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On the Importance of Carbocation Intermediates in Bimolecular Nucleophilic Substitution Reactions in Aqueous Solution

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Abstract: The effect of nucleophilic anions on the rate constants for reaction of 1-(4-methoxyphenyl)-2,2,2-trifluoroethyl iodide (**1-I**) and bromide (**1-Br**) in water at 25 °C and a constant ionic strength of 6.00 maintained with perchlorate ion has been determined. These substrates react by a $D_N + A_N$ (S_N1) mechanism through the 1-(4-methoxyphenyl)-2,2,2-trifluoroethyl carbocation intermediate (**2**), which is captured by I^-, N_3^-, and SCN^- in diffusion-limited reactions. There are also reactions of **1-I** in the presence of the strong nucleophiles N_3^- and SCN^- that are kinetically bimolecular at low nucleophile concentrations (0–1.00 M), but higher nucleophile concentrations (2.00–4.00 M) cause decreases in the velocity of the reaction. Decreases in velocity are observed for the reaction of **1-I** in the presence of the weak nucleophiles Cl^-, AcO^-, and SO_4^{2-} and for the reaction of **1-Br** in the presence of N_3^-. These data are consistent with a stepwise preassociation mechanism for the bimolecular substitution reactions of N_3^- and SCN^- with **1-I** because this pathway will be significant only when the reactions of both the leaving group ion (I^-) *and* the nucleophile (N_3^- or SCN^-) with the free carbocation **2** are diffusion limited. The fit of the data for the reaction of N_3^- with **1-I** to a rate equation derived for the stepwise preassociation mechanism gives $K_{as} = 0.67\ M^{-1}$ for the formation of the [N_3^-·**1-I**] preassociation complex and the rate constant ratio $k_{Nu}/k_{solv} = 2$ for reaction of **1-I** with N_3^- within this complex (k_{Nu}) and for reaction of **1-I** in the presence of solvent alone (k_{solv}). The largest rate increase observed at $[Nu^-] = 1.00$ M is only 40% for the reaction of **1-I** in the presence of SCN^-, so the rate accelerations resulting from bimolecular nucleophilic substitution reactions through a carbocation intermediate are small even when this reaction is favored by the choice of nucleophile and leaving group.

Introduction

It has been over 20 years since the provocative suggestion of Sneen that *all* aliphatic nucleophilic substitution reactions that are kinetically bimolecular proceed by a stepwise mechanism in which the nucleophile traps an ion pair or an ion–dipole pair intermediate in the rate-determining step.[1] This extreme proposal has been discredited by the demonstration that many bimolecular nucleophilic substitution reactions proceed by a concerted mechanism which avoids the formation of a carbocation reaction intermediate.[2-6]

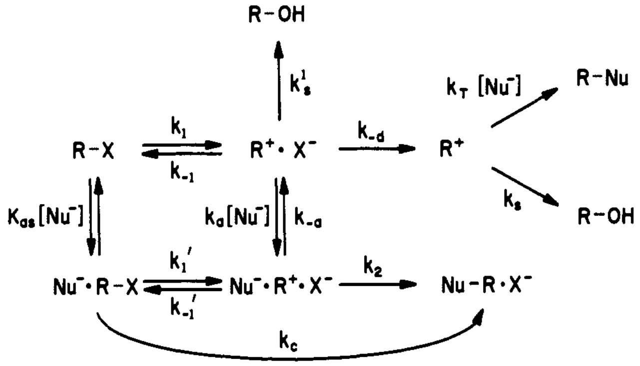
Bimolecular nucleophilic substitution reactions that proceed through carbocation reaction intermediates are not expected to be common because strict conditions must be met if the reaction of the nucleophilic reagent with an ion pair intermediate is to give a detectable increase in the rate of disappearance of the substrate.[5] These conditions may be summarized with reference to Scheme I:

(1) The rate of formation of the carbocation intermediate (by k_1 or k_1') must be faster than the rate of formation of nucleophile adducts by a concerted reaction mechanism (by K_{as} and k_c).

(2) The formation of the ion pair intermediate [R^+·X^-] from substrate must be *reversible* in order for its reaction with nucleophilic reagents to lead to an increase in the rate of disappearance of substrate. This requires that the rate constant for the return of ion pair to substrate (k_{-1}) be larger than the rate constants for the irreversible reactions of the ion pair (k_{-d} and k_s'), i.e., $k_{-1} > k_{-d} + k_s'$.

(3) In order for the reaction through the triple ion complex [Nu^-·R^+·X^-] to lead to a detectable increase in the rate of disappearance of the substrate, the rate of formation of products from this complex must be faster than that for the formation of products from the ion pair [R^+·X^-], i.e., $k_2 > k_{-d} + k_s'$.

Scheme I



These conditions will be most easily met in nonpolar solvents in which free ions are relatively unstable so that the rate constant k_{-d} for their formation from ion pairs is relatively small. They are much more unlikely to be met in water or largely aqueous solvents in which the free ions are more stable and k_{-d} is very large.[5-8] There are several examples of bimolecular aliphatic nucleophilic substitution reactions in organic solvents that proceed through ion–molecule or ion pair intermediates,[9,10] but it is not clear whether stepwise pathways are ever followed for kinetically bimolecular nucleophilic substitution reactions in largely aqueous solutions.

This paper addresses the question of whether stepwise pathways are viable for bimolecular nucleophilic substitution reactions in water or largely aqueous solutions. The substrate used in these studies, 1-(4-methoxyphenyl)-2,2,2-trifluoroethyl iodide (**1-I**), was chosen because it can be shown to satisfy the stringent requirements for detectable bimolecular nucleophilic substitution through ion pair and/or triple ion complex intermediates in aqueous solution. We report that **1-I** shows weak bimolecular reactions with azide and thiocyanate ions in water at a high constant ionic

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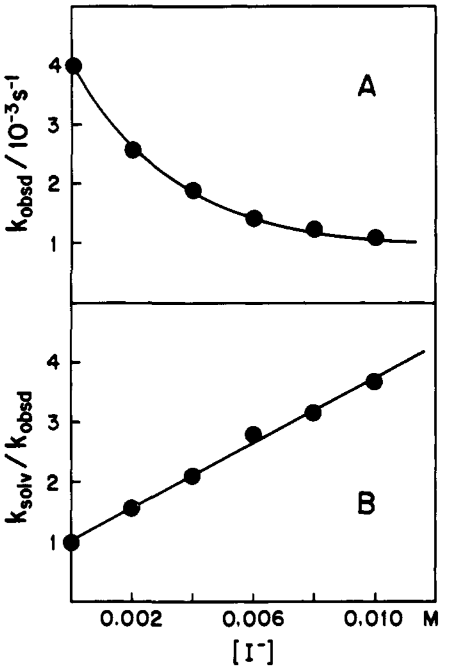


Figure 1. (A) Dependence of k_{obsd} (s^{-1}) on the concentration of added iodide ion for the solvolysis of **1-I** in water at 25 °C and I = 6.00 ($NaClO_4$). (B) The linear reciprocal replot of the data from A according to eq 1 of the text.

Scheme II

$$\mathbf{1\text{-}I} \underset{k_I[I^-]}{\overset{k_{solv}}{\rightleftharpoons}} \mathbf{2} \xrightarrow{k_s} \mathbf{1\text{-}OH}$$

strength of 6.00 maintained with $NaClO_4$. Evidence is presented that these reactions proceed by a stepwise preassociation mechanism[11] through triple ion complexes $[Nu^-{\cdot}\mathbf{2}{\cdot}I^-]$ (Scheme I).

Experimental Section

Materials. Reagent grade inorganic salts were used without further purification. The water used for kinetic studies was distilled and then passed through a Milli-Q water purification system. **1-Br** and **1-I** were prepared according to published procedures.[12b]

Kinetic Analyses. Kinetic studies were done at 25 °C, and constant ionic strength was maintained with $NaClO_4$. Solutions of salts in mixed methanol/water solvents were prepared by diluting a measured volume of methanol with an aqueous solution of $NaClO_4$ or NaN_3 to the appropriate final volume. The progress of the reactions of **1-Br** and **1-I** was followed by monitoring the decrease in absorbance at 280 nm. Solutions of substrates were prepared in acetonitrile, and the reactions were initiated by making a 100-fold dilution into the reaction mixtures. The final concentration of **1-I** was ~5 × 10^{-6} M. There is a decrease in the solubility of **1-Br** in solutions of increasing $[NaN_3]$. The final concentration of **1-Br** was 4 × 10^{-5} M for reactions at $[NaN_3]$ = 0–1.00 M, and this was reduced to 1 × 10^{-5} M for reactions at $[NaN_3]$ > 1.00 M. The reactions at the lower concentrations of **1-Br** were monitored in cuvettes with a 6-cm path length instead of the standard 1-cm cells.

Observed first-order rate constants for these reactions were determined as the slope of a semilogarithmic plot of reaction progress against time. The plots were linear for ≥3 half-lives of the reaction. The rate constants were reproducible to ±5%.

The NFIT nonlinear curve fitting program from Island products was used to fit kinetic data to the rate equation derived for a preassociation reaction mechanism.

Results

Table I. Effect of Sodium Azide on the Pseudo-First-Order Rate Constants for the Reactions of 1-(4-Methoxyphenyl)-2,2,2-trifluoroethyl Derivatives in Water[a]

	$k_{obsd}/10^{-3}\ s^{-1}$ [b]	
$[NaN_3]$/M	4-MeOArCH(CF_3)I	4-MeOArCH(CF_3)Br
0.00	1.98	21.9
0.20	2.38	21.0
0.40	2.62	19.5
0.60	2.72	20.9
0.80	2.90	20.6
1.00	3.02	19.3

[a] At 25 °C and I = 1.00 ($NaClO_4$). [b] The slope of a logarithmic plot of the change in absorbance at 280 nm against time.

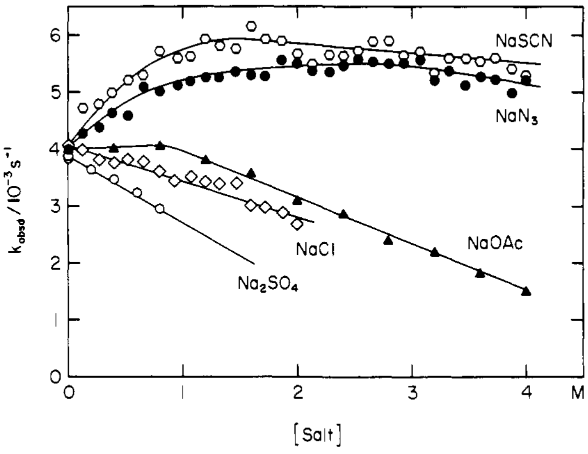
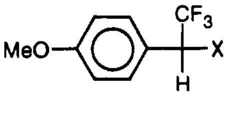


Figure 2. Dependence of k_{obsd} (s^{-1}) on the concentration of added nucleophilic salts for the reaction of **1-I** in water at 25 °C and I = 6.00 ($NaClO_4$).

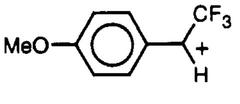
Figure 1A shows the effect of increasing concentrations of iodide ion on the observed first-order rate constants, k_{obsd}, for the reaction of **1-I** in water at 25 °C and I = 6.00 ($NaClO_4$). Figure 1B shows the fit to eq 1, derived for Scheme II, of the data from Figure

$$k_{solv}/k_{obsd} = 1 + (k_I/k_s)[I^-] \qquad (1)$$

1A: k_{solv} in eq 1 is k_{obsd} at [NaI] = 0 M. The data define a line of slope k_I/k_s = 270 M^{-1}, where k_I and k_s are the rate constants for the capture of **2** by iodide ion and solvent, respectively. A rate constant ratio of k_{az}/k_s = 220 M^{-1} for partitioning of **2** between reaction with azide ion and solvent in water (I = 6.00, $NaClO_4$) was determined in an earlier study.[8] This can be combined with the value of k_I/k_s obtained from Figure 1B to give k_I/k_{az} = 1.2 for partitioning of **2** between reaction with iodide and azide ions.



1-X



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The observed first-order rate constants k_{obsd} for the reaction of **1-I** and **1-Br** in water at 25 °C and I = 1.00 ($NaClO_4$) and at increasing concentrations of sodium azide are given in Table I. The observed first-order rate constants k_{obsd} for the reaction of **1-I** in water at 25 °C and I = 6.00 ($NaClO_4$) and at increasing concentrations of several nucleophilic salts or for the reaction of **1-I** in the presence of increasing concentrations of $NaClO_4$ in water that contains no other salt are given in Table II. Figure 2 is a plot of some of the data from Table II.

Figure 3 shows the effect of increasing concentrations of added sodium azide on k_{obsd}/k_{solv} for the reaction of **1-Br** in water at 25 °C and I = 6.00 ($NaClO_4$), for which k_{solv} = 0.049 s^{-1}.[8] These data were fit to eq 2 to give a value of b = −0.104 for the specific salt effect of replacing ClO_4^- with N_3^-.

$$k_{obsd}/k_{solv} = 1 + b[N_3^-] \qquad (2)$$

The observed first-order rate constants k_{obsd} for the reaction of **1-I** in mixed methanol/water solvents at 25 °C and constant

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Table II. Effect of Added Salts on the Pseudo-First-Order Rate Constants for the Reaction of 1-(4-Methoxyphenyl)-2,2,2-trifluoroethyl Iodide in Water[a]

	$k_{obsd}/10^{-3}$ s^{-1} [b]						
[Nu] (M)	NaN_3	NaSCN	NaOAc	NaO_2CCF_3	Na_2SO_4	NaCl	$NaClO_4$[c]
0.00	4.02	3.91	4.01	3.93	3.88	4.08	1.08
0.13	4.28	4.72				3.99	
0.20					3.64		1.35
0.27	4.40	4.75				3.82	
0.40	4.79	4.98	4.01	4.09	3.47	3.76	1.56
0.53	4.77	5.21				3.84	
0.60					3.23		1.83
0.67	5.12	5.28				3.79	
0.80	5.03	5.72	4.05	3.86	2.95	3.61	1.98
0.93	5.12	5.59				3.44	
1.00							2.12
1.07	5.20	5.64				3.52	
1.20	5.28	5.95	3.79	3.81		3.43	
1.33	5.28	5.81				3.38	
1.47	5.37	5.71				3.39	
1.60	5.31	6.15	3.56	3.31		2.99	
1.73	5.26	5.93				2.97	
1.87	5.58	5.91				2.92	
2.00	5.51	5.65	3.08	3.25		2.64	2.87
2.13	5.38	5.48					
2.27	5.39	5.67					
2.40	5.49	5.64	2.87	3.72			
2.53	5.59	5.73					
2.67	5.55	5.89					
2.80	5.51	5.92	2.40	2.68			
2.93	5.51	5.62					
3.00							3.37
3.07	5.56	5.70					
3.20	5.21	5.34	2.19	2.24			
3.33	5.39	5.59					
3.47	5.13	5.59					
3.60	5.28	5.53	1.81	2.04			
3.73	5.23	5.59					
3.87	4.97	5.40					
4.00	5.21	5.27	1.49	1.70			3.77
5.00							3.91
6.00							4.02

[a] At 25 °C and $I = 6.00$ ($NaClO_4$). [b] The slope of a logarithmic plot of the change in absorbance at 280 nm against time. [c] Sodium perchlorate was the only salt added.

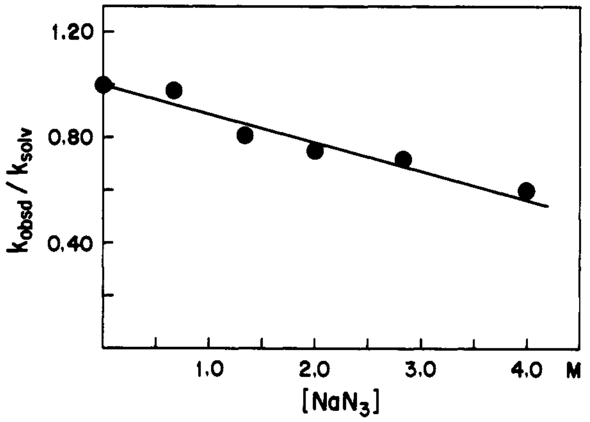

Figure 3. Dependence of k_{obsd}/k_{solv} on the concentration of added sodium azide for the reaction of **1-Br** in water at 25 °C and $I = 6.00$ ($NaClO_4$), for which $k_{solv} = 0.049$ s^{-1}.[8] The slope of the line gives $b = -0.104$.

ionic strength ($NaClO_4$) and at increasing concentrations of sodium azide are given in Table III. Apparent second-order rate constants [$(k_{Nu})_{app}$] for the reaction of sodium azide with **1-I** in these solvents, determined as the slopes of linear plots of k_{obsd} against [NaN_3], are also listed in Table III.

Discussion

The following observations show that the reactions of **1-X** proceed by stepwise $D_N + A_N$ (S_N1)[14] mechanisms through the common reaction intermediate **2**.

Table III. Effect of Sodium Azide on the Pseudo-First-Order Rate Constants and Apparent Second-Order Rate Constants for the Reactions of 1-(4-Methoxyphenyl)-2,2,2-trifluoroethyl Iodide in Methanol/Water Solvents[a,b]

	$k_{obsd}/10^{-4}$ s^{-1} [c]				
[NaN_3]/M	10%[e] 3.28	20%[f] 3.02	30%[g] 2.75	40%[h] 2.39	50%[i] 1.97
0.00	19.3	5.87	2.48	1.05	0.50
0.20	21.9	6.61	2.69	1.19	0.56
0.40	23.5	6.94	2.93	1.30	0.60
0.60	23.9	7.26	3.08	1.38	0.63
0.80	25.3	7.52	3.27	1.45	0.65
1.00	26.6	7.86	3.36	1.52	0.69
$(k_{Nu})_{app}/10^{-4}$ M^{-1} s^{-1} [k]	6.7	1.86	0.90	0.46	0.178

[a] Columns of k_{obsd} values are labeled with % MeOH[d]/Y[j]. [b] At 25 °C and constant ionic strength maintained with $NaClO_4$. [c] The slope of a logarithmic plot of the change in absorbance at 280 nm against time. [d] Percent methanol in water. [e] $I = 5.00$. [f] $I = 4.00$. [g] $I = 3.00$. [h] $I = 2.00$. [i] $I = 1.00$. [j] The Grunwald–Winstein Y value for the mixed methanol/water solvent (ref 19). [k] The slope of a plot of k_{obsd} against [NaN_3].

(1) The reactions of these substrates with azide ion and other nucleophilic anions[12] or amines[13] give good yields of the nucleophile adducts by a pathway that is kinetically zero order in the concentration of the nucleophilic reagent.

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(2) The yields of the nucleophile adducts from the reactions of **1-X** are independent of the leaving group X^- for $X^- = I^-$, Br^-, mesylate ion, and tosylate ion.[12]

(3) The reactions of **1-Br**[8,12] and **1-I** (Figure 1) are subject to strong inhibition by added bromide and iodide common ions, respectively.

Most of our previous studies on the stepwise nucleophilic substitution reactions of **1-X** were at the relatively low concentrations of nucleophilic anions that were required to trap the carbocation reaction intermediate **2** [$k_T \gg k_s$ (Scheme I) for $Nu^- = I^-$, Br^-, and N_3^-].[8,12,13] The present experiments at much higher nucleophile concentrations have been carried out in order to determine whether **1-I** or **1-Br** also undergoes weak bimolecular substitution reactions.

The values of k_{obsd} for the reaction of **1-I** in water and at a constant ionic strength of 1.00 ($NaClO_4$) increase by ca. 50% as the concentration of sodium azide is increased from 0 to 1.00 M, but there is little change in k_{obsd} for the reaction of **1-Br** over the same range of azide ion concentrations (Table I). The study of the reaction of **1-I** at the higher ionic strength of 6.00 ($NaClO_4$) and over a broader range of azide ion concentrations shows that k_{obsd} for **1-I** increases by ca. 40% as $[NaN_3]$ is increased from 0 to 2.00 M and then decreases as $[NaN_3]$ is further increased to 4.00 M (Table II and Figure 2). There is a similar change in k_{obsd} for the reaction of **1-I** in water at a constant ionic strength of 6.00 ($NaClO_4$) as the concentration of sodium thiocyanate is increased from 0 to 4.00 M, but there are marked decreases in k_{obsd} at increasing concentrations of sodium acetate, sodium chloride, or sodium sulfate (Table II and Figure 2).

There are two possible explanations for the increases in the reactivity of **1-I** in water as perchlorate ion is replaced by thiocyanate or azide ion: (1) they may represent specific salt effects or (2) there may be bimolecular displacement reactions of thiocyanate and azide ions with **1-I** by either a stepwise or a concerted reaction mechanism (Scheme I).

Specific Salt Effects. The following observations show that the data in Figure 2 and Table II for the reaction of **1-I** cannot be explained solely by simple specific salt effects of azide or thiocyanate ions.

(1) A specific salt effect should not cause an increase in k_{obsd} at low salt concentrations and then a decrease at higher concentrations, as is observed for the reaction of **1-I** in the presence of N_3^- and SCN^-.

(2) The 4-fold increase in k_{obsd} for the reaction of **1-I** as the concentration of sodium perchlorate is increased from 0 to 6.00 M shows that these reactions are subject to a large positive perchlorate ion salt effect which may be attributed to stabilization of the carbocation-like transition state for the solvolysis reaction by ClO_4^-.[15] The decreases in k_{obsd} for this reaction upon replacement of ClO_4^- by Cl^-, AcO^-, and SO_4^{2-} (Figure 2) show that these anions provide a weaker stabilization of this transition state. Similarly, substitution of perchlorate ion by azide ion normally causes little change or small decreases in k_{obsd} for solvolysis reactions that proceed by a stepwise mechanism rather than the increases in k_{obsd} that are seen for the reaction of **1-I** (Figure 2). For example, k_{obsd} for the reaction of 1-(4-methylphenyl)ethyl chloride in 50% methanol in water remains constant as 0.50 M sodium perchlorate is substituted by 0.50 M sodium azide,[3] while substitution of N_3^- for ClO_4^- causes a small decrease in k_{obsd} for the solvolysis of **1-Br** in 50:50 (v:v) trifluoroethanol/water.[12b]

(3) The specific azide ion salt effects on the reactions of the structurally homologous substrates **1-I** and **1-Br** would be expected to be similar, but in fact the effects of sodium azide on k_{obsd} for these two reactions are very different. The effect of azide ion on k_{obsd} for the reaction of **1-I** is complex (Figure 2), but increasing concentrations of this anion cause a steady linear decrease in k_{obsd} for the reaction of **1-Br** (Figure 3).

The data in Figures 2 and 3 are consistent with a negative specific azide ion salt effect, which causes k_{obsd} to decrease for the reactions of both **1-I** and **1-Br**, and a second positive specific azide ion salt effect, which causes k_{obsd} to increase for only the reaction of **1-I**. This second salt effect dominates the overall change in k_{obsd} at $[NaN_3] = 0$–2.00 M but not at higher $[NaN_3]$ where the negative specific azide ion salt effect appears to be dominant (Figure 2).

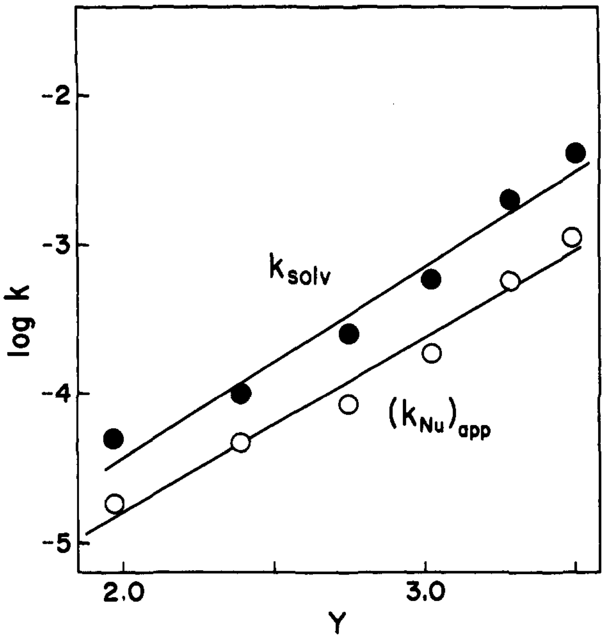

Figure 4. Dependence of log k_{solv} (s^{-1}, ●) for the solvolysis reactions of **1-I** and log $(k_{Nu})_{app}$ ($M^{-1}\,s^{-1}$, ○) for the apparent bimolecular substitution reactions of azide ion with **1-I** on the Grunwald–Winstein *Y* value of the solvent for reactions in mixed methanol/water solvents.

Bimolecular Displacement Reactions. The simplest explanation for the increases in k_{obsd} for the reaction of **1-I** in the presence of azide and thiocyanate ions (Figure 2) is that there are bimolecular nucleophilic substitution reactions of these ions with **I-I** which may proceed by either a stepwise or a concerted reaction mechanism.

A bimolecular substitution reaction of nucleophiles with **1-I** requires that there be a correlation between the effect of increasing concentrations of the nucleophile on k_{obsd} and the yields of the nucleophile adduct. We were unable to determine whether this correlation exists because the yields of the nucleophile adduct from the putative bimolecular substitution reaction, calculated from the increases in k_{obsd} (Figure 2), are too small to be detected against the background of near quantitative yields of the nucleophile adduct obtained from trapping of the liberated carbocation intermediate **2** ($k_T[Nu^-]$, Scheme I). For example, the reaction of **1-I** at $[NaN_3] = 0.40$ M would give a 98.89% yield of the azide adduct if trapping of **2** by azide ion ($k_{az}/k_s = 220$ M^{-1})[8] were the only pathway for its formation but only a slightly larger yield of 99.06% if the 19% rate increase at $[NaN_3] = 0.40$ M were due to a concurrent bimolecular substitution reaction of azide ion (Figure 2). The precision of our experiments is insufficient for the detection of such small differences in product yields, so such *direct* confirmation of bimolecular nucleophilic substitution reactions at **1-I** is not possible. We rely instead on indirect evidence to support this reaction pathway.

Bimolecular displacement reactions at **1-I** by a *concerted* A_ND_N (S_N2)[14] mechanism (K_{as} and k_c, Scheme I) are unlikely because α-CF_3-substituted centers are known to be extremely resistant to concerted displacement reactions.[16-18] The nearly parallel Grunwald–Winstein correlations[19] of k_{solv} for the solvolysis re-

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actions of **1-I** ($m = 1.3$) and $(k_{Nu})_{app}$ for the bimolecular substitution reactions of azide ion with **1-I** ($m = 1.2$) in mixed methanol/water solvents (Figure 4) are consistent with transition states of nearly identical polarity for the two reactions. Therefore, bonding between the nucleophile or the leaving group and the benzylic carbon, which would decrease the polarity of the transition state for a concerted bimolecular substitution reaction, must be minimal. By comparison, smaller values of $m = 0.75$ and 0.80 are observed for the bimolecular substitution reactions of N_3^- with 1-(4-fluorophenyl)ethyl chloride and 1-(3-methoxyphenyl)ethyl chloride, respectively,[3] both of which proceed by a concerted mechanism through a transition state that is stabilized by partial bonding of the nucleophile and the leaving group to the benzylic carbon.

We now consider whether the increases in k_{obsd} for the reaction of **1-I** at increasing concentrations of azide or thiocyanate ion are due to *stepwise* bimolecular substitution reactions of these anions (Scheme I). For this to be a viable mechanism, it must first be shown that the following conditions are satisfied:

(1) A stepwise reaction through the triple ion complex $[Nu^-{\cdot}\mathbf{2}{\cdot}I^-]$ will increase the rate of disappearance of substrate only when the ion pair intermediate $[\mathbf{2}{\cdot}I^-]$ is formed reversibly [$k_{-1} > k_{-d}$ ($k_{-d} \gg k_s'$, so k_s' can be neglected),[20] Scheme I]. This condition is equivalent to that for a diffusion-limited reaction of the leaving group I^- with the free carbocation **2**, because this requires that when the ion pair $[\mathbf{2}{\cdot}I^-]$ is formed by diffusional encounter of **2** and I^-, its collapse to **1-I** (k_{-1}) occurs essentially every time it is formed so that it rarely dissociates to re-form free ions (k_{-d}). The reaction of I^- with **2** must be diffusion limited because the rate constant k_1 for trapping of **2** by iodide ion is slightly larger than the diffusional rate constant k_{az}[12] for the trapping of **2** by azide ion ($k_1/k_{az} = 1.2$). We conclude that $k_{-1} > k_{-d}$ for partitioning of $[\mathbf{2}{\cdot}I^-]$, so this ion pair must be formed reversibly from **1-I** and undergo internal return to reactant.[21]

(2) The partitioning of the triple ion complex $[Nu^-{\cdot}\mathbf{2}{\cdot}I^-]$ to products $[k_2/(k_2 + k_{-1}' + k_{-a})]$ must be more favorable than the partitioning of the ion pair $[\mathbf{2}{\cdot}I^-]$ to products for the reaction in the absence of Nu^- $[(k_{-d}/(k_{-d} + k_{-1})]$. Since $k_{-1} \approx k_{-1}'$ for internal return and $k_{-d} \approx k_{-a}$ for diffusional separation of ions, this requires $k_2 > k_{-d}$. This condition is equivalent to that for a diffusion-limited reaction of Nu^- with the free carbocation **2**, which requires that the encounter complex $[\mathbf{2}{\cdot}Nu^-]$ collapse to products (with a rate constant $\approx k_2$) much faster than it separates to reform free ions (with a rate constant $\approx k_{-d}$). This requirement is met by both N_3^-[12] and SCN^-[23a] because the reactions of these anions with free **2** are diffusion limited.

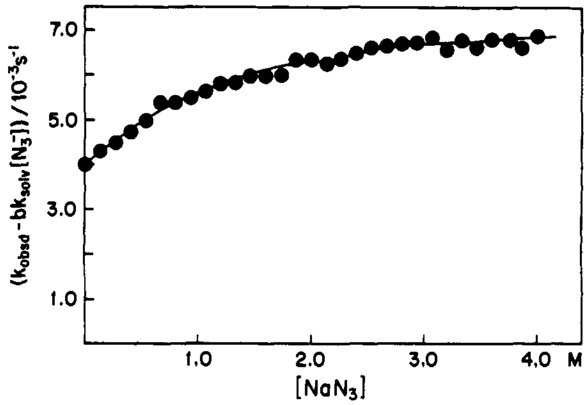
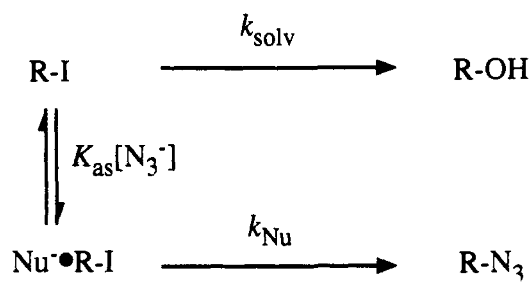


Figure 5. Replot of data from Figure 2 for the reaction of **1-I** in the presence of sodium azide after correction of k_{obsd} for the negative specific azide ion salt effect using $k_{solv} = 4.0 \times 10^{-3}$ s^{-1} and $b = -0.104$ determined for the reaction of **1-Br** (see text). The solid line shows the fit of the data to eq 3 of the text with $K_{as} = 0.67$ M^{-1} and $k_{Nu} = 8.0 \times 10^{-3}$ s^{-1}.

Scheme III



The stepwise bimolecular substitution reaction may proceed by a trapping (Sneen) mechanism (k_1 and $k_a[Nu^-]$, Scheme I)[1] or a stepwise preassociation mechanism ($K_{as}[Nu^-]$ and k_1', Scheme I),[5,11,25,26] depending upon which of these pathways for the formation of $[Nu^-{\cdot}\mathbf{2}{\cdot}I^-]$ proceeds through the rate-determining transition state of lowest energy. This pathway can be determined by comparison of the rate constants k_{-1}' and k_{-a} for the breakdown of $[Nu^-{\cdot}\mathbf{2}{\cdot}I^-]$.[5,11,25,26] The observation of a diffusion-limited reaction between I^- and the free carbocation **2** requires $k_{-1} > k_{-d}$ (see above). Since $k_{-1} \approx k_{-1}'$ for internal return and $k_{-d} \approx k_{-a}$ for breakdown by diffusional separation, respectively, at the ion pair and ion triplet, then $k_{-1}' > k_{-a}$. We conclude that the fastest pathway for the breakdown of $[Nu^-{\cdot}\mathbf{2}{\cdot}I^-]$ is by k_{-1}' and K_{as}, and so, by the principle of microscopic reversibility, K_{as} and k_1' is the preferred pathway for formation of the triple ion complex. In fact, the stepwise preassociation mechanism must be followed whenever the reaction of the leaving group with the free carbocation intermediate is diffusion limited.[5]

The stepwise preassociation mechanism is not only a viable mechanism for the bimolecular nucleophilic substitution reactions of azide ion and thiocyanate ion with **1-I**, but this mechanism also provides a sensible and self-consistent explanation for several of our experimental results which are otherwise difficult to rationalize:

(1) The stepwise preassociation mechanism will be observed only when the reaction of the leaving group ion with free **2** is diffusion limited. The observation of a bimolecular reaction of azide ion with **1-I** but not with **1-Br** can be explained by this requirement for the stepwise preassociation mechanism, because k_1 for trapping of **2** by I^- is diffusion limited but k_{Br} for trapping of **2** by Br^- is 3-fold smaller than a diffusional rate constant [$k_{az}/k_{Br} = 2.9$ for partitioning of **2** in water at $I = 6.00$ ($NaClO_4$)].[8]

(2) The stepwise preassociation mechanism will be observed only for nucleophilic ions whose reactions with free **2** are diffusion limited. The observation of kinetically bimolecular substitution reactions of azide ion and thiocyanate ion with **1-I** but of only negative specific salt effects of chloride, acetate, and sulfate ions can be explained by this requirement for a stepwise preassociation mechanism because the reactions of N_3^-[12] and SCN^-[23a] with **2**

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(20) The value for k_{-d} is expected to be similar to $k_{-d} \approx 1.6 \times 10^{10}$ s^{-1} for separation of ion-pair intermediates of solvolysis of 1-(4-methylphenyl)ethyl derivatives.[7] By contrast, $k_s = 2.3 \times 10^7$ s^{-1} for the reaction of **2** in water ($I = 6.0$, $NaClO_4$) and the ion-pair intermediate of solvolysis of **1-Br** is (2–6)-fold less reactive than the liberated carbocation **2** so that $k_{-d} \gg k_s'$ for this reaction.[8]

(21) Internal return has been detected for the solvolysis reactions of 1-phenyl-2,2,2-trifluoroethyl triflate in the weakly nucleophilic solvents hexafluoro-2-propanol and trifluoroacetic acid as the difference in the rate constants for the loss of optical activity and the formation of products for the reaction of a chiral substrate.[22]

(22) Allen, A. D.; Ambidge, C.; Che, C.; Michael, H.; Muir, R.; Tidwell, T. T. *J. Am. Chem. Soc.* **1983**, *105*, 2343–2350.

(23) (a) The rate constant ratio $k_{SCN}/k_{az} = 1.0$ has been determined from product ratios for the reaction of **2** in 20% methanol in water: J. P. Richard, manuscript in preparation. (b) The rate constant ratios for the partitioning of **2** in 50:50 (v:v) trifluoroethanol/water of $k_{az}/k_{Cl} = 6.7$[24] and $k_{az}/k_{AcO} = 31$[12b] show that the capture of **2** by chloride and acetate ions is slower than the diffusion-limited trapping by azide ion. The further decreases in these ratios with increasing carbocation reactivity to $k_{az}/k_{Cl} = 2.8$ for capture of the 4-methoxybenzyl carbocation[6] and $k_{az}/k_{AcO} = 10$ for capture of the 1-(4-methylphenyl)ethyl carbocation[7] show that neither k_{AcO} nor k_{Cl} for the capture of **2** has reached the constant value expected for an encounter-limited reaction.

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are diffusion limited but the reactions of Cl$^-$, AcO$^-$,[23b] and probably SO$_4^{2-}$ with **2** are slower than diffusion.

(3) The stepwise preassociation mechanism predicts a limiting reaction velocity at high nucleophile concentrations when essentially all of the substrate exists in the encounter complex [Nu$^-$·R-X] with the nucleophile (Scheme I). This provides an explanation for the downward curvature that is observed in the plots of k_{obsd} against the concentration of nucleophile for the reaction of azide ion and thiocyanate ion with **1-I** (Figure 2).

Figure 5 shows a replot of the data for N$_3^-$ from Figure 2 according to eq 3 which was derived for Scheme III. Scheme

$$k_{obsd} - bk_{solv}[N_3^-] = \frac{k_{solv} + k_{Nu}K_{as}[N_3^-]}{1 + K_{as}[N_3^-]} \qquad (3)$$

III is a simplified version of Scheme I in which k_{solv} is the observed first-order rate constant for solvolysis of **1-I**, K_{as} is the association constant for formation of the substrate–nucleophile encounter complex, and k_{Nu} is the macroscopic first-order rate constant for conversion of this encounter complex to the nucleophile adduct. The left-hand side of eq 3 is the observed rate constant for the reaction of **1-I** corrected for the negative specific azide ion salt effect that is observed at high [NaN$_3$] (Figure 2). The specific azide ion salt effect on the reaction of **1-I** (by k_1, Scheme I) and the reaction of the preassociation complex [N$_3^-$·**1-I**] (by k_1', Scheme I) were assumed to be the same as that on the reaction of **1-Br** for which $b = -0.104$ (Figure 3). The value of $k_{solv} = 4.0 \times 10^{-3}$ s^{-1} (Table II) was used to obtain a nonlinear least-squares fit of the data to eq 3 (solid line, Figure 5), which gave $K_{as} = 0.67$ M^{-1} and $k_{Nu} = 8.0 \times 10^{-3}$ s^{-1}.

The values for K_{as} and k_{Nu} obtained from this analysis are reasonable. A value of $K_{as} = 0.3$ M^{-1} has been estimated for formation of an encounter complex between 1-propanethiol and 1-(4-methylphenyl)ethyl chloride in 50:50 trifluoroethanol/water.[7] The somewhat larger value of $K_{as} = 0.67$ M^{-1} estimated here could refect stabilizing electrostatic interactions between the azide anion and the positive end of the dipole of the CF$_3$ group at [N$_3^-$·**1-I**].

The ratio $k_{Nu}/k_{solv} = 2$ requires that the reaction of **1-I** in the encounter complex with azide ion be 2-fold faster than in the presence of solvent alone. Most or all of this difference must be due to the more favorable partitioning of [N$_3^-$·**2**·I$^-$] than of [**2**·I$^-$] to products ($k_2 > k_{-d}$, Scheme I). There is no evidence for a significant difference between k_1 and k_1', so nucleophilic assistance to the reaction of **1-I** is minimal.

The large Grunwald–Winstein values of $m = 1.3$ and 1.2 for the solvolysis reaction of **1-I** and the apparent bimolecular substitution reaction of azide ion with **1-I**, respectively, are consistent with similar changes in polarity on moving from the ground state to the transition state for these reactions. A detailed evaluation of data for reactions in mixed methanol/water solvents with respect to a stepwise preassociation mechanism would require additional experiments at higher concentrations of azide ion (see Figure 5), which are not feasible because of the limited solubility of sodium azide in aqueous/organic solvents.

Summary. These experiments provide a relatively simple protocol for determining if kinetically bimolecular nucleophilic substitution reactions proceed through a carbocation reaction intermediate. The reactions of nucleophilic anions with **1-X** are kinetically second order in nucleophile only when the reactions of *both* the nucleophile and the leaving group anion with the free carbocation **2** are diffusion limited. This is consistent with a stepwise preassociation mechanism for the bimolecular substitution reaction. The relative rate acceleration observed at [Nucleophile] = 1.00 M is small (≤40%, Figure 2 and Table II), even for those reactions which particularly favor the observation of a stepwise bimolecular substitution reaction. These results suggest that large rate accelerations should not be expected for nucleophilic substitution reactions in water which follow the stepwise preassociation reaction mechanism.

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Evaluation of Potential Ferromagnetic Coupling Units: The Bis(TMM) Approach to High-Spin Organic Molecules

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Abstract: Four new hydrocarbon tetraradicals, **1–4**, each composed of two triplet trimethylenemethane (TMM) subunits linked by a potential ferromagnetic coupling unit (FC), were synthesized and characterized by variable-temperature electron paramagnetic resonance (EPR) spectroscopy. Simulation of the EPR powder spectra and a priori calculation of the zero-field splitting parameters aided spectral assignment. The Heisenberg Hamiltonian appears to quantitatively model relative spin-state energies in **1–4**. In three cases ferromagnetic coupling was achieved, as evidenced by quintet ground states in the resulting tetraradicals. In one case, strong evidence for antiferromagnetic coupling was obtained.

Introduction

A key to the rational design of magnetic organic materials is the ability to control spin–spin coupling of unpaired electrons.[1,2] One approach we have been pursuing is shown schematically in Figure 1a. We conceptually divide a high-spin material into two components: the spin-containing fragment (SC), which provides the unpaired electrons, and the ferromagnetic coupling unit (FC).[3,4]

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