mode) have γ,δ-C_mH contributions.

Table VI collects our information on the more prominent modes that have C_mH contributions. From the discussion above and the summary in the table, it is clear that normal modes with substantial contributions from C_mH deformations can be divided into three classes: (a) those that are localized to the α,β porphyrin-like part of the molecule, (b) those that are γ,δ localized, and (c) those that are substantially delocalized throughout the macrocycle. In this regard, the C_mH motions echo behavior that occurs for the skeletal motions themselves.

Ethyl Group Vibrations. The IR spectrum of CuOEC shows seven modes at 1464, 1452, 1375, 1064, 1058, 1015, and 956 cm^{-1} that are insensitive to metal substitution, methine deuteration, and a change in peripheral substituents and are therefore assigned to ethyl group vibrations. These modes are not observed in the resonance Raman spectra, except for the 1464-cm^{-1} mode that is present in nearly all of the resonance Raman spectra of the chlorin complexes that we have examined. The chlorin macrocycle does not appear to influence the internal vibrations of the ethyl groups greatly, since the frequencies are all close to the values reported by Kincaid et al.[32] from the IR spectrum of NiOEP in an argon matrix. However, a detailed vibrational analysis, using methylene-deuterated chlorin samples analogous to the OEP-d_{16} samples examined by Spiro and co-workers,[2e] will be necessary to establish this with certainty.

Conclusions

From our analysis of the resonance Raman and IR spectra of the MOEC complexes, we have shown that the vibrational modes of metallochlorins, while retaining many characteristics of metalloporphyrins including core size and peripheral substituent sensitivity, cannot be assigned by direct comparison with the normal modes of metalloporphyrins. The normal-coordinate analysis of NiOEC performed by Boldt et al.,[21] therefore, represents the starting point for the description of the vibrational modes of metallochlorins. In the work presented here, the mode compositions deduced for metallochlorins by metal substitution, methine deuteration, and a change in the peripheral substituents of OEC have been used to test their analysis. The overall agreement is surprisingly good, although some mode assignments need to be modified. Such agreement is gratifying, considering that it is the first normal-coordinate treatment of a metallochlorin and the data we have presented here may be used to refine it.

Abbreviations: DC = deuterochlorin IX dimethyl ester; diol chlorin = *cis*-3′,4′-dihydroxy-2,4-dimethyldeuterochlorin IX dimethyl ester; ECI = etiochlorin I; EPI = etioporphyrin I; Im = imidazole; IR = infrared; lactone chlorin = 5′-hydroxy-6,6′-*trans*-γ-spirolactone-2,4-dimethyldeuterochlorin IX monomethyl ester; $(Me)_7$chlorin = 3′-hydro-4′-methyl-2,4-dimethyldeuterochlorin IX dimethyl ester; OEC = octaethylchlorin, specifically, the trans derivative; OEP = octaethylporphyrin; pPP = photoprotoporphyrin IX dimethyl ester; RR = resonance Raman; TMC = *meso*-tetramethylchlorin; TPC = *meso*-tetraphenylchlorin; TPiBC = *meso*-tetraphenylisobacteriochlorin; TPP = *meso*-tetraphenylporphyrin.

Note Added in Proof. Kushmeider and Spiro (*J. Phys. Chem.*, in press) have recently completed a normal-coordinate analysis of NiOEC. They report the absence of mode localization and a clear correlation between chlorin and porphyrin modes. Their calculated meso-deuterium shifts, however, deviate noticeably from those we report here for CuOEC. Whether these deviations arise from mode-localization effects or from metal dependency in mode composition remains to be established.

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Concurrent Stepwise and Concerted Substitution Reactions of 4-Methoxybenzyl Derivatives and the Lifetime of the 4-Methoxybenzyl Carbocation

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Abstract: The rates of reaction of 4-methoxybenzyl chloride, pentafluorobenzoate, and 3,5-dinitrobenzoate in 50:50 (v/v) trifluoroethanol/water are zero order in the concentration of azide ion. These reactions give good yields of the azide adduct from trapping of the 4-methoxybenzyl carbocation intermediate, and there is also strong common chloride ion inhibition of the reaction of 4-$MeOArCH_2Cl$. The yields of the azide and solvent adducts give the rate constant ratio $k_{az}/k_s = 25\ M^{-1}$, and analysis of the chloride common ion effect gives $k_{Cl}/k_s = 9\ M^{-1}$, for partitioning of the carbocation intermediate. The reaction of azide ion with the carbocation intermediate serves as a diffusion-controlled "clock" ($k_{az} = 5 \times 10^9\ M^{-1}\ s^{-1}$) for the reactions of solvent ($k_s = 2 \times 10^8\ s^{-1}$) and chloride ion ($k_{Cl} = 2 \times 10^9\ M^{-1}\ s^{-1}$). There is a solvent-induced change in mechanism and in the less ionizing solvents of 80:20 (v/v) and 70:30 (v/v) acetone/water; the reaction of azide ion with **1** produces the azide adduct by both trapping of the carbocation intermediate and by a concerted bimolecular substitution reaction.

Introduction

The substitution reactions of benzyl derivatives have been studied for most of this century, and these investigations have been central to the development of the theory of nucleophilic substitution at saturated carbon[1-3] and in the understanding of solvent effects on the mechanism of solvolysis reactions.[4] However, there are many unanswered questions regarding the precise mechanism for solvolysis in partially aqueous solvents, and the mechanism for the substitution reactions of 4-methoxybenzyl derivatives is particularly unclear.

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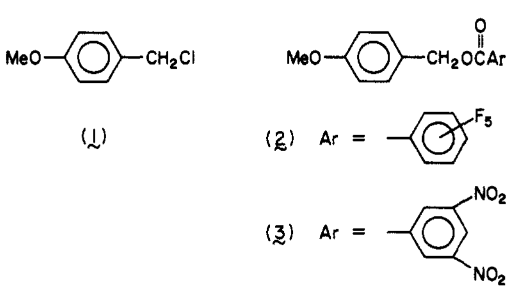
Bimolecular reactions of both anionic and neutral nucleophiles with 4-methoxybenzyl derivatives have been observed in a variety of solvents.[5-12] Kohnstam[13] has published limited data on the reaction of 4-methoxybenzyl chloride (**1**) with sodium azide in 70% acetone/water. However, these experiments were not performed at constant ionic strength, and the interpretation of the results depends on the estimate for the specific salt effect of azide ion. They have been said to be consistent with concurrent S_N1 ($D_N + A_N$)[14] and S_N2 (A_ND_N)[14] reactions,[13] stepwise reaction through an ion pair intermediate,[15] and also with S_N2 displacement alone.[16,17] Although there is evidence from Hammett correlations,[18] α-deuterium isotope,[19a] and solvent[17,20] effects that the transition state for nucleophilic substitution at 4-methoxybenzyl derivatives is carbocation-like, this is *not* sufficient to demonstrate that the reaction in fact proceeds through a carbocation intermediate.[21] For example, concerted bimolecular substitution reactions at acetals[22] and 1-phenylethyl derivatives[23] proceed through transition states which resemble the corresponding carbocations.

In this paper we report experiments, performed at constant ionic strength. on the 4-methoxybenzyl derivatives **1**, **2**, and **3** which settle the question of the mechanism for nucleophilic substitution in acetone/water and trifluoroethanol/water solvents. We also report the lifetime of the 4-methoxybenzyl carbocation in these solvents.



Experimental Section

Materials. 4-Methoxybenzyl chloride, 4-methoxybenzyl alcohol, 3,5-dinitrobenzoyl chloride, pentafluorobenzoyl chloride, triethylamine, 4-(dimethylamino)pyridine, spectroscopic grade acetone, 2,2,2-trifluoroethanol, 1-propanethiol, and sodium azide were purchased from Aldrich. 4-Methoxybenzyl chloride was distilled under reduced pressure and was stored over $CaCO_3$. 1-Propanethiol was distilled under nitrogen. Water was obtained from a Milli-Q purification system. All other chemicals were of reagent grade and were used without further purification.

4-Methoxybenzyl Pentafluorobenzoate (2). 4-Methoxybenzyl alcohol (2.2 g, 16 mmol) and triethylamine (3.3 mL, 24 mmol) were dissolved in dry dichloromethane (80 mL) and cooled to O °C. Pentafluorobenzoyl chloride (5 g, 22 mmol) was added, and the mixture was stirred at room temperature for 3 h. The solution was then washed with 0.5 M HCl (100 mL), 0.1 M NaOH (100 mL), and brine (100 mL), dried ($MgSO_4$), and evaporated to give a yellow solid. This was recrystallized from chloroform/hexane to give the ester (4.3 g, 81%) as plates: mp 98 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 7.37 (2 H, d, J = 9 Hz, Ar), 6.92 (2 H, d, J = 9 Hz, Ar), 5.34 (2 H, s, CH_2), 3.82 (3 H, s, CH_3); MS, found M^+ 332.0473, $C_{15}H_9F_5O_3$ requires 332.0473. Anal. Calcd for $C_{15}H_9F_5O_3$: C, 54.2; H, 2.73. Found: C, 54.2; H, 2.80.

4-Methoxybenzyl 3,5-Dinitrobenzoate (3). 3,5-Dinitrobenzoyl chloride (5.5 g, 24 mmol) was dissolved in dry dichloromethane (60 mL), and to this was added 4-methoxybenzyl alcohol (3 g, 22 mmol), 4-(dimethylamino)pyridine (100 mg, 0.8 mmol), and triethylamine (7 mL, 50 mmol). The mixture was stirred at room temperature under argon for 16 h. The solution was washed with 1 M HCl (100 mL), 1 M NaOH (100 mL), and brine (100 mL), dried ($MgSO_4$), and evaporated to give a brown solid. This was recrystallized from ethyl acetate/hexane to give the ester (4.1 g, 58%) as yellow needles: mp 101-102 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 9.22 (1 H, t, J = 2 Hz, Ar), 9.16 (2 H, d, J = 2 Hz, Ar), 7.43 (2 H, d, J = 9 Hz, Ar), 6.95 (2 H, d, J = 9 Hz, Ar), 5.42 (2 H, s, CH_2), 3.84 (3 H, s, CH_3); MS, found M^+ 332.0642, $C_{15}H_{12}N_2O_7$ requires 332.0645. Anal. Calcd for $C_{15}H_{12}N_2O_7$: C, 54.2; H, 3.64; N, 8.4. Found: C, 54.3; H, 3.67; N, 8.4.

Preparation of Solutions. Solutions of 50:50 (v/v) trifluoroethanol/water at ionic strength 0.50 were prepared as described previously,[24b] except that aqueous solutions that contained NaN_3 were adjusted to pH $\approx$ 7 with concentrated $HClO_4$ before use. The stock solution of 5:45:50 PrSH/TFE[25]/H_2O was prepared by mixing equal volumes of an appropriate aqueous salt solution at ionic strength 1.0 ($NaClO_4$) and a solution of 9:1 (v/v) TFE/PrSH. This stock solution was diluted with known volumes of 50:50 (v/v) TFE/H_2O at ionic strength 0.50, to give solvents consisting of 50% H_2O, $(50 - x)$% TFE, and x% PrSH (v/v/v). Solutions of 80:20 (v/v) and 70:30 (v/v) acetone/water at ionic strength 0.50 were prepared by mixing specified volumes of appropriate aqueous salt solutions and acetone.

Kinetic Methods. Reactions were initiated by making a 100-fold dilution of a solution of the substrate in acetonitrile into the reaction mixture. The solvolysis of 4-methoxybenzyl chloride (2.5 mM) in 50:50 (v/v) trifluoroethanol/water was followed spectrophotometrically by monitoring the decrease in absorbance at 240 nm.

The reaction of 4-methoxybenzyl chloride (0.25–1 mM) in 80:20 (v/v) and 70:30 (v/v) acetone/water was followed spectrophotometrically at 452 nm by monitoring the protonation of 4-nitrophenoxide ion by the hydrochloric acid that is produced during solvolysis. Reaction volumes of 3 mL containing 15 μL of 0.1 M 4-nitrophenol (90% anion in 50% acetone) were used.

Rate constants for the reactions of 4-methoxybenzyl pentafluorobenzoate and 3,5-dinitrobenozate (1 mM) in 50:50 (v/v) trifluoroethanol/water were determined by following the disappearance of the substrate by HPLC, with peak detection at 273 nm. 3-(4-Methoxyphenyl)-1-propanol (1 mM) was used as an injection standard.

In all cases, pseudo-first-order rate constants, k_{obsd}, were obtained from the slopes of linear semilogarithmic plots of reaction progress against time, which covered at least 3 halftimes of the reaction. The values of k_{obsd} were reproducible to within ±5%.

Procedures for Product Studies. Reactions of 4-methoxybenzyl chloride in 2 mL of PrSH/TFE/H_2O containing 50% H_2O at 22 ± 2 °C were initiated by injecting 25 μL of a solution of substrate in acetonitrile to give a final concentration of 1.25 mM. The reactions were analyzed by HPLC after 5–10 min.

Reactions of 4-methoxybenzyl chloride in 80:20 (v/v) and 70:30 (v/v) acetone/water in a volume of 2 mL were initiated by injecting 20 μL of a solution of substrate in acetonitrile to give a final concentration of 1 mM. The solutions were incubated at 25 °C for 10–20 halftimes of the reaction, were then diluted with 2 mL of water, and analyzed by HPLC. Failure to dilute the mixtures with water resulted in very broad peaks.

Studies of the reactions of 4-methoxybenzyl pentafluorobenzoate and 3,5-dinitrobenzoate in 50:50 (v/v) trifluoroethanol/water were conducted

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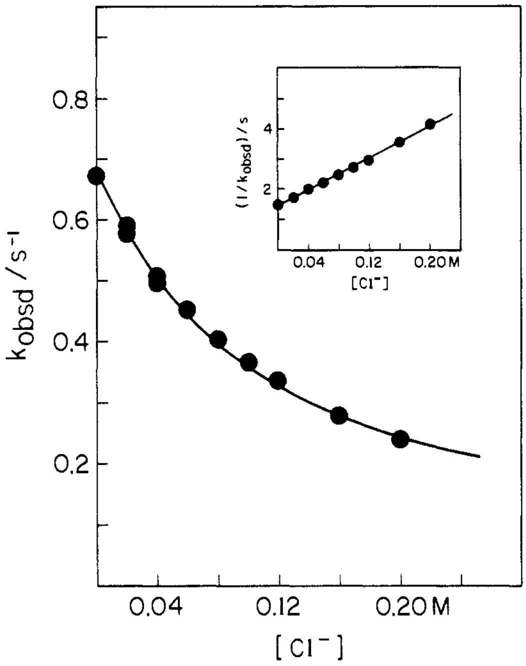

Figure 1. The dependence of k_{obsd} on the concentration of added chloride ion for the solvolysis of 4-methoxybenzyl chloride (**1**) in 50:50 (v/v) TFE/H_2O at 25 °C and ionic strength 0.50 ($NaClO_4$). The inset shows the linear reciprocal plot of the data, according to eq 2 of the text. The curve through the data of the main figure was calculated by using the values of k_{solv} and k_{Cl}/k_s that were obtained from the linear plot by least-squares analysis.

as described for the kinetic methods.

Product Analysis by HPLC. The products were separated by HPLC as described previously[24b,26] and were detected by the UV absorbance of the 4-methoxyphenyl ring at 273 nm.

The solvent and nucleophile substitution products were identified by methods described previously.[24b,26] The extinction coefficients of 4-methoxybenzyl alcohol and trifluoroethyl ether at 273 nm, which is λ_{max} for the alcohol, were assumed to be identical. The extinction coefficients at 273 nm of all other substitution products were shown to be identical with those for the solvent adducts by methods described previously.[24b,26]

Product ratios were determined periodically over several halftimes of the reactions, in order to show that the products were stable to the solvolysis reaction conditions.

Calculation of Product Yields and Rate Constant Ratios. The fractional yields of the individual substitution products were calculated as the HPLC peak area for the adduct divided by the sum of the peak areas for all the solvent and nucleophile adducts. Rate constants ratios were calculated from the peak areas for the azide (RN_3) and solvent (ROS) adducts, by using eq 1. The values of k_{az}/k_s determined in different experiments agreed to within 10%.

$$k_{az}/k_s\ (M^{-1}) = \{\text{area of } RN_3 \text{ peak}\}/\{(\text{total area of ROS peaks}) \times [N_3^-]\} \quad (1)$$

Results

Figure 1 shows that k_{obsd} for the solvolysis of **1** in 50:50 (v/v) trifluoroethanol/water, determined spectrophotometrically by following the disappearance of the substrate, is decreased by a chloride common ion effect. The values of k_{obsd} were fit to eq 2 (Figure 1, inset) which was derived for a stepwise mechanism with a carbocation intermediate (Scheme I). The slope and intercept of this reciprocal plot give $k_{Cl}/k_s = 9\ M^{-1}$.

Scheme I

$$\text{4-MeOArCH}_2\text{Cl} \underset{k_{Cl}[Cl^-]}{\overset{k_{solv}}{\rightleftharpoons}} \text{4-MeOArCH}_2^+ \xrightarrow{k_s} \text{4-MeOArCH}_2\text{OS} + H^+$$

$$1/k_{obsd} = 1/k_{solv} + (k_{Cl}/k_{solv}k_s)[Cl^-] \quad (2)$$

Table I. Rate Constants for Solvolysis and Nucleophilic Selectivities for the Reactions of 4-Methoxybenzyl Derivatives in 50:50 (v/v) Trifluoroethanol/Water[a]

compd	leaving group	k_{solv}, s^{-1}	k_{az}/k_s,[b] M^{-1}	k_{HOH}/k_{TFE}[b,c]
1	chloride	0.67	25[d]	2.0
2	pentafluorobenzoate	2.3×10^{-5}	26[e]	1.7
3	3,5-dinitrobenzoate	1.3×10^{-6}	25[f]	1.7

[a] At 25 °C and ionic strength 0.50 ($NaClO_4$). [b] Obtained from product analysis by HPLC. [c] Determined in the absence of azide ion. [d] Average of values obtained at 0.03, 0.125, and 0.25 M azide ion. [e] Average of values obtained at eight concentrations of azide ion in the range 0.01–0.50 M. [f] Determined at 0.01 M azide ion, where the addition of solvent to the carbonyl group of the substrate is negligible (see text).

Table II. Pseudo-First- and -Second-Order Rate Constants, Yields of Azide Adduct, and Product Rate Constant Ratios for the Reaction of 4-Methoxybenzyl Chloride with Sodium Azide in 80:20 (v/v) and 70:30 (v/v) Acetone/Water[a]

acetone/water	$[N_3^-]$ M	10^4k_{obsd},[b] s^{-1}	10^3k_N, $M^{-1}\ s^{-1}$	$(f_{az})_{rates}$[c]	$(f_{az})_{obsd}$[d]	$(k_{az}/k_s)_{obsd}$,[e] M^{-1}
80:20 (v/v)	0	1.39[f] (0.31)[g]	2.1[h]			
	0.02	1.81		0.23	0.33	24.7
	0.04	2.25		0.38	0.53	27.7
	0.06	2.64		0.47	0.64	29.5
	0.08	3.02		0.54	0.72	32.3
	0.10	3.12		0.55	0.78	34.5
70:30 (v/v)	0	7.60[f] (2.71)[i]	5.1[h] (3.5)[j]			
	0.04	10.2		0.25	0.39	15.7
	0.08	11.7		0.35	0.58	17.5
	0.12	12.6		0.40	0.70	19.2
	0.16	13.9		0.45	0.77	21.0
	0.20	14.7		0.48	0.82	22.9

[a] At 25 °C and ionic strength 0.50 ($NaClO_4$). [b] Determined by monitoring the protonation of a 4-nitrophenoxide ion indicator by the acid produced during solvolysis. [c] Expected fractional yield of the azide adduct due to bimolecular reaction, calculated from the increases in k_{obsd}. [d] Observed fractional yield of the azide adduct, determined experimentally from product analysis by HPLC. [e] Calculated by using eq 1 in the Experimental Section. [f] The rate constant for reaction in the absence of azide ion is k_{solv}. [g] At 20 °C and zero ionic strength: ref 20. [h] Obtained by least-squares analysis of the values of k_{obsd} at 0–0.08 M azide ion. [i] At 20 °C and zero ionic strength: ref 13. [j] At 20 °C: ref 5.

Table I gives the values of k_{solv} and the product rate constant ratios k_{az}/k_s and k_{HOH}/k_{TFE} for the reactions of **1**, **2**, and **3** in 50:50 (v/v) trifluoroethanol/water.

The observed rate constant for the disappearance of **2** in 50:50 (v/v) trifluoroethanol/water, determined by HPLC from the decrease in the area of the substrate peak, was found to be independent of the concentration of azide ion in the range 0–0.50 M.

At 0.01 M azide ion a product rate constant ratio of k_{az}/k_s = 25 M^{-1} was determined for the reaction of **3** in 50:50 (v/v) trifluoroethanol/water. An increase to 0.50 M azide ion was accompanied by a 30% increase in k_{obsd} (determined by HPLC from the decrease in the area of the substrate peak) and changes in the product rate constant ratios k_{HOH}/k_{TFE} (from 1.7 to 7.3) and k_{az}/k_s (from 25 to 5 M^{-1}). These results show that azide ion catalyzes the attack of solvent at the carbonyl group of the substrate to produce 4-methoxybenzyl alcohol.

The effect of replacing trifluoroethanol with 1-propanethiol on the yields of the azide, solvent, and thiol adducts obtained from the reaction of **1** in the presence of 0.03 M azide ion is given in the supplementary material. The solvent was varied from an initial composition of 50:50 (v/v) TFE/H_2O to a final composition of 5:45:50 (v/v/v) PrSH/TFE/H_2O.

Table II gives the observed rate constants for the reaction of **1** with sodium azide in 80:20 (v/v) and 70:30 (v/v) acetone/water, determined spectrophotometrically by following the protonation of 4-nitrophenoxide ion by the hydrochloric acid produced during solvolysis. The values of k_{obsd} are linear with $[N_3^-]$ up to 0.08 M in both solvents, and second-order rate constants, k_N, were calculated by least-squares analysis of these data (Table II). At higher concentrations of azide ion the values of k_{obsd} show small

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(25) Abbreviation: TFE, 2,2,2-trifluoroethanol.

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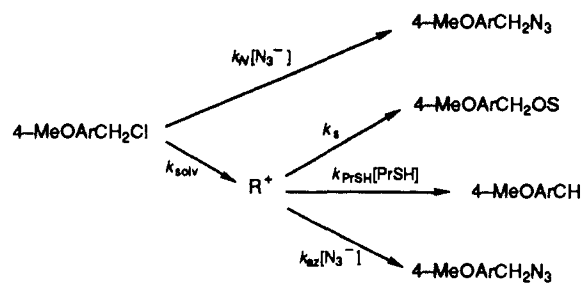
Scheme II



negative deviations (10–20%) from the calculated least-squares lines. Table II also gives the fractional yields of the azide adduct and the values of $(k_{az}/k_s)_{obsd}$ that were calculated from the product yields at increasing azide ion concentration.

Discussion

Mechanism of Reaction of 4-Methoxybenzyl Derivatives in 50:50 (v/v) Trifluoroethanol/Water. The following results show that the solvolysis of **1**, **2**, and **3** in 50:50 (v/v) trifluoroethanol/water is stepwise through the diffusionally equilibrated 4-methoxybenzyl carbocation intermediate which can be trapped by azide and chloride ions, solvent, and 1-propanethiol.

(1) The inhibition of the solvolysis of **1** by added chloride ion (Figure 1) shows that chloride ion competes with solvent for reaction with a diffusionally equilibrated intermediate to regenerate the substrate. The good fit of all the experimental data to eq 2, which was derived for solvolysis through a carbocation intermediate (Scheme I), shows that the reaction of the carbocation with solvent can be completely inhibited by chloride ion and therefore that there is no significant reaction of the solvent with the neutral substrate or with the carbocation–chloride ion pair.

(2) The reactions in the presence of azide ion give good yields of the azide adducts for **1**, **2**, and **3**. For **2** and **3**, there are no increases in k_{obsd} that are due to bimolecular substitution by azide ion at the benzylic carbon. Therefore, the reaction of azide ion with **2** and **3** occurs by an S_N1 mechanism.

(3) The ratio of rate constants for the reaction with azide ion and solvent determined from product ratios, k_{az}/k_s, is identical for **1**, **2**, and **3** (Table I). This suggests that the leaving group is not involved in the product-determining step and that there is partitioning of a common liberated carbocation intermediate between reaction with solvent and with azide ion.

(4) We were unable to determine directly the kinetic order of the reaction of **1** with respect to azide ion, because the latter absorbs very strongly at $\lambda \leq 260$ nm where the reaction would have been monitored.[27] Therefore, the mechanism of the reaction of **1** with azide ion was established indirectly from the effect of 1-propanethiol, an efficient trapping reagent for carbocations,[28] on the yields of the azide and solvent adducts.[23] Figure 2 shows that for reaction of **1** in the presence of 0.03 M azide ion, the replacement of trifluoroethanol by 1-propanethiol leads to the *same* fractional decrease in the yield of the solvent (total water and trifluoroethanol) and azide ion substitution products. Therefore, the formation of the thiol, solvent, and azide adducts must occur by a common pathway. The solvolysis reaction is S_N1 through the 4-methoxybenzyl carbocation intermediate, so that the azide and thiol adducts must also arise from trapping of this carbocation (Scheme II. lower pathway). If part of the reaction of **1** with azide ion proceeded through a pathway not involving the carbocation (Scheme II, upper pathway), then the yield of the azide adduct from this pathway would be independent of [PrSH]. This would result in a leveling off of the normalized fractional yield of the azide adduct at high [PrSH] to a larger value than that for the solvent adducts. The product rate constant ratios k_{PrSH}/k_{az} and k_{PrSH}/k_s (M^{-1}) both decrease by 30% when the amount of PrSH is increased from 1% to 5%. A similar medium effect on the reactivity of these nucleophiles has been observed in previous work.[29]

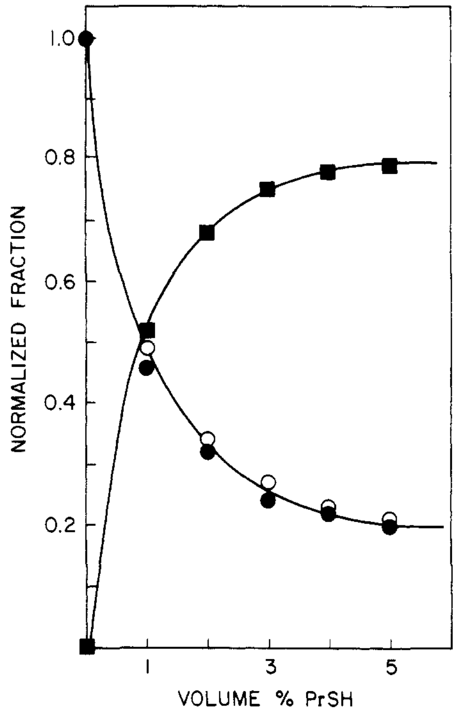


Figure 2. The effect of replacing trifluoroethanol with 1-propanethiol on the normalized fractional yields of the azide (○) and total water and trifluoroethanol (●) adducts obtained from the reaction of 4-methoxybenzyl chloride (**1**) in the presence of 0.03 M azide ion at 22 ± 2 °C and ionic strength 0.50 ($NaClO_4$). The solvent was varied from an initial composition of 50:50 (v/v) TFE/H_2O to a final composition of 5:45:50 (v/v/v) PrSH/TFE/H_2O. The normalized fractional yield is the yield of the adduct divided by the yield of that adduct obtained in the absence of PrSH. The yields of the PrSH adduct (■) are reported as the fraction of the total products. (Data are given in the supplementary material.)

Lifetimes of Benzyl Carbocations and Mechanism of Solvolysis of Benzyl Derivatives. The 1-(4-methoxyphenyl)ethyl carbocation, with $k_{az}/k_s = 100$ M^{-1} in 50:50 (v/v) trifluoroethanol/water, reacts with azide ion at the diffusion limit,[24] and the reaction of azide ion with the 4-methoxybenzyl carbocation, which is more unstable, should also be diffusion controlled. Therefore, the ratio of rate constants for reaction of the 4-methoxybenzyl carbocation with azide and solvent in 50:50 (v/v) trifluoroethanol/water, $k_{az}/k_s = 25$ M^{-1}, can be combined with an estimated value of $k_{az} = 5 \times 10^9$ M^{-1} s^{-1} to obtain a rate constant $k_s = 2 \times 10^8$ s^{-1}.[24,30] This value of k_s can then be combined with the rate constant ratio $k_{Cl}/k_s = 9$ M^{-1} (Results) to give $k_{Cl} = 2 \times 10^9$ M^{-1} s^{-1} for reaction of the 4-methoxybenzyl carbocation with chloride ion. The values of k_{az}/k_s for reaction of the carbocation in 80:20 (v/v) and 70:30 (v/v) acetone/water (see below) give $k_s = 6 \times 10^8$ and 7×10^8 s^{-1}, respectively. The small effect of a change in solvent on k_s for this carbocation is similar to the solvent effect on the values of k_s for the reaction of several other carbocations in acetonitrile/water solvents.[31,32]

The rate constant for capture of 4-MeOArCH(CH_3)$^+$ in 50:50 (v/v) trifluoroethanol/water is $k_s = 5 \times 10^7$ s^{-1},[24b] so that the

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[27] The 4-nitrophenoxide ion indicator method that was used to follow the reaction of 4-methoxybenzyl chloride in acetone/water solvents at 452 nm cannot be employed in trifluoroethanol/water solvents because the 4-nitrophenoxide ion is protonated by the trifluoroethanol.

[28] Richard, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 1373–1383.

[29] See Figure 4 of ref 23.

[30] Diffusion-limited rate constants of 4–7 × 10^9 M^{-1} s^{-1} have been measured directly for the reaction of azide ion with unstable carbocations in water or predominantly aqueous solutions: McClelland, R. A.; Banait, N.; Steenken, S. *J. Am. Chem. Soc.* **1986**, *108*, 7023–7027. McClelland, R. A.; Kanagasabapathy, V. M.; Steenken, S. *Ibid.* **1988**, *110*, 6913–6914.

[31] Amyes, T. L.; Jencks, W. P. *J. Am. Chem. Soc.* **1989**, *111*, 7888–7900.

[32] McClelland, R. A.; Kanagasabapathy, U. M.; Banait, N. S.; Steenken, S. *J. Am. Chem. Soc.* **1989**, *111*, 3966–3972.

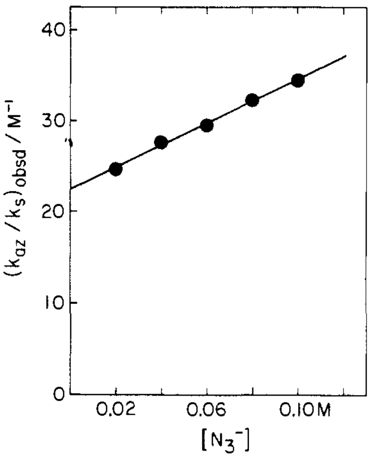

Figure 3. The dependence of the observed rate constant ratio calculated from the yields of the azide and solvent substitution products for the reaction of 4-methoxybenzyl chloride (**1**) with azide ion in 80:20 (v/v) acetone/water at 25 °C and ionic strength 0.50 ($NaClO_4$). The data are from Table II, and the line was calculated by least-square analysis. The slope and intercept of this line were used to calculate the value of k_{az}/k_s = 8 M^{-1} for partitioning of the 4-methoxybenzyl carbocation, according to eq 3.

substitution of a methyl group for an α-hydrogen in the 4-methoxybenzyl system leads to about a 4-fold decrease in k_s.[33] Therefore, the estimated values of k_s for $PhCH(CH_3)^+$ and 4-$NO_2ArCH(CH_3)^+$ in 50:50 (v/v) trifluoroethanol/water[24b] can be multiplied by a factor of 4 to give rate constants for the capture of benzyl and 4-nitrobenzyl carbocations of $k_s \approx 4 \times 10^{11}$ and 4×10^{13} s^{-1}, respectively. These values are lower limits because the demand for stabilization of benzyl carbocations by the aromatic ring is expected to be larger than that for 1-phenylethyl carbocations, so that the effect on k_s of changing the aromatic substituent should be larger for the former. This is illustrated by the increase in the Hammett ρ values for the addition of solvent to carbocations when the α-substituent is made more electron-withdrawing along the series $ArC(CH_3)OMe^+$,[34] $ArCH(CH_3)^+$,[24b] and $ArCH(CF_3)^+$.[26]

The value of $1/k_s \approx 3 \times 10^{-12}$ s for $PhCH_2^+$ suggests that the lifetime of this species is so short that it reacts with solvent before it can diffuse up to added solutes. This is consistent with the observation that the solvolyses of benzyl tosylate[35] and azoxytosylate[36] in 50:50 (v/v) trifluoroethanol/water do not proceed through the liberated benzyl carbocation.

The estimated lifetime of 4-$NO_2ArCH_2^+$, $1/k_s \approx 3 \times 10^{-14}$ s, is around the time for a bond vibration ($\approx 10^{-13}$ s), so that there is little or no barrier for its capture by partially aqueous solvent.[21] The solvolysis of 4-nitrobenzyl derivatives probably occurs by direct attack of the solvent on the substrate because the 4-nitrobenzyl carbocation does not have a significant lifetime. This conclusion is consistent with the decreases in secondary α-deuterium isotope effects,[19b,37] Grunwald–Winstein m values,[2,4a,b,d,37] and Hammett ρ values[18] for the solvolysis of benzyl derivatives that are observed when the aromatic substituent is changed from 4-methoxy to 4-nitro.

Mechanism of Reaction of 4-Methoxybenzyl Chloride with Azide Ion in Acetone/Water Solvents. The data in Table II show the effect of added azide ion at constant ionic strength on the values of k_{obsd} for the reaction of **1** in 80:20 (v/v) and 70:30 (v/v) acetone/water. There is a good linear correlation of the rate data up to 0.08 M azide ion in both solvents. The negative deviations of the points above 0.08 M azide do not arise from a change in rate-limiting step for the reaction of azide ion (see below). They are probably due to a specific salt effect that arises from the replacement of ClO_4^- by N_3^-.

Scheme III

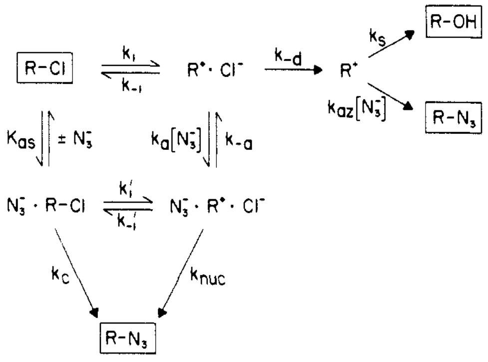

Table II also shows that the fractional yields of the azide adduct obtained from reaction of **1** in 80:20 (v/v) and 70:30 (v/v) acetone/water, $(f_{az})_{obsd}$, are significantly larger than the expected fractional yields, $(f_{az})_{rates}$, that are calculated from the increases in k_{obsd} caused by azide ion. These results show that, in addition to bimolecular displacement, there is also a pathway for the formation of the azide substitution product which is zero-order in the concentration of azide ion.

Figure 3 shows that the rate constant ratio that is calculated from the yields of the azide and solvent adducts from the reaction of **1** in 80:20 (v/v) acetone/water, $(k_{az}/k_s)_{obsd}$ (Table II), increases linearly with the concentration of azide ion. This is unusual because values of $(k_{az}/k_s)_{obsd}$ do not usually depend on $[N_3^-]$.[24] The result is required for a reaction in which the azide adduct is formed by concurrent S_N1 and S_N2 pathways (Scheme II), because for this mechanism, the rate of formation of the azide adduct (RN_3) depends on $[N_3^-]$, whilst the rate of formation of the solvent adduct (ROH) depends on $1/[N_3^-]$, so that $[RN_3]/[ROH]$ depends on $[N_3^-]^2$.[38] The data in Figure 3 were fit to eq 3, which was derived for the concurrent mechanisms shown in Scheme II.[39] The value of k_N/k_{solv} = 15 M^{-1} in 80:20 (v/v) acetone/water (Table II) can be combined with the slope and the intercept of the line drawn in Figure 3 to give a value of k_{az}/k_s = 8 M^{-1} for partitioning of the 4-methoxybenzyl carbocation between azide ion and solvent. The corresponding data for the reaction in 70:30 (v/v) acetone/water give k_N/k_{solv} = 7 M^{-1} and k_{az}/k_s = 7 M^{-1}.

$$(k_{az}/k_s)_{obsd} = (k_{az}/k_s)(k_N/k_{solv})[N_3^-] + \{(k_{az}/k_s) + (k_N/k_{solv})\} \quad (3)$$

We now consider the mechanism for the observed bimolecular reaction of azide ion with **1** in acetone/water solvents. Some possible pathways for the formation of the azide adduct from **1** are shown in Scheme III. The top pathway (k_1) is the mechanism proposed by Sneen[15,40] that involves reversible formation of the carbocation–chloride intimate ion pair which is then trapped by azide ion ($k_a[N_3^-]$) to give the azide adduct. The lower pathway (through K_{as} and k_1') is a stepwise preassociation mechanism[21] for the bimolecular reaction of azide ion with **1**, and concerted displacement of the leaving group occurs through K_{as} and k_c. A unimolecular reaction of **1** occurs when the ion pair separates (k_{-d})

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[33] This decrease is smaller than the 20–40-fold decrease in the reactivity of oxocarbenium ions toward water when an α-hydrogen is replaced by a methyl group.[31] This, and the effects of other α-substituents on the kinetic and thermodynamic stability of carbocations, will be discussed in a later paper.

[34] Young, P. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 8238–8248.

[35] Maskill, H. *J. Chem. Soc., Perkin Trans. 2* **1986**, 1241–1246.

[36] Maskill, H.; Jencks, W. P. *J. Chem. Soc., Chem. Commun.* **1984**, 944–946. Maskill, H.; Jencks, W. P. *J. Am. Chem. Soc.* **1987**, *109*, 2062–2070.

[37] Shiner, V. J., Jr.; Rapp, M. W.; Pinnick, H. R., Jr. *J. Am. Chem. Soc.* **1970**, *92*, 232–233.

[38] Sneen[15] has argued that the constant value of $(k_{az}/k_s)_{obsd}$ = 21.6 M^{-1} that can be calculated from Kohnstam's data[13] in 70% acetone at all of the concentrations of azide used is inconsistent with reaction of azide ion with **1** by concurrent S_N1 and S_N2 mechanisms. However the data in Table II show that the constant value of $(k_{az}/k_s)_{obsd}$ can also be explained by the limited range of $[N_3^-]$ (0–0.04 M) that was studied.

[39] The good fit of the point at 0.10 M azide, which deviates from the linear correlation of the rate data in Table II, suggests that there are compensatory salt effects on at least two of the rate constants in eq 3.

to give the free carbocation which is then trapped by azide ion ($k_{az}[N_3^-]$) or by solvent (k_s).

The following show that the bimolecular reaction of **1** with azide ion in 80:20 (v/v) and 70:30 (v/v) acetone/water occurs by concerted displacement of the leaving group (S_N2) rather than by a stepwise preassociation mechanism[21] or the ion pair trapping mechanism.[15,40]

(1) The values of k_{solv} in Table II give a Grunwald–Winstein *m* value that is similar to the value of 1.08 reported in the literature.[20] The large *m* value is consistent with solvolysis through a carbocation intermediate. The much smaller value of $m \approx 0.5$ that can be calculated from the values of k_N in Table II shows that there is much less change in charge on moving from the ground to the transition state for the bimolecular compared with the solvolysis reaction. This implies that there is considerable bonding of both azide and chloride to the benzylic carbon in the transition state, which is consistent with a concerted displacement mechanism.

(2) For both the stepwise preassociation mechanism and the Sneen trapping mechanism, nucleophiles that are stronger than chloride ion should react with **1** with identical second-order rate constants.[22,41] Therefore, the increase in the second-order rate constants along the series SCN^-, N_3^-, and $S_2O_3^{2-}$ for the reaction of **1** in 80% dioxane/water[6] is inconsistent with both mechanisms.

(3) The ratio of rate constants for the bimolecular reaction of thiosulfate and thiocyanate ions with ring-substituted benzyl bromides in 80% dioxane increases along the series 4-MeO, 4-H, and 4-NO_2.[6] These changes are consistent with *concerted* displacement and a diagonal reaction coordinate on a two-dimensional reaction-coordinate diagram.[42]

(4) The rate constant for collapse of the carbocation–azide ion pair (k_{nuc}, eq 4) can be estimated from $k_s = 2 \times 10^8$ s^{-1}, $k_{az}/k_s = 10^6$ M^{-1} for reactions in which there is a chemical barrier to capture of the carbocation by azide ion,[43] $K_{as} = 0.3$ M^{-1},[28] and $k_{nuc} = k_{az}/K_{as}$ to be $k_{nuc} \approx 10^{15}$ s^{-1}. Therefore, the lifetime of

$$\text{4-MeOArCH}_2^+ + N_3^- \overset{K_{as}}{\rightleftharpoons} R^+{\cdot}N_3^- \xrightarrow{k_{nuc}} \text{4-MeOArCH}_2N_3 \qquad (4)$$

the carbocation–azide ion pair, $1/k_{nuc} \approx 10^{-15}$ s, is much shorter than the time for a bond vibration ($\approx 10^{-13}$ s). If the ion pair (or the triple ion complex, Scheme III) does not exist for the time of a single bond vibration, then it cannot be an intermediate in the reaction of **1** with azide ion, and the concerted displacement mechanism is enforced.[21]

(5) In 50:50 trifluoroethanol/water, and in more strongly ionizing solvents (e.g., water), the reaction of **1** with azide ion is exclusively S_N1; but, the reaction of azide ion with 4-methoxybenzyl dimethylsulfonium nitrate in water is largely bimolecular.[11] The appearance of the second-order term for azide when the leaving group is changed from chloride to dimethyl sulfide is an example of a synergistic interaction between the incoming nucleophile and the leaving group that stabilizes the transition state for the bimolecular reaction of azide ion.[23,41] This is consistent with only a concerted mechanism, in which there is partial bonding of both the nucleophile and the leaving group to the benzylic carbon in the transition state.

The Appearance of Concurrent S_N1 and S_N2 Reactions for 4-Methoxybenzyl Derivatives. The results of these studies show that the transition states for the unimolecular and bimolecular reactions of 4-methoxybenzyl chloride and the 4-methoxybenzyl carbocation intermediate of the stepwise reaction each lie at discrete positions on a three-dimensional energy diagram. The relative energies of the transition states for the S_N1 and S_N2 reactions vary independently with changes in solvent ionizing power. In 50:50 (v/v) trifluoroethanol/water, the transition state for the unimolecular reaction of **1** is much lower in energy than that for the concerted reaction of **1** with azide ion, and the latter is therefore not observed. However, in 70:30 (v/v) acetone/water, the bimolecular substitution reaction of azide ion makes a significant contribution to k_{obsd} for the reaction of **1**, which shows that this change in solvent causes a larger increase in the energy of the highly polar transition state for the S_N1 reaction, compared with that for the S_N2 reaction. Further decreases in solvent polarity eventually lead to the rate of the S_N1 reaction of azide ion becoming insignificant compared with the rate of the S_N2 reaction.

There have been other reports of concurrent S_N1 and S_N2 reactions of 4-methoxybenzyl derivatives, and it is possible that this is a common mechanism for the reaction of these substrates. 4-Methoxybenzyl 2,4,6-triphenylpyridinium salts react with secondary amines in chlorobenzene by pathways zero- and first-order in [Nu].[10] There is evidence that the racemization of 4-methoxybenzyl ethylmethylsulfonium perchlorate in methanol occurs by both dissociation of the substrate to give an ion–dipole pair and by direct displacement of the leaving group by ethylmethyl sulfide.[12]

4-Methoxybenzyl halides have been reported to undergo bimolecular reactions with several nucleophiles in 70% acetone[5] and in 80% dioxane,[6] with ArS^- in methanol,[7,19a] with $ArNH_2$ in ethanol,[8] and with bromide ion in ethylene glycol diacetate.[9] In all of these studies the effects of the nucleophile on the rate constants, but not on the product distribution, were determined. Additional product studies here would likely reveal further examples of nucleophilic substitution by concurrent S_N1 and S_N2 pathways.

Acknowledgment is made to the National Institutes of Health, Grant GM39754, for support of this work.

Supplementary Material Available: Table of product yields for the reaction of 4-methoxybenzyl chloride in a solvent of 50:50 (v/v) trifluoroethanol/water containing 0.03 M NaN_3 and increasing concentrations of 1-propanethiol (1 page). Ordering information is given on any current masthead page.

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