed in a thermostat at 65 °C. The reaction mixture was analyzed the following day by HPLC; no trace of the starting material was detected. The desired compound was isolated by semipreparative HPLC. Extraction of the eluate with pentane gave pure material as shown by analytical HPLC.

Kinetics and Product Studies. The reactions were run at constant ionic strength in solutions prepared by mixing three volumes of water solution of the salt(s) (at constant ionic strength of 1.00 M, maintained with sodium perchlorate) with one volume of the organic solvent at room temperature, ca. 22 °C. The reaction vessel was either a 2-mL HPLC flask sealed with a tight PTFE septum which was placed in an aluminum block in the water thermostat or, in the slower reactions, a 4-mL pear-shaped flask,[28] equipped with a PTFE stop cock (high-vacuum type). The reactions were initated by rapid addition of the substrate dissolved in acetonitrile with a spring-loaded syringe. The concentration of the substrate in the reaction solution was usually about 0.02 mM. At appropriate intervals, samples (300 μL) of the reaction solution were transferred with a thermostated syringe (water-jacketed) to an HPLC flask (in some experiments containing acetic acid or saturated sodium hydrogen carbonate solution to neutralize the sample) and analyzed. The components of the reaction solution were chromatographically well separated. The mol % of the starting material and each of the products were measured. The phenomenological rate constants for the disappearance of the starting material were calculated from plots of ln (mol % starting material) vs. time and product data.

All experiments at 100 °C were carried out as 1-point kinetics. The reactions were run in the 4-mL flasks described above, which were placed in a thermostat (filled with polyethylene glycol instead of water). At appropriate time the reactions were halted rapidly by cooling the flasks in a stream of cold tap water, and the contents were transferred to HPLC flasks and analyzed.

The elimination–substitution ratios given in Table I are calculated from the product compositions at "infinity" time, i.e., reaction time greater than 10 half-lives.

Rate constants for the reactions with hydroxide anion were obtained in the following way. First, the observed rate constant (k_{obsd}) of the disappearance of **1-Cl** combined with the product data at the reaction time t (the time for sampling of the reaction solution) was employed to calculate the composition in mol % of **1-Cl**, **3**, and **4** "corrected" for the substitution reaction, i.e., the mol % values that would be measured in the absence of the substitution product:

$$\text{mol \% } \mathbf{1}_{\mathrm{c}} = 100/\exp(k_{\mathrm{obsd}}t([\mathbf{3}] + [\mathbf{4}])/([\mathbf{2}] + [\mathbf{3}] + [\mathbf{4}])) \quad (15)$$

$$\text{mol \% } \mathbf{3}_{\mathrm{c}} = \{[\mathbf{3}]/([\mathbf{3}] + [\mathbf{4}])\}(100 - \text{mol \% } \mathbf{1}_{\mathrm{c}}) \quad (16)$$

$$\text{mol \% } \mathbf{4}_{\mathrm{c}} = [\mathbf{4}/(\mathbf{3} + \mathbf{4})](100 - \text{mol \% } \mathbf{1c}) \quad (17)$$

In this way, a set of "corrected" mol % values was calculated. These were then used for a computer simulation of the rate constants k_{13} and k_{14}; k_{43} was measured in a separate experiment starting from pure **h-4**.

$$\begin{tikzcd}
\mathbf{1}_{\mathrm{c}} \arrow[rr, "k_{14}"] \arrow[dr, "k_{13}"'] & & \mathbf{4}_{\mathrm{c}} \arrow[dl, "k_{43}"] \\
& \mathbf{3}_{\mathrm{c}} &
\end{tikzcd}$$

Since it was found that the results of the simulation are not very sensitive to small changes in k_{43} and since $k_{43}{}^{d_6}$ is expected to have a value close to the one measured for $k_{43}{}^{\mathrm{H}}$, the measured value of $k_{43}{}^{\mathrm{H}}$ is used also in the simulation of the reaction with ***d*₆-1-Cl**. It is assumed that the isotope effect $k_{43}{}^{\mathrm{H}}/k_{43}{}^{\mathrm{D}}$ has a value close to the one measured for $k_{13}{}^{\mathrm{H}}/k_{13}{}^{\mathrm{D}}$;[29] a smaller isotope effect results in a larger $k_{13}{}^{\mathrm{H}}/k_{13}{}^{\mathrm{D}}$ (a value of ~1 corresponds to a maximum $k_{13}{}^{\mathrm{H}}/k_{13}{}^{\mathrm{D}}$ of ca. 9.3).

The equations used in the simulation describe the "corrected" concentrations of the starting material **1** and the products **3** and **4** at the reaction time t as

$$\text{mol \% } \mathbf{1}_{\mathrm{c}} = ae^{-m_1t} + (100 - a)e^{-m_2t}$$

$$\text{mol \% } \mathbf{3}_{\mathrm{c}} = be^{-m_1t} - be^{-m_2t}$$

$$\text{mol \% } \mathbf{4}_{\mathrm{c}} = 100 - \text{mol \% } \mathbf{1}_{\mathrm{c}} - \text{mol \% } \mathbf{3}_{\mathrm{c}}$$

where

$$a = 100(k_{13} + k_{14} - m_2)/(m_1 - m_2)$$

$$b = 100k_{14}/(m_2 - m_1)$$

$$m_1 = [(k_{13} + k_{14} + k_{41} + k_{43})^2/4 - k_{14}k_{43} - (k_{41} + k_{43})k_{13}]^{1/2} + (k_{13} + k_{14} + k_{41} + k_{43})/2$$

$$m_2 = -[(k_{13} + k_{14} + k_{41} + k_{43})^2/4 - k_{14}k_{43} - (k_{41} + k_{43})k_{13}]^{1/2} + (k_{13} + k_{14} + k_{41} + k_{43})/2$$

$$k_{41} = 0$$

This type of computer simulation has been used previously.[23a]

The reactions of **1-OAc** were also computer simulated with the same method. The rearrangement rate constant (k_{43}) for the conversion of **h-4** to **h-3**, measured as 5.8 × 10^{-6} s^{-1}, was utilized also for the simulation of the reaction with ***d*₆-1-OAc**. A somewhat smaller rate constant is expected for $k_{43}{}^{d_6}$. However, even a 20% decrease in $k_{43}{}^{d_6}$ has only a minor effect on the simulated rate constants $k_{13}{}^{d_6}$ and $k_{14}{}^{d_6}$ and an insignificant effect on $k_{14}{}^{\mathrm{H}}/k_{14}{}^{d_6}$.

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

Acknowledgment. The Swedish Natural Science Research Council has financially supported this work.

Registry No. **h-1-Cl**, 56954-89-3; **h-1-Br**, 56954-88-2; **h-1-OAc**, 85055-86-3; D_2, 7782-39-0.

---

[28] Lövås, S.; Ahlberg, P. *J. Am. Chem. Soc.* **1985**, *107*, 7534–7541.

[29] It is very reasonable that the isotope effects on the rearrangement and the elimination have similar values (ref 23a).