Mechanism for Nucleophilic Substitution and Elimination Reactions at Tertiary Carbon in Largely Aqueous Solutions: Lifetime of a Simple Tertiary Carbocation

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Abstract: The rate constants and the yields of the products of the nucleophilic substitution and elimination reactions of 1-(4-methoxyphenyl)-3-methyl-3-butyl derivatives (**1-X**) have been determined in mostly aqueous solvents, and the absolute rate constant for reaction of the simple tertiary carbocation $\mathbf{1}^+$ in 50:50 (v/v) trifluoroethanol/water has been estimated as $k_s = 3.5 \times 10^{12}$ s^{-1}. Product studies show that the acid-catalyzed reactions of **1-OH** and 4-(4-methoxyphenyl)-2-methyl-1-butene (**2**) do not proceed exclusively through a common carbocation intermediate $\mathbf{1}^+$. The observed formation of small amounts of the azide ion adduct $\mathbf{1\text{-}N_3}$ likely occurs by a preassociation reaction mechanism. The reactions of **1-Cl** and $\mathbf{1\text{-}O_2CC_6F_5}$ in 50:50 (v/v) trifluoroethanol/water give 39% and 56%, respectively, of the alkene products of elimination, and the yields of the alkenes are unaffected by the addition of 0.50 M of the good nucleophile N_3^-. This result is consistent with a concerted unimolecular mechanism for the elimination reactions of **1-X**.

Introduction

The stepwise $D_N + A_N$ (S_N1)[1] mechanism for nucleophilic substitution at tertiary derivatives is strongly favored by the large steric barrier to concerted bimolecular substitution at tertiary carbon and the large stabilization of the putative carbocation intermediate by hyperconjugative electron donation from three alkyl groups.[2] However, there is no consensus about the dynamics of solvolysis and elimination reactions at tertiary carbon. In one textbook on physical organic chemistry, it has been concluded that the solvolysis of *tert*-butyl derivatives proceeds through ion pair or ion−molecule pair intermediates which undergo separation to free species in water,[3] and in another that this classical S_N1 mechanism is "*now recognized as an extreme situation, though one which can occur when a particularly stabilized carbocation such as Ph_3C^+ is involved*".[4] These contradictory conclusions reflect the difficulties in interpreting results from the literature which pertain to the lifetime of simple tertiary carbocations in water.

The yields of methylpropene and the solvent adducts from the reaction of *tert*-butyl chloride, bromide, and iodide in ethanol vary with the leaving group, but they are almost constant when the reactions are carried out in water.[5] These results are consistent with the conclusion that in an organic solvent, where the diffusional separation of ion pair intermediates is relatively slow, simple tertiary carbocations undergo deprotonation by the leaving group within the carbocation-leaving group ion pair, but that in the highly polar solvent water, the diffusional separation to free ions is faster than the formation of alkene products by proton transfer from the carbocation to the leaving group. However, it is not clear why a significant amount of alkene product should be formed by proton transfer from the carbocation to chloride, bromide, or iodide ion leaving groups, because these anions are less basic than the ethanol solvent which surrounds the carbocation-leaving group ion pair. Furthermore, there is no experimental evidence that *requires* that ion pairs form as intermediates of the elimination reactions of *tert*-butyl halides: the decreasing yields of alkene products in solvents of increasing ionizing power may reflect the higher polarity of the transition state for solvolysis than of that for a concerted elimination reaction,[6] which would favor formation of the solvolysis products in the polar solvent water.

There is no significant common ion inhibition of the reaction of *tert*-butyl bromide in 90% acetone in water[7] and very little exchange of ^{36}Cl from $Na^{36}Cl$ into unreacted *tert*-butyl chloride during its reaction in methanol[8] or of ^{18}O between the bridging and nonbridging positions during the reaction of ^{18}O-labeled *tert*-butyl *p*-nitrobenzoate in 80% acetone in water,[9] and the solvolysis of chiral tertiary chlorides proceeds with partial inversion of configuration in 80% acetone in water[10] and in methanol.[11] These results are consistent with the conclusion that the direct reaction of solvent with tertiary carbocation-leaving group ion pair intermediates of solvolysis reactions in mostly organic solvents is faster than their separation to free ions, and that the chloride ion leaving group acts to shield the ion pair intermediate from frontside attack of solvent. However, the change to a mostly aqueous solvent will favor separation of the ion pair intermediates to the free carbocations.

Tertiary carbocations will be formed as liberated intermediates of solvolysis reactions in water provided that the rate constant

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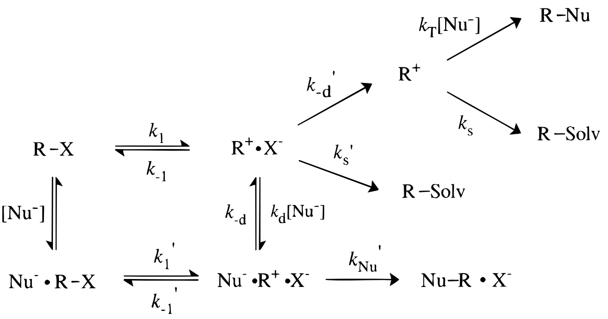
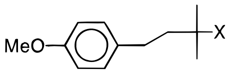
Scheme 1



for separation of the ion pair to give free ions ($k_{-d}' \approx 10^{10}$ s^{-1}, Scheme 1) is larger than that for the direct reaction of solvent with the ion pair (k_s', Scheme 1). The two best estimates from the chemical literature of $k_s = 4 \times 10^9$ s^{-1} [12−14] and $k_s = 10^{10}$ s^{-1} [15−17] for the rate constant for reaction of the *tert*-butyl carbocation with water both suggest that this carbocation will form as a liberated intermediate of solvolysis reactions in water.

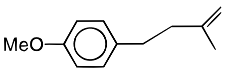
Rate constants for the reaction of tertiary carbocations with solvent might be calculated from the azide ion selectivity determined from product analysis, k_{az}/k_s (M^{-1}), using a diffusional rate constant for the reaction of N_3^-: $k_{az} = k_T = 5 \times 10^9$ M^{-1} s^{-1} (Scheme 1).[18,19] However, this azide "clock"[20,21] should be used only when trapping of the *free* carbocation ($k_T[\mathrm{Nu}^-]$, Scheme 1) is a step on the pathway to formation of the azide ion adduct. It is unclear whether the low yields of the azide ion adduct obtained from nucleophilic substitution at tertiary derivatives[22] represent diffusion-controlled trapping of a free tertiary carbocation by N_3^- or the alternative conversion of an encounter complex of N_3^- and the substrate to the azide ion adduct by a preassociation mechanism (K_{as}, k_1', and k_{Nu}', Scheme 1).[23] The preferred reaction pathway depends on the balance between the rate constants for the direct reaction of solvent with the ion pair intermediate (k_s') and its diffusional separation to give free ions (k_{-d}').[24] If the direct reaction of solvent with the ion pair is significantly faster than its separation to free ions ($k_s' > k_{-d}'$), then the free carbocation will not be formed and the azide ion adduct *must* be formed from an encounter complex between the substrate and the nucleophile by a preassociation mechanism (K_{as}, Scheme 1).[24] In the case that the reaction of N_3^- does occur mainly by a preassociation mechanism, then the observed value of k_{az}/k_s (M^{-1}) determined from product analysis will be an *overestimate* of the rate constant ratio for partitioning of the carbocation between reaction with N_3^- and solvent, and the value of k_s (s^{-1}) calculated from this observed ratio using $k_{az} = 5 \times 10^9$ M^{-1} s^{-1} will then be an *underestimate* of the reactivity of the carbocation toward solvent.

In summary, the uncertainty regarding the lifetime of simple tertiary carbocations in aqueous solvents is due to difficulties in drawing generalizations from the results obtained in mostly organic solvents, and to the relative scarcity and sometimes questionable accuracy of data for the product distributions of these reactions.[25] We report here a comprehensive systematic study of the kinetics and product distributions of the reactions of **1-X** and **2** in mostly aqueous solvents, which was directed toward (a) estimating or establishing a limit for the rate constants for reaction of the simple tertiary carbocation $\mathbf{1}^+$ and the *tert*-butyl carbocation with these solvents, (b) characterizing any intermediate that is common to the acid-catalyzed reactions of **1-OH** and **2**, (c) determining the extent of trapping of the simple tertiary carbocation $\mathbf{1}^+$ by external nucleophilic reagents in mostly aqueous solvents, and (d) characterizing the mechanism of the elimination reactions of **1-X** to give alkene products.



1-X

X = Cl, OH, $O_2CC_6F_5$



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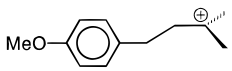
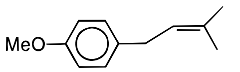


$\mathbf{1}^+$



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Experimental Section

Syntheses. The materials and procedures for the synthesis of the following compounds, along with spectral data for these compounds are given in the Supporting Information: 3-hydroxy-1-(4-methoxyphenyl)-3-methylbutane (**1-OH**), 1-(4-methoxyphenyl)-3-methyl-3-butyl pentafluorobenzoate (**1-O₂CC₆F₅**), 4-(4-methoxyphenyl)-2-methyl-1-butene (**2**), and 3-chloro-1-(4-methoxyphenyl)-3-methylbutane (**1-Cl**).

Product Studies. Reactions were carried out at 25 °C and a constant ionic strength of 0.50 maintained with sodium perchlorate, and product distributions were determined by HPLC analysis. Reactions were initiated by making a 100-fold dilution of a solution of substrate in acetonitrile into the reaction mixture to give a final substrate concentration of *ca.* 7×10^{-4} M for the reactions of **1-Cl** and **2**, or 0.02 M for the reactions of **1-OH**. The reactions of **1-O₂CC₆F₅** in 50:50 (v/v) TFE/H_2O were initiated by making a 50-fold dilution of a solution of this substrate in acetonitrile into trifluoroethanol, and then mixing the resulting solution with an equal volume of 1.0 M aqueous sodium perchlorate to give a final substrate concentration of 0.02 M. 9-Fluorenyl methyl ether (3×10^{-5} M) was used as an internal standard to correct the observed areas of the substrate and product peaks for small variations in the HPLC injection volume.

The yields of the products of the spontaneous reactions of **1-O₂CC₆F₅** and **1-Cl** were determined during the first 2% of reaction and after at least ten reaction halftimes, respectively. The yields of the products of the acid-catalyzed reaction of **1-OH** were determined during the appearance of up to 3% total products, and product yields for the acid-catalyzed reaction of **2** were determined during the first three halftimes of the reaction. The conversion of **1-OH** (20 mM) or of **2** (20 mM) to an equilibrium mixture of reaction products in 50:50 (v/v) TFE/H_2O containing 1.00 M $HClO_4$ and 3-(4-methoxyphenyl)-1-propanol (5 ×

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(25) Dimensionless ratios of k_{az}/k_{HOH} = 3.9, 7, 12, 14.5, and 74 have been reported for the partitioning of the putative intermediate of solvolysis of *tert*-butyl bromide in aqueous acetone between reaction with N_3^- and water. Experimental and typographical errors have been suggested to account for this range of values, and a "best" value has been identified.[22]

10^{-4} M) as an internal standard was monitored by withdrawal of an aliquot (120 μL) of the reaction mixture at various times, which was neutralized with 2 M sodium acetate before analysis by HPLC.

HPLC Analyses. The products of the spontaneous reactions of **1-Cl** and **1-O$_2$CC$_6$F$_5$** and the acid-catalyzed reactions of **1-OH** and **2** were separated and quantified by HPLC analysis as described in previous work.[20,26,27] The reaction products were detected at 278 nm, which is λ_{max} for **1-OH**.

The alcohol (**1-OH**) and the disubstituted alkene (**2**) products of the reactions of **1-X** were identified by comparison of their HPLC retention times with those of authentic materials. The ethers **1-OMe** and **1-OCH$_2$CF$_3$** were identified as the peaks which appear during reaction of **1-X** in mixed MeOH/H$_2$O and TFE/H$_2$O solvents, respectively. The trisubstituted alkene **3** was identified as the additional product peak that appears during the acid-catalyzed reactions of **1-OH** and **2** and the spontaneous reactions of **1-Cl** and **1-O$_2$CC$_6$F$_5$**.

When the reactions of **1-Cl** and **1-O$_2$CC$_6$F$_5$** were carried out in the presence of increasing concentrations of NaN$_3$, there was no change in the normalized peak area for **3**, but there was an increase in the normalized area of the peak for **2** that was identical, within experimental error, with the accompanying decrease in the sum of the normalized peak areas for the solvent adducts (**1-Solv**). This suggests that **1-N$_3$** and **2** have nearly identical retention times. A partial resolution of the peaks for **1-N$_3$** and **2** was achieved by use of very long HPLC analysis times, but these conditions were not practical for the routine determination of product yields. The extinction coefficients of **1-Solv** and **1-N$_3$** at 278 nm are identical (see below). Therefore, the peak areas for **1-N$_3$** were estimated as either (a) the difference between the sum of the normalized areas for the solvent peaks (**1-Solv**) for reactions in the presence and absence of N_3^- or (b) the difference between the normalized peak areas for the mixture of **1-N$_3$** and **2** for reactions in the presence of N_3^- and the peak area for **2** for reactions in the absence of N_3^-. As required by mass balance, there is good agreement between these two determinations.

The ratios of product yields were calculated using eq 1, where A_1 and A_2 are the HPLC peak areas for the products P$_1$ and P$_2$ and ϵ_2/ϵ_1 is the ratio of the extinction coefficients for P$_2$ and P$_1$ at 278 nm, the

$$[\mathrm{P}]_1/[\mathrm{P}]_2 = (A_1/A_2)(\epsilon_2/\epsilon_1) \tag{1}$$

wavelength used for these analyses. A ratio of $\epsilon_{\mathbf{1-OH}}/\epsilon_{\mathbf{1-Cl}} = 1.0$ was determined from HPLC analysis using authentic **1-OH** and **1-Cl**, and ratios of $\epsilon_{\mathbf{1-OH}}/\epsilon_{\mathbf{1-X}} = 1.0$ were used for the N_3^- (**1-N$_3$**) and alkoxide ion (**1-OMe** and **1-OCH$_2$CF$_3$**) adducts, because it has been shown in previous work that, at λ_{max}, the extinction coefficients of α-substituted 4-methoxybenzyl alcohols do not change when the hydroxy group is replaced by azido or simple alkoxy groups.[20,27−29] A ratio of $\epsilon_{\mathbf{1-OH}}/\epsilon_{\mathbf{2}} = 1.0$ at 278 nm was determined by showing that the decrease in the normalized HPLC peak area for **2** during its acid-catalyzed (0.50 M HClO$_4$) reaction in 50:50 (v/v) TFE/H$_2$O is identical, within experimental error, with the increase in the sum of the normalized peak areas for the reaction products, which are mostly the solvent adducts **1-OH** and **1-OCH$_2$CF$_3$** (97%). A ratio of $\epsilon_{\mathbf{1-Cl}}/\epsilon_{\mathbf{3}} = \epsilon_{\mathbf{1-OH}}/\epsilon_{\mathbf{3}} = 0.82$ was calculated using eq 2, where $A_{\mathbf{1-Cl}}$ is the initial normalized HPLC peak area for **1-Cl**, and $A_{\mathbf{1-Solv}}$, $A_{\mathbf{2}}$, and $A_{\mathbf{3}}$ are the final normalized peak areas of the products of the complete reaction of **1-Cl** in 50:50 (v/v) MeOH/H$_2$O. The 7% increase in absorbance that is observed when the reaction of **1-Cl** in 50:50 (v/v) TFE/H$_2$O is followed spectrophotometrically at 278 nm is consistent with the conclusion that the extinction coefficient for **3** at 278 nm is slightly larger than that for **1-Cl**.

$$\epsilon_{\mathbf{1-Cl}}/\epsilon_{\mathbf{3}} = (A_{\mathbf{1-Cl}} - A_{\mathbf{1-Solv}} - A_2)/A_{\mathbf{3}} \tag{2}$$

Calculation of Rate Constant Ratios. Dimensionless rate constant ratios for the reactions of **1-X** with nucleophilic reagents Nu1 and Nu2 were calculated from the ratio of product yields using eq 3. Rate constant ratios (M^{-1}) for partitioning of **1-X** between reaction with N_3^- and solvent were calculated using eq 4, where $\sum$[**1-Solv**] is the sum of the concentrations of the products of the reaction of solvent with **1-X**. A similar equation that treats the elimination reaction as a first-order process was used to calculate rate constant ratios for partitioning of **1-X** between nucleophilic substitution and alkene-forming elimination reactions.

$$k_{\mathrm{Nu1}}/k_{\mathrm{Nu2}} = ([\mathbf{1\text{-}Nu1}][\mathrm{Nu2}])/([\mathbf{1\text{-}Nu2}][\mathrm{Nu1}]) \tag{3}$$

$$k_{\mathrm{az}}/k_{\mathrm{s}} = [\mathbf{1\text{-}N_3}]/(\Sigma[\mathbf{1\text{-}Solv}][\mathrm{N_3}^-]) \tag{4}$$

The integrated HPLC peak areas and the rate constant ratios calculated directly from the ratios of product peak areas are reproducible to better than ±5% and ±10%, respectively. The product rate constant ratios for reaction of N_3^- are estimated to be accurate to ± 20%, because the yields of the azide ion adduct **1-N$_3$** were determined from the difference between the normalized areas of the product peaks for reactions in the presence and absence of this nucleophile (see above).

Kinetic Studies. Kinetic studies were carried out at 25 °C and a constant ionic strength of 0.50 maintained with sodium perchlorate.

The reactions of **1-Cl** were initiated by making a 100-fold dilution of a solution of substrate in acetonitrile into the reaction mixture to give a final substrate concentration of *ca.* 6×10^{-4} M. Reactions in the presence of perchlorate, lyoxide, and halide ions were monitored spectrophotometrically by following the increase in absorbance at 234 nm. Reactions in 50:50 (v/v) MeOH/H$_2$O in the presence of N_3^- were monitored by following the protonation of a phenoxide anion indicator (8×10^{-4} M) at 290 nm.[30] Argon was bubbled through both the aqueous salt solutions (1.0 M) and the methanol cosolvent immediately before preparation of the mixed solvent used in the phenoxide indicator assay, in order to minimize the amount of dissolved oxygen in the final solvent. In most cases this eliminated the downward drift in the end points for these reactions, which is probably due to oxidation of phenoxide ion. In cases where the end point was unstable, it was calculated by adding 3% to the change in A_{290} observed after five reaction halftimes. Observed first-order rate constants, k_{obsd} (s^{-1}), for the reaction of **1-Cl** were calculated from the slopes of semilogarithmic plots of reaction progress against time, which were linear for at least three reaction halftimes. The values of k_{obsd} were reproducible to within ±5%.

The reactions of **1-O$_2$CC$_6$F$_5$** in 50:50 (v/v) TFE/H$_2$O were carried out as described for the product studies. The relative concentrations of products (Σ[P]) and substrate ([S]$_0$) were monitored by HPLC analyses during the first 2% of this reaction, and k_{obsd} was determined as the slope of a plot of $\Sigma[\mathrm{P}]/[\mathrm{S}]_0$ against time.

The acid-catalyzed reactions of **1-OH** and **2** in 50:50 (v/v) TFE/H$_2$O were carried out as described for the product studies. The first-order rate constant for conversion of **1-OH** to **1-OCH$_2$CF$_3$** was determined as the slope of a linear plot of $A_{\mathbf{1-OTFE}}/A_{\mathbf{1-OH}}$ against time during the first 12% of the approach to an equilibrium concentration of **1-OCH$_2$CF$_3$**, where $A_{\mathbf{1-OTFE}}$ and $A_{\mathbf{1-OH}}$ are the integrated HPLC peak areas for **1-OCH$_2$CF$_3$** and **1-OH**, respectively. The first-order rate constant for the disappearance of **2** was determined as the slope of a semilogarithmic plot of reaction progress against time which covered three reaction halftimes.

Results

The first-order rate constants for the reaction of **1-Cl** at 25 °C in 50:50 (v/v) TFE/H$_2$O, determined by monitoring the increase in absorbance at 234 nm, are $k_{obsd} = 3.1 \times 10^{-4}$ s^{-1} ($I = 0.50$, NaClO$_4$) and 2.1×10^{-4} s^{-1} ($I = 0$). Figure 1 shows the dependence of k_{obsd}/k_0 for the reaction of **1-Cl** at 25 °C on the concentration of added Cl$^-$ in 50:50 (v/v) MeOH/H$_2$O ($I = 0.50$, NaClO$_4$) and on the concentration of added Cl$^-$ or Br$^-$ in 50:50 (v/v) TFE/H$_2$O ($I = 0.50$, NaClO$_4$), where k_0 is the rate constant for reaction in the absence of added halide ion.

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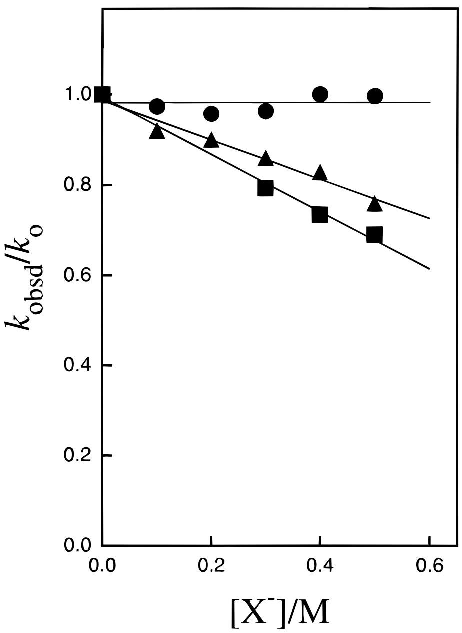


Figure 1. The dependence of k_{obsd}/k_0 for the reaction of **1-Cl** on the concentration of added X^- at 25 °C and $I = 0.50$ ($NaClO_4$), where k_0 is the rate constant for reaction in the absence of added halide ion. Key: ●, effect of added Cl^- in 50:50 (v/v) $MeOH/H_2O$; ■, effect of added Cl^- in 50:50 (v/v) TFE/H_2O; ▲, effect of added Br^- in 50:50 (v/v) TFE/H_2O.

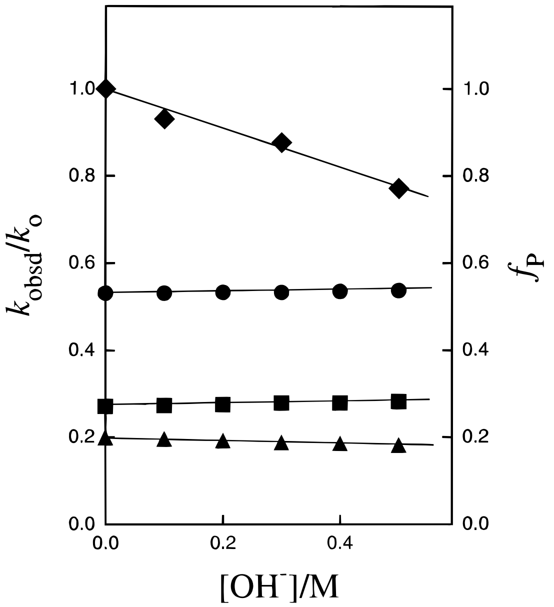


Figure 2. The dependence of k_{obsd}/k_0 and the fractional yields of substitution and elimination products (f_P) for the reaction of **1-Cl** on the concentration of added HO^- in 50:50 (v/v) $MeOH/H_2O$ at 25 °C and $I = 0.50$ ($NaClO_4$), where k_0 is the rate constant for reaction in the absence of added HO^-. Key: ◆, k_{obsd}/k_0; ●, fractional yield of **1-OH**; ▲, fractional yield of **1-OMe**; ■, total fractional yield of **2** and **3**.

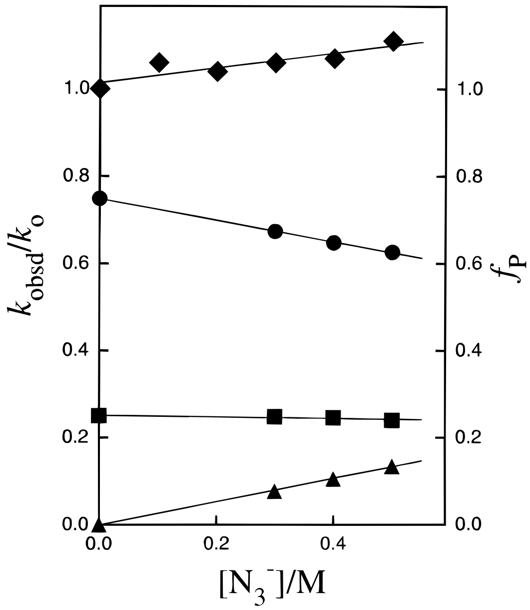


Figure 3. The dependence of k_{obsd}/k_0 and the fractional yields of nucleophilic substitution and elimination products (f_P) for the reaction of **1-Cl** on the concentration of added N_3^- in 50:50 (v/v) $MeOH/H_2O$ at 25 °C and $I = 0.50$ ($NaClO_4$), where k_0 is the rate constant for reaction in the absence of added N_3^-. Key: ◆, k_{obsd}/k_0; ●, total fractional yield of **1-OH** and **1-OMe**; ▲, fractional yield of **1-N₃**; ■, total fractional yield of **2** and **3**.

Table 1. Product Rate Constant Ratios for the Partitioning of **1-X** between Reaction with Azide Ion and Solvent at 25 °C and $I = 0.50$ ($NaClO_4$)[a]

substrate	solvent	k_{az}/k_s[b] (M^{-1})	k_{az}/k_{HOH}[c]	k_{az}/k_{ROH}[d]
1-Cl	50:50 (v/v) trifluoroethanol/water	0.38	13	14[e]
	50:50 (v/v) methanol/water	0.41	15	19[f]
1-O₂CC₆F₅[g]	50:50 (v/v) trifluoroethanol/water	0.31	11	10[e]

[a] The rate constant ratios are estimated to be accurate to ±20% (see Experimental Section). [b] Rate constant ratio for partitioning between reaction with azide ion and solvent, calculated using eq 4. [c] Dimensionless ratio of second-order rate constants for reaction with azide ion and water, calculated using eq 3. [d] Dimensionless ratio of second-order rate constants for reaction with azide ion and ROH, calculated using eq 3. [e] ROH = CF_3CH_2OH. [f] ROH = MeOH. [g] Determined from the product yields during the first 2% of the reaction.

Figure 2 shows the effect of increasing concentrations of added lyoxide ion on k_{obsd}/k_0 and on the product yields, determined by HPLC analysis, for the reaction of **1-Cl** at 25 °C in 50:50 (v/v) $MeOH/H_2O$ ($I = 0.50$, $NaClO_4$), where k_0 is the rate constant for reaction in the absence of added lyoxide ion. The addition of 0.25 M lyoxide ion has no effect on the product distribution for the reaction of **1-Cl** in the presence of 0.25 M N_3^- in this solvent.

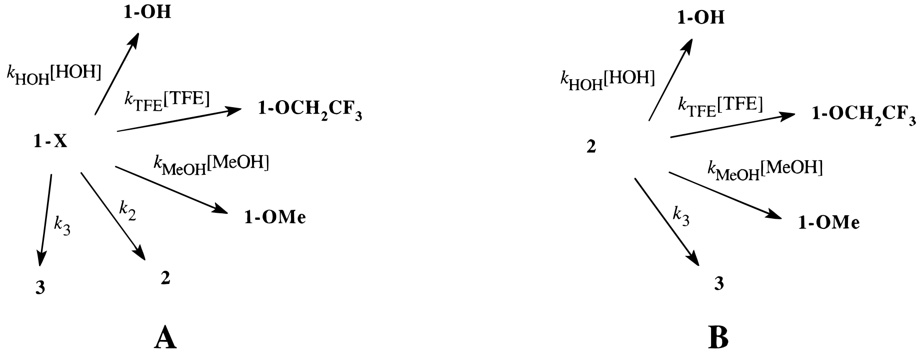
Figure 3 shows the effect of increasing concentrations of added N_3^- on k_{obsd}/k_0, determined by monitoring the protonation of a phenoxide anion indicator at 290 nm, and on the product yields, determined by HPLC analysis, for the reaction of **1-Cl** at 25 °C in 50:50 (v/v) $MeOH/H_2O$ ($I = 0.50$, $NaClO_4$), where k_0 is the rate constant for reaction in the absence of added N_3^-. Rate constant ratios for partitioning of **1-Cl** between reaction with N_3^- and with solvent, calculated from the product yields, are reported in Table 1. These ratios were calculated by treating the reactions of solvent either as a first-order process (k_{az}/k_s, M^{-1}) using eq 4, or as bimolecular reactions of methanol and water (k_{az}/k_{MeOH} and k_{az}/k_{HOH}) using eq 3. Azide ion (up to 0.50 M) has no effect on the total yield of 25% of the alkenes **2** and **3** from the reaction of **1-Cl** in this solvent, and the observed product rate constant ratios k_{az}/k_e (M^{-1}, not reported) for partitioning of **1-Cl** between formation of the azide ion adduct and elimination to form alkenes decrease with increasing concentrations of N_3^-. Table 1 also gives the product rate constant ratios for the reaction of **1-Cl** with N_3^- and solvent in 50:50 (v/v) TFE/H_2O ($I = 0.50$, $NaClO_4$) at 25 °C; there is also no effect of N_3^- on the yields of **2** and **3** from the reaction of **1-Cl** in this solvent. Nucleophile selectivities k_{az}/k_{HOH}

Table 2. Yields of the Products of the Spontaneous Reactions of **1-X** and the Acid-Catalyzed Reactions of **1-OH** and **2** in Mixed Alcohol/Water Solvents at 25 °C and $I = 0.50$ ($NaClO_4$)

solvent	substrate	yield of product (%)[a]				
		1-OH	**1-OCH$_2$CF$_3$**	**1-OMe**	**2**	**3**
TFE/H_2O 50:50 (v/v)	**1-Cl**	50	12		13	26
	1-O$_2$CC$_6$F$_5$[b]	35	9.3		30	26
	1-OH[c]		58		13	29
	2[d]	87	10			3.4
MeOH/H_2O 50:50 (v/v)	**1-Cl**	54		21	7.2	18
	1-OH[c]			66	13	21
	2[d]	64		32		3.9
MeOH/TFE/H_2O 5:45:50 (v/v/v)	**1-Cl**	51	9.8	2.7	14	23
	1-OH[c]		47	12	15	27
	2[d]	83	7.7	6.1		3.5
TFE/H_2O 20:80 (v/v)	**1-Cl**	74	3.3		6.8	15
	1-OH[c]		24		22	54
	2[d]	95	2.6			2.7
MeOH/TFE/H_2O 2:18:80 (v/v/v)	**1-Cl**	75	2.2	0.88	6.9	15
	1-OH[c]		24	8.6	20	48
	2[d]	94	1.8	1.4		2.6

[a] Product yields were determined by HPLC analysis at 278 nm and are given to two significant figures. [b] Product yields determined during the first 2% of the reaction. [c] Acid-catalyzed reaction in the presence of 0.50 M $HClO_4$. These yields were determined by short extrapolations to zero time of plots of product yield against time during appearance of up to 3% total products. [d] Acid-catalyzed reaction in the presence of 0.50 M $HClO_4$. Product yields were determined during the first three halftimes of the reaction.

Scheme 2



determined in these experiments fall within the broad range of values reported for the reactions of *tert*-butyl derivatives.[25]

The first-order rate constant for the reaction of **1-O$_2$CC$_6$F$_5$** at 25 °C in 50:50 (v/v) TFE/H_2O ($I = 0.50$, $NaClO_4$), determined by following the formation of products during the first 2% of reaction, is $k_{obsd} = 7.1 \times 10^{-8}$ s^{-1}. There is no detectable change in k_{obsd} (±5%) for this reaction when the concentration of N_3^- is increased from zero to 0.50 M, and the yields of the alkenes **2** and **3** are also independent of the concentration of N_3^-. Rate constant ratios for partitioning of **1-O$_2$CC$_6$F$_5$** between reaction with N_3^- and solvent, calculated from the product yields using either eq 3 or 4, are reported in Table 1.

Table 2 gives the yields, determined by HPLC analysis, of the products of the spontaneous solvolysis and elimination reactions of **1-Cl** and **1-O$_2$CC$_6$F$_5$** in several mixed alcohol/water solvents. Rate constant ratios for partitioning of **1-X** between nucleophilic substitution and elimination (Scheme 2A), calculated from the product yields in Table 2, are given in Table 3.

The variation with time of the yields of the products of the acid-catalyzed reaction of **1-OH**, determined during the appearance of up to 3% total products, at 25 °C in 50:50 (v/v) TFE/H_2O containing 0.50 M $HClO_4$ is shown in Table 1S of the Supporting Information. The small changes in the apparent product yields over time are due to the acid-catalyzed reaction of **2**. Table 2 gives the initial yields of the products that were determined by a linear extrapolation of product yields to zero time. The absolute difference between the yields of **2** (11%) and **1-OCH$_2$CF$_3$** (60%) observed at early reaction times and their yields determined by extrapolation of the data to zero time (Table 2) is only 2−3%. A similar procedure was used to determine the initial yields of the products of the acid-catalyzed reactions of **1-OH** in other mixed alcohol/H_2O solvents (Table 2). Rate constant ratios for partitioning of **1-OH** between nucleophilic substitution and elimination (Scheme 2A), calculated from the product yields in Table 2, are given in Table 3.

The change in the observed yields of the products of the acid-catalyzed reaction of **2** at 25 °C in 50:50 (v/v) TFE/H_2O containing 0.50 M $HClO_4$ is ≤10% during the first three halftimes of the reaction (Table 1S, Supporting Information). The yields of the products of the reaction of **2** in several mixed alcohol/H_2O solvents are given in Table 2. Rate constant ratios for partitioning of **2** between nucleophilic addition of solvent and isomerization (Scheme 2B), calculated from the product yields in Table 2, are given in Table 3.

The first-order rate constant for the acid-catalyzed conversion of **1-OH** to **1-OCH$_2$CF$_3$**, determined under initial velocity conditions, at 25 °C in 50:50 (v/v) TFE/H_2O containing 0.50 M $HClO_4$ is $k_h = 1.5 \times 10^{-7}$ s^{-1}. This can be converted to the second-order rate constant for the acid-catalyzed cleavage of **1-OH** to give the carbocation **1**$^+$, $k_H = 1.8 \times 10^{-6}$ M^{-1} s^{-1}, using eq 5 ([H$^+$] = 0.50 M) and 6, which were derived for the

$$k_H = \frac{k_h(1/f_p)}{0.50\ \mathrm{M}} \tag{5}$$

$$1/f_p = 1 + \frac{k_{HOH}[\mathrm{HOH}]}{k_{TFE}[\mathrm{TFE}]} + \frac{k_2}{k_{TFE}[\mathrm{TFE}]} + \frac{k_3}{k_{TFE}[\mathrm{TFE}]} \tag{6}$$

Table 3. Product Rate Constant Ratios for the Spontaneous Reactions of **1-X** and the Acid-Catalyzed Reactions of **1-OH** and **2** in Mixed Alcohol/Water Solvents at 25 °C and $I = 0.50$ ($NaClO_4$) (Scheme 2)

		rate constant ratio[a]							
solvent	substrate	k_{HOH}/k_{MeOH}[b]	k_{HOH}/k_{TFE}[b]	k_{MeOH}/k_{TFE}[b]	k_2/k_{TFE} (M)	k_2/k_{MeOH} (M)	k_3/k_{TFE} (M)	k_3/k_{MeOH} (M)	k_3/k_2[c]
TFE/H_2O 50:50 (v/v)	**1-Cl**		1.1		7.6		15		2.0
	1-O₂CC₆F₅		0.92		22		19		0.89
	1-OH[d]				1.6		3.4		2.1
	2[d]		2.1				2.3		
$MeOH/H_2O$ 50:50 (v/v)	**1-Cl**	1.1				4.2		10	2.4
	1-OH[d]					2.3		4.0	1.7
	2[d]	0.90						1.5	
$MeOH/TFE/H_2O$ 5:45:50 (v/v/v)	**1-Cl**	0.83	1.2	1.4	8.6	6.2	15	11	1.7
	1-OH[d]			1.2	1.9	1.6	3.5	2.8	1.8
	2[d]	0.60	2.4	4.0			2.8	0.70	
TFE/H_2O 20:80 (v/v)	**1-Cl**		1.4		5.6		13		2.3
	1-OH[d]				2.6		6.3		2.4
	2[d]		2.2				2.8		
$MeOH/TFE/H_2O$ 2:18:80 (v/v/v)	**1-Cl**	0.94	1.9	2.0	7.7	3.9	17	8.7	2.2
	1-OH[d]			1.8	2.0	1.1	4.8	2.7	2.4
	2[d]	0.74	2.9	3.9			3.5	0.91	

[a] Calculated from the product yields in Table 2. Rate constants are defined in Scheme 2. [b] Dimensionless ratio of second-order rate constants, calculated using eq 3. [c] Dimensionless ratio of first-order rate constants, calculated as the ratio of the yields of **3** and **2** (Table 2). [d] Acid-catalyzed reaction in the presence of 0.50 M $HClO_4$.

Scheme 3

$$\textbf{1-OH} \underset{k_{HOH}[HOH]}{\overset{k_H[H^+]}{\rightleftharpoons}} \textbf{1}^+ \xrightarrow{k_{TFE}[TFE] + k_2 + k_3} \textbf{1-OCH}_2\textbf{CF}_3 + \textbf{2} + \textbf{3}$$

mechanism shown in Scheme 3. A value of $f_p = 0.17$ for the fractional yield of **1-OCH₂CF₃** from partitioning of $\mathbf{1}^+$ was estimated from the relative yields of **1-OCH₂CF₃**, **2**, and **3** from the reaction of **1-OH** and with the assumption that the rate constant ratio for partitioning of the intermediate of the acid-catalyzed reaction of **1-OH** between reaction with water and trifluoroethanol is equal to $k_{HOH}/k_{TFE} = 1.1$ determined for the spontaneous reaction of **1-Cl** (Table 3).[31] By comparison, a value of $k_H = 4 \times 10^{-6}$ M^{-1} s^{-1} has been determined for the acid-catalyzed cleavage of *tert*-butyl alcohol to form the *tert*-butyl carbocation in water.[14]

The first-order rate constant for the disappearance of **2** at 25 °C in 50:50 (v/v) TFE/H_2O containing 0.50 M $HClO_4$ is $k_h = 4.0 \times 10^{-5}$ s^{-1}. This can be converted to the second-order rate constant for the protonation of **2** to give $\mathbf{1}^+$, $k_H = 8.1 \times 10^{-5}$ M^{-1} s^{-1}, using eq 5 with $f_p = (1.0 - 0.016) = 0.984$, where 0.016 is the fraction of the carbocation intermediate $\mathbf{1}^+$ that partitions to reform **2**. This fraction was calculated from the yield of 3.4% of **3** from the acid-catalyzed reaction of **2** (Table 2) and the rate constant ratio $k_3/k_2 = 2.1$ for the formation of **3** and **2** from the acid-catalyzed reaction of **1-OH** in 50:50 (v/v) TFE/H_2O (Table 3).

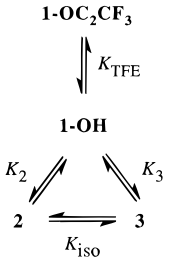
The reaction of **1-OH** or of **2** for 6 days at 25 °C in 50:50 (v/v) TFE/H_2O containing 1.0 M $HClO_4$ leads to the formation of the *same* (±5% in the yield of the individual products) equilibrium mixture of **1-OH**, **1-OCH₂CF₃**, **2**, and **3** (Scheme 4). Table 4 gives the equilibrium constants for the acid-catalyzed interconversion of **1-OH**, **1-OCH₂CF₃**, **2**, and **3** shown in Scheme 4 that were calculated from the relative concentrations of these species at chemical equilibrium. The value of $K_2 = 1.1 \times 10^{-3}$ for the interconversion of **1-OH** and **2** in 50:50 (v/v) TFE/H_2O (Table 4) is larger than the $K = 1.3 \times 10^{-4}$ values reported for the dehydration of *tert*-butyl alcohol to give methylpropene in water.[32]

Table 4. Equilibrium Constants for Interconversion of the Products of the Acid-Catalyzed Reactions of **1-OH** and **2** at 25 °C in 50:50 (v/v) Trifluoroethanol/Water (Scheme 4)[a]

equilibrium constant[b]	
K_{TFE}[c]	0.11
K_2[d]	1.1×10^{-3}
K_3[d]	1.1×10^{-2}
K_{iso}[e]	10
$f_{alk} = 0.011$[f]	$f_{RSolv} = 0.989$[g]

[a] Equilibria were established in solutions that contained 1.0 M $HClO_4$. The reactions of **1-OH** and **2** lead to the same equilibrium mixture of products. [b] The equilibrium constants are defined in Scheme 4. [c] Ratio of the concentrations of **1-OCH₂CF₃** and **1-OH** at equilibrium. [d] Ratio of the concentrations of the respective alkene and the solvent adduct **1-OH** at equilibrium. [e] Ratio of the concentrations of the trisubstituted alkene **3** and the disubstituted alkene **2** at equilibrium. [f] The total fraction of the alkenes **2** and **3** at equilibrium. [g] The total fraction of the solvent adducts **1-OH** and **1-OCH₂CF₃** at equilibrium.

Scheme 4



Discussion

The addition of a β-(4-methoxybenzyl) group to *tert*-butyl chloride to give **1-Cl** leads to a small decrease in the first-order rate constant for reaction at 25 °C in 50:50 (v/v) TFE/H_2O ($I = 0$), from $k_{obsd} = 9 \times 10^{-4}$ s^{-1} for *tert*-butyl chloride[33] to 2.1×10^{-4} s^{-1} for **1-Cl** (Results), which can be attributed to the polar effect of the electron-withdrawing 4-methoxybenzyl group. There is no nucleophilic assistance to the ionization of **1-Cl** by

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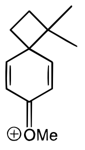
(31) The very weak Brønsted base Cl^- should have little or no effect on the relative reactivity of water and trifluoroethanol toward the carbocation intermediate $\mathbf{1}^+$ of these reactions.

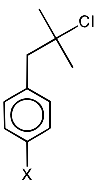
(32) Eberz, W. F.; Lucas, H. J. *J. Am. Chem. Soc.* **1934**, *56*, 1230–1234.

(33) Estimated by linear interpolation from $k_{obsd} = 7.3 \times 10^{-4}$ and 1.6×10^{-3} s^{-1} for reaction of *tert*-butyl chloride in TFE/H_2O ($I = 0$) containing 40 wt % and 50 wt % water, respectively,[34] to 50:50 (v/v) TFE/H_2O, which contains 42 wt % water.

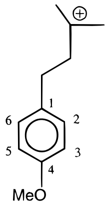
the 4-methoxyphenyl group to form the arenium ion **4**, because no nucleophilic assistance by formation of a phenonium ion was observed in earlier studies of the reaction of **MeO-5**,[35] and intramolecular nucleophilic displacement to form four-membered rings is typically 10^2-10^3-fold slower than the corresponding displacement reactions to form three-membered rings.[36] The concentrations of $\mathbf{1}^+$ and the arenium ion **4** at chemical equilibrium depend on the balance between the stabilization of $\mathbf{1}^+$ obtained from intramolecular addition of the 4-methoxyphenyl group to the tertiary carbocation and the *ca*. 26 kcal/mol of strain energy in the four-membered ring of **4**.[37] However, the stabilization obtained from addition of the 4-methoxyphenyl group to the tertiary cationic center must be significantly smaller than 26 kcal/mol, because the addition of water to $\mathbf{1}^+$ form the *neutral* alcohol **1-OH**, which is thermodynamically more stable than **4**, is favored by only by 23 kcal/mol.[38] Similar arguments exclude the more unlikely possibility of participation by C-1 of the 4-methoxyphenyl ring as a Brønsted base in intramolecular deprotonation of $\mathbf{1}^+$ to form alkenes.[39] We conclude that there is no internal nucleophilic assistance to the ionization of **1-Cl** to form $\mathbf{1}^+$, and that this carbocation exists essentially exclusively in the open form as a simple tertiary carbocation.



4



X-5



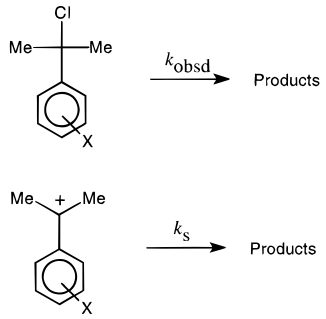
$\mathbf{1}^+$

Estimated Rate Constants for Reactions of Tertiary Carbocations. The rate constants k_s (s^{-1}) for reaction of this solvent with a series of ring-substituted cumyl carbocations were determined in previous work, by using the reaction of N_3^- with the carbocation as a "clock" for the slower reaction of solvent.[42b] The extended Hammett relationship established by these data was then extrapolated to give estimated rate constants for the reactions of cumyl carbocations with solvent which were too large to determine using the azide ion clock method.[42a,b] These data establish a linear logarithmic relationship (eq 7) between

$$\log k_s = -0.53 \log k_{obsd} + 10.6 \qquad (7)$$

k_{obsd} (s^{-1}) for reaction of ring-substituted cumyl chlorides in 50:50 (v/v) TFE/H_2O[6] and the values of k_s (s^{-1}) for reaction of the corresponding cumyl carbocations (Scheme 5). The values of k_{obsd} for reaction of **1-Cl** and *tert*-butyl chloride in 50:50 (v/v) TFE/H_2O at $I = 0$ (see Experimental Section) were substituted into eq 7 to give estimated values of $k_s = 3.5 \times 10^{12}$ s^{-1} and 1.6×10^{12} s^{-1} for reaction of $\mathbf{1}^+$ and the *tert*-butyl carbocation, respectively, with this solvent. This estimate of k_s for reaction of the *tert*-butyl carbocation with solvent is *more than 100-fold larger* than the best available literature estimates of this rate constant cited in the introduction.[12,15,16] We prefer the estimate made in this work to the earlier estimates because of the close structural similarity between cumyl chlorides, which were used to establish the linear relationship given by eq 7, and simple tertiary alkyl chlorides. By contrast, one of the earlier estimates of the lifetime of the *tert*-butyl carbocation required extrapolation of a rate-equilibrium relationship established for oxocarbenium ions,[15,16] and the other[12] was based on the extrapolation of a linear logarithmic relationship between equilibrium constants for formation of highly resonance-stabilized triarylmethyl carbocations in water and in the gas phase.[13]

Scheme 5



We are interested in understanding the factors which determine when a kinetic barrier appears for the reaction of carbocations with nucleophilic solvents, and the factors which control the height of that barrier.[43] The data in this work suggest that the requirement for the partial loss of stabilizing hyperconjugative interactions between the β-hydrogens and the cationic center in the transition state for the nucleophilic addition of aqueous solvents to simple tertiary alkyl carbocations does not create a large kinetic barrier to this reaction.

The estimated rate constants for reaction of the *tert*-butyl carbocation and $\mathbf{1}^+$ with solvent, $k_s \approx 10^{12}$ s^{-1}, are larger than both the rate constant for their diffusional encounter with external nucleophilic reagents, $k_T[Nu^-] \approx (5 \times 10^9$ M^{-1} $s^{-1})[Nu^-]$ (Scheme 1),[18,19] and that for reorganization of the local solvation shell by the dielectric relaxation of solvent (k_{reorg}

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[34] Shiner, V. J., Jr.; Dowd, W.; Fisher, R. D.; Hartshorn, S. R.; Kessick, M. A.; Milakofsky, L.; Rapp, M. W. *J. Am. Chem. Soc.* **1969**, *91*, 4838–4843.

[35] The small 1.5-fold difference in k_{obsd} for reaction of **H-5** and **MeO-5** is consistent with only a small inductive effect of the 4-MeO substituent on the reaction, and it shows that there is no significant movement of positive charge from the developing carbocation onto the aromatic ring [Brown, H. C.; Kim, C. J. *J. Am. Chem. Soc.* **1968**, *90*, 2082–2096].

[36] (a) Kirby, A. *Adv. Phys. Org. Chem.* **1980**, 183–278. (b) Knipe, A. C.; Stirling, C. J. M. *J. Chem. Soc. B* **1968**, 67–71. (c) Bird, R.; Knipe, A. C. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1215–1220.

[37] Winnik, M. C. *Chem. Rev.* **1981**, *81*, 491–524.

[38] Calculated from $pK_R = -16.7$ for $\mathbf{1}^+$ which was determined in this work.

[39] There will be no significant intramolecular proton transfer to C-1 of the 4-methoxyphenyl ring in the presence of the fast competing proton transfer and nucleophilic addition reactions of solvent for the following reasons: (i) This site is much more weakly basic than solvent: A pK_a of -6.74 has been determined for protonation of methoxybenzene at oxygen [Arnett, E. M.; Wu, C. Y. *J. Am. Chem. Soc.* **1960**, *82*, 5660–5665], and the pK_a for protonation of C-4 of the aromatic ring must be even more negative than this. (ii) Proton transfer between two carbon atoms is intrinsically slower than proton transfer between carbon and an electronegative atom such as oxygen (see ref 41b, p 166). (iii) The effective molarities for intramolecular proton transfer reactions are generally close to unity,[36a] so that there is no large kinetic advantage to intramolecular deprotonation of $\mathbf{1}^+$.

[40] Saunders, W. H. *J. Am. Chem. Soc.* **1994**, *116*, 5400–5404.

[41] (a) Kresge, A. J. *Acc. Chem. Res.* **1975**, *8*, 354–360. (b) Bernasconi, C. F. *Adv. Phys. Org. Chem.* **1992**, *27*, 119–238.

[42] (a) Richard, J. P.; Amyes, T. L.; Vontor, T. *J. Am. Chem. Soc.* **1991**, *113*, 5871–5873. (b) The azide "clock" assumes a value of $k_{az} = 5 \times 10^9$ M^{-1} s^{-1} for diffusion-limited trapping of carbocations by N_3^-. This assumption has been verified by direct measurement of second-order rate constants for the diffusion-limited reaction of N_3^- with triarylmethyl,[18] diarylmethyl,[18] and α-substituted 4-methoxybenzyl[19] carbocations. The rate constants for these diffusion-limited reactions range from 5×10^9 to 7×10^9 M^{-1} s^{-1}, which sets an error limit of ≤40% for the value of k_s calculated from the N_3^- selectivity k_{az}/k_s (M^{-1}). (c) This relationship has been determined using the following data, where X indicates the benzene ring substituent(s) (Scheme 5): X = 3-F, $\log k_{obsd} = -0.92$, $\log k_s = 11.1$; X = 4-NO_2, $\log k_{obsd} = -3.63$, $\log k_s = 12.3$; X = 3,5-(CF_3), $\log k_{obsd} = -4.50$, $\log k_s = 13.1$.

[43] Richard, J. P. *Tetrahedron* **1995**, *51*, 1535–1573.

$\approx 10^{11}$ s^{-1}).[44] They suggest that the ion pair or ion molecule intermediates of the reactions of simple tertiary derivatives undergo direct reaction with a molecule of solvent within the solvation shell that is present at the time of their formation, with $k_s' \approx k_s = k_{reorg}$,[56] and that there is no significant chemical reaction between these intermediates and *bulk* solvent, because $k_s' > k_{-d} \approx 10^{10}$ s^{-1}.

Chloride ion is approximately 100-fold more reactive than water toward stable carbocations ($k_{Cl}/k_s \approx 100$ M^{-1}),[45,46] so that the *chemical* barrier to collapse of a contact ion pair between Cl^- and **1**$^+$, in which the Cl^- is correctly aligned to allow reaction to give **1-Cl**, should be even smaller than the barrier to the reaction of solvent with the carbocation. Therefore, the *rate constant* for the reaction of Cl^- within the ion pair **1**$^+$**·Cl**$^-$ will lie close to the vibrational limit of 10^{13} s^{-1}, so that this ion pair may not exist as an intermediate in a potential well for the time of even one bond vibration ($\approx 10^{-13}$ s).[23] By comparison, Abraham has estimated a barrier of $\Delta G^\ddagger = 5 \pm 5$ kcal/mol for collapse of the contact ion pair between Cl^- and the *tert*-butyl carbocation to give *tert*-butyl chloride.[47] The results reported here suggest that the barrier to collapse of the contact ion pair **1**$^+$**·Cl**$^-$ to give **1-Cl** is much smaller than 5 kcal/mol. For example, the Eyring equation [$\ln k = \ln (k_BT/h) - (\Delta G^\ddagger/RT)$] predicts a barrier of $\Delta G^\ddagger = 1.1$ kcal/mol for a reaction with a rate constant of 10^{12} s^{-1} at 25 °C.

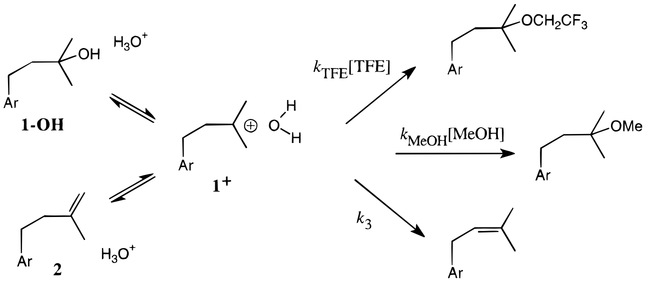
Estimated Equilibrium Constants for Formation of Tertiary Carbocations. The estimated rate constant for conversion of an ion−molecule pair between **1**$^+$ and solvent, in which the solvent molecule is orientated to allow its reaction with **1**$^+$ to give the solvent adduct, is $k_s \approx 10^{12}$ s^{-1} (see above). Therefore, the rate-limiting step for reaction of **1**$^+$ with a molecule of water within the solvation shell which surrounds this carbocation at the time of its formation as an intermediate in the acid-catalyzed reaction of **1-OH** (Scheme 3) must be the rotation of a water molecule into a reactive orientation, with a rate constant similar to that for the dielectric relaxation of water ($k_s = k_{reorg} \approx 10^{11}$ s^{-1}).[44] This value of $k_s = k_{HOH}[HOH] = 1 \times 10^{11}$ s^{-1} and $k_H = 1.8 \times 10^{-6}$ M^{-1} s^{-1} for the acid-catalyzed cleavage of **1-OH** were substituted into eq 8 that was derived for Scheme 3, to give an estimated value of $pK_R = -16.7$ for the simple tertiary carbocation **1**$^+$ in 50:50 (v/v) TFE/H_2O. Similarly, the value

$$pK_R = \log (k_H/k_{HOH}[HOH]) \qquad (8)$$

of $k_s = k_{HOH}[HOH] = 1 \times 10^{11}$ s^{-1} and $k_H = 4.0 \times 10^{-6}$ M^{-1} s^{-1} for the acid-catalyzed exchange of ^{18}O from $H_2{}^{18}O$ into *tert*-butyl alcohol[14] gives $pK_R = -16.4$ for the *tert*-butyl carbocation in water. This is more negative than the earlier estimates of $pK_R = -15$[13] and -15.5[48] for the *tert*-butyl carbocation, which were obtained by extrapolation of linear free energy correlations between data for reactions in the gas phase[13] or organic solvents[48] and H_2O.

Acid-Catalyzed Reactions of 1-OH and 2. One of the goals of this work was to determine rate constant ratios for the partitioning of **1**$^+$ which were free of the effects of the presence of an anionic leaving group in an ion pair reaction intermediate. In principle, this can be accomplished by determining the product distributions of the acid-catalyzed reactions of **1-OH** or **2** in aqueous solvents, because these reactions are expected to proceed through tertiary carbocation intermediates that are virtually identical (**1**$^+$, Scheme 6).

Scheme 6



The data in Table 2 show that the reactions of **1-OH** and **2** in several mixed alcohol/water solvents give different *relative* yields of the solvolysis and elimination reaction products. Since the major fate of **1**$^+$ generated from the acid-catalyzed cleavage of **1-OH** is its "invisible" reaction with water to regenerate **1-OH** (Scheme 3), these differences are best illustrated as differences in the product rate constant ratios k_3/k_{TFE} (M), k_3/k_{MeOH} (M), and k_{MeOH}/k_{TFE} given in Table 3. These data require the following: (a) that **1-OH** and **2** do not undergo exclusive reaction through a common, identical, reaction intermediate **1**$^+$, and (b) that the rate constant ratios for partitioning of **1**$^+$ in nucleophilic solvents cannot be easily determined from these product studies.

This failure, in very favorable circumstances, to observe acid-catalyzed reactions of **1-OH** and **2** through a common tertiary carbocation intermediate **1**$^+$ emphasizes the fleeting lifetime of such carbocations, and the resulting difficulties in the determination of the distribution of the products of their reaction in aqueous solution. The observed differences in the relative yields of the products from the acid-catalyzed reactions of **1-OH** and **2** might be explained by the following:

(1) There may be differences in the composition and reactivity of the solvation shell which surrounds **1**$^+$ at the time of its formation from the respective substrates (Scheme 6). However, the data in Table 3 require that such differences be maintained even in 20:80 (v/v) TFE/H_2O and 2:18:80 (v/v/v) MeOH/TFE/H_2O (Table 3) which contain 94 mol % water.

(2) Acid-catalyzed nucleophilic substitution of solvent at **1-OH** proceeds by partitioning of the nonselective carbocation **1**$^+$, because *tertiary* aliphatic carbon is extremely resistant to concerted nucleophilic substitution. A significant fraction of the reaction of the acid-catalyzed addition of solvent to **2** may occur by a concerted reaction mechanism, because of the greater steric ease of concerted nucleophilic addition of solvent at the planar sp^2 carbon of **2** than at the tertiary carbon of **1-OH.** The larger nucleophilic selectivity $k_{MeOH}/k_{TFE} = 4$ for the acid-catalyzed reaction of **2** in 5:45:50 (v/v/v) MeOH/TFE/H_2O compared to the acid-catalyzed reaction of **1-OH** for which $k_{MeOH}/k_{TFE} = 1.2$ (Table 3) shows that the former reaction proceeds through a transition state in which the bonding to the incoming nucleophile is stronger than for addition of solvent to the nonselective carbocation **1**$^+$. This is consistent with stabilization of the transition state by the incoming nucleophile, whose addition to **2** is concerted with proton transfer to carbon.

Reactions of 1-X in the Presence of Nucleophilic Reagents. (a) Chloride Ion. The kinetic data for the reaction of **1-Cl** in the presence of increasing concentrations of Cl^- serve to illustrate the difficulty in distinguishing chloride common ion and induced common ion inhibition[49] of solvolysis from specific Cl^- salt effects.

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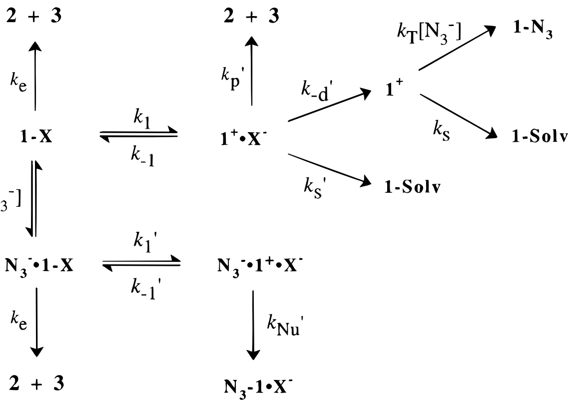
Figure 1 (●) shows that the addition of 0.50 M Cl^- leads to no detectable common ion inhibition of the reaction of **1-Cl** in 50:50 (v/v) MeOH/H_2O ($I = 0.50$, $NaClO_4$). However, the replacement of 0.50 M sodium perchlorate with 0.50 M sodium chloride results in a 30% decrease in k_{obsd} for reaction of this substrate in 50:50 (v/v) TFE/H_2O (Figure 1, ■). By contrast, when sodium chloride is the only salt present, k_{obsd} for reaction of **1-Cl** in this solvent remains constant ($k_{obsd} = 2.1 \times 10^{-4}$ s^{-1}) when the concentration of this salt is increased from 0 to 0.50 M. The decreases in k_{obsd} that are observed when perchlorate ion is replaced by Cl^- in 50:50 (v/v) TFE/H_2O (Figure 1, ■) might be attributed to perchlorate-ion-induced common ion inhibition of the reaction of **1-Cl**.[49] However, these decreases are more likely due to differences in the *specific* perchlorate and halide ion salt effects on k_{obsd}, for the following reasons: (a) Sodium bromide and sodium chloride lead to similar decreases in k_{obsd} for reaction of **1-Cl** at constant ionic strength of 0.50 maintained with sodium perchlorate (Figure 1).[50] (b) There are only low yields of the azide ion adduct **1-N$_3$** from the trapping of 1^+ by the good nucleophile N_3^- (below), so that there should be little or no common ion inhibition of the reaction of **1-Cl** from trapping of 1^+ by Cl^-, which is more weakly nucleophilic than N_3^-.

(b) Lyoxide Ion. Figure 2 shows that there is no change in the product distribution of the reaction of **1-Cl** in 50:50 (v/v) MeOH/H_2O when the concentration of lyoxide ion is increased from 0 to 0.50 M ($I = 0.50$, $NaClO_4$), but that there is an accompanying 23% decrease in k_{obsd} for this reaction (Figure 2, ◆), which can be attributed to a specific lyoxide ion salt effect. An increase from 0 to 0.75 M sodium hydroxide also has no effect on the relative yields of the solvolysis and elimination products of the reaction of 2-chloro-2-methyl-1-phenylpropane (**H-5**) in 25% acetonitrile in water.[51]

General base catalysts and lyoxide ion often cause an increase in the fractional yield of alkene from the partitioning of α-methylbenzyl carbocations between loss of a proton and capture by solvent, because these bases provide stronger catalysis of the deprotonation of the carbocation than of the nucleophilic addition of solvent.[52−55] By contrast, lyoxide ion leads to no detectable change in the total yields of 25% of the alkenes **2** and **3** and 75% of the solvent adducts **1-OH** and **1-OMe** from the reaction of **1-Cl** in 50:50 (v/v) MeOH/H_2O (Table 2 and Figure 2). This does not result from catalysis by lyoxide ion of both the deprotonation of 1^+ *and* its capture by solvent, because the addition of 0.25 M lyoxide ion also has no effect on the product distribution of the reaction of **1-Cl** in the presence of 0.25 M N_3^- in this solvent (Results), for which the 7.2% yield of the azide ion adduct **1-N$_3$** is formed at the expense of only the solvent adducts. We conclude that the reactions of the carbocation 1^+ are so fast that it undergoes no detectable competing bimolecular reaction with lyoxide ion.

(c) Azide Ion. Figure 3 (◆) shows that there is a 10% increase in k_{obsd} for the reaction of **1-Cl** in 50:50 (v/v) MeOH/H_2O ($I = 0.50$, $NaClO_4$) when the concentration of N_3^- is increased from 0 to 0.50 M. This is accompanied by the formation of 13% of the azide ion adduct **1-N$_3$** at the expense of the solvent adducts, but there is no change in the total yield of 25% of the alkenes **2** and **3** (Figure 3). We attribute the very small (<0.1 kcal/mol) stabilization of the transition state for the reaction of **1-Cl** by 0.50 M N_3^- to either a specific N_3^- salt effect or to a very weak bimolecular reaction of N_3^- with **1-Cl**. The absence of any detectable increase in k_{obsd} for the reaction of **1-O$_2$CC$_6$F$_5$** in 50:50 (v/v) TFE/H_2O when the concentration of N_3^- is increased from 0 to 0.50 M (Results) shows that there is also no significant bimolecular nucleophilic substitution reaction of N_3^- with this substrate. Rate constant ratios for the reaction of **1-Cl** and **1-O$_2$CC$_6$F$_5$** with N_3^- and solvent, calculated from the yields of the N_3^- and solvent adducts using eq 3 or eq 4, are reported in Table 1. The dimensionless selectivities k_{az}/k_{HOH} for the reaction of **1-X** in mixed alcohol/water solvents (Table 1) are close to $k_{az}/k_{HOH} = 19$ determined for the reaction of **H-5** in 25% acetonitrile in water.[51]

Scheme 7



We now consider the detailed mechanism for the formation of the small amounts of the azide ion adduct **1-N$_3$** from the reactions of **1-Cl** and **1-O$_2$CC$_6$F$_5$** (Table 1). The yield of **1-N$_3$** from the diffusion-controlled trapping of the ion pair **1^+·X^-** to give the triple ion complex **N_3^-·1^+·X^-** ($k_d[Nu^-]$, Scheme 1) is negligible even at the highest concentration of N_3^- used in our experiments, because the first-order rate constant for this reaction, $k_d[N_3^-] \approx (5 \times 10^9\ M^{-1}\ s^{-1})\ (0.50\ M)$,[18,19,42c] is much smaller than the estimated rate constant $k_s' \approx k_s = 10^{11}\ s^{-1}$ for the direct reaction of solvent with the ion pair (see above). Therefore, the possibility of diffusional encounter of the ion pair **1^+·X^-** with N_3^- to give the triple ion complex **N_3^-·1^+·X^-** has been omitted from Scheme 7.[30,56] The remaining possibilities are that **1-N$_3$** is formed either by trapping of the free carbocation **1^+** (k_1, k_{-d}' and $k_T[N_3^-]$, Scheme 7), or by a preassociation mechanism through the association complex **N_3^-·1-X** (K_{as}, k_1', and k_{Nu}', Scheme 7).[23,42,57] The following observations are consistent with the conclusion that the ion pair intermediates **1^+·X^-** of the reactions of **1-X** are so reactive that they undergo little or no diffusional separation to the free carbocation ($k_s' > k_{-d}'$, Scheme 7), so that most or all of the observed azide ion adduct *must* be formed by a preassociation mechanism.[23]

(1) There is no decrease in the product rate constant ratio k_{az}/k_s (M^{-1}) for the reaction of **1-Cl** when the nucleophilicity

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[50] **1-Br** is too reactive to accumulate during the reaction of **1-Cl** in the presence of NaBr because k_{obsd} values for reaction of *tert*-butyl bromide in mixed aqueous/organic solvents are *ca*. 40-fold larger than those for reaction of *tert*-butyl chloride under the same conditions [Harris, J. M.; Mount, D. L.; Smith, M. R.; Neal, W. C., Jr.; Dukes, M. D.; Raber, D. J. *J. Am. Chem. Soc.* **1978**, *100*, 8147−8155].

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[57] There should be no significant formation of the solvent adducts from reaction of the triple ion complex **N_3^-·1^+·X^-**, because the chemical reactivity of N_3^- within this complex is much greater than that of the surrounding solvent molecules.

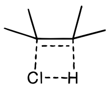
of the solvent is increased by replacing TFE in 50:50 (v/v) TFE/H_2O by methanol (Table 1). This is inconsistent with the formation of **1-N$_3$** and **1-Solv** by trapping of a diffusionally-equilibrated carbocation intermediate, because an increase in the nucleophilicity of the solvent would lead to an increase in the rate constant for the activation-limited reaction of solvent (k_s), but to little or no change in k_T for the diffusion-limited reaction of N_3^-, resulting in an overall decrease in the observed azide ion selectivity k_{az}/k_s (M^{-1}). For example, there is a large decrease from $k_{az}/k_s = 105$ to 10 M^{-1} for reaction of the 1-(4-methoxyphenyl)ethyl carbocation when the solvent is changed from 50:50 (v/v) TFE/H_2O to 50:50 (v/v) MeOH/H_2O.[20] The almost identical product rate constant ratios k_{az}/k_s (M^{-1}) for the reaction of **1-Cl** in these solvents (Table 1) strongly suggest that the yield of the azide ion adduct is determined by the magnitude of the association constant K_{as} (M^{-1}) for formation of the preassociation complex between N_3^- and the substrate (**N_3^-·1-Cl**).

(2) The dimensionless selectivities k_{MeOH}/k_{TFE} for partitioning of 1-arylethyl carbocations between reaction with methanol and trifluorethanol in 5:45:50 (v/v/v) MeOH/TFE/H_2O exhibit a large dependence on the stability of the carbocation when the carbocations are solvent-equilibrated species, but they decrease sharply to a limiting value of $k_{MeOH}/k_{TFE} \leq 3.0$ when the carbocation is so unstable that it reacts directly with the surrounding solvent pool.[42,52] Therefore, the small values of $k_{MeOH}/k_{TFE} \leq 2.0$ for the reactions of **1-Cl** in 5:45:50 (v/v/v) and 2:18:80 (v/v/v) MeOH/TFE/H_2O (Table 3) are consistent with the partitioning of a short-lived ion pair intermediate between reaction with methanol and trifluoroethanol within the small pool of surrounding solvent molecules.[42,52]

The rate constant for reaction of the free carbocation **1$^+$** with a solvent of 50:50 (v/v) TFE/H_2O cannot be calculated directly from the product azide ion selectivity $k_{az}/k_s = 0.38$ M^{-1} for the reaction of **1-Cl** by using the diffusion-limited trapping of **1$^+$** by N_3^- ($k_T[N_3^-]$, Scheme 7) as a "clock" for the reaction of solvent,[20,21] because very little of the observed **1-N$_3$** is formed by trapping of the free carbocation **1$^+$**. However, this observed azide ion selectivity *can* be used to estimate a *lower limit* on k_s' for the direct reaction of solvent with the ion pair **1$^+$·Cl$^-$**, provided it is possible to estimate the relative yields of **1-N$_3$** obtained from the trapping and preassociation reaction pathways.[52] The yield of **1-N$_3$** from the reaction of **1-Cl** with N_3^- by a preassociation mechanism depends on the stability of the preassociation complex (K_{as}, Scheme 7) and on the relative rates of ionization of **1-Cl** within this complex (k_1') and of free **1-Cl** (k_1). In the limit that *all* of the azide ion adduct is formed by a preassociation mechanism in which N_3^- provides no assistance to ionization of the substrate ($k_1' = k_1$, Scheme 7), then $k_{az}/k_s = K_{as}$, so that the value of K_{as} for formation of the preassociation complex between N_3^- and the substrate can be determined directly from the yield of the azide ion adduct. Such a value of $K_{as} = k_{az}/k_s = 0.20$ M^{-1} has been estimated for the reaction of (3,5-bis(trifluoromethyl)phenyl)diazomethane in 50:50 (v/v) TFE/H_2O, for which the putative 3,5-bis(trifluoromethyl)-benzyl carbocation intermediate of the stepwise reaction of this substrate is too unstable to undergo diffusion-limited trapping by azide ion.[58] The total yield of 39% of the alkenes **2** and **3** from the reaction of **1-Cl** in 50:50 (v/v) TFE/H_2O (Table 2) is unaffected by the addition of 0.50 M N_3^- (Results). Therefore, at $[N_3^-] = 0.50$ M, the yield of **1-N$_3$** from the reaction of **1-Cl** by a preassociation mechanism with $K_{as} = 0.20$ M^{-1} is expected to be 5.5%, which is only *ca.* 50% of the observed yield of 10.4% **1-N$_3$** under these conditions. This suggests that, at most, only *ca.* 50% of the azide ion adduct can be formed by the diffusion-controlled trapping of the liberated carbocation **1$^+$** ($k_T[N_3^-]$, Scheme 7). In fact, if K_{as} is larger than 0.20 M^{-1}, and/or if N_3^- provides a small amount of assistance to the ionization of **1-Cl** within the complex **N_3^-·1-Cl**, so that $k_1' > k_1$ (Scheme 7), then the preassociation mechanism could account for the formation of *all* of the observed azide ion adduct. In any event, the conclusion that no more than 50% of the observed azide ion adduct **1-N$_3$** can result from trapping of the free carbocation **1$^+$** requires that the diffusional separation of the ion pair **1$^+$·Cl$^-$** to give the free carbocation **1$^+$** be no faster that its direct reaction with solvent, so that $k_s' \geq k_{-d}'$ (Scheme 7). The estimated rate constant for diffusional separation of a carbocation-anion ion pair, $k_{-d} \approx 2 \times 10^{10}$ s^{-1},[52,58] then gives $k_s' \geq 2 \times 10^{10}$ s^{-1}. This lower limit is consistent with the value estimated above of $k_s' \approx k_s = k_{reorg} \approx 1 \times 10^{11}$ s^{-1} for the reaction of **1$^+$** with solvent.

Alkene-Forming Elimination. The yield of 13% of the disubstituted alkene **2** from the elimination of HCl across the methyl groups of **1-Cl** in 50:50 (v/v) TFE/H_2O (Table 2) is similar to the yield of 14% methylpropene from the reaction of *tert*-butyl chloride under similar reaction conditions.[34] However, the total yield of the alkenes **2** and **3** from the reaction of **1-Cl** is somewhat larger than this, because the yield of the thermodynamically favored alkene **3** is two-fold greater than the yield of **2** (Table 2). The large increases in the rate constant ratios k_2/k_{ROH} and k_3/k_{ROH} for partitioning of **1-X** between elimination and solvolysis as the leaving group is changed from water to chloride to pentafluorobenzoate (Table 3) show that the leaving group must be present in the transition state for the product determining step for the reactions of **1-Cl** and **1-O$_2$CC$_6$F$_5$**. The possibility that solvent acts as a Brønsted base to promote a concerted E2 elimination reaction[59,60] of the tertiary chloride **1-Cl** can be excluded, because the much stronger base lyoxide ion does not promote this reaction (Figure 2). We therefore conclude that the leaving group acts as the proton acceptor for the elimination reactions of **1-Cl**, and probably for the reactions of **1-O$_2$CC$_6$F$_5$**.

The alkene-forming elimination reactions of tertiary halides and benzoate esters in polar solvents are generally assumed to proceed by a stepwise mechanism through the carbocation-leaving group ion pair intermediates of the solvolysis reaction (k_p', Scheme 7),[51,53–55,61–63] and the possibility of *concerted unimolecular elimination* through a cyclic transition state such as **6** and **7** is not considered in the interpretation of experimental data for these reactions.[6] However, the mechanism for the elimination reactions of tertiary alkyl derivatives such as **1-Cl** and **1-O$_2$CC$_6$F$_5$** in aqueous solutions deserves very close scrutiny for the following reasons:



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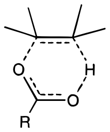

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(1) It is not clear why the partitioning of the **1$^+$·Cl$^-$** ion pair should lead to the formation of significant amounts of an alkene

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product. The reason for this is two-fold: (a) Cl^- is a very weak Brønsted base ($pK_a = -7$ in water);[64] and (b) the alkene products are thermodynamically less stable than the adducts of the carbocation to solvent ($f_{alk} = 0.011$, Table 4).[29]

(2) Increasing concentrations of N_3^- lead to *different* changes in the yields of the solvolysis and elimination reaction products (Figure 3). The constant total yield of the alkenes **2** and **3** from the reactions of **1-Cl** and **1-O$_2$CC$_6$F$_5$** in the presence of increasing concentrations of N_3^- in 50:50 (v/v) MeOH/H_2O and TFE/H_2O (Figure 3 and Results) is inconsistent with the formation of an ionic reaction intermediate which partitions between addition of solvent (k_s', Scheme 7) and loss of a proton (k_p', Scheme 7). These results are consistent with the following mechanistic interpretation: (a) As discussed above, the solvent adducts **1-Solv** are formed primarily from reaction of the free substrate (**1-Cl**) and the azide ion adduct **1-N$_3$** is formed from reaction of the preassociation complex of the substrate with N_3^- (**N$_3^-$·1-Cl**, Scheme 7). (b) The conversion of **1-Cl** to the preassociation complex **N$_3^-$·1-Cl** leads to the formation of **1-N$_3$** at the expense of only **1-Solv**. (c) The yield of the alkenes **2** and **3** is insensitive to the conversion of **1-Cl** into the preassociation complex **N$_3^-$·1-Cl**, because these products are formed by concerted elimination reactions of both free **1-Cl** and **1-Cl** within the preassociation complex **N$_3$·1-Cl**, with the same first-order rate constant (k_e, Scheme 7).[6]

(3) The *rate constant* for the collapse of **1$^+$·Cl$^-$** to **1-Cl** was estimated above to lie close to the vibrational limit of 10^{13} s^{-1} so that this ion pair may not exist as an intermediate in a potential energy well for the time of even one bond vibration ($\approx 10^{-13}$ s).[23] If there is no significant *chemical* barrier to collapse of **1$^+$·Cl$^-$** to neutral reactant, then elimination of HX from **1-X** may proceed by a concerted mechanism which is enforced because the ion pair intermediate of the stepwise reaction is too unstable to exist in an energy well for the time of a bond vibration.[23]

(4) A concerted pathway for elimination of HCl from *tert*-butyl chloride has been identified in a recent quantum mechanical/molecular mechanical coupled potential simulation of the ionic fragmentation of *tert*-butyl chloride in water.[65]

The Question of Solvent Assistance to the Ionization of 1-Cl. The effects of changes in bulk solvent on the rate constants for solvolysis represent the sum of many contributing factors which are extremely difficult to separate and quantify. The rate constants for reaction of *tert*-butyl halides show an apparent larger sensitivity to changes in the nucleophilicity of bulk solvent than those for adamantyl derivatives which react by a limiting unassisted stepwise mechanism.[66-69] These data may correspond to nucleophilic solvent assistance to the ionization of *tert*-butyl chloride to form a nucleophilically "solvated" ion pair intermediate. There is a strong correlation between the nucleophilicity of protic solvents and their Brønsted acidity, so that the data may also be explained by different sensitivities of the reactions of *tert*-butyl and adamantyl derivatives to changes in the acidity of the solvent, with differing degrees of electrophilic "pull" by solvent to the ionization of these substrates.[70-72] Changes in the ground state solvation of the substrate may also contribute to solvent effects on the rate constants for solvolysis,[73-75] and it has been suggested that some apparent relationships between solvolysis rate and solvent nucleophilicity in fact represent correlations of rate with the ground state solvation of a phenyl group.[76]

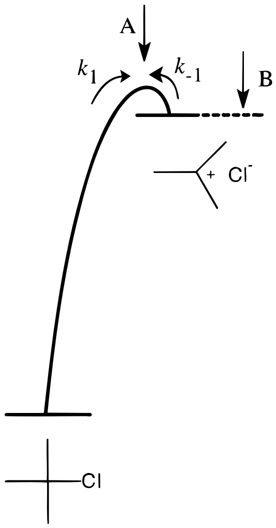

Figure 4. The free energy profile for ionization of a tertiary chloride to give the carbocation−chloride ion pair. A nucleophilic interaction between the tertiary carbocation and solvent may increase the rate of formation of the ion pair by either of the following mechanisms: (A) a decrease in the intrinsic kinetic barrier to the reaction, which will result in equal decreases in the kinetic barriers to both the formation (k_1) and collapse (k_{-1}) of the ion pair; and (B) a decrease in the thermodynamic barrier to the reaction, which will result in a decrease in the kinetic barrier to formation of the ion pair through a late carbocation-like transition state.

The small product rate constant ratios $k_{MeOH}/k_{TFE} = 1.4$ and 2.0 determined for the reaction of **1-Cl** with methanol and trifluoroethanol in 5:45:50 and 2:18:80 (v/v/v) MeOH/TFE/H_2O, respectively, show that the replacement of trifluoroethanol by methanol results in only a small nucleophilic stabilization of the *product-determining* transition state, which is the addition of solvent to the carbocation within the ion pair **1$^+$·Cl$^-$** (see **8A**). There are also only small stabilizations of the transition states for the rate- and product-determining steps of the reaction of **1-Cl** by the very good nucleophile N_3^- (Table 1). This suggests that there also is no assistance to the reaction of this substrate by the much more weakly nucleophilic solvent.[77]

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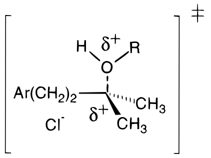
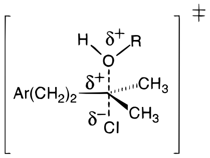


8A



8B

Our results show that tertiary carbocation−chloride ion pairs lie in a shallow potential energy well, with very small barriers to collapse of the carbocation by the addition of solvent or Cl^- ($k_{-1} \geq k_s' \approx 10^{11}$ s^{-1}, Scheme 7 and Figure 4). A nucleophilic interaction with solvent might lead either to a reduction in the "intrinsic" kinetic barrier, which would lead to equal increases in the rate constants for both the formation and collapse of the ion pair (Figure 4, A), or to a net thermodynamic stabilization of the carbocation, which would be expressed primarily as a decrease in the kinetic barrier to formation of the ion pair, which proceeds through a late carbocation-like transition state (Figure 4, B). The former effect cannot be large, because the rate constant for collapse of the tertiary carbocation back to reactants (k_{-1}, Figure 4) is already close to the vibrational limit of 10^{13} s^{-1}.[23] Similarly, it is difficult to understand how there can be a large equilibrium stabilization of the carbocation by a nucleophilic interaction with solvent ("nucleophilic solvation"), because once nucleophilic (i.e., bonding) interactions between these reactants become stabilizing it is simplest that the reactants should continue to products in a strongly exothermic reaction, without passage over an free energy maximum. We know of no theoretical support for the alternative coordinate for a reaction through nucleophilically solvated carbocation reaction intermediate in which partial bond formation between solvent and tertiary carbocation is first stabilizing as the solvated intermediate is formed, then destabilizing with the approach to the transition state for nucleophilic addition of solvent, and again stabilizing after passage over the reaction transition state.

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Supporting Information Available: Details of procedures for the synthesis of the compounds used in this work, and a table showing the change with time in the yields of the products of the perchloric acid-catalyzed reactions of **1-OH** and **2** in 50:50 (v/v) TFE/H_2O (5 pages). See any current masthead page for ordering and Internet access instructions.

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