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Participation by Ether Oxygen (RO-3) in the Hydrolysis of Sulfonate Esters of 2-Methoxyethanol and 2-Methoxy-2-methyl-1-propanol. Implications Regarding the Nonlinear Ethanol–Trifluoroethanol Plot for Mustard Chlorohydrin

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The lack of scrambling with deuterium-labeled reactants, a nonlinear ethanol–trifluoroethanol plot, and rate acceleration by added thiourea are used to show that sulfonate esters of methoxyethanol ($MeOCH_2CH_2OH$) undergo solvent-assisted displacement in a variety of solvents; neighboring group participation by ether oxygen (RO-3 participation) does not occur. This conclusion is in accord with predictions of rate based on the Taft treatment of substituent effects. On the other hand, the branched derivative $MeOCMe_2CH_2OBs$ reacts with concerted RO-3 participation to give completely rearranged product. Its solvolysis rate is insensitive to added thiourea, the Taft treatment predicts modest anchimeric assistance, and a linear ethanol–trifluoroethanol plot is observed. We discuss the implications of these results relative to the previously observed nonlinear plot for mustard chlorohydrin.

In discussing intramolecular nucleophilic assistance by a neighboring group, Winstein found it useful to define solvolytic rate constants in mechanistic terms: k_Δ being the rate constant for anchimerically assisted ionization, k_s being the rate constant for nucleophilically assisted displacement by solvent, and k_c being the rate constant for the idealized process that involves neither neighboring group nor solvent nucleophilic assistance. In their pioneering studies, Winstein and his co-workers found that oxygen in the five or six position of $MeO(CH_2)_nOBs$ gave large solvolytic rate enhancements although oxygen in the three or four position slowed solvolysis.[1,2] They concluded that RO-5 and RO-6 participation to form five- and six-membered rings was strong, while RO-3 and RO-4 participation to form three- and four-membered rings was weaker; the RO-3 system was described as a borderline k_s–k_Δ system.

Recently, Eliel and co-workers have shown RO-4 participation to be absent from the system with $n = 4$.[3] However, in branched systems such as $PhCH_2O$- and $MeOCMe_2(CH_2)_nX$ ($n = 1, 2$), Winstein[1] and Eliel[3] have shown that RO-3 and RO-4 participation can be enhanced relative to direct displacement by solvent. Branching favors neighboring group participation by sterically slowing solvent displacement,[4] by stabilizing the cyclic ions,[5] and by the Thorpe–Ingold effect.[6] Although the branched RO-3 substrate gives complete rearrangement, the RO-4 system gives a variable amount of rearrangement dependent on the number and position of methyl branches and medium effects. Neither study yielded compelling data to confirm significant anchimeric assistance by the neighboring oxygen atom.

In contrast with their oxygen analogues, substrates with neighboring sulfur groups show a different trend with position of the neighboring group. In the substrates $RS(CH_2)_nX$, RS-3 participation is the most effective,[7] while five-membered ring formation is found to be the fastest with other neighboring groups.[2] Eliel and co-workers have recently shown that RS-4 participation is weak, occurring only in branched systems.[8]

In this article we apply additional mechanistic probes to more clearly understand RO-3 participation in compounds **1** and **2**. Additionally, the oxygen systems are used to better our understanding of the ethanol (EtOH)–trifluoroethanol (TFE) probe. We recently reported that the EtOH–TFE plot for mustard chlorohydrin is nonlinear despite the fact that it solvolyzes with strong assistance by the neighboring sulfur group (a k_Δ process) and without nucleophilic solvent assistance (a k_s process).[9] Previously, nonlinear EtOH–TFE plots have been observed for k_s processes and linear plots have been observed for k_c and k_Δ processes.[10,11] Hence the mustard chlorohydrin result was considered a failure of the EtOH–TFE probe. A possible cause of the failure is that rates are retarded in TFE by hydrogen bonding to the sulfur neighboring group. If this is the failure mode, substrates bearing a neighboring oxygen group should be even more sensitive to hydrogen bonding by TFE and hence should also give a nonlinear EtOH–TFE plot. Consequently, we have examined the solvolysis rates of **1**-OMs and **2**-OBs in aqueous EtOH and TFE.

$$MeOCR_2CR'_2X$$

$$\mathbf{1}\text{:}\ R = R' = H$$

$$\mathbf{2}\text{:}\ R = Me;\ R' = H$$

$$\mathbf{3}\text{:}\ R = H;\ R' = D$$

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(7) Reference 2, Chapter 6. Also see: McManus, S. P.; Yorks, K.; Harris, J. M. *J. Polym. Sci., Polm. Chem. Ed.* **1985**, *23*, 379. Harris, J. M.; Paley, M. S.; Sedaghat-Herati, M. R.; McManus, S. P. *J. Org. Chem.* **1985**, *50*, 5230.

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Table I. Solvolysis of 2-Methoxyethyl Mesylate in Water, Aqueous Ethanol (v/v), and Aqueous Trifluoroethanol (w/w)

solvent (Y_{OMs})	temp, °C	10^4K, s^{-1}
H_2O (4.12[a])	68.3	1.41[b,c]
	60.0	0.818 ± 0.018
	70.0	1.57 ± 0.08
20% EtOH (3.21[d])	68.3	1.16[b,c]
	70.0	1.23 ± 0.01
	75.0	1.43 ± 0.04
40% EtOH (2.17[e])	68.3	0.386[b,c]
	70.0	0.446 ± 0.009
	75.0	0.677 ± 0.014
	80.0	1.01 ± 0.05
60% EtOH (1.13[d])	68.3	0.203[b,c]
	75.0	0.334 ± 0.008
	85.0	0.680 ± 0.007
60% TFE (2.24[f])	68.3	0.125 ± 0.001
70% TFE (2.15[d])	68.3	0.0702[b,c]
	72.0	0.114 ± 0.005
	79.1	0.276 ± 0.009
	94.8	1.81 ± 0.09
97% TFE (1.92[d])	68.3	0.0207[b,c]
	92.4	0.0769 ± 0.0012
	104.9	0.143 ± 0.008

[a] Extrapolated from the linear relationship (r = 0.992) for Y_{OMs} of 80%, 60%, 50%, and 20% EtOH and 40% and 20% acetone vs. Y_{OTs}; see ref 12. [b] Extrapolated from rates at other temperatures. [c] Because of the narrow temperature range the ΔH^* and ΔS^* values obtained are not reliable for wide extrapolations. [d] From the rate data of Table I, ref 12. [e] Extrapolated by using the linear relationship between Y_{OMs} and Y_{OTs} for 80%, 60%, 50% and 20% ethanol. [f] Extrapolated by using the linear relationship between Y_{OMs} for 97%, 70% and 50% TFE and the 1-AdBr rates at 35° (r = 0.992); Kaspi, J.; Rappoport, Z. *J. Am. Chem. Soc.* **1980**, *102*, 3829.

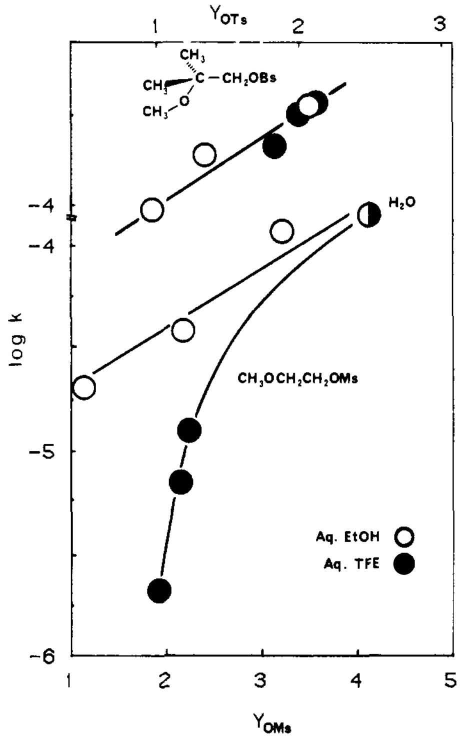

Figure 1. Ethanol–trifluoroethanol plots of log k vs. Y_{OMs} (bottom scale) for 1-OMs and vs. Y_{OTs} (top scale) for 2-OBs.

Results

Ethanol–Trifluoroethanol Probe. 2-Methoxyethyl mesylate (1-OMs) was sovolyzed in pure water and in three concentrations of aqueous EtOH and TFE. At least duplicate determinations of rate constants were obtained conductimetrically at two or more temperatures (Table I).

Table II. Solvolysis of 2-Methoxy-2-methyl-1-propyl Brosylate (2) in Aqueous Ethanol and Trifluoroethanol at 90.0 °C

solvent	10^4K, s^{-1} (no. of detns)	solvent	10^4K, s^{-1} (no. of detns)
40% EtOH	2.05 ± 0.24 (9)	50% TFE	2.07 ± 0.15 (6)
50% EtOH	1.31 ± 0.116 (7)	70% TFE	1.89 ± 0.25 (5)
60% EtOH	0.859 ± 0.006 (2)	97% TFE	1.48 ± 0.40 (7)

Table III. Effect of Thiourea on the Rate of 2-Methoxyethyl Mesylate Solvolysis in Water (75 °C) and of the Tosylate in 50% Aqueous Trifluoroethanol (80 °C)

system	M, thiourea	10^4k, s^{-1}	k/k_0
ROMs/H_2O	0.0	2.15[a]	1.0
	0.2	3.13 ± 0.09	1.45
	0.5	5.06 ± 0.09	2.35
ROTs/50% TFE	0.0	0.420 ± 0.08	1.00
	0.1	0.710 ± 0.07	1.69
	0.2	1.19 ± 0.05	2.86
	0.5	2.50 ± 0.16	5.94
	1.0	5.16 ± 0.12	12.4

[a] Computed from rates at other temperatures from Table I.

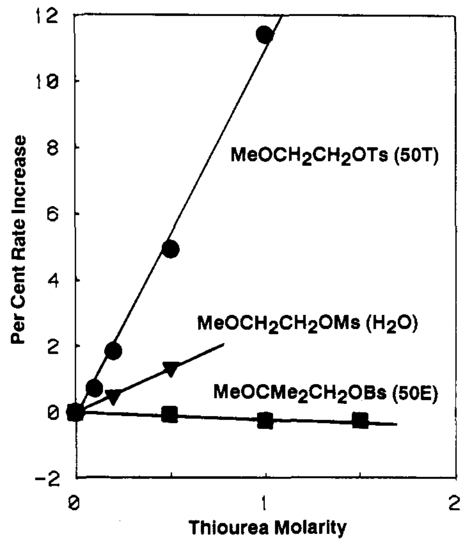

Figure 2. Effect of added thiourea on pseudo-first-order rates for 1-OMs in water (▼), 1-OTs in 50% aqueous TFE (●), and 2-OBs in 50% aqueous EtOH (■).

Since McLennan[11] found that use of Y values determined for leaving groups different from that under study may present interpretational problems, we have plotted (Figure 1) log k for 1-OMs against Y_{OMs} values, calculated from the available rate data for 1-adamantyl mesylate.[12] Separate correlations for the aqueous EtOHs and TFEs are found.

2-Methoxy-2-methyl-1-propyl brosylate (2-OBs) was synthesized and its kinetics in aqueous EtOHs and TFEs were determined (Table II). The average standard deviation of the pseudo-first-order rate constants determined for **2** in these solvents is much larger than that normally found for well-behaved substrates. Therefore, several individual rate determinations (Table II) were made in some solvent compositions to provide a higher confidence factor. A plot of Y_{OTs} vs. log k values (Figure 1) shows a reasonable

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[12] Bentley, T. W.; Carter, G. E. *J. Org. Chem.* **1983**, *48*, 579. A referee has suggested that Y_{OTs} values should be used rather than construction of a new scale of Y values. While Bentley and Carter did not calculate Y_{OMs} values in the referenced article, their determination is straightforward. Numerically, Y_{OMs} and Y_{OTs} values are not the same yet they do give a good correlation (correlation coefficient = 0.998). By using the available mesylate data we are avoiding any question of the leaving group causing the two correlation lines in our figure.

Table IV. First-Order Rate Constants for Solvolysis of 2 in 50% Aqueous Ethanol at 90.0 °C with Thiourea

M, thiourea	10^4k	k/k_0	M, thiourea	10^4k	k/k_0
0.0	1.31	1.0	1.0	1.05	0.80
0.5	1.19	0.91	1.5	1.07	0.82

linear correlation (r = 0.969).

Effect of Thiourea on Rates. Conductimetric rates were determined for solvolysis of 1-OMs in water and of 1-OTs in 50% aqueous TFE with and without added thiourea (Table III). A plot of k/k_0 vs. thiourea molarity in each case has a positive slope and is linear (r = 0.997), Figure 2.

The branched brosylate 2-OBs was also subjected to solvolysis with varying amounts of added thiourea (Table IV). A plot of k/k_0 vs. thiourea molarity is shown in Figure 2.

Deuterium-Labeling Studies. Methoxyethanol-*1,1*-d_2, 3-OH, was prepared in 80% yield by reduction of methyl 2-methoxyacetate with lithium aluminum deuteride. The alcohol was converted to its tosylate 3-OTs by using the standard pyridine procedure.[13] In 70:30 CD_3COCD_3–D_2O, the ^1H NMR spectra at 200 MHz of the deuteriated and nondeuteriated alcohols and tosylates were uncomplicated. The aliphatic portion of the deuteriated tosylate consisted of the methoxy singlet at 3.27 ppm, the CH_2 singlet at 3.60 ppm, and the aryl CH_3 singlet at 2.47 ppm. The aryl region consisted of doublets at 7.82 and 7.52 ppm. Upon heating this solution at 80 °C for 12 h, the NMR spectrum indicated the hydrolysis to be about 20% complete. On the basis of comparison with a known sample, new singlet peaks at 3.36 and 3.51 ppm were assignable to CH_3O and $MeOCH_2$ resonances in $MeOCH_2CD_2OH$, respectively. The new aryl CH_3 was at 2.36 ppm, and in the aromatic region two new doublets from the sulfonate group appeared at 7.25 and 7.72 ppm. No new peak appeared at either 4.15 ppm where the CH_2OSO_2 resonance in the nondeuteriated tosylate appears or at 3.71 ppm where the CH_2OH resonance in the nondeuteriated alcohol appears. After further heating at 80 °C for an additional 24 h, ^1H NMR showed that the hydrolysis had proceeded to about 50% completion. Again, the only peaks present were those assigned to unreacted 3, the unscrambled alcohol hydrolysis product, and TsOD.

Discussion

Application of Solvent Assistance Probes to 1 and 2. Recently we have found that assignment of mechanism for k_s, k_c, and k_Δ substrates is aided by an analysis of the rate behavior when thiourea is added.[14] Thiourea, a powerful neutral nucleophile, accelerates the rate for k_s substrates, giving a linear correlation between rate increase and thiourea molarity. When thiourea is added to solvolytic reactions of k_c or k_Δ substrates, the rates are slightly depressed nonlinearly with respect to thiourea concentration.[14] Application of this probe to the methoxyalkyl substrates (Figure 2) shows linear acceleration for the unbranched substrate 1, consistent with reaction by a k_s mechanism, and slight rate depression for the branched system 2, consistent with reaction by either a k_c or k_Δ mechanism.

To confirm reaction of 1 by a k_s mechanism, we synthesized 2-methoxyethanol specifically deuterated at C-1, 3-OH. The tosylate ester 3-OTs was prepared and subjected to hydrolysis conditions by being heated in 50% aqueous acetone. Having characterized the deuteriated and nondeuteriated alcohols and tosylates by ^1H NMR, it was readily determined by NMR that hydrolysis of 1-OTs proceeds without rearrangement, and it was shown that reaction does not produce a cyclic oxonium ion that returns to neutral tosylate. In the latter case a new resonance owing to CH_2OSO_2 would have appeared at 4.15 ppm. The spectrum was clean in this region at 20% and at 50% reaction. This experiment also revealed that no 2-methoxyethanol with C-1 and C-2 scrambled is formed. Had this been the case, a new peak at 3.71 ppm, owing to the CH_2OD resonance, would have appeared. Therefore, there is no evidence from this hydrolysis experiment to implicate any mechanism other than direct nucleophilic displacement of the leaving group by solvent. In contrast, the branched compound 2-OBs undergoes acetolysis to give completely rearranged products.[1]

Raber, Harris and co-workers[10] have shown that there is a linear correlation of rates in aqueous EtOHs and aqueous TFEs with Y values for a number of k_c and k_Δ substrates. By constrast, k_s substrates give separate correlation lines for aqueous EtOH and aqueous TFE rates. Our application of this probe to 1-OMs and 2-OBs, Figure 1, shows a typical, nonlinear k_s plot for 1 and a linear k_c–k_Δ plot for 2.

In summary, the EtOH–TFE probe, the thiourea probe, and product studies are consistent with reaction of compound 1 by a k_s mechanism. The EtOH–TFE probe and the thiourea probe are consistent with the assignment of either a k_c or k_Δ mechanism for 2-OBs. Because the product is 100% rearranged, a k_Δ mechanism seems to be strongly indicated. Before this is assigned, evidence that anchimeric assistance is occurring is necessary. That issue is addressed in the following section.

On the Question of Anchimeric Assistance in 2-OBs. Rate Comparisons. We noted above that 2-OBs undergoes solvolysis without nucleophilic solvent assistance; thus it is indicated to react by either a k_c or a k_Δ mechanism. Two factors strongly suggest that the substrate is reacting by a k_Δ and not a k_c mechanism. First, formation of a primary cation under these conditions is unprecedented. Past experience would suggest that a superacid medium, which is both highly electrophilic and highly ionizing, would be necessary.[15] Because primary carbocations are quite unstable and are normally sterically unhindered, primary substrates undergo solvolysis with nucleophilic solvent assistance. If this nucleophilic attack is made sterically unattractive by placing branched substituents near the reactive site, then the primary substrates will react with neighboring carbon or hydrogen assistance to give a rearranged carbocation.[15] An excellent example of this sort of behavior is provided by solvolysis of neopentyl derivatives, which have recently been unequivocally demonstrated to react by a k_Δ process.[16]

Since 2-OBs rearranges completely,[1,17] it seems reasonable that this rearrangement and ionization are concurrent.

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[14] McManus, S. P.; Neamati-Mazraeh, N.; Karaman, R. M.; Harris, J. M. *J. Org. Chem.* **1986**, *51*, 4876.

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[17] In aqueous dioxane, Winstein, Lindegren, and Ingraham (ref 1c) found that the only product of rearrangement of 2-OBs is isobutyraldehyde. They propose a reasonable reaction mechanism that involves a methoxy shift to form $Me_2C^+CH_2OMe$ followed by a hydride shift to form the oxonium ion $Me_2CHCH{=}O^+Me$, which is the precursor to isobutyraldehyde.

Table V. Taft Treatment for $MeOCH_2CH_2OBs$ (1-OBs) and $MeOC(Me)_2CH_2OBs$ (2-OBs)

	σ^* for R in	log k/k_0		
structure	RCH_2OBs^a	$EtOH^b$	$HCOOH^b$	$AcOH^b$
$CH_3CH_2CH_2CH_2OBs$	−0.115	−0.283	−0.108	−0.258
$ClCH_2CH_2CH_2OBs$	+0.385	−0.697	−0.880	−0.786
$PhCH_2CH_2CH_2OBs$	+0.08	−0.346	−0.360	−0.405
$MeOCH_2CH_2CH_2OBs$	+0.14	−0.459	−0.583	−0.444
1-OBs				
(actual)[c]	+0.52	−0.880	−1.125	
(calcd)		(−0.787)[e]	(−1.11)[f]	
2-OBs				
(actual)[c]	+0.32[d]			−0.191
(calcd)				(−0.683)[g]

[a] From ref 14. [b] From ref 1. [c] Not included in the correlation. [d] From ref 18 by summation of listed values.[21] [e] R = −0.968. [f] R = −0.987. [g] R = −0.982.

Table VI. Comparison of Rates of Different Substrate Types in Solvents of Varying Nucleophilicities

$\dfrac{k^{Me_2CRCH_2OSO_2Ar}}{k^{RCH_2OSO_2Ar'}}$	solvent[a]						
	EtOH	AcOH	60E	40E	70T	97T	TFA
Me[b]	1100	7.3					0.0155
MeO[c]			3.24	3.13	1.60	0.133	

[a] AcOH = acetic acid; 60E = 60 aqueous EtOH; T = aqueous TFE; TFA = trifluoroacetic acid. [b] Reference 15. [c] Rates are at 90 °C. Rates for 1-OBs are obtained by extrapolating rates of 1-OMs (Table I) from other temperatures and multiplying by 2.9.

If this is the case, then the rate will be enhanced as compared to an appropriate k_s model system. The key in detecting this rate enhancement is to compare solvolysis rates with an appropriate model. An excellent method for achieving this comparison is Taft's σ^* method.[2,15,18] By correlating the reactivity of a series of primary model compounds that react by a k_s mechanism, the k_s rate of the suspect derivative can be calculated and compared to the observed value. As mentioned above, Winstein et al.[1] used this method for 1-OBs, but some of their model substrates have since been shown to react with anchimeric assistance. For example, it is now well-known that 2-(*p*-anisyl)ethyl substrates, and even 2-phenylethyl derivatives in some solvents, are complex in that they react by competing k_s and k_Δ mechanisms.[19] Also, some neighboring halogens are suspected of participation even when they may have to form four-membered rings.[20] Therefore, to achieve our goal of providing a reasonable k_s model, we have conservatively selected four model substrates for which no compelling evidence of anchimeric assistance exists. Our revised treatment is shown in Table V. The actual and calculated values for log k/k_0 for 1-OBs and 2-OBs are shown as the last entry in the respective columns in Table V.[21]

As can be seen by comparing the calculated and measured rates, and as would be expected from the studies above, 1-OBs is predicted by this probe to be a k_s substrate; the calculated k_s rates in both ethanol and formic acid are very close to the observed rates. However, when the computed rate of 2-OBs is compared with its observed rate in acetic acid, the calculated rate is found to be significantly slower than the observed rate. Since all the model compounds in this correlation are receiving substantial (approximately 10^4) nucleophilic solvent assistance,[15] and since it is known that 2-OBs does not receive this assistance, it is reasonable to conclude that 2-OBs is receiving neighboring carbon assistance, i.e., reaction by a k_Δ mechanism (with weak anchimeric assistance) is indicated.

It is also revealing simply to compare rate trends of **1** and **2** with mechanistically well characterized models having similar structures. The evidence is very strong for reaction of *n*-propyl substrates by a k_s mechanism and neopentyl substrates by a k_Δ mechanism.[15,16] The steric differences between those models and **1** and **2** are essentially the same. Reaction by a k_Δ mechanism in the case of neopentyl is due to loss of nucleophilic solvent assistance, which the *n*-propyl substrate enjoys, and the availability through methyl migration of the more stable tertiary carbocation. A bridged carbocation intermediate has not been proposed.[15,16] Instead, the transition state involves a bridged species with one pentavalent methyl carbon.

An analysis of medium effects is also revealing. There is a trend to smaller rate ratios for *n*-propyl/neopentyl tosylates and 1-OBs/2-OBs in solvents of decreasing nucleophilicity, Table VI. A similar trend is found if rates for 1-OTs are compared with those of 2-adamantyl tosylate, a weak k_Δ substrate.[22] A final point is that the Winstein–Grunwald *m* values in aqueous ethanols for 1-OMs and 2-OBs are 0.30 and 0.31, respectively. It has previously been shown that *m* values of this magnitude are found for k_s and k_Δ substrates.[15] On the other hand the *m* value for 1-adamantyl tosylate is very different, being 1.0.

To summarize, with 2-OBs, anchimeric assistance is weak, hence the indicators do not unambiguously require the k_Δ mechanism. Nevertheless, when solvent assistance is sterically prevented and rearrangement provides a much more stable cation than can be directly obtained, concerted rearrangement to form the more stable intermediate is favored a priori and commonly occurs.[15,22] With 2-OBs, the bridged ion is probably not an intermediate. Such a process has generally been called a "downhill reaction" with the first intermediate being the rearranged cation. In connection with this discussion Eliel and his co-workers[3] have recently suggested that RO-4 participation occurs without anchimeric assistance in the primary and secondary derivatives that they studied. As we indicated above, we are skeptical of this viewpoint, as we view the possibility of forming primary or unhindered secondary carbocations in an unassisted process as unlikely, especially in a nucleophilic solvent such as methanol. The problem that these authors faced is similar to ours; when anchimeric assistance is weak, its detection is difficult. This point has been well made by the recent finding that 2-adamantyl, long thought to be a pure k_c secondary substrate, reacts with carbon participation.[22]

Implications Regarding Ethanol–Trifluoroethanol Plots. We have shown in a previous study that mustard chlorohydrin, $HOCH_2CH_2SCH_2CH_2Cl$, **4**, undergoes solvolysis by a k_Δ mechanism, and yet it gives a nonlinear EtOH–TFE plot typical of a k_s derivative.[9] We have suggested that one possible reason why the probe failed for **4** may be that **4** has a lower susceptibility to electro-

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(19) Review: Lancelot, C. J.; Cram, D. J.; Schleyer, P. v. R. In *Carbonium Ions*; Olah, G. A., Schleyer, P. v. R., Eds.; Wiley: New York, 1972; Vol. 3, Chapter 27.

(20) Peterson, P. E. *Acc. Chem. Res.* **1971**, *4*, 407. Olah, G. A. *Halonium Ions*; Wiley: New York, 1975, Chapters 7–9.

(21) The Taft constant for the $MeOC(CH_3)_2$ substituent was estimated by adding the value for two methyls (2 × −0.1) to the value (0.52) of $MeO\text{-}CH_2$. This method of estimating σ^* values gives the accepted value for *tert*-butyl (0.0 + 3 × −0.100 = −0.300).

(22) Cheung, C. R.; Tseng, L. T.; Lin, M.-H.; Srivastara, S.; le Noble, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 1598. For evidence favoring a k_c mechanism for 2-adamantyl, see: Bentley, T. W.; Schleyer, P. v. R. *Ibid.* **1976**, *98*, 7658.

philic solvent assistance than 1-adamantyl chloride, the model for the plot.[9,23] This difference would lead to a relative rate retardation for **4** in the highly electrophilic (strongly hydrogen bonding) TFEs. A logical source for this difference in electrophilicity would be solvation of the sulfur neighboring group in **4** by TFE. The oxygen neighboring group of compound **2** should be even more strongly solvated than the sulfur of **4**, and one might expect the EtOH–TFE plot for **2**-OBs to be even more strongly curved than that for **4**. However, as shown in Figure 1, **2**-OBs gives a linear plot, the usual result for k_Δ substrates.

Before rejecting our previous explanation for failure of the plots with **4**, we must consider possible reasons why a comparison of **2** and **4** may be improper. Three such reasons seem plausible. First, compound **2** may be a poor model for the solvation effects on the neighboring group of **4** because of steric hinderance by the geminal methyls to solvent approach to the neighboring oxygen in **2**. Second, neighboring group assistance is much more powerful in **4** than in **2**, and this difference may lead to neighboring group desolvation being important in the transition state for **4** but not for **2**. And third, the proposed low sensitivity of **4** to solvent electrophilicity may be unassociated with the neighboring group. For example, it is predicted from potential energy surface diagrams[24] that a better neighboring group will lead to a transition state in which bond cleavage to the leaving group is reduced; the observation that **4** has a low OTs/Cl rate ratio[25] is consistent with this prediction. A reduction in charge development on the leaving group could easily give a reduction in sensitivity to electrophilic solvent assistance.

In summary, we have shown that esters of the unbranched structure **1** react by a k_s mechanism, while the branched analogue **2**-OBs reacts with weak neighboring oxygen participation (a k_Δ mechanism). The linear EtOH–TFE plot observed for **2** is in sharp contrast to the nonlinear plot observed for **4**, despite the similar reaction mechanisms; the reason for the nonlinear plot for **4** remains unclear.[25a]

Experimental Section

General. Solvents used for kinetic measurements were dried and purified by using standard literature procedures and were sealed and stored in a desiccator until mixed with cosolvents. NMR measurements were made on an IBM-Bruker AFT-200 system. Melting points and boiling points are uncorrected.

Isobutylene oxide was prepared by using the procedure of Pasto and Cumbo:[26] bp 58 °C; ^{1}H NMR ($CDCl_3$) 2.61 (s, 2 H, CH_2O) and 1.34 ppm (s, 6 H, CH_3).

2-Methoxy-2-methyl-1-propanol was prepared in 60% yield from isobutylene oxide as described by Winstein et al.:[1] bp 140 °C; ^{1}H NMR ($CDCl_3$) 3.42 (s, 2 H, CH_2OH), 3.23 (s, 3 H, CH_3O), 3.13 (ns, 1 H, OH), and 1.16 ppm (s, 6 H, $C(CH_3)_2$).

2-Methoxy-2-methyl-1-propyl brosylate (2-OBs) was prepared by using the standard pyridine procedure[13] and was crystallized from hexane: mp 47.5 °C; ^{1}H NMR ($CDCl_3$) 7.78, 7.69 (dd, J = 3.8 Hz, 4 H, ArH), 3.90 (s, 2 H, OCH_2), 3.14 (s, 3 H, CH_3O), and 1.16 ppm (s, 6 H, $C(CH_3)_2$).

2-Methoxyethanol-*1,1*-d_2 (3-OH). Under a nitrogen atmosphere, 20 g methyl 2-methoxyacetate in 50 mL of anhydrous ethyl ether was slowly added to a cooled, stirred suspension of 4.5 g of $LiAlD_4$ in 75 mL of anhydrous ethyl ether. The resulting solution was gently heated at reflux for 1.5 h and then worked up[27] by the slow, stepwise addition of 4.5 mL of H_2O, 6 mL of 3 M NaOH, and 12 mL of H_2O. The solution was filtered and the solid residue was extracted with three 100-mL portions of CH_2Cl_2. These extracts were combined with the ether filtrate and the combined extracts were concentrated in vacuo to give the deuteriated alcohol. Distillation gave 12 g (80%) of pure material (GC), bp 40 °C (40 mmHg). The ^{1}H NMR spectrum of the deuteriated alcohol was consistent with that of 2-methoxyethanol (**1**-OH) except for the absence of the peak at 3.71 ppm owing to the CH_2OH resonance. Also, the resonance for the remaining CH_2 group (at 3.51 ppm) is a singlet in **3**-OH.

2-Methoxyethyl-*1,1*-d_2 tosylate (3-OTs) was prepared by using the pyridine procedure[13] and purified by low temperature precipitation from hexane: ^{1}H NMR (70% $(CD_3)_2CO/D_2O$) 7.82, 7.52 (dd, 8.3 Hz, 4 H, ArH), 3.60 (s, 2 H, $MeOCH_2$), 3.27 (s, 3 H, OCH_3), and 2.47 ppm (s, 3 H, $ArCH_3$).

Kinetics. Pseudo-first-order rate constants were determined conductimetrically by using an automated procedure previously described.[28] Substrates were ca. 10^{-3} M in 10 mL of solvent. 2,6-Lutidine was added (ca. 10^{-3} M) to scavenge liberated acid. At least duplicate determinations were made unless otherwise noted in the tables.

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[23] Harris, J. M.; McManus, S. P.; Sedaghat-Herati, M. R.; Neamati-Mazraeh, N.; Kamlet, M. J.; Taft, R. W.; Doherty, R. M.; Abraham, M. H. In *Nucleophilicity*; Harris, J. M., McManus, S. P., Eds.; Adv. in Chem. Series, No. 215, American Chemical Society: Washington, D.C., 1987; pp 247–254.

[24] Shafer, S. G.; Harris, J. M. *J. Org. Chem.* **1981**, *46*, 2164.

[25] (a) McManus, S. P.; Neamati-Mazraeh, N.; Paley, M. S.; Hovanes, B. A.; Harris, J. M. *Tetrahedron Lett.* **1985**, *26*, 4571. (b) **Note Added in Proof**: Recent evidence with ArP (P-4), PhS (S-5), and PhSe (Se-3) neighboring groups confirms the present finding that electrophilic solvation of the neighboring group is not the cause of the EtOH–TFE probe failure. Instead, ion pair return, which is solvent dependent, is involved; cf. McManus, S. P.; et al., unpublished results.

[26] Pasto, D. J.; Cumbo, C. C. *J. Org. Chem.* **1965**, *30*, 1271.

[27] Reference 13, pp 581–595.

[28] Hovanes, B. A.; Harris, J. M.; McManus, S. P. *Am. Lab.* **1984**, *16*, No. 6, 22. McManus, S. P.; Lam, D. H. *J. Org. Chem.* **1978**, *43*, 650.