Substitution at simple secondary carbon centers is known to be subject to nucleophilic assistance, and the rate constants for reactions of 1-(4-nitrophenyl)-2-propyl tosylate, iodide, and bromide with solvent components fall on the same Swain-Scott plots as those for reagents that react by second-order nucleophilic substitution.[4] This suggests that oxygen exchange occurs through a coupled concerted mechanism, as suggested for other leaving groups in secondary systems.[3] On the other hand, the absence of a large difference in the ratio of hydride transfer to solvent attack for the protonation of 1-butene in water and 1-hexene in trifluoroacetic acid[13] suggests that there is little nucleophilic assistance for solvent attack in this reaction, so that the 1,2-addition may be uncoupled concerted. It is likely that the solvent is directly involved in proton transfer to and from carbon.

The appearance of the transition state, as indicated by structure-reactivity correlations, isotope effects, and other characteristics, is often used to diagnose the nature of reaction mechanisms. However, the appearance of the transition state does not distinguish between a two-step mechanism and a concerted, one-step mechanism with a transition state that resembles the presumed intermediate. As pointed out by Hammett, different reactions with similar, carbocation-like transition states can actually occur through parallel pathways of similar energy.[25] The similar response of these different reactions to changing substituents, solvent, temperature, and other variables does not prove that the reactions proceed through a common intermediate; it only shows that the transition states have similar structures.

Reactions that proceed through carbocation intermediates have carbocation-like transition states, and there is a strong tendency in the literature to fit experimental data to the paradigm that reactions with carbocation-like transition states proceed through carbocation intermediates. We suggest that it is time to reject this paradigm and that the conclusion that a reaction proceeds by an S_N1 (or $D_N + A_N$ or $D_N{}^*A_N$)[2] mechanism should be based on evidence that a carbocation is formed as an intermediate in the reaction.

Acknowledgment. We are grateful to Prof. J. Manassen for helpful communication.

(25) Hammett, L. P. *Physical Organic Chemistry*, 2nd ed.; McGraw Hill: New York, 1970; pp 157-167.

Solvolysis of Benzyl Azoxytosylate and the Effect of Added Bases and Nucleophiles in Aqueous Trifluoroethanol and Aqueous Acetonitrile

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Abstract: The rates and products of reaction of benzyl azoxytosylate (**1b**) in 1:1 (v/v) aqueous trifluoroethanol containing sodium perchlorate, sodium thiocyanate, sodium iodide, sodium bromide, sodium chloride, sodium hydroxide, sodium acetate, perchloric acid, and imidazole (buffered and unbuffered) have been measured at 42 °C as part of an investigation into its mechanism of solvolysis. Nonbasic solutes give only small rate effects (some rate enhancing, others rate retarding), but, if nucleophilic, they lead to substitution products—the classic evidence of an S_N1 reaction mechanism. After the initial rate-determining fragmentation, about half of the total solvolytic reaction proceeds through an electrophilic benzylic intermediate which is sufficiently long-lived to be trapped by nucleophilic solutes such as thiocyanate and the halide anions to give benzyl thiocyanate and benzyl halides. The other half gives the solvent-derived products benzyl alcohol and benzyl trifluoroethyl ether by a route which is not affected by dilute nonbasic solutes. Sodium acetate, which leads to negligible formation of benzyl acetate, and imidazole lead to the formation of trifluoroethyl tosylate; imidazole also produces *N*-tosylimidazole. These two base-induced bimolecular reactions involve nucleophilic attack at the sulfur of the tosyl group and involve electronic polarization of **1b** in the opposite sense from that in the unimolecular fragmentation. One of the minor products in the presence of bases from the trappable intermediate of the solvolysis reaction is benzaldehyde, which suggests that the intermediate is $C_6H_5CH_2ON_2^+$, a new type of reactive electrophile. It is not yet certain whether the half of the unimolecular fragmentation reaction which does not proceed through the trappable intermediate involves another electrophilic intermediate which is simply too short-lived to be intercepted by dilute nucleophiles or whether about half of the initial fragmentation is followed by a concerted uncoupled capture of the nascent benzyl cation by solvent. Replacing a small proportion of the trifluoroethanol in the reaction medium by the more nucleophilic ethanol does not have a drastic effect upon the overall course of the reaction, and a very similar mechanism also appears to be operative in aqueous acetonitrile.

Alkyl azoxytosylates (**1**) have been known for many years,[1,2] but only recently have they been recognized as solvolytic substrates.[3] Structurally, these compounds relate both to alkyl tosylates (**2**) and to diazo compounds that intervene as intermediates in solvolytic deamination reactions.[3-5] We have already described an investigation into the mechanism of solvolysis of 2-adamantyl azoxytosylate (**1a**).[3,5] The results were interpreted in terms of a rate-determining fragmentation followed by nu-

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(1) Stevens, T. E. *J. Org. Chem.* **1964**, *29*, 311-315.
(2) Freeman, J. P.; Lillwitz, L. D. *J. Org. Chem.* **1970**, *35*, 3107-3110. White, E. H.; Lewis, C. P.; Ribi, M. A.; Ryan, T. J. *Ibid.* **1981**, *46*, 552-558. White, E. H.; Todd, M. J.; Ribi, M.; Ryan, T. J.; Sieber, A. A. F.; Dickerson, R. E.; Bordner, J. *Tetrahedron Lett.* **1970**, 4467-4472.
(3) Maskill, H.; Murray-Rust, P.; Thompson, J. T.; Wilson, A. A. *Chem. Commun.* **1980**, 788-789.

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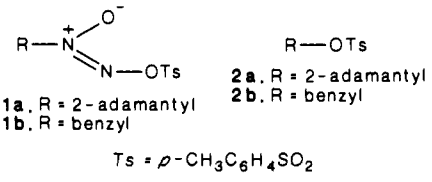
cleophilic capture of the 2-adamantyl cation either by solvent or, in certain circumstances, by the tosylate anion. 2-Adamantyl tosylate (**2a**) also reacts by an S_N1 mechanism,[6] but comparison of the detailed results from **1a** and **2a** constitutes evidence that, for **2a**, a subsequent step of the first-formed (intimate) ion pair, rather than its formation, is rate determining.[5,7]



We now report results of an investigation of the solvolysis of benzyl azoxytosylate (**1b**) in 1:1 (v/v) aqueous trifluoroethanol (1:1 TFE–H_2O). This compound was chosen as the first of the simplest series which would allow a Hammett-type study of substituent effects upon the solvolysis of alkyl azoxytosylates.[8] A prior investigation of the solvolysis of benzyl tosylate (**2b**) in the same solvent mixture was necessary because it was thought to be a possible intermediate in the solvolysis of **1b**.[9] Our interpretation of the results of that investigation[10] was in terms of a solvent-induced bimolecular (S_N2) mechanism[11] rather than an S_N1 process,[12] so we could not assume the same relationship between the mechanisms of reaction of azoxytosylate and tosylate for benzyl as had been found for the 2-adamantyl system.

However, the activation parameters in 1:1 TFE–H_2O are $\Delta H^{\ddagger} = 100$ (±4) kJ mol^{-1} and $\Delta S^{\ddagger} = -12$ (±8) J K^{-1} mol^{-1} for **1b**[13] compared with $\Delta H^{\ddagger} = 99$ (±4) kJ mol^{-1} and $\Delta S^{\ddagger} = -3$ (±8) J K^{-1} mol^{-1} for **1a**,[14] and the sensitivities of the rates of solvolysis of both compounds to changes in the nature of the solvent are also very similar.[15] Consequently, we took as a working hypothesis that **1b** reacts by an initial rate-determining fragmentation, and the main thrust of the present study was to elucidate the subsequent steps by a combination of product analytical and kinetics methods. Our prior investigation of benzyl tosylate had served to establish and validate our methodology.[10]

Experimental Section

Benzylhydroxylamine.[16] Portions of sodium cyanoborohydride (1.20 g, 19.1 mmol) and a solution cautiously made up from ice-cold methanol (30 cm^3) and acetyl chloride (10 cm^3) were added alternately over about 15 min to a magnetically stirred solution of benzaldehyde oxime (freshly redistilled under reduced pressure; 3.25 g, 26.8 mmol) and a single small crystal of methyl orange in methanol (5 cm^3), sufficient methanolic HCl being added to maintain the color on the pink side of the red–yellow color change.[5,17] The methanol was then evaporated under reduced pressure with slight warming. The waxy residue was treated with sufficient dilute aqueous sodium hydroxide to give a solution of pH ~9 which was then saturated with sodium chloride and extracted several times with dichloromethane. The combined organic phase was dried (Na_2SO_4), filtered, and evaporated to give an oil which crystallized under a stream of nitrogen and then was dried in a vacuum desiccator: 3.10 g, 25.2 mmol, 94%; mp 49–53 °C [lit.[16] mp 57 °C]; ^{1}H NMR δ ($CDCl_3$, 60 MHz) 7.25 (5 H, s), 5.8–6.3 (2 H, exch D_2O), 3.89 (2 H, s). This material was used without further purification.

***N*-Nitrosobenzylhydroxylamine.**[18] An ice-cold solution of sodium nitrite (0.80 g, 11.6 mmol) in water (2 cm^3) was added over about 2 min to a stirred solution of benzylhydroxylamine (0.83 g, 6.75 mmol), aqueous hydrochloric acid (2 M, 5.5 cm^3), and methanol (3 cm^3) under argon at 0 °C.[5] After about 5 min, a thick white precipitate was formed whereupon the solution was diluted with ice-cold water and filtered by using suction and a precooled glass sinter. The crystals were dried at room temperature under vacuum: 0.46 g, 3.03 mmol, 45%; mp 67–75 °C [lit.[19] mp 74–76 °C]; ^{1}H NMR δ ($CDCl_3$, 60 MHz) 7.38 (5 H, s), 5.20 (2 H, s), 4.6 (1 H, br; in another preparation, this D_2O-exchangeable signal was observed at δ 10.4). The aqueous filtrate was extracted with ether 3 times. The combined ether phase was dried overnight at 0 °C (Na_2SO_4), filtered, and evaporated under reduced pressure to leave pale-yellow crystals identical by NMR with the first batch (0.38 g, 2.50 mmol, 37%). Both samples were stored below 0 °C and used without further purification.

Benzyl Azoxytosylate. *p*-Toluenesulfonyl chloride (recrystallized, 0.53 g, 2.77 mmol) was added portionwise to a stirred solution of *N*-nitrosobenzylhydroxylamine (0.28 g, 1.84 mmol) in dry pyridine (1.5 cm^3) at 0 °C under argon.[5,20] The reaction mixture was kept at 0 °C for about 14 h and then ice-cold water was added dropwise. After a brief period of further stirring, the mixture was diluted with water and extracted 3 times with diethyl ether. The combined ether phase was washed twice with ice-cold aqueous copper sulfate and ice-cold aqueous sodium bicarbonate, dried ($MgSO_4$), filtered, and then evaporated down to give almost colorless crystals (0.54 g, 1.76 mmol, 96%). Recrystallization at low temperature from ether–pentane followed by trituration with pentane at room temperature gave very pale-yellow crystals: mp 90.5–91.5 °C [lit.[1] mp 92 °C]; ^{1}H NMR δ ($CDCl_3$, 60 MHz) 7.78, 7.24 (4 H, ABq, J = 8.4 Hz), 7.25 (5 H, s), 5.12 (2 H, s), 2.42 (3 H, s).

Trifluoroethyl Tosylate. This compound was prepared by the usual Tipson[20] method at room temperature in good yield and recrystallized from pentane: mp 39.5–40.5 °C [lit.[21] mp 40–42 °C]; ^{1}H NMR δ ($CDCl_3$, 90 MHz) 7.81, 7.37 (4 H, ABq, J = 8.1 Hz), 4.35 (2 H, q, J_{HF} = 8.1 Hz), 2.41 (3 H, s).

***N*-Tosylimidazole.** This compound was prepared as described by Hicks and Fraser-Reid[22] and recrystallized from pentane–ether: ^{1}H NMR δ ($CDCl_3$, 90 MHz) 7.84, 7.34 (4 H, ABq, J = 8.1 Hz), 8.03–7.11 (3 H, m), 2.41 (3 H, s).

Thermolysis of Benzyl Azoxytosylate. The 60-MHz NMR spectrum of a sample of benzyl azoxytosylate (ca. 20 mg) in $CDCl_3$ (ca. 0.6 cm^3) was recorded, and then the NMR tube was put in a thermostated water bath at 65.5 °C. The tube was withdrawn and rapidly cooled, the spectrum was recorded, and the tube was returned to the water bath at recorded times. The relative intensities of the benzylic signals of the azoxytosylate at δ 5.12 and of the tosylate[10] at δ 4.99 were used to calculate the percentage conversion. The first-order rate constant of the reaction was determined by the usual linear regression analysis using data from nine spectra recorded during 92% of the conversion ($k = 1.1 \times 10^{-5}$ s^{-1}, $R > 0.99$). At the end of the reaction, the spectrum was indistinguishable from that of pure authentic benzyl tosylate prepared by the Tipson method.[10]

Solvolysis of Benzyl Azoxytosylate. (i) Kinetics. Rates of solvolysis of benzyl azoxytosylate in 1:1 (v/v) aqueous trifluoroethanol (ca. 10^{-5} M) with or without added electrolytes at 42 °C were measured by monitoring the decrease in UV absorbance at 245 or 275 nm in the thermostated cell compartment of a Gilford spectrophotometer. First-order rate constants were calculated from Kezdy–Swinbourne plots[23] by

(4) White, E. H.; Woodcock, D. J. In *The Chemistry of the Amino Group*; Patai, S., Ed.; Wiley: New York, 1968; Chapter 8, pp 407–497. Kirmse, W. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 251–261.
(5) Maskill, H.; Thompson, J. T.; Wilson, A. A. *Chem. Commun.* **1981**, 1239–1240. Maskill, H.; Thompson, J. T.; Wilson, A. A. *J. Chem. Soc., Perkin Trans. 2* **1984**, 1693–1703.
(6) Bentley, T. W.; Schleyer, P. v. R. *Adv. Phys. Org. Chem.* **1977**, *14*, 1. Bentley, T. W.; Bowen, C. T.; Morten, D. H.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1981**, *103*, 5466–5475. Bentley, T. W.; Schleyer, P. v. R. *Ibid.* **1976**, *98*, 7658–7666. Schadt, F. L.; Bentley, T. W.; Schleyer, P. v. R. *Ibid.* **1976**, *98*, 7666–7674. Fry, J. L.; Lancelot, C. J.; Lam, L, K. M.; Harris, J. M.; Bingham, R. C.; Raber, D. J.; Hall, R. E.; Schleyer, P. v. R. *Ibid.* **1970**, *92*, 2538–2540. Raber, D. J.; Harris, J. M.; Hall, R. E.; Schleyer, P. v. R. *Ibid.* **1971**, *93*, 4821–4828. Harris, J. M.; Hall, R. E.; Schleyer, P. v. R. *Ibid.* **1971**, *93*, 2551–2553.
(7) Paradisi, C.; Bunnett, J. F. *J. Am. Chem. Soc.* **1981**, *103*, 946–948. Shiner, V. J.; Fisher, R. D. *Ibid.* **1971**, *93*, 2553–2554.
(8) Johnson, C. D. *The Hammett Equation*; Cambridge University Press: London, 1973.
(9) Maskill, H.; Jencks, W. P. *Chem. Commun.* **1984**, 944–946.
(10) Maskill, H. *J. Chem. Soc. Perkin Trans. 2* **1986**, 1241.
(11) Streitwieser, A. *Chem. Rev.* **1956**, *56*, 571. Shiner, V. J. In *Isotope Effects in Chemical Reactions*; Collins, C. J.; Bowman, N. S., Eds.; Van Nostrand Reinhold: New York, 1970; Chapter 2, pp 90–159. Shiner, V. J.; Rapp, M. W.; Pinnick, H. R. *J. Am. Chem. Soc.* **1970**, *92*, 232–233.
(12) Hammond, G. S.; Peloquin, J.; Fang, F. T.; Kochi, J. K. *J. Am. Chem. Soc.* **1960**, *82*, 443–445. Aronovitch, H.; Pross, A. *J. Chem. Soc., Perkin Trans. 2* **1978**, 540–545. Karton, Y.; Pross, A. *Ibid.* **1980**, 250–254.
(13) Galloway, I. M.; Maskill, H.; unpublished results.
(14) Conner, J. K.; Maskill, H., unpublished results.
(15) Maskill, H.; Thompson, J. T., unpublished results.
(16) Feuer, H.; Vincent, B. F.; Bartlett, R. S. *J. Org. Chem.* **1965**, *30*, 2877–2880.
(17) Borch, R. F.; Bernstein, M. D.; Durst, H. D. *J. Am. Chem. Soc.* **1971**, *93*, 2897–2904.
(18) Axenrod, T.; Wieder, M. J.; Milne, G. W. A. *Tetrahedron Lett.* **1969**, 401–405.
(19) Müller, E.; Metzger, H. *Chem. Ber.* **1956**, *89*, 396–406; *Chem. Abstr.* **1956**, *50*, 14600g.
(20) Tipson, R. S. *J. Org. Chem.* **1944**, *9*, 235–241.
(21) Wentworth, S. E.; Scieraffa, P. L. *Org. Prep. Proced.* **1969**, *1*, 225–228; *Chem. Abstr.* **1970**, *72*, 54954u.
(22) Hicks, D. R.; Fraser-Reid, B. *Synthesis* **1974**, 203.

Table I. Rates of Solvolysis of Benzyl Azoxytosylate (**1b**) in 1:1 (v/v) H_2O–TFE Containing Nonbasic Electrolytes

solute	concentration, mol dm^{-3}	ionic strength[a]	temp, °C	10^5k, s^{-1}
$NaClO_4$	0	0	41.6	4.12
	0.25	0.25	41.6	4.49
	0.50	0.50	41.6	4.73
NaI	0	0.50	41.2	4.47
	0.08	0.50	41.2	4.32
	0.16	0.50	41.2	4.25
$HClO_4$	0	0.50	41.8	4.85
	0.10	0.50	41.8	4.85
	0.20	0.50	41.8	4.84
NaSCN	0	0.50	41.9	4.87
	0.08	0.50	41.9	4.93
	0.16	0.50	41.9	5.0

[a] Ionic strength made up with $NaClO_4$.

using 20–50 data points covering about five half-lives. No deviation from linearity could be detected with a simple first-order plot and an experimental infinity absorbance reading.

(ii) Product Analyses. Reaction mixtures were analyzed by reverse-phase (C-18) HPLC using aqueous methanol as eluant and direct injection as described for the analogous reactions of benzyl tosylate.[10]

Isolation and Characterization of Products from the Large-Scale Solvolysis of Benzyl Azoxytosylate in the Presence of Sodium Acetate. Aqueous sodium acetate (1 M, 50 cm^3) was added to a solution of benzyl azoxytosylate (ca. 0.65 g) in trifluoroethanol (50 cm^3) with warming and stirring. The reaction mixture in a sealed flask was maintained at 42 °C for 49 h with occasional releases of gas pressure. The solution was cooled, and the trifluoroethanol was evaporated under reduced pressure. The residual aqueous oil was extracted twice with ether, each ether phase being washed with brine. The combined ether solution was dried (Na_2SO_4), filtered, evaporated, and then pumped hard at room temperature to leave a pale-yellow oil (0.59 g) which crystallized at 0 °C overnight. The crystals were recrystallized twice from ether–pentane at low temperature (mp 73–75 °C) and shown to be identical by NMR, melting point, and HPLC with an authentic sample of *N*-nitrosobenzylhydroxylamine.[18] (This compound undergoes slow decomposition under the solvolytic conditions to give benzylhydroxylamine, which was also detected in solvolytic product mixtures by HPLC comparison with an authentic sample.[16])

The mother liquors from the recrystallizations were combined and chromatographed on neutral alumina (Woelm, deactivated by 10% water, 20 g) with 50% ether–pentane. Evaporation of the combined first few fractions gave a wax which was recrystallized from pentane at low temperature (mp 40.0–40.5 °C) and shown to be identical by NMR, melting point, and HPLC with an authentic sample of trifluoroethyl tosylate.[21]

HPLC Molar Response Factors. (i) Determination of the HPLC detector's molar response factor for benzyl alcohol, benzyl trifluoroethyl ether, benzyl thiocyanate, and benzyl acetate toward naphthalene, the internal standard, has already been described.[10] (ii) Benzaldehyde (redistilled under nitrogen, bp 175–176 °C, 56.15 mg) and naphthalene (89.45 mg) were made up to 15.0 cm^3 with acetonitrile. A sample of this solution was injected into 1:1 (v/v) H_2O–CH_3CN in a screw-capped HPLC vial, and the solution was analyzed in the usual way. From 10 analyses using the conditions employed in analysis of reaction mixtures, a molar response factor (mrf) of 5.60 (±0.28) was obtained. In a duplicate experiment on a similar scale but using 3 times the ratio of $C_{10}H_8$ to benzaldehyde, a result of 5.46 (±0.22) was obtained. A mean value of 5.53 was used. From this result and that of 0.0572 for benzyl alcohol vs. naphthalene,[10] a calculated value of 97 is obtained for the mrf of benzaldehyde vs. benzyl alcohol at 257 nm. A direct determination by multiple analysis of an accurately made up standard solution of benzaldehyde and benzyl alcohol in acetonitrile gave 96 ± 1. (iii) By the same general method of multiple analysis of standard solutions in acetonitrile made up from accurately weighed pure samples, mrf results vs. naphthalene at 257 nm were obtained for trifluoroethyl tosylate (0.217) and *N*-tosylimidazole (1.38).

Results

1. In Aqueous Trifluoroethanol. The rates and products of the reaction of **1b** in 1:1 H_2O–TFE containing nonbasic electrolytes are shown in Tables I and II, and the modest rate-enhancing effect of sodium perchlorate is illustrated in Figure 1. Clearly, there are neither acid catalysis nor any second-order contributions to the overall rate, only specific salt effects upon the solvolytic reaction.[10,24]

Whilst SCN^- and I^- have minimal (but opposite) rate effects, both lead to substantial yields of substitution product. The effect of the former in producing benzyl thiocyanate (Table II), which was shown to be quite stable to the reaction conditions, has already been illustrated in Figure 1 of our preliminary communication,[9] and the intercept in the double reciprocal plot of $[SCN^-]^{-1}$ vs. (mole fraction yield of $PhCH_2SCN)^{-1}$ gives the limiting yield of $PhCH_2SCN$ at the hypothetical infinite concentration of SCN^-. The results from Table II give the plot in Figure 2, and the result is 47% ($R > 0.99$), representing a trivial refinement of our earlier report of 45%.[9] The yields of benzyl alcohol and benzyl trifluoroethyl ether are estimated to be 36% and 17% at the hypothetical infinite concentration of sodium thiocyanate (a ratio of

Table II. Products from Solvolysis of Benzyl Azoxytosylate (**1b**) in 1:1 (v/v) H_2O–TFE Containing NaSCN at 42 °C

[NaSCN], mol dm^{-3}	ionic strength[a]	% $PhCH_2OH$	% $PhCH_2OCH_2CF_3$	% $PhCH_2SCN$
0	0.50	76	24	0
0.10	0.50	69	22	8.7
		(76)	(24)[b]	
0.25	0.50	63	21	16
		(75)	(25)[b]	
0.50	0.50	57	21	22
		(73)	(27)[b]	
1.0	1.0	47	18	35
		(73)	(27)[b]	
1.5	1.5	43	19	38
		(69)	(31)[b]	
1.8	1.8	39	19	42
		(67)	(33)[b]	

[a] Ionic strength made up with $NaClO_4$. [b] Proportions of solvent-derived product.

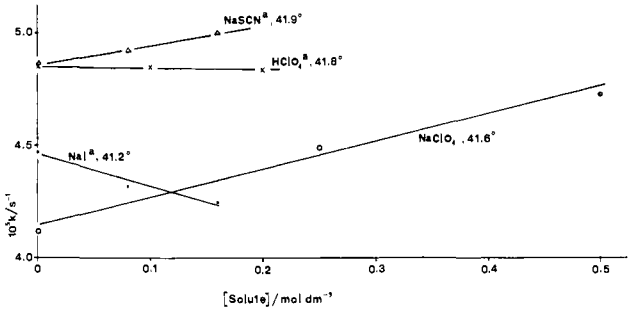


Figure 1. Effects of nonbasic solutes upon the rate of solvolysis of benzyl azoxytosylate (**1b**) in 1:1 (v/v) trifluoroethanol–water: a, constant ionic strength maintained with $NaClO_4$.

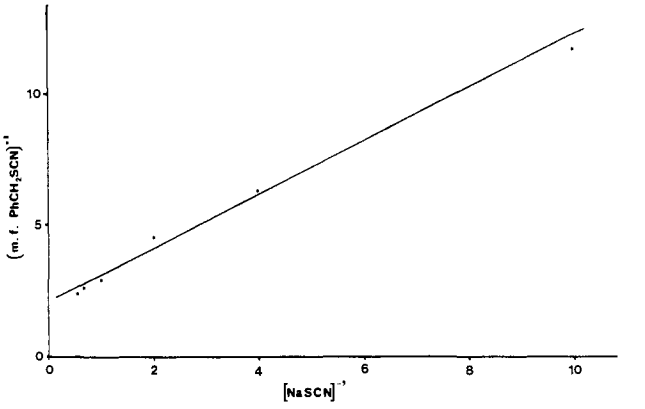


Figure 2. Plot of (mole fraction yield of $PhCH_2SCN)^{-1}$ vs. $[NaSCN]^{-1}$ for the solvolysis of benzyl azoxytosylate (**1b**) in 1:1 (v/v) trifluoroethanol–water, 42 °C.

(23) Swinbourne, E. S. *Analysis of Kinetic Data*; Nelson: London, 1971.

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

Table III. Products from Solvolysis of Benzyl Azoxytosylate (**1b**) in 1:1 (v/v) H_2O–TFE in the Presence of Halide Anions and Thiocyanate at 42 °C

SCN^-		$SCN^- + I^-$			$SCN^- + Br^-$		
$[SCN^-]$, mol dm^{-3}	% $PhCH_2SCN$	$[SCN^-]$, mol dm^{-3}	$[I^-]$, mol dm^{-3}	% $PhCH_2SCN$	$[SCN^-]$, mol dm^{-3}	$[Br^-]$, mol dm^{-3}	% $PhCH_2SCN$
0.5	22[a]	0.15	0.5	25[b]	0.12	0.5	16[d]
0.15	11[e]	0.05	0.5	23	0.03	0.5	12
0.12	10[e]	0.015	0.5	22[c]			
0.045	4[e]	0.045	0.15	12			
0.03	3[e]						

[a] $PhCH_2OH$:$PhCH_2OCH_2CF_3$ = 73:27. [b] $PhCH_2OH$:$PhCH_2OCH_2CF_3$ = 71:29. [c] $PhCH_2OH$:$PhCH_2OCH_2CF_3$ = 73:27 (total recovery = 98%). [d] $PhCH_2OH$:$PhCH_2OCH_2CF_3$ = 72:28 (total recovery = 101%). [e] Estimated from results at other concentrations, see Table II and Figure 2.

Table IV. Rate Results for Solvolysis of Benzyl Azoxytosylate (**1b**) in 1:1 (v/v) H_2O–TFE Containing Unbuffered Sodium Acetate at 42 °C

$[NaOAc]$, mol dm^{-3}	ionic strength[a]	10^5k, s^{-1}
0	0.5	4.6
0.2	0.5	27
0.3	0.5	29
0.5	0.5	57
1.0	1.0	105

[a] Ionic strength = $[NaOAc] + [NaClO_4]$.

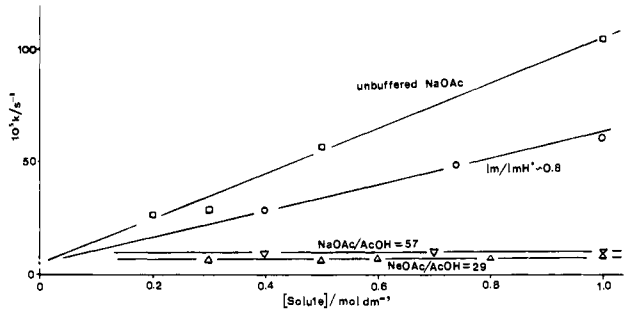


Figure 3. Effects of NaOAc, NaOAc/AcOH, and Im/ImH^+ buffers upon the rate of solvolysis of benzyl azoxytosylate (**1b**) in 1:1 (v/v) trifluoroethanol–water, 42 °C.

2.1:1) compared with 76% and 24% (3.2:1) at zero thiocyanate concentration.

Benzyl iodide, although unmistakably formed during the solvolysis of **1b** in the presence of iodide, is unstable to the reaction conditions, so reliable analyses of the kinetic products could not be obtained directly. Benzyl azoxytosylate was solvolyzed in the presence of sodium iodide and sodium thiocyanate, the latter sufficiently low in concentration that it did not compete significantly with the much higher concentrations of iodide as a nucleophile in the reaction of **1b**. The concentration of SCN^- was, however, sufficiently high that it preempted solvolysis of the benzyl iodide by converting it into benzyl thiocyanate. At the end of the reaction, therefore, the yield of benzyl thiocyanate could be related back to the prior formation of $PhCH_2I$. Results of these experiments are given in Table III along with those from comparable experiments using sodium thiocyanate as a trap for benzyl bromide produced in the solvolysis of **1b** in the presence of sodium bromide.

The effects of unbuffered sodium acetate upon both the rate and the products from **1b** were also investigated, and the results are shown in Tables IV and V. Clearly, there is an appreciable rate effect, and the plot of the overall rate constant against acetate concentration appears linear, Figure 3. Direct analysis of the reaction mixture in the normal way showed two new products. The major one was shown to be trifluoroethyl tosylate by isolation and comparison with an authentic synthetic sample,[21] and the minor one was benzaldehyde. (Only the merest trace of a peak was found in chromatograms at the retention time corresponding to that of authentic benzyl acetate.) Acidification of reaction mixtures which contained trifluoroethyl tosylate allowed analysis of *N*-nitrosobenzylhydroxylamine, which was identified by isolation and comparison with an authentic sample.[18] Additionally, benzylhydroxylamine was detected in amounts which increased with time and was almost certainly formed by denitrosation of the *N*-nitrosobenzylhydroxylamine.

Table V. Products from Solvolysis of Benzyl Azoxytosylate (**1b**) in 1:1 (v/v) H_2O–TFE Containing Unbuffered Sodium Acetate at 42 °C

$[NaOAc]$, mol dm^{-3}	ionic strength[a]	% $PhCH_2OH$	% $PhCH_2OCH_2CF_3$	% PhCHO	% CF_3CH_2OTs
0	0.5	76	24	0	0
0.005	0.5	69	24	0.1	7
		(74)	(26)	(0.1)[b]	
0.05	0.5	45	15	0.5	40
		(74)	(25)	(0.9)[b]	
0.10[c]	0.5	40	12	0.7	47
		(76)	(23)	(1.3)[b]	
0.25	0.5	18	6	1	75
		(73)	(23)	(4)[b]	
0.5[d]	0.5	14	5	1	80
		(69)	(24)	(7)[b]	
1.0	1.0	7	3	1	89
		(63)	(26)	(11)[b]	

[a] Ionic strength = $[NaOAc] + [NaClO_4]$. [b] Relative proportions of $PhCH_2OH + PhCH_2OCH_2CF_3 + PhCHO$ = 100; calculated directly from chromatographic data rather than from the normalized yields. [c] Total recovery = 98%. [d] Total recovery = 104%.

Table VI. Effect of Sodium Acetate/Acetic Acid upon the Rate of Solvolysis of Benzyl Azoxytosylate (**1b**) in 1:1 (v/v) H_2O–TFE at 42 °C

$[NaOAc]$, mol dm^{-3}	buffer ratio[a]	10^5k, s^{-1}
0.3	29	6.53
0.5	29	6.73
0.6	29	7.14
0.8	29	7.93
1.0	29	7.96
0.4	57	9.96
0.7	57	10.1
1.0	57	10.8

[a] Buffer ratio = [NaOAc]/[AcOH].

Two trends are evident within the product distributions shown in Table V. Firstly, the yields of CF_3CH_2OTs increase rapidly as the concentration of unbuffered sodium acetate increases, and secondly, the yields of benzaldehyde, although remaining small in absolute terms, increase significantly as a proportion of the total solvolytic product ($PhCH_2OH + PhCH_2OCH_2CF_3 + PhCHO$) virtually entirely at the expense of the $PhCH_2OH$.

The effect of buffering the sodium acetate with acetic acid in the aqueous trifluoroethanol is quite dramatic (Tables VI and VII and Figure 3). The rate of the reaction is now almost (but not quite) independent of the buffer concentration with a small dependence upon the buffer ratio, and benzaldehyde has become a very minor product, but, as a proportion of the solvolysis yield, it still increases slightly as the buffer concentration increases. There also appears to be some tendency for the proportion of $PhCH_2OCH_2CF_3$ within the solvolytic yield to increase at the expense of the $PhCH_2OH$ as the buffer concentration (at constant buffer ratio) increases. The yield of CF_3CH_2OTs is also suppressed as the buffer ratio $[AcO^-]$:[AcOH] is decreased, but, at constant buffer ratio, the yield of CF_3CH_2OTs still increases with the buffer concentration.

Table VII. Products from Solvolysis of Benzyl Azoxytosylate (**1b**) in 1:1 (v/v) H_2O–TFE Containing Sodium Acetate/Acetic Acid Buffers at 42 °C

[NaOAc],[a] mol dm^{-3}	ionic strength[b]	% $PhCH_2OH$	% $PhCH_2OCH_2CF_3$	% PhCHO	% CF_3CH_2OTs
0	0.5	76	24	0	0
0.05	0.5	63	23	0.2	14
		(74)	(26)	(0.3)[c]	
0.10[d]	0.5	60	22	0.3	18
		(73)	(27)	(0.4)[c]	
0.08[e,f]	0.5	72	23	0.1	5
		(76)	(24)	(0.1)[c]	
0.25	0.5	57	22	0.4	21
		(72)	(28)	(0.5)[c]	
0.24[e]	0.5	69	24	0.2	7
		(74)	(26)	(0.2)[c]	
0.5	0.5	52	21	0.4	27
		(71)	(28)	(0.6)[c]	
0.4[e]	0.5	66	26	0.2	8
		(72)	(28)	(0.3)[c]	
1.0	1.0	45	21	0.5	33
		(67)	(32)	(0.8)[c]	
1.6	1.6	41	22	0.6	36
		(64)	(35)	(0.9)[c]	

[a] $[AcO^-]/[AcOH]$ = 17. [b] Ionic strength = [NaOAc] + $[NaClO_4]$. [c] Relative proportions of $PhCH_2OH$ + $PhCH_2OCH_2CF_3$ + PhCHO calculated directly from chromatographic data rather than the normalized results. [d] Total recovery = 96%. [e] $[AcO^-]/[AcOH]$ = 4. [f] Total recovery = 101%.

Table VIII. Rate Effect of Imidazole Buffers upon Solvolysis of Benzyl Azoxytosylate (**1b**) in 1:1 (v/v) TFE–H_2O at 42 °C

$[Im/ImH^+]$,[a] mol dm^{-3}	10^5k, s^{-1}
0[b]	4.6
0.40	29
0.74	49
1.0	61

[a] Aqueous solution of Im adjusted to pH ~6.4 with concentrated $HClO_4$ at which total buffer concentration = 2.0 mol dm^{-3}; samples of this were then diluted to give solutions 1.48 and 0.80 mol dm^{-3}, and each of these was diluted 1:1 with TFE. [b] 1:1 H_2O–TFE with no buffer and no $NaClO_4$.

Table IX. Products from Solvolysis of Benzyl Azoxytosylate (**1b**) in 1:I (v/v) H_2O–TFE at 42 °C in the Presence of Imidazole Buffers

$[Im/ImH^+]$,[a] mol dm^{-3}	% $PhCH_2OH$	% $PhCH_2OCH_2CF_3$	% PhCHO	% ImTs	% CF_3CH_2OTs
0	76	24	0	0	0
0.05	42	17	0.4	11	30
	(71)	(28)	(1)[b]		
0.25	26	6	0.8	14	53
	(79)	(19)	(2)[b]		
0.50	10	4	0.5	23	63
	(70)	(27)	(3)[b]		

[a] Im/ImH^+ ~ 0.8; in the absence of perchloric acid, virtually no $PhCH_2OH$ or $PhCH_2OCH_2CF_3$ was detected at 0.5 mol dm^{-3} imidazole. [b] $PhCH_2OH$ + $PhCH_2OCH_2CF_3$ + PhCHO = 100.

In contrast to the small effect of buffer concentration when sodium acetate/acetic acid is used, an appreciable dependence was found between the overall rate constant and the concentration of imidazole/imidazolium perchlorate buffers, Table VIII and Figure 3. Correspondingly, CF_3CH_2OTs is formed in greater yields by using buffered imidazole (Table IX) rather than buffered acetate (Table VII); there is also a new product which was identified as *N*-tosylimidazole by isolation and comparison with an authentic sample.[22] Since this compound is itself susceptible to base-catalyzed solvolyses,[25] its yields in Table IX must be regarded as minimum values. As in the reaction with buffered acetate, very little benzaldehyde was produced with buffered imidazole, but again, as a proportion of the solvolysis product, it increases as the buffer concentration increases. In the absence of an acid buffer, *N*-tosylimidazole, trifluoroethyl tosylate, and *N*-nitrosobenzylhydroxylamine are virtually the only products in 1:1 H_2O–TFE at 0.5 mol dm^{-3} imidazole.

Table X. Products from Solvolysis of Benzyl Azoxytosylate (**1b**) in H_2O–TFE–EtOH[a] at 42 °C

[NaSCN], mol dm^{-3}	ionic strength[b]	% $PhCH_2OH$	% $PhCH_2OCH_2CF_3$	% $PhCH_2OEt$	% $PhCH_2SCN$
0	0.5	74	23	2.9	0
0.25[c]	0.5	64	19	2.5	15
		(75)	(22)	(3)[e]	
0.5	0.5	57	18	3.0	22
		(73)	(23)	(4)[e]	
1.0[d]	1.0	48	17	3.3	32
		(70)	(25)	(5)[e]	
1.5	1.5	42	19	3.0	36
		(66)	(29)	(5)[e]	

[a] Mole fractions = 0.80:0.185:0.015 (50:47:3 by volume). [b] Ionic strength = [NaSCN] + $[NaClO_4]$. [c] Total recovery = 103%. [d] Total recovery = 98%. [e] Proportions of solvent-derived products.

Table XI. Rates of Solvolysis of Benzyl Azoxytosylate (**1b**) in 1:1 (v/v) H_2O–CH_3CN Containing Various Solutes at 42 °C

solute	[solute], mol dm^{-3}	ionic strength[a]	10^5k, s^{-1}
0	0	0	3.29
$NaClO_4$	0.50	0.5	3.51
NaSCN	0.20	0.5	3.42
NaOAc	0.15	0.5	3.28
NaOAc	0.25	0.5	3.16
NaOAc/AcOH[b]	0.2	0.5	3.15
NaOAc/AcOH[b]	0.3	0.5	2.86

[a] Ionic strength made up with $NaClO_4$. [b] $[AcO^-]/[AcOH]$ = 29.

Table XII. Effect of [NaSCN] upon Products from Benzyl Azoxytosylate (**1b**) in 1:1 (v/v) H_2O–CH_3CN at 42 °C[a]

[NaSCN], mol dm^{-3}	% $PhCH_2OH$	% $PhCH_2SCN$
0	100	0
0.2	89	11
0.5	80	20
1.0	71	29

[a] Ionic strength = 0.50 mol dm^{-3} ($NaClO_4$).

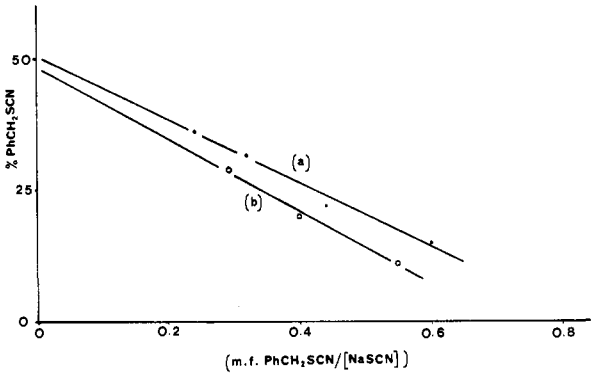


Figure 4. Plots of percent $PhCH_2SCN$ vs. (mole fraction yield of $PhCH_2SCN$)/[NaSCN] for the solvolysis of benzyl azoxytosylate (**1b**) in (a) H_2O–TFE–EtOH and (b) H_2O–CH_3CN, 42 °C.

2. In Aqueous Trifluoroethanol Containing Ethanol. The effect of sodium thiocyanate upon the product distribution from the solvolysis of **1b** in this ternary solvent is shown in Table X. The limiting yield of $PhCH_2SCN$ was calculated to be 50% at infinite concentration of sodium thiocyanate by an Eadie–Hofstee plot[26]

(25) Monjoint, P.; Laloi-Diard, M. *Bull. Soc. Chim. Fr.* **1973**, 2357–2361. Monjoint, P.; Ruasse, M.-F. *Tetrahedron Lett.* **1984**, *25*, 3183–3186.

(26) Eadie, G. S. *J. Biol. Chem.* **1942**, *146*, 85–93. Hofstee, B. H. J. *Ibid.* **1952**, *199*, 357–364.

Table XIII. Products from Solvolysis of Benzyl Azoxytosylate (**1b**) in 1:1 (v/v) H_2O–CH_3CN at 42 °C in the Presence of Sodium Acetate

[NaOAc], mol dm^{-3}	ionic strength[a]	% $PhCH_2OH$	% PhCHO	% $PhCH_2OAc$
0	0	100	0.03	0
0.06	0.06	99.6	0.4	0
0.10[b]	0.10	99.3	0.7	0
0.10[c]	0.5	99.6	0.4	≤0.1
0.2[d]	0.2	98.9	1.1	0
0.2[c]	0.5	99.2	0.8	≤0.2
0.3[e]	0.3	98.3	1.7	0
0.3[c]	0.5	98.7	1.3	≤0.3
0.4[f]	0.5	97.7	2.3	0

[a] Ionic strength = [NaOAc] + [$NaClO_4$]. [b] Total recovery = 99%. [c] Buffered with AcOH, ratio [AcO^-]:[AcOH] = 29. [d] Total recovery = 96%. [e] Total recovery = 100%. [f] Final reaction mixture had to be diluted at room temperature to obtain a single liquid phase for HPLC analysis.

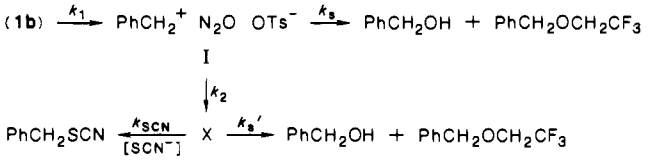
shown in Figure 4. This result is gratifyingly similar to the result of 47% found in the absence of the ethanol. The small proportion of $PhCH_2OC_2H_5$ within the solvent-derived product is hardly affected by the sodium thiocyanate, and the trends for $PhCH_2OH$ and $PhCH_2OCH_2CF_3$ are very similar to what was found in the binary solvent system without the ethanol.

3. In Aqueous Acetonitrile. The effects of several solutes upon the rate of solvolysis of **1b** in 1:1 (v/v) H_2O–CH_3CN are given in Table XI. Sodium perchlorate is weakly rate enhancing, thiocyanate has virtually no effect at constant ionic strength, and sodium acetate has a rate-retarding effect which is enhanced by acetic acid buffering. Effects of sodium thiocyanate and acetate (unbuffered and buffered with acetic acid) upon product distributions are given in Tables XII and XIII. From the limited results of Table XII, a three-point Eadie–Hofstee plot (Figure 4) indicates a limiting yield of about 48% $PhCH_2SCN$ at infinite sodium thiocyanate concentration in this medium. This is in line with what was found in the aqueous trifluoroethanol with and without ethanol. Sodium acetate leads to the formation of small yields of benzaldehyde but barely detectable amounts of benzyl acetate. As in aqueous trifluoroethanol, the formation of benzaldehyde is suppressed by buffering the acetate with acetic acid, but it still increases with increasing buffer concentration.

Discussion

1. Reaction in Aqueous Trifluoroethanol. The results in Tables I and II show that nonbasic electrolytes introduce no appreciable second-order kinetic terms. In view of the normal susceptibility of benzylic electrophiles to bimolecular attack by soft nucleophiles such as SCN^- and I^-, these results are quite unusual and are probably due to the driving force for the reaction coming mainly from the departure of the N_2O and TsO^- in tandem. Increasing concentrations of sodium thiocyanate at constant ionic strength, however, lead to increasing yields of benzyl thiocyanate. This result demonstrates that at least some extent of the reaction proceeds through a reactive intermediate which is sufficiently long-lived to be intercepted by dilute nucleophiles. The intercept in the double reciprocal plot of $[SCN^-]^{-1}$ vs. (mole fraction yield of $PhCH_2SCN)^{-1}$, Figure 2, gives 47% as the limiting yield of $PhCH_2SCN$ as $[SCN^-]$ increases. This corresponds to the proportion of the overall reaction which proceeds through the trappable intermediate. The remaining 53% of the reaction gives only solvent-derived product (36% $PhCH_2OH$ and 17% $PhCH_2OCH_2CF_3$) by a route with which even very high concentrations of powerful nucleophiles cannot compete. Iodide and bromide were also used as nucleophilic traps for the long-lived intermediate, using an indirect method necessitated by the instability of the benzyl halides themselves to the solvolytic conditions. As $[I^-]$ increases from 0.15 to 0.5 mol dm^{-3} (with $[SCN^-]$ = 0.05 mol dm^{-3} or lower), the extent of trapping increases from 12% to 23%. These results are about the same as those obtained using SCN^- as the direct nucleophilic trap. From a more limited set of data, bromide appears to be a less effective trap for the long-lived intermediate. Qualitatively, these relative nucleophilicities of Br^-, I^-, and SCN^- toward an electrophile are unexceptional,[27] but if we take the results of Table III to indicate a factor of only 2 in the rate constants of the long-lived intermediate with I^- and Br^-, a rather low Swain–Scott s value of about 0.2 is indicated in this medium compared with an s value of about 0.4 for benzyl tosylate based upon n_{CH_3I} values in methanol.[10,27]

Scheme I



The most obvious mechanism which accommodates these results so far involves an initial rate-determining step of **1b** to give a very short-lived species which is not trappable by solutes but which partitions between capture by solvent and formation of the long-lived intermediate before undergoing any appreciable extent of diffusion through the solvent.

Whilst there have been claims that the benzyl cation itself can be a trappable intermediate,[12] recent results[10,28] indicate that it would be far too short-lived to be intercepted by thiocyanate in the present investigation. Two experimental observations suggested that benzyl tosylate might be the long-lived intermediate. In the first case, we had detected 2-adamantyl tosylate in the solvolysis of the corresponding 2-adamantyl azoxytosylate even in media as nucleophilic as aqueous ethanol.[5] Secondly, thermolysis of **1b** in nonsolvolytic media such as chloroform in the absence of nucleophiles gave complete conversion to benzyl tosylate in a clean first-order reaction. Accordingly, Scheme I was formulated with the benzyl cation as a nontrappable very short-lived electrophilic intermediate, I, separated from its tosylate counterion by only the nitrous oxide molecule and with X = $PhCH_2OTs$ as the trappable long-lived intermediate formed by ion pair combination from the N_2O-separated ion pair. By applying the steady-state approximation to X (estimates of the reactivity of $PhCH_2OTs$ in 1:1 TFE–H_2O at 42 °C indicate that it would be very reactive),[10-12] eq 1 is obtained as the relationship between the yield of $PhCH_2SCN$ and the concentration of SCN^- in the medium (see Appendix).

$$\frac{1}{\text{mole fraction of } PhCH_2SCN} = \frac{k_s'(k_s + k_2)}{k_2 k_{SCN}[SCN^-]} + \frac{(k_s + k_2)}{k_2} \quad (1)$$

In qualitative agreement, a plot of (mole fraction yield of $PhCH_2SCN)^{-1}$ against $[SCN^-]^{-1}$ is linear (Figure 2). However, according to eq 1, the ratio of the gradient to the intercept allows calculation of $k_s'/k_{SCN} = 0.4_5$ mol dm^{-3} for the intermediate X. This ratio allows us to calculate an approximate minimum half-life of 3×10^{-10} s for the long-lived intermediate in 1:1 (v/v) aqueous trifluoroethanol without additional nucleophiles assuming a diffusion-controlled rate constant of 5×10^9 dm^3 mol^{-1} s^{-1} for its reaction with SCN^-. If the reaction with SCN^- is less than diffusion controlled, then the solvolytic half-life is correspondingly longer. We established by direct measurements that this ratio of the first-order solvolytic rate constant to that of the second-order reaction with thiocyanate for $PhCH_2OTs$ is actually only 0.08 mol dm^{-3} in 1:1 (v/v) TFE–H_2O.[10] In other words, a much lower concentration of SCN^- (5 times lower) is sufficient to trap $PhCH_2OTs$ in this medium than is required for the long-lived intermediate in the reaction of **1b**, so we are dealing with a more reactive and shorter lived species than $PhCH_2OTs$. The same deductions follow from the low estimated Swain–Scott s value (see above). Whilst these results rule out $PhCH_2OTs$ as the long-lived intermediate in the solvolysis of **1b**, they do not, of

(27) Pearson, R. G.; Sobel, H.; Songstad, J. *J. Am. Chem. Soc.* **1968**, *90*, 319–326. Swain, C. G.; Scott, C. B. *Ibid.* **1953**, *75*, 141–147.
(28) Richard, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1982**, *104*, 4689–4691; **1984**, *106*, 1373–1383.

course, invalidate the mechanism of Scheme I altogether.

2. Selectivities of the Intermediates in Scheme I. As $[SCN^-]$ is increased, the yields of $PhCH_2OH$ and $PhCH_2OCH_2CF_3$ tend toward limiting values of 36% and 17%, respectively, a ratio of 2.1:1. These represent the yields of solvent-derived products through that proportion of the reaction via a species which cannot be intercepted by even very high concentrations of nucleophilic solutes. Since the molar proportion of H_2O–CF_3CH_2OH in the solvent is 4:1, we are witnessing an approximately 2-fold selectivity of some electrophile in favor of CF_3CH_2OH over the much more nucleophilic water.

The total yields of $PhCH_2OH$ and $PhCH_2OCH_2CF_3$ in the absence of SCN^- are 76:24, so the yields of these two products via the long-lived intermediate are 76–36 and 24–17, i.e., 40% and 7%, respectively. This represents a molar ratio of about 6:1, or a small selectivity in the expected sense in favor of water. For comparison, $PhCH_2OTs$ gives $PhCH_2OH$:$PhCH_2OCH_2CF_3$ = 81:19 (approximately 4:1, or no selectivity) in its reaction with 1:1 TFE–H_2O, 0.5 mol dm^{-3} in $NaClO_4$,[10] which constitutes corroborative evidence that it is not the trappable intermediate X in Scheme I. These differences in selectivity for benzyl substitution by nucleophilic components of a mixed solvent as the leaving group is changed (a p_{xy} effect) are exceptionally large and comparable with the changes more usually associated with changes in the nucleophile (measured by β_{nuc}) or with substituent effects in the benzylic residue (p_{xy} effects).

3. Effect of Ethanol upon the Reaction in Aqueous Trifluoroethanol. The results in Table X demonstrate the effect upon the products of replacing a small proportion of the very weakly basic trifluoroethanol by a cosolvent ethanol which is not very dissimilar in size and molecular shape but which is much more nucleophilic.[29] The mole fraction composition of this medium is H_2O:CF_3CH_2OH:EtOH = 0.80:0.185:0.015 compared with 0.8:0.2 H_2O:TFE in the 1:1 (v/v) medium. This small proportion of ethanol should not cause any major perturbation of the overall reaction or drastically alter the bulk properties of the medium. In agreement with this expectation, the Eadie–Hofstee plot[26] in Figure 4 based upon eq 2 of the Appendix leads to a calculated limiting yield of 50% $PhCH_2SCN$ as $[SCN^-] \rightarrow \infty$ compared with 47% in the absence of the ethanol.

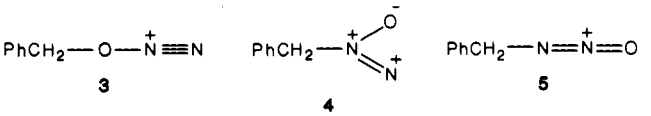
The overall yield of $PhCH_2OC_2H_5$ at about 3% is largely unaffected by the presence or concentration of NaSCN, so very little of this product can arise from the long-lived intermediate which is trappable by the SCN^-. Taking the yields of $PhCH_2OTFE$ as 23% at $[SCN^-] = 0$ and 17% as $[SCN^-] \rightarrow \infty$ about 6% of the 50% of reaction via the long-lived intermediate is captured by CF_3CH_2OH in the absence of SCN^- and 44% by H_2O. Consequently, 74 – 44 = 30% of the reaction is formed by H_2O reacting with some electrophile not trappable by SCN^-. Thus, in H_2O–TFE–EtOH (0.80:0.185:0.015),

	$PhCH_2OH$	+ $PhCH_2OCH_2CF_3$	+ $PhCH_2OC_2H_5$
trappable intermediate ⟶	44	6	⩽1
nontrappable species ⟶	30	17	3

Again, therefore, we see that the trappable intermediate demonstrates a small selectivity in favor of water over trifluoroethanol whereas the selectivity of the nontrappable electrophile between these two solvent components is in the opposite and unexpected sense by a factor of about 2.4:1 ($PhCH_2OH$:$PhCH_2OCH_2CF_3$ ~ 1.8:1 compared with H_2O:TFE = 4.3:1). However, comparison of the ratio of $PhCH_2OCH_2CF_3$:$PhCH_2OC_2H_5$ (6:1) from the nontrappable electrophile with the molar proportion CF_3CH_2OH:C_2H_5OH (12.3:1) indicates an approximately 2-fold selectivity in favor of the more nucleophilic ethanol, which suggests that the anomaly in the $PhCH_2OH$:$PhCH_2OCH_2CF_3$ ratio may be more to do with a suppressed nucleophilicity of water in the vicinity of the electrophile rather than a real selectivity in favor of CF_3CH_2OH.

4. The Identity of the Long-Lived Intermediate and the Possible Nonexistence of a Short-Lived Intermediate. The kinetic and product analytical evidence so far discussed requires two product-forming routes followed to similar extents but leading to characteristically different proportions of solvent-derived products in a mixed solvent. According to the mechanism in Scheme I as originally propounded,[9] the product-forming routes diverge from a very short-lived intermediate I, the N_2O-separated ion pair, which is produced in the initial rate-determining step of the reaction. One route involves a relatively long-lived (trappable) intermediate, the other involves solvent capture of the benzyl carbonium ion, and it is the standard free energy barriers of the respective routes from the first-formed cationic intermediate I which describe (or determine) the partitioning between the two routes according to this mechanism.

Tosylate anion has been shown to intercept carbocations in even quite nucleophilic solvents, and its effectiveness in such cases must be due to its close proximity to the nascent carbonium ion rather than to its inherent base strength.[5,30,31] Nitrous oxide must be at least equally well positioned to intercept the benzyl cation produced in the initial heterolysis of **1b** in Scheme I as tosylate anion even though it too is inherently a weak nucleophile. The reversible departure of the even more weakly nucleophilic N_2 from arenediazonium ions[32] is a precedent for such a reaction. Whilst combination of $PhCH_2^+$ with N_2O could in principle be at one of three sites to give **3**, **4**, or **5**, formation of benzaldehyde in the solvolysis of **1b** in the presence of bases (see below) is direct evidence that the trappable intermediate is in fact **3**. Supportive evidence has been provided by recent ab initio molecular orbital calculations on the relative stabilities of the products obtained from the addition of R^+ to N_2O in the gas phase where R = H, CH_3, and $PhCH_2$.[33,34]



3 4 5

Although the mechanism of Scheme I appears to accommodate the results so far discussed, an alternative matter of detail needs to be considered. If there were no free energy barrier to the capture of the benzyl cation by a solvent molecule, then the N_2O-separated ion pair corresponds not to an intermediate but to an activated complex in an uncoupled concerted process.[35] And, if there is no barrier in the reaction of the benzyl cation with solvent, there can be none in its reaction with N_2O to give the long-lived intermediate 3; otherwise none of the reaction would follow this route. If, in this migration from nitrogen to oxygen, the $PhCH_2^+$ becomes sufficiently detached that orbital overlap is insignificant, then orbital symmetry considerations need not be a (theoretical) constraint. An alternative partial mechanism to the early part of Scheme I, therefore, involves fragmentation

(29) Bentley, M. D.; Lacadie, J. A. *Tetrahedron Lett.* **1971**, 741–744. Kaspie, J.; Rappoport, Z. *Ibid.* **1977**, 2035–2038. Harris, J. M.; Raber, D. J.; Neal, W. C.; Dukes, M. D. *Ibid.* **1974**, 2331–2334. Allard, B.; Casadevall, A.; Casadevall, E.; Largeau, C. *Nouv. J. Chimie* **1979**, *3*, 335–342.

(30) Albert, A.; Serjeant, E. P. *Ionization Constants of Acids and Bases*; Methuen: London, 1962. Dinius, R. H.; Choppin, G. R. *J. Phys. Chem.* **1962**, *66*, 268–270.

(31) Zefirov, N. S.; Koz'min, A. S. *Acc. Chem. Res.* **1985**, *18*, 154–158.

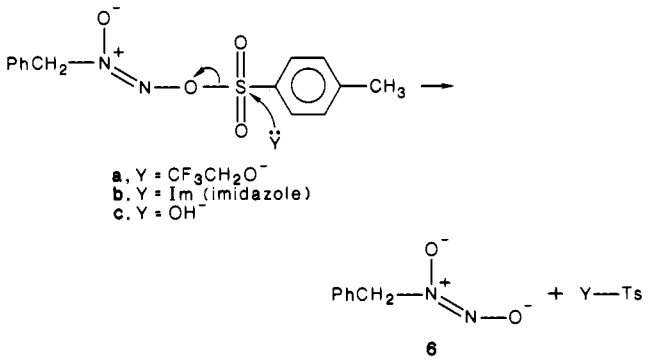
(32) Bergstrom, R. G.; Wahl, G. H.; Zollinger, H. *Tetrahedron Lett.* **1974**, 2975–2978. Hegarty, A. F. In *The Chemistry of Diazonium and Diazo Groups*; Patai, S., Ed.; Wiley-Interscience: Chichester, England, 1978; Chapter 12.

(33) Gill, P. M. W.; Maskill, H.; Poppinger, D.; Radom, L. *J. Chem. Res.*, in press.

(34) Alternative mechanisms involving stepwise fragmentation of **1b** were also considered. The kinetic effects of substituents in the benzyl residue and in the arenesulfonate leaving group are $\rho(\sigma^+) = -3.23$ and $\rho(\sigma) = 1.27$, respectively (unpublished work, H. Maskill and I. M. Galloway). These results indicate that the bonds to *both* the benzyl *and* the nucleofuge are undergoing heterolysis in the rate-determining step, hence the fragmentation must be concerted. They also rule out an initial Meisenheimer-type rearrangement of **1b** as the route to the formation of **3**.

(35) Jencks, W. P. *Chem. Soc. Rev.* **1981**, *10*, 345–375.

Scheme II



of **1b** and uncoupled concerted capture of the incipient benzyl cation either by a solvent molecule or, if none is appropriately positioned, then by the N_2O molecule through its oxygen. An equivalent description of this alternative partial mechanism is in terms of three parallel uncoupled processes from **1b** in which the electrophilic (benzylic) moieties and the nucleofuges are identical; in one, the nucleophile (N_2O) is a reorientated part of the nucleofuge, and in the other two, the nucleophiles are H_2O and CF_3CH_2OH. The proportions of these three routes from **1b** (47:36:17) are determined (or described) by the relative standard free energies of the respective activated complexes in the three parallel routes from **1b**. However, since the routes with H_2O and CF_3CH_2OH take place to relative extents different from the molar proportions of H_2O and CF_3CH_2OH in the medium, these must take place via preassociation steps. This is entirely compatible with the selectivity in favor of CF_3CH_2OH since the pendant oxygen of the azoxy group will be a basic site to form a better hydrogen bond with the more acidic solvent component thereby facilitating heterolysis and leaving a CF_3CH_2OH molecule especially well placed to capture the nascent benzyl cation.

The significant difference between the alternative mechanisms, both of which appear to account for the results so far, is that in one the N_2O-separated ion pair is an intermediate, admittedly a very short-lived one which does not survive diffusion through the solvent, and in the other it is the major part of three very closely related activated complexes. Whilst the conceptual distinction is clear enough, an experimental differentiation is more problematical, and further evidence, perhaps theoretical, may need to be considered.

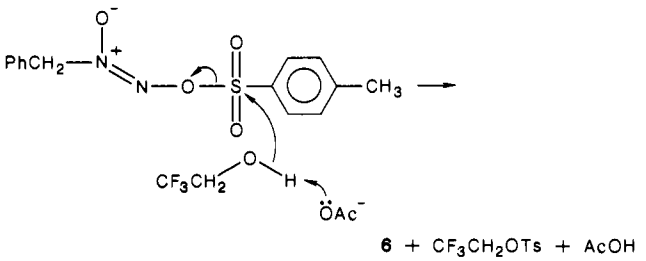
5. Effect of Bases upon the Reaction of 1b in 1:1 TFE–H_2O.

(a) Sodium Acetate. There is a substantial approximately linear dependence between the concentration of unbuffered sodium acetate and the overall rate of reaction of **1b** in 1:1 TFE–H_2O (Table IV, Figure 3). When the sodium acetate is buffered with acetic acid, the rate enhancements become very small and dependent upon the buffer ratio (Table VI, Figure 3). The results in the buffered media indicate catalysis mainly by the small equilibrium concentration of the conjugate base of the solvent, principally $CF_3CH_2O^-$. However, since pK_{AH} (CH_3CO_2H) << pK_{AH} (CF_3CH_2OH),[30,36] unbuffered sodium acetate in the 1:1 TFE–H_2O system will lead to only a very low extent of solvent deprotonation, and [$CF_3CH_2O^-$] should be proportional to [NaOAc]$^{1/2}$. Consequently, the observed rate constants in reactions with unbuffered acetate should be proportional to [NaOAc]$^{1/2}$, rather than [NaOAc] as is found, if the rate enhancements were exclusively due to $CF_3CH_2O^-$. The results in the buffered solutions are quite compelling, so we deduce that the rate enhancements in the unbuffered acetate solutions are due to reaction induced mainly by $CF_3CH_2O^-$ but that there is some small extent of reaction facilitated by acetate itself and probably minor complications due to specific salt effects. Some small extent of catalysis by acetate itself is also indicated by the product analytical results.

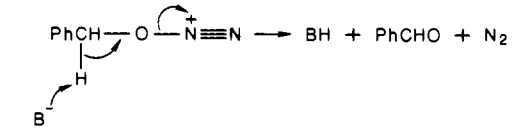
In both buffered and unbuffered reactions, two new products were detected by HPLC and identified as benzaldehyde (minor)

(36) Ballinger, P.; Long, F. A. *J. Am. Chem. Soc.* **1960**, *82*, 795–798.

Scheme III



Scheme IV



and trifluoroethyl tosylate (major); although the formation of benzyl acetate had been expected, it occurs to a barely detectable extent. In the unbuffered reactions, the yield of trifluoroethyl tosylate increased rapidly as [$CH_3CO_2^-$] increased. The formation of CF_3CH_2OTs is substantially suppressed by buffering, but even at constant buffer ratio there is still some increase in its yield as the buffer concentration is increased. The formation of CF_3CH_2OTs, therefore, seems principally to be due to direct reaction of **1b** with the low equilibrium concentration of $CF_3CH_2O^-$ (Scheme II, Y = $CF_3CH_2O^-$) but with some contribution due to reaction of **1b** with solvent catalyzed by acetate (Scheme III).

Regardless of detail, the formation of CF_3CH_2OTs requires nucleophilic attack at the sulfur of the substrate in a nonsolvolytic route and displacement of the *N*-benzylazoxy anion **6** perhaps with some extent of assistance to departure by hydrogen bonding. Other reactions involving nucleophilic attack at the sulfur of the tosyl group have been reported.[25] The mechanisms of Schemes I, II, and III represent an interesting case of a substrate (**1b**) whose unimolecular and bimolecular reactions with nucleophiles take place with different heterolytic bond cleavages involving electron flow in opposite directions.[37] The electron flow in the unimolecular heterolysis of **1b** implied by the mechanism of Scheme I is in one direction and that in the bimolecular reactions of **1b** in Schemes II and III is in the other, although both will be facilitated by H bonding by the solvent at the pendant oxygen of the azoxy group.

The minor product in the reaction of **1b** in 1:1 TFE–H_2O containing unbuffered acetate is benzaldehyde, the absolute yield of which levels off at about 1% as [AcO^-] increases and solvolysis is overtaken by the reaction of **1b** to form CF_3CH_2OTs. However, within the yield of $PhCH_2OH$ + $PhCH_2OCH_2CF_3$ + PhCHO, the proportion of PhCHO increases as [$CH_3CO_2^-$] increases (Table V) almost wholly at the expense of benzyl alcohol. These results are compatible with benzaldehyde being a product of the long-lived intermediate within the solvolytic mode. Freeman and Lillwitz[2] have already shown that much more basic conditions than those employed here are necessary for direct reaction of **1b** with a base via abstraction of a proton from the benzylic carbon.

A well-precedented mechanism which accounts for the formation of benzaldehyde and which provides structure **3** for the long-lived intermediate implicated in the trapping experiments with nucleophiles is given in Scheme IV.[38] The base in this E2 mechanism could, in principle, be acetate itself or the equilibrium concentration of $CF_3CH_2O^-$ generated by acetate with the solvent. Whilst the formation of benzaldehyde is suppressed by buffering, its yield does increase with buffer concentration at constant buffer ratio. Consequently, although the major route from **3** to PhCHO involves B^- = $CF_3CH_2O^-$, there is also catalysis by acetate.

(37) Maskill, H. *Chem. Commun.* **1986**, 1433.

(38) Smith, P. J.; Pollock, C. A.; Bourns, A. N. *Can. J. Chem.* **1975**, *53*, 1319–1326. Bartsch, R. A.; Cho, B. R. *J. Am. Chem. Soc.* **1979**, *101*, 3587–3591. Hoffman, R. V.; Balfoure, E. L. *Ibid.* **1979**, *101*, 5687–5692.

Increasing the buffer concentration also causes the proportion of $PhCH_2OCH_2CF_3$ to increase at the expense of $PhCH_2OH$, Table VII. This result implicates acetate catalysis in the displacement of N_2O by CF_3CH_2OH and relates to catalysis in the capture of relatively stable 1-arylethyl carbocations by CF_3CH_2OH.[39] Such a mechanism would also be operative in the unbuffered reactions and explains why the proportion of $PhCH_2OCH_2CF_3$ did not decrease along with that of $PhCH_2OH$ as the proportion of benzaldehyde increases with increasing acetate concentrations.

Four principal reactions of the long-lived intermediate **3** have, therefore, been identified: (i) uncatalyzed displacement of N_2O by solvent with H_2O more effective than CF_3CH_2OH, (ii) acetate-catalyzed displacement of N_2O by CF_3CH_2OH to give $PhCH_2OCH_2CF_3$, (iii) displacement of N_2O by dilute nucleophiles such as SCN^-, and (iv) base-induced proton abstraction with loss of N_2 to give benzaldehyde—the E2 mechanism. Displacements of N_2 from primary alkyldiazonium ions by either solvent molecules or nucleophilic solutes are well known analogies of reaction modes i and iii above.[4,40]

(b) Imidazole. In contrast to the results obtained by using acetate–acetic acid, imidazole–imidazolium perchlorate buffers lead to appreciable increases in the observed overall reaction rate. The increasing yields of CF_3CH_2OTs with increasing buffer concentration indicate that imidazole is an effective catalyst for the reaction of CF_3CH_2OH with **1b** in a way that acetate is not. The detection and identification of another major product, *N*-tosylimidazole, implicates an additional nonsolvolytic reaction: direct nucleophilic attack by the base at the sulfur of **1b**, Scheme II, Y = imidazole. At 0.5 mol dm^{-3} unbuffered imidazole, *N*-tosylimidazole, trifluoroethyl tosylate, and, presumably, the *N*-benzylazoxy anion **6** are the only detectable products. For comparison, 0.5 mol dm^{-3} unbuffered acetate still allows 20% solvolysis in addition to 80% CF_3CH_2OTs.

The total yield of solvolysis product obviously decreases with increasing buffer concentration; consequently, it was not possible to investigate how the ratio $PhCH_2OH$:$PhCH_2OCH_2CF_3$:PhCHO varied at higher imidazole concentrations with any sort of precision. The limited results in Table IX indicate, however, that imidazole is more effective than acetate in producing PhCHO from the long-lived intermediate via the E2 mechanism but not more effective in catalyzing the solvent-induced displacement of N_2O.

6. Reaction in Aqueous Acetonitrile. The effects of solutes upon rates in aqueous acetonitrile are shown in Table XI and are similar to those found in aqueous trifluoroethanol. The estimated limiting yield of $PhCH_2SCN$ at high concentrations of SCN^- is about 48% via the Eadie–Hofstee plot[26] of Figure 4 using the data of Table XII, which is virtually the same as in aqueous trifluoroethanol. We take this as evidence of a very closely related mechanism, but, in aqueous CH_3CN, $PhCH_2OH$ is the only solvent-derived product.

As in the reaction in H_2O–TFE, sodium acetate produces virtually no benzyl acetate, and the low yields of benzaldehyde are partly suppressed by buffering with acetic acid, Table XIII. This is the expected result if proton abstraction from the long-lived intermediate **3** in the E2 mechanism is both by the equilibrium concentration of the conjugate base of the solvent, this time OH^-, and by acetate itself. There is also an indication that the rate decrease as perchlorate (with a substantial rate-enhancing specific salt effect) is replaced by acetate (with a rate-retarding effect) is greater when the acetate is buffered (Table XI). This suggests that the rate-retarding salt effect by acetate in the absence of buffer is partially offset by a small base catalysis contribution via OH^-. By analogy with our findings in the aqueous trifluoroethanol, this would be the nonsolvolytic reaction via the mechanism in Scheme II with Y = OH^-.

Acknowledgment. We thank the University of Stirling for granting sabbatical leave to H.M. Most of the experimental work was carried out at Brandeis University supported by the National Institutes of Health (GM 20888) and the National Science Foundation (PCM 81-17816), to whom we are grateful.

Appendix

Assuming that the reaction of Scheme I is kinetically controlled, the mole fraction yield of $PhCH_2SCN$ is

$$\frac{k_{SCN}[X]\,[SCN^-]}{k_s[I] + (k'_s + k_{SCN}[SCN^-])[X]}$$

and if the steady-state approximation may be applied to the reactive intermediate X

$$k_2[I] = (k'_s + k_{SCN}[SCN^-])[X]$$

Substituting for [X] in the former equation by using the latter and simplifying the outcome gives the mole fraction yield of $PhCH_2SCN$ as

$$\frac{k_2 k_{SCN}[SCN^-]}{k'_s(k_s + k_2) + k_{SCN}(k_s + k_2)[SCN^-]}$$

which may be transformed into

$$\frac{1}{\text{mole fraction yield of } PhCH_2SCN} = \frac{k'_s(k_s + k_2)}{k_2 k_{SCN}[SCN^-]} + \frac{(k_s + k_2)}{k_2} \quad (1A)$$

or

$$\text{mole fraction of } PhCH_2SCN = \frac{k_2}{(k_s + k_2)} - \left(\frac{\text{(mole fraction of } PhCH_2SCN)}{[SCN^-]}\right)\frac{k'_s}{k_{SCN}} \quad (2A)$$

Registry No. 1b, 25370-91-6; NaSCN, 540-72-7; NaBr, 7647-15-6; NaOAc, 127-09-3; HOAc, 64-19-7; $PhCH_2OH$, 100-51-6; $PhCH_2SCN$, 3012-37-1; $PhCH_2OCH_2CF_3$, 67696-28-0; CF_3CH_2OTs, 433-06-7; $NaClO_4$, 7601-89-0; NaI, 7681-82-5; $HClO_4$, 7601-90-3; CF_3CH_2OH, 75-89-8; CH_3CN, 75-05-8; PhCH=NOH, 932-90-1; $PhCH_2NHOH$, 622-30-0; $PhCH_2N(N{=}O)OH$, 28571-11-1; NaCl, 7647-14-5; NaOH, 1310-73-2; imidazole, 288-32-4.

(39) Richard, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 1396–1401.

(40) Kirmse, W.; Arold, H. *Chem. Ber.* **1970**, *103*, 23–26.