Effect of Solvent on β-Arylalkyl Solvolysis[1]

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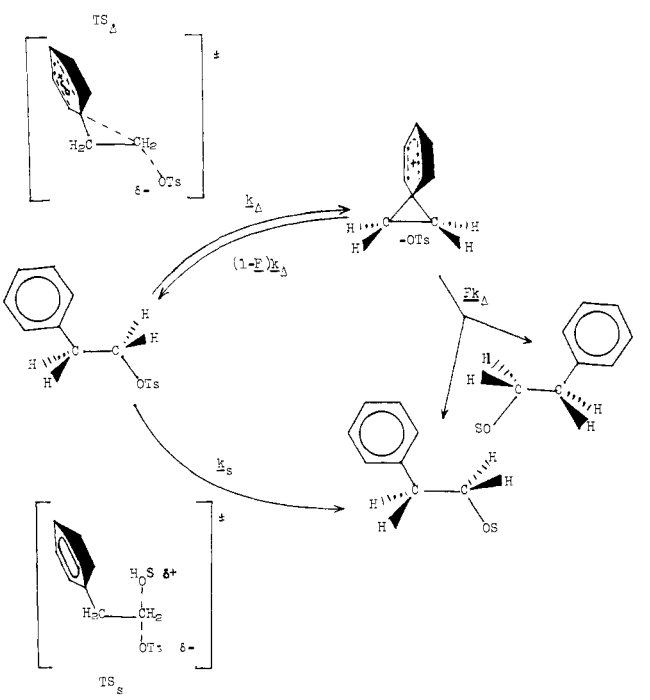
Abstract: Solvolysis rate constants, k_t, for a series of β-arylethyl and 1-aryl-2-propyl tosylates in solvents ranging from EtOH to CF_3CO_2H were dissected into their aryl assisted (Fk_Δ) and aryl unassisted (k_s) components in order to determine the effect of solvent on each reaction pathway. Correlations of k_s and k_Δ for $PhCH_2CH_2OTs$ and $PhCH_2CH(OTs)CH_3$, and of k_t for appropriate model substrates, EtOTs and 2-PrOTs, by the full Winstein-Grunwald equation, $\log (k/k_0) = mY + lN$, demonstrate quantitatively the different sensitivities evidenced by the k_s and k_Δ mechanisms to solvent ionizing power (Y) and solvent nucleophilicity (N): $PhCH_2CH_2OTs$, k_s ($m = 0.33$, $l = 0.78$), k_Δ ($m = 0.67$, $l \approx 0$), and EtOTs, k_t ($m = 0.36$, $l = 0.82$); $PhCH_2CH(OTs)CH_3$, k_s ($m = 0.50$, $l = 0.46$), k_Δ ($m = 0.82$, $l \approx 0$), and 2-PrOTs, k_t ($m = 0.60$, $l = 0.47$). Combinations of these constants allow the calculation of the $k_t(PhCH_2CH_2OTs)/k_t(EtOTs)$ ratios, which vary 7500-fold in going from CH_3CH_2OH to CF_3CO_2H, to within a factor of 2 of the experimental values and the $k_t(PhCH_2CH(OTs)CH_3)/k_t(2\text{-PrOTs})$ ratios to within factors of 2-4. Increased solvent ionizing power does not appear to change the kinetically significant degree of aryl participation in transition states leading to the phenonium intermediate appreciably, as is shown by the slight solvent variation of $\rho(k_\Delta)$ and by linear $m_\Delta Y$ plots. All available evidence supports the interpretation that primary and secondary β-arylalkyl substrates solvolyze by competition between discrete aryl assisted and aryl unassisted pathways, each leading to distinct sets of products. Nucleophilic solvent assistance plays a dominant role in the k_s pathway.

Solvolyses of all primary and most secondary β-arylalkyl systems proceed through discrete aryl assisted (k_Δ) and/or aryl unassisted (k_s) pathways (Scheme I).[3] Although Cram adopted this formulation when phenonium ions were first proposed as solvolysis intermediates,[4,5] two decades of intense investigation were required before the implications were quantitatively understood and all challenges could be answered satisfactorily. These studies also helped lead to the realization that simple[6a] secondary solvolysis, termed "borderline" in the S_N1-S_N2 spectrum of Hughes and Ingold, occurs with substantial nucleophilic solvent assistance.[6b]

Symmetrical phenonium ions were postulated to account for dominant retention of product stereochemistry in solvolyses of the 3-aryl-2-butyl system (I).[4a] However, the observed rate constants (k_t) of I were *lower,* in some cases, than those of a nonparticipating model, 2-butyl (k_t(*threo*-I-OTs)/k_t(2-butyl-OTs) = 0.6, acetic acid).[7] When corrected by even the most liberal factors for decelerative phenyl inductive effects[5,8] and internal return from the phenonium ions,[9] only moderate relative rate ratios were obtained (24,[5a] 43[5c]). If the model system, 2-butyl, solvolyzed by simple ionization (k_c), i.e. involved the formation of a nonnucleophilically solvated "open" ion ($k_s \equiv k_c$), the corrected rate enhancements would indicate too small a driving force[7,10] for participation in ionization (1.5-2.2 kcal/mol) to be consistent with the formation of a σ-bonded phenonium intermediate. As an "escape from the dilemma",[11b] Brown proposed weak π participation during ionization leading to a pair of rapidly equilibrating ions.[11,12]

Beginning in 1967, a series of treatments[1,5b,c,13-15] appeared which employed substrates containing *deactivated* phenyl groups as better models for the anchimerically unassisted route (k_s). Rate enhancements observed with *activated* phenyl groups would result from the incursion of the k_Δ process. This provided, for the first time, methods for the accurate dissection of the total rate constant (k_t) into its k_s and Fk_Δ[16] components, and allowed a clear test of mechanism. Solvent-vs.-aryl competition would predict quantitative agreement between values of Fk_Δ/k_t determined independently from rate data and from product stereochemistry, while the interpretation involving equilibrating ions would not predict such a correlation. Since remarkably exact rate-product correlations *were* found,[3,13d,14] the k_s and k_Δ pathways must be discrete, implying strong assistance by solvent or neighboring group compared to a limiting ionization process (k_c). Subsequent studies using the hindered 2-adamantyl substrate as a model for limiting (k_c) secondary

Scheme I



solvolyses quantitatively confirmed that simple secondary substrates are substantially assisted by nucleophilic solvent participation in all but the most ionizing, least nucleophilic media.[17-20]

To understand better the nature of k_s-k_Δ competition, we analyzed the effect of solvent on β-arylalkyl solvolysis. Changing the solvent from ethanol to trifluoroacetic acid causes a dramatic variation in the relative rate ratio (eq 1: the solvolysis rate, k_t, of a substrate capable of neighboring-group assistance relative to that of a nonparticipating model) for β-phenethyl tosylate (7500-fold, R = H) and for 1-phenyl-2-propyl tosylate (100-fold, R = CH_3).

$$\frac{k_t(PhCH_2CHROTs)}{k_t(CH_3CHROTs)} = \frac{Fk_\Delta(PhCH_2CHROTs) + k_s(PhCH_2CHROTs)}{k_s(CH_3CHROTs)} \quad (1)$$

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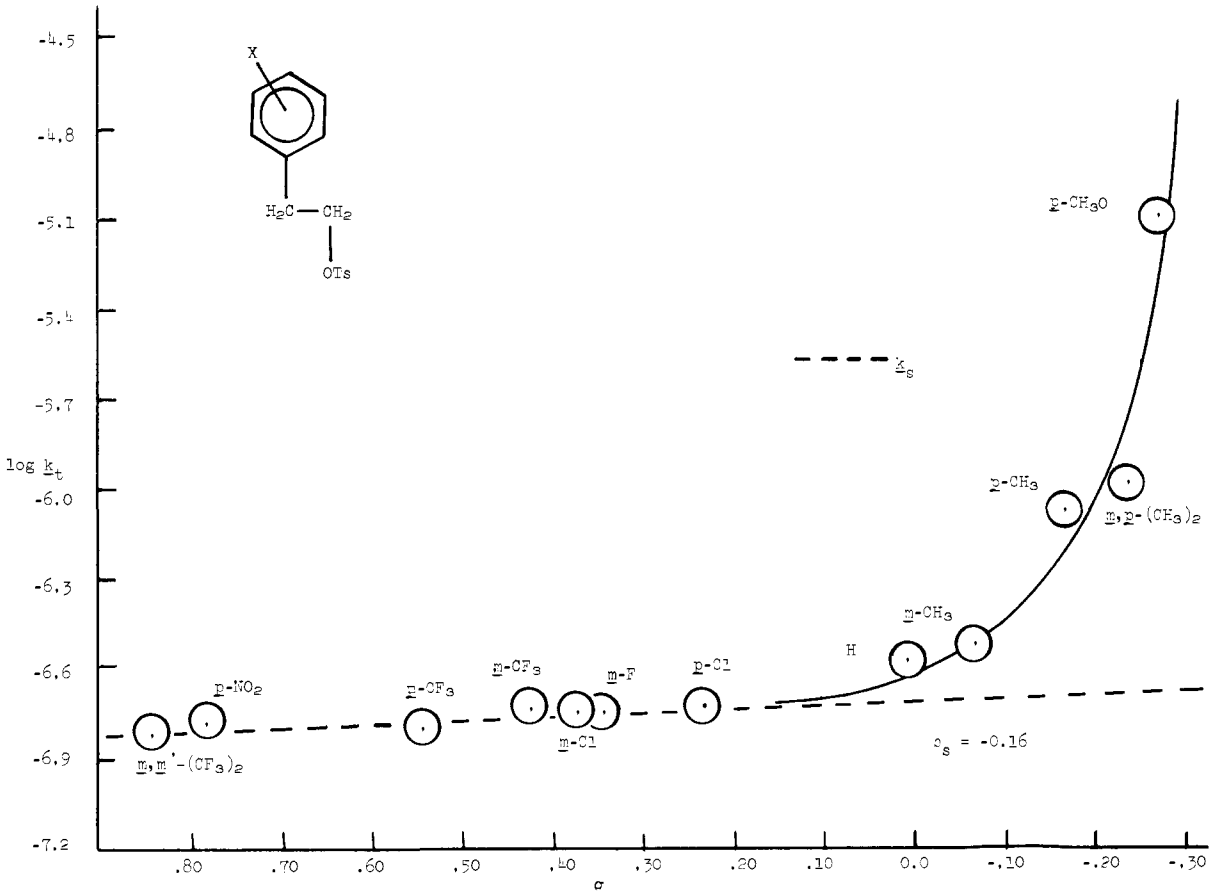


Figure 1. Plot of log k_t(β-arylethyl tosylates), acetic acid, vs. σ, 75 °C.

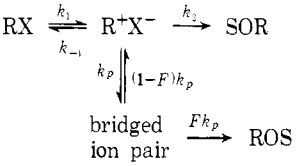
These large changes, indicating a shift in mechanism from aryl unassisted (k_s) to aryl assisted (k_Δ), could be caused by either of two effects or their combination:[21] (1) by a decrease in k_s($PhCH_2CHROTs$) and k_s($CH_3CHROTs$) relative to Fk_Δ as solvent nucleophilicity is decreased and/or (2) by an enhancement of the relative magnitude of Fk_Δ as solvent ionizing power is increased, caused by (a) different responses of the two dissimilar pathways to solvent ionizing power ($m_\Delta > m_s$)[21] or (b) an increase of aryl bridging in transition states (TS_Δ) leading to the phenonium intermediate.[5c,22] Dissected values of k_s and k_Δ for β-phenethyl tosylate (II) and 1-phenyl-2-propyl tosylate (III) were correlated with measures of solvent nucleophilicity (N) and solvent ionizing power (Y), and other parameters to determine which factors dominate.

With regard to the more intimate questions of mechanistic detail, it has been suggested that tight ion pairs are the species for which neighboring group and solvent compete in the solvolyses of secondary systems[14b,15,23-26] or substrates generally.[26-28] This mechanism[14b,15,23c,29,30] (Scheme II) is kinetically consistent with the original one involving attack on neutral substrate if the rate of internal return of the intimate ion pair (k_{-1}) is fast compared to k_2 or k_p ($k_{-1} \geq 20\ k_2$ and k_p[14b]). The wide range of solvent data presented here will be analyzed in light of these two mechanistic alternatives.

Results

Kinetics. A series of substituted β-arylalkyl tosylates were solvolyzed in a range of solvents possessing greatly different nucleophilicities and ionizing powers. Ethanolyses, acetolyses, and formolyses were studied by standard techniques; trifluoroacetolyses were determined by a special procedure, involving complete evaporation of the acidic solvent, developed here and described in the Experimental Section.

Scheme II



Primary β-Arylethyl Tosylates. The total rate constants, k_t (Table I), in all solvents except trifluoroacetic acid were dissected into their k_s and Fk_Δ components by the Hammett treatment[3,13-15] (Figure 1). Log k_t values for deactivated β-aryl substrates were plotted *vs.* σ constants to define a k_s line. Differences between log k_t for activated compounds and the extrapolated k_s line yield values of Fk_Δ. When several compounds defined the k_s line, an iterative procedure[13e] was employed to calculate and eliminate small percentages of Fk_Δ from the rates of these deactivated substrates. Initially, this was accomplished by constructing a plot of Fk_Δ for activated compounds vs. σ^+ and extending it through the σ^+ constants of the k_s substrates.[13e,31] Extrapolated Fk_Δ rate constants for these deactivated substrates were then deducted from their k_t values to give refined k_s points from which a new k_s line was constructed. Since slight curvatures have been noted in Fk_Δ(β-aryl)-σ^+ plots which include both activating and deactivating groups,[1b,5c,29,32-34] a scale of substituent constants more appropriate for β-aryl participation was devised with neophyl as standard.[1b,32,35] Using the Yukawa-Tsuno correlation[34] of Fk_Δ ($\equiv k_t$) for substituted neophyl brosylates in acetic acid (75 °C),[33,34,36] eq 2 (correln coeff 0.997), values of σ(neophyl) were calculated from experimental data (log $(k^X/k^H)/-3.96$) or from known values of σ and σ^+ ($\sigma + 0.43(\sigma^+ - \sigma)$).

Table I. Summary of Kinetic Data for β-Arylethyl Tosylates

Solvent	Substituent	Temp, °C	k_t, s^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
Ethanol	*p*-H	75.04	$(7.52 \pm 0.09) \times 10^{-6}$		
		75.01[a]	$(7.08 \pm 0.06) \times 10^{-6}$		
	p-CH_3	75.01	$(8.10 \pm 0.10) \times 10^{-6}$		
	p-CH_3O	75.01	$(1.38 \pm 0.02) \times 10^{-5}$		
		75.01[a]	$(1.35 \pm 0.03) \times 10^{-5}$		
50% (v/v) aq ethanol	*m,m'*-$(CF_3)_2$	75.03	$(3.47 \pm 0.10) \times 10^{-5}$	19.8	−22.4
		100.6	$(2.64 \pm 0.07) \times 10^{-4}$		
		75.0[b]	3.46×10^{-5}		
	p-NO_2	75.05	$(4.09 \pm 0.06) \times 10^{-5}$	20.0	−21.5
		100.6	$(3.17 \pm 0.08) \times 10^{-4}$		
		75.0[b]	4.07×10^{-5}		
	p-CF_3	75.08	$(4.16 \pm 0.02) \times 10^{-5}$	20.6	−19.6
		100.6	$(3.42 \pm 0.28) \times 10^{-4}$		
		75.0[b]	4.13×10^{-5}		
	m-CF_3	100.6	$(3.17 \pm 0.05) \times 10^{-4}$		
	m-Cl	75.05	$(4.26 \pm 0.09) \times 10^{-5}$	19.6	−22.7
		100.6	$(3.16 \pm 0.05) \times 10^{-4}$		
		75.0[b]	4.24×10^{-5}		
	m-F	74.99	$(4.48 \pm 0.03) \times 10^{-5}$	19.3	−23.4
		100.6	$(3.24 \pm 0.04) \times 10^{-4}$		
		75.0[b]	4.48×10^{-5}		
	p-Cl	75.02	$(4.40 \pm 0.02) \times 10^{-5}$	19.8	−21.8
		100.6	$(3.36 \pm 0.01) \times 10^{-4}$		
		75.0[b]	4.39×10^{-5}		
	p-H	75.04	$(5.39 \pm 0.06) \times 10^{-5}$	20.1	−20.8
		100.6	$(4.20 \pm 0.14) \times 10^{-4}$		
		75.0[b]	5.37×10^{-5}		
	p-C_6H_5	90.19	$(1.87 \pm 0.01) \times 10^{-4}$	19.7	−21.7
		103.37	$(5.04 \pm 0.04) \times 10^{-4}$		
		75.0[b]	5.44×10^{-5}		
	m-CH_3	75.01	$(5.48 \pm 0.04) \times 10^{-5}$	20.4	−19.6
		100.6	$(4.45 \pm 0.05) \times 10^{-4}$		
		75.0[b]	5.48×10^{-5}		
	p-CH_3	75.05	$(7.39 \pm 0.17) \times 10^{-5}$	21.4	−16.4
		100.7	$(6.61 \pm 0.04) \times 10^{-4}$		
		75.0[b]	7.36×10^{-5}		
	m,p-$(CH_3)_2$	75.03	$(8.88 \pm 0.10) \times 10^{-5}$	22.3	−13.5
		90.14	$(3.53 \pm 0.07) \times 10^{-4}$		
		75.0[b]	8.86×10^{-5}		
	p-CH_3O	75.05	$(2.87 \pm 0.11) \times 10^{-4}$	21.5	−13.4
		84.43[c]	6.40×10^{-4}		
		100.6	$(2.56 \pm 0.07) \times 10^{-3}$		
		75.0[b]	2.81×10^{-4}		
Acetic acid	*m,m'*-$(CF_3)_2$	75.0[b,d]	1.52×10^{-7}	23.8	−21.7
	p-NO_2	75.0[b,d]	1.66×10^{-7}	23.7	−21.7
	p-CF_3	75.0[b,d]	1.62×10^{-7}	24.6	−19.4
	m-CF_3	75.0[b,d]	1.90×10^{-7}	23.4	−22.5
	m-Cl	75.0[b,d]	1.86×10^{-7}	23.9	−21.0
	m-F	75.0[b,d]	1.87×10^{-7}	24.2	−20.2
	p-Cl	75.0[b,d]	1.94×10^{-7}	24.6	−18.9
	p-H	75.0[a,b,d,e]	2.85×10^{-7}	24.8	−17.7
	m-CH_3	103.60	$(5.75 \pm 0.02) \times 10^{-6}$	25.7	−14.8
		123.63	$(3.42 \pm 0.02) \times 10^{-5}$		
		75.0[b]	3.18×10^{-7}		
	p-CH_3	75.0[b,e]	8.46×10^{-7}	25.6	−13.0
	m,p-$(CH_3)_2$	103.56	$(2.12 \pm 0.02) \times 10^{-5}$	26.1	−11.1
		123.70	$(1.31 \pm 0.02) \times 10^{-4}$		
		75.0[b]	1.12×10^{-6}		
	2-Fluorenyl	103.85[c]	2.53×10^{-5}	25.8	−11.6
		124.09[c]	1.54×10^{-4}		
		75.0[b]	1.35×10^{-6}		
	p-CH_3O	75.0[b,d]	8.53×10^{-6}	25.1	−10.0
Formic acid	*p*-NO_2	75.24[c]	2.24×10^{-6}	22.1	−21.3
		84.43[c]	5.22×10^{-6}		
		75.0[b]	2.19×10^{-6}		
	p-Cl	60.82	$(1.91 \pm 0.01) \times 10^{-6}$	24.4	−12.0
		75.55	$(9.41 \pm 0.32) \times 10^{-6}$		
		75.0[b]	8.89×10^{-6}		
	p-H	75.0[f]	4.29×10^{-5}	24.2	−9.4
	p-C_6H_5	60.82	$(1.84 \pm 0.03) \times 10^{-5}$	23.8	−9.1
		75.54	$(8.75 \pm 0.19) \times 10^{-5}$		
		75.0[b]	8.28×10^{-5}		

Table I (*Continued*)

Solvent	Substituent	Temp, °C	k_t, s^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
	m-CH_3	75.0[f]	7.93×10^{-5}	24.1	−8.4
	p-CH_3	75.0[f]	2.94×10^{-4}	23.0	−8.8
	m,p-$(CH_3)_2$	60.78	$(1.30 \pm 0.02) \times 10^{-4}$	22.6	−8.9
		75.56	$(5.75 \pm 0.05) \times 10^{-4}$		
		75.0[b]	5.45×10^{-4}		
	p-CH_3O	75.0[a]	1.77×10^{-3}	21.7	−9.3
Trifluoroethanol	*p*-NO_2	75.0[b,g]	1.68×10^{-8}	19.3[h]	−28.2[h]
	p-H	75.0[g]	4.82×10^{-6}	20.5	−24.4
	p-CH_3	75.0[g]	5.31×10^{-5}		
	p-CH_3O	75.0[g]	3.39×10^{-4}		
Trifluoroacetic acid	*p*-Cl	49.66	$(9.59 \pm 0.69) \times 10^{-6}$	16.6	−30.3
		75.16	$(6.85 \pm 0.29) \times 10^{-5}$		
		75.0[b]	6.78×10^{-5}		
	p-H	49.75	$(7.09 \pm 0.20) \times 10^{-5}$	15.6	−29.4
		75.11	$(4.49 \pm 0.38) \times 10^{-4}$		
		75.0[b]	4.46×10^{-4}		
		75.0[i]	$(3.95 \pm 0.11) \times 10^{-4}$	19.7	−17.8
		75.0[b,j]	3.22×10^{-4}	20.2	−16.8
	p-C_6H_5	35.07	$(4.31 \pm 0.20) \times 10^{-5}$	17.6	−21.5
		49.76	$(1.67 \pm 0.26) \times 10^{-4}$		
		75.0[b]	1.32×10^{-3}		
	2-Naphthyl	49.79[c]	1.75×10^{-4}	16.4	−25.2
		59.85[c]	3.90×10^{-4}		
		75.0[b]	1.20×10^{-3}		
	m-CH_3	36.09	$(4.15 \pm 0.37) \times 10^{-5}$	17.8	−21.2
		49.81	$(1.48 \pm 0.07) \times 10^{-4}$		
		75.0[b]	1.18×10^{-3}		
	p-CH_3	36.03	$(1.61 \pm 0.07) \times 10^{-4}$	17.3	−20.0
		49.76	$(5.57 \pm 0.31) \times 10^{-4}$		
		75.0[b]	4.24×10^{-3}		
	m,p-$(CH_3)_2$	36.08	$(3.46 \pm 0.15) \times 10^{-4}$	17.7	−17.4
		49.85	$(1.23 \pm 0.02) \times 10^{-3}$		
		75.0[b]	9.67×10^{-3}		
	2-Fluorenyl	35.99[c]	2.13×10^{-4}	14.7	−27.7
		49.85[c]	6.23×10^{-4}		
		75.0[b]	3.53×10^{-3}		
	p-C_6H_5O	35.09	$(1.65 \pm 0.07) \times 10^{-4}$	15.7	−25.0
		49.77	$(5.54 \pm 0.45) \times 10^{-4}$		
		75.0[b]	3.51×10^{-3}		
	p-CH_3O	30.08	$(9.70 \pm 0.20) \times 10^{-5}$	15.3	−26.4
		49.76	$(4.87 \pm 0.12) \times 10^{-4}$		
		75.0[b]	2.97×10^{-3}		

[a] Reference 10. [b] Calculated from data at other temperatures. [c] One run. [d] Reference 13e. [e] Reference 32. [f] Reference 22. [g] Reference 38. [h] For ethyl nosylate; see ref 38c. [i] Reference 42. [j] Reference 72.

$$\log (k^X/k^H) = -3.96[\sigma + 0.43(\sigma^+ - \sigma)] \quad (2)^{37}$$

These are listed in Table II. The β-arylethyl data for 50% aqueous ethanol and acetic acid (Figure 1) were analyzed by the iterative dissection method, using the deactivated substrates *m,m'*-$(CF_3)_2$ to *m*-F to define the k_s line. The k_s lines for formic acid and trifluoroethanol were constructed using the $k_t(\approx k_s)$ value for the *p*-NO_2 compound and label scrambling data for the parent substrate ($k_s \approx 0.1k_t$).[38,39] A similar two point k_s line was obtained for ethanol using label scrambling data for the *p*-H ($k_s = 0.994k_t$)[39] and *p*-CH_3O ($k_s = 0.56k_t$)[40] compounds. The k_s pathway makes a negligible contribution in trifluoroacetic acid.[41-43] Resultant Fk_Δ values for each solvent are given in Table III.

A preliminary observation from the data in Table III is the reduced influence in trifluoroacetic acid of the highly activating ether substituents. Both the *p*-CH_3O and less basic *p*-C_6H_5O compounds are slower than *p*-CH_3. Ample evidence exists for this type of deactivation through hydrogen bonding of oxygen and nitrogen-containing substituents in trifluoroacetic acid,[44,45] and in other acidic solvents (i.e., HCO_2H[45] and CF_3CH_2OH[45-47]). Therefore, the most activated, most k_Δ prone aryl groups are unfortunately eliminated from correlations involving the effect of solvent on the anchimeric pathway (vide infra). Brown, at one time, interpreted the slight downward curvature of a $k_t(\approx Fk_\Delta)$–σ^+ plot for activated β-aryl-

Table II. Values of Substitutent Constants

Substituent	σ[a]	σ^+[a]	σ(neophyl)
m,m'-$(CF_3)_2$[b]	0.84	1.04	(0.93)[c]
p-NO_2	0.7801	0.79	0.78
p-CF_3	0.54	0.61	(0.57)[c]
m-CF_3	0.42	0.52	(0.46)[c]
m-Br	0.39	0.41	(0.40)[c]
m-Cl	0.37	0.40	(0.38)[c]
m-F	0.34	0.35	(0.34)[c]
p-Cl	0.23	0.11	0.18[d]
H	0.0	0.0	0.0
m-CH_3	−0.07	−0.07	−0.07
p-CH_3	−0.17	−0.31	−0.22
m,p-$(CH_3)_2$[b]	−0.24	−0.38	−0.29
p-CH_3O	−0.27	−0.78	−0.50

[a] L. M. Stock and H. C. Brown, *Adv. Phys. Org. Chem.*, **1**, 35 (1963). [b] Additivity of substituent effects is assumed.[a,55] [c] Determined from eq 2 and values of σ and σ^+. [d] Determined from tosylate data.[32]

Table III. Fk_Δ Values for β-Arylethyl Tosylates in Various Solvents, 75 °C, s^{-1}

Substituent	Solvent					
	EtOH	50% aq EtOH	AcOH	HCO_2H	CF_3CH_2OH	CF_3CO_2H
p-NO_2		4.53×10^{-9} [a]	3.53×10^{-11} [a]			2.14×10^{-8} [b,c]
m-Br						4.80×10^{-6} [b,c]
p-Cl				5.34×10^{-6}		6.78×10^{-5}
p-H	4.52×10^{-8}	4.24×10^{-6}	7.49×10^{-8}	3.86×10^{-5}	4.34×10^{-6}	4.46×10^{-4}
m-CH_3		4.13×10^{-6}	1.03×10^{-7}	7.47×10^{-5}		1.18×10^{-3}
p-CH_3	6.7×10^{-7}	2.12×10^{-5}	6.23×10^{-7}	2.89×10^{-4}	5.21×10^{-5}	4.24×10^{-3}
m,p-$(CH_3)_2$		3.49×10^{-5}	8.91×10^{-7}	5.40×10^{-4}		9.67×10^{-3}
p-CH_3O	6.35×10^{-6}	2.27×10^{-4}	8.30×10^{-6}	1.77×10^{-3}	3.38×10^{-4}	2.97×10^{-3}
p-C_6H_5O						3.51×10^{-3}
2-Fluorenyl			1.14×10^{-6}			3.53×10^{-3}
F (*p*-H)	≈1 [d]	≈1 [d]	0.32 [e]	0.91 [f]	0.94 [g]	0.42,[h] 0.22,[i] 0.28 [j]

[a] Calculated by the iterative method. [b] Reference 43. [c] Corrected for leaving group (ONs/OTs = 6.0) and contribution from k_s.[43,72] [d] References 40 and 41. [e] Reference 32, 90 °C. [f] J. W. Clayton and C. C. Lee, *Can. J. Chem.*, **39**, 1510 (1961), 74 °C. [g] Reference 38, 75 °C. [h] Reference 42, 75 °C. [i] Calculated for *m*-Br-II nosylate, 70 °C.[b] [j] Calculated for *p*-NO_2-II nosylate, 110 °C.[b]

ethyl tosylates in formic acid as evidence for considerably weaker aryl charge delocalization in Fk_Δ than in aromatic substitution reactions.[22] Since it is now agreed that k_Δ transition state is strongly bound,[3] the observed nonlinearity probably results from deactivation of the important *p*-CH_3O compound by hydrogen bonding in formic acid.[45]

An initial attempt to extend the range of correlation by combining data for meta- and para-substituted compounds with those for polynuclear aromatic substrates[48] was abandoned for several reasons. While σ^0 constants are available for the latter substrate class,[49] σ^+ values depend on the method of determination.[38c,50,51] In addition, the most activated site for attachment to the polynuclear aryl is the α position, introducing peri or ortho steric interactions.[52] There does exist a *tert*-cumyl chloride derived σ^+ constant for 2-fluorenyl,[53] and a good fit is obtained to the ρ^+ line defined by the log Fk_Δ values for other activated substituents in acetic acid.[13e] However, Fk_Δ for β-(2-fluorenyl)ethyl tosylate, approximately twice that of the *p*-CH_3 substrates in acetic acid, is lower than the value for the *p*-CH_3 compound in trifluoroacetic acid. The fluorenyl derivative is the only member of the series to form a colored solution (blue-green[54]) initially in trifluoroacetic acid, perhaps indicating radical cation formation in this solvent. The correlational range was extended somewhat with the *m,p*-dimethyl substituted compound. The σ constants for such limited alkyl substitution have been shown to be additive.[55]

Secondary 1-Aryl-2-propyl Tosylates. Table IV presents total rate constants, k_t, for a series of 1-aryl-2-propyl tosylates which were dissected into k_s and Fk_Δ components by Hammett[3,13a] and Taft treatments.[3,13c] Table V lists k_t values for 1,3-diaryl-2-propyl tosylates which were analyzed using a multiple substitution technique[3,13b] to estimate the magnitude of aryl assisted and aryl unassisted pathways for each 1-aryl-2-propyl unit. Values of Fk_Δ for each 1-aryl-2-propyl tosylate calculated by the three treatments (Table VI) show good agreement.

Table VII compares the percent of aryl assisted reaction ($100\ Fk_\Delta/k_t$) calculated by the three treatments with experimentally observed percent yield of ester with retained configuration. The values for 1-phenyl-2-propyl tosylate increase 3-11% on going from one to 25 iterations in the Hammett treatment. Although this reduces somewhat agreement with the observed percentage of Fk_Δ as determined from product data,[56] we believe the iterative procedure ideally to be the more appropriate method of analysis. Small inaccuracies or lack of kinetic data to sufficiently define the k_s line can cause significant variations in the calculated value of Fk_Δ, especially for compounds where this contribution is small. The percentages of Fk_Δ(1-phenyl-2-propyl tosylate) obtained by the three kinetic methods, 39 ± 10 (AcOH) and 80 ± 10 (HCO_2H) are in close agreement, considering the different assumptions made, and correspond reasonably well with results obtained from stereochemical studies, 25 (AcOH) and 68 (HCO_2H). Acetolyses of *threo*-3-aryl-2-butyl brosylates for which there are more kinetic and product data, when analyzed by the iterative Hammett method, agree very well with the results determined from product stereochemistry. The success of these treatments provides strong evidence[13a-d] that the 1-aryl-2-propyl system solvolyzes by discrete aryl assisted and aryl unassisted processes.

Influence of Solvent Nucleophilicity (N) and Solvent Ionizing Power (Y). Winstein emphasized the discrete nature of the aryl unassisted (k_s) and aryl assisted (k_Δ) pathways by plotting k_s($PhCH_2CHROTs$) vs. k_t($CH_3CHROTs$) and k_Δ($PhCH_2CHROTs$) vs. k_t(neophyl-OTs) in a variety of solvents for primary (R = H)[41] and secondary (R = CH_3)[35] β-aryl substrates. These correlations can be obtained directly against measures of solvent nucleophilicity (N) and solvent ionizing power (Y) in the general Winstein-Grunwald equation for solvolytic processes (eq 3):[1b,19,57,58]

$$\log (k/k_0) = mY + lN \qquad (3)$$

Values of N have been determined[19] for a wide range of solvents by evaluating eq 3 for methyl tosylate (eq 4). The acetic-formic m_{AF} value (0.3) was used as a measure of the substrate's sensitivity to ionizing power, and l = 1.0 in view of the extremely high sensitivity of methyl derivatives to solvent nucleophilicity (eq 4).

$$N = \log (k/k_0)_{CH_3OTs} - 0.3Y \qquad (4)$$

Choice of a proper solvent ionizing power scale for use in eq 3 to correlate the tosylate rate data of the present study and in eq 4 posed difficulties. The standard measure of Y, based on the solvolysis of *tert*-butyl chloride,[59,60] generally produces dispersion when employed to correlate limiting (k_c) substrates having other leaving groups.[19,61] This standard has proved deficient in certain fluorinated solvents[62,63] (the Y value of 1.84 measured for trifluoroacetic acid on the *tert*-butyl chloride scale[64] is below that of formic acid, 2.05), because of ion pairing effects.[62a] We have chosen 2-adamantyl tosylate as the reference compound.[1b,18,19] Although a secondary substrate, it ionizes through a limiting k_c mechanism.[17] Rate constants for 2-adamantyl tosylate plot linearly (correln coeff 0.999) with those for *p*-methoxyneophyl tosylate, a k_Δ substrate suggested by Winstein as a standard to measure ionizing power uncomplicated by internal return,[20] for compounds containing sulfonate leaving groups.[61b] While literature data for the latter

Table IV. Solvolysis Rate Constants of 1-Aryl-2-propyl Tosylate, $XC_6H_4CH_2CH(OTs)CH_3$

Solvent	X	Temp, °C	k_t, s^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
Ethanol	*p*-H	50.0[a]	$(1.41 \pm 0.03) \times 10^{-6}$		
	p-CH_3O	49.60[a]	$(8.28 \pm 0.13) \times 10^{-6}$		
		50.0[b]	8.65×10^{-6}		
80% v/v aq ethanol	*p*-NO_2	50.0[c,d]	4.39×10^{-6}	21.4	−17.1
	p-CF_3	50.0[e,d]	5.25×10^{-6}	21.6	−15.9
	m-CF_3	50.0[c,d]	6.11×10^{-6}	20.1	−20.4
	m-Cl	50.0[c,d]	5.24×10^{-6}	21.9	−15.0
	p-Cl	50.0[c,d]	6.20×10^{-6}	22.1	−14.2
	p-H	50.0[c,d]	9.42×10^{-6}	22.3	−12.8
	p-CH_3	50.0[c,d]	1.85×10^{-5}	22.1	−11.8
	p-CH_3O	50.0[c,d]	9.55×10^{-5}	22.6	−7.2
Acetic acid	*p*-NO_2	50.0[c,e]	1.21×10^{-7}	26.1	−9.7
		100.0[c,e]	3.22×10^{-5}		
	m-CF_3	100.4[e]	$(5.68 \pm 0.06) \times 10^{-5}$		
		50.0[f]	1.92×10^{-7}		
		100.0[f]	5.46×10^{-5}		
	m-Cl	75.12	$(4.77 \pm 0.07) \times 10^{-6}$	26.7	−6.7
		100.30[e]	$(6.86 \pm 0.14) \times 10^{-5}$		
		50.0[c]	2.22×10^{-7}		
		100.0[c]	6.66×10^{-5}		
	p-Cl	75.13	$(5.72 \pm 0.08) \times 10^{-6}$	26.4	−6.9
		100.0[e]	$(7.82 \pm 0.07) \times 10^{-5}$		
		50.0[c]	2.72×10^{-7}		
	p-H	50.0[c,e]	6.36×10^{-7}	26.5	−5.0
		100.0[e]	$(1.83 \pm 0.02) \times 10^{-4}$		
	p-CH_3	75.11	$(3.27 \pm 0.06) \times 10^{-5}$	25.6	−5.9
		99.92	$(4.09 \pm 0.06) \times 10^{-4}$		
		50.0[c]	1.72×10^{-6}		
		100.0[c]	4.12×10^{-4}		
		101.1[c]	4.57×10^{-4}		
		101.1[e,g]	$(4.72 \pm 0.03) \times 10^{-4}$		
	p-CH_3O	50.0[a,c]	1.24×10^{-5}	24.1	−6.4
		100.0[a,c]	2.21×10^{-3}		
Formic acid[g]	*p*-NO_2	50.0[e]	$(1.32 \pm 0.03) \times 10^{-5}$	24.8	−4.4
		75.0[e]	$(2.22 \pm 0.10) \times 10^{-4}$		
	p-CF_3	75.04[e]	$(2.55 \pm 0.20) \times 10^{-4}$		
		50.0[h]	1.67×10^{-5}		
	m-CF_3	50.0[c,e]	2.33×10^{-5}	22.9	−9.1
		75.0[c,e]	3.23×10^{-4}		
	m-Cl	50.0[c,e]	3.22×10^{-5}	23.6	−6.2
		75.0[c,e]	4.86×10^{-4}		
	p-Cl	50.0[c,e]	6.74×10^{-5}	23.0	−6.7
		75.0[c,e]	9.48×10^{-4}		
	p-H	50.0[e]	$(3.04 \pm 0.01) \times 10^{-4}$	22.4	−5.6
		75.0[c,e]	3.99×10^{-3}		
	p-CH_3	50.0[e]	$(1.66 \pm 0.05) \times 10^{-3}$	21.7	−4.4
		75.0[c,e]	1.97×10^{-2}		
	p-CH_3O	50.0[c,e]	9.06×10^{-3}	22.7	2.3
		75.0[c,e]	1.24×10^{-1}		
Trifluoroacetic acid	*p*-H	50.0[i]	$(3.47 \pm 0.02) \times 10^{-3}$	19.2	−10.5
		50.0[c,j,k]	5.11×10^{-3}	19.5	−8.9

[a] S. Winstein, M. Brown, K. C. Schreiber, and A. H. Schlesinger, *J. Am. Chem. Soc.*, **74,** 1140 (1952). [b] Calculated using the divisor 1.05 decrease in rate for the *p*-CH_3O substrate (80% v/v ethanol[d]) in going from 50 to 49.60 °C. [c] Calculated from data at other temperatures. [d] References 13f. [e] Reference 13a. [f] Calculated using divisors of 1.04 and 296 ± 18 decreases in rate in going from 100.4 to 100.0 and 50.0 °C, respectively, for other k_s substrates (AcOH) *p*-NO_2, *m*-Cl, and *p*-Cl. [g] Determined by a conductometric method, as were all formolyses. [h] Calculated using the divisor of 15.3 ± 1.4 decrease in rate in going from 75 to 50 °C for other k_s substrates (HCO_2H), *p*-NO_2, *m*-CF_3, and *m*-Cl. [i] Reference 35. [j] Reference 74. [k] Buffered with sodium trifluoroacetate.

compound are limited to the ethanol-formic acid range, rate data for 2-adamantyl tosylate are also linear (correln coeff 0.994) with those for neophyl tosylate in the complete ethanol-trifluoroacetic acid spectrum.[41,61b,65] Fortunately, the difference in Y value between acetic and formic acid in the *tert*-butyl chloride and 2-adamantyl tosylate scales is virtually the same (3.69 vs. 3.65 Y units), thereby allowing calculation of N values for both Y scales using the same m_{AF} value, 0.3, in eq 4.

Primary β-Phenethyl Tosylate. Values of k_s (75 °C) for β-phenethyl tosylate for the solvents in which k_s was observable (ethanol, 50% ethanol, acetic acid, and formic acid) were correlated by eq 5 (correln coeff 0.998). The value of k_s in CF_3CH_2OH was not included because of the difficulty in obtaining accurate rate data, as well as N and Y values in this anhydrous medium[62a,63c,66] (see Table VIII, footnote *f*). The k_Δ rate constants[68] (75 °C) in these same four solvents and trifluoroacetic acid were correlated by eq 6 (correln coeff 0.997). Comparison of eq 5 and 6 clearly shows the very different sensitivities to solvent nucleophilicity and ionizing power of the k_s and k_Δ pathway, as Winstein's results anticipated.[41]

Table V. Solvolysis Rate Constants of 1,3-Diaryl-2-propyl Tosylates, $XC_6H_4CH_2CH(OTs)CH_2C_6H_4Y$

Solvent	X	Y	Temp, °C	k_t, s^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
AcOH	*p*-H	*p*-H	75.0[a]	$(5.68 \pm 0.02) \times 10^{-6}$	27.5	−3.7
			100.0[a,b]	$(8.98 \pm 0.05) \times 10^{-5}$		
			125.0[a]	$(9.65 \pm 0.11) \times 10^{-4}$		
	p-CH_3O	*p*-CH_3O	100.0[a,b]	$(1.68 \pm 0.13) \times 10^{-3}$		
	p-NO_2	*p*-NO_2	100.0[b]	$(3.71 \pm 0.06) \times 10^{-6}$	27.0	−11.5
			125.0	$(3.90 \pm 0.05) \times 10^{-5}$		
	p-H	*p*-CH_3O	75.13	$(6.58 \pm 0.16) \times 10^{-5}$	25.3	−5.2
			100.0[b]	$(8.09 \pm 0.49) \times 10^{-4}$		
	p-H	*p*-NO_2	100.0[b,c]	$(2.10 \pm 0.02) \times 10^{-5}$	24.5	−14.6
			125.20	$(1.82 \pm 0.03) \times 10^{-4}$		
	p-CH_3O	*p*-NO_2	75.13	$(1.33 \pm 0.03) \times 10^{-5}$	26.5	−5.1
			100.40[b,c]	$(1.90 \pm 0.02) \times 10^{-4}$		
			100.0[d]	1.83×10^{-4}		
HCO_2H[c]	p-H	*p*-H	50.21	$(1.71 \pm 0.05) \times 10^{-4}$	23.7	−2.5
			75.0[b]	$(2.56 \pm 0.08) \times 10^{-3}$		
	p-CH_3O	*p*-CH_3O	24.12	$(1.70 \pm 0.05) \times 10^{-4}$	22.5	0.0
			50.10	$(3.96 \pm 0.10) \times 10^{-3}$		
			75.0[b,d]	5.24×10^{-2}		
	p-NO_2	*p*-NO_2	75.0[b]	$(1.14 \pm 0.04) \times 10^{-5}$	26.9	−4.3
			84.6	$(3.15 \pm 0.10) \times 10^{-5}$		
	p-H	*p*-CH_3O	24.12	$(8.21 \pm 0.24) \times 10^{-5}$	22.3	−2.1
			50.20	$(1.88 \pm 0.06) \times 10^{-3}$		
			75.0[b,d]	2.40×10^{-2}		
	p-H	*p*-NO_2	50.12	$(8.48 \pm 0.40) \times 10^{-6}$	26.5	0.2
			75.10[b]	$(1.77 \pm 0.02) \times 10^{-4}$		
			75.0[d]	1.75×10^{-4}		
	p-CH_3O	*p*-NO_2	24.12	$(1.29 \pm 0.04) \times 10^{-5}$	23.9	−0.5
			50.10	$(3.63 \pm 0.14) \times 10^{-4}$		
			75.0[b,d]	5.60×10^{-3}		

[a] J. J. Harper, Ph.D. Thesis, Princeton University, 1968. [b] Reference 13b. [c] Determined by an automatically recording conductometric method, as were all formolyses. [d] Calculated from data at other temperatures.

Table VI. Values of Fk_{Δ} of 1-Aryl-2-propyl Tosylates Determined by Various Methods, 50 °C[a], s^{-1}

		Solvent				
Substituent	Method	EtOH	80% EtOH	AcOH (temp, °C)	HCO_2H (temp, °C)	CF_3CO_2H
p-Cl	Hammett[b]				4.70×10^{-5}	
					6.52×10^{-4} (75)	
p-H	Hammett[b]	1.0×10^{-7}	2.56×10^{-6}	3.24×10^{-7}	2.79×10^{-4}	3.46×10^{-3} [c]
				8.56×10^{-5} (100)	3.64×10^{-3} (75)	
	Taft			7.6×10^{-5} (100)	3.12×10^{-3} (75)	
	Mult subst			5.02×10^{-5} (100)	2.68×10^{-3} (75)	
p-CH_3	Hammett[b]		1.10×10^{-5}	1.34×10^{-6}	1.63×10^{-3}	
				2.87×10^{-4} (100)	1.93×10^{-2} (75)	
	Taft		0.62×10^{-5}	2.83×10^{-4} (100)	1.86×10^{-2} (75)	
p-CH_3O	Hammett[b]	7.04×10^{-6}	8.75×10^{-5}	1.20×10^{-5}	9.03×10^{-3}	
				2.07×10^{-3} (100)	1.24×10^{-1} (75)	
	Taft		8.32×10^{-5}	2.08×10^{-3} (100)	1.23×10^{-1} (75)	
	Mult subst			2.02×10^{-3} (100)	1.19×10^{-1} (75)	
F values (*p*-H)[c]		≈1	≈1[d]	0.19[e]	1	0.09[f]

[a] Other temperatures are indicated in parentheses. [b] For data in 80% aqueous ethanol, acetic acid, and formic acid, deactivated substrates *p*-NO_2 to *m*-Cl were used to define the k_s line (iterative technique). The k_s line for ethanol was estimated from percent inversion of configuration for 1-phenyl-2-propyl tosylate ($k_s = 0.93\ k_t$; Table IV, footnote *a*) and the ρ_s value for 80% aqueous ethanol (−0.24) [c] Reference 35. [d] Reference 13f. [e] 75°C. [f] 25°C.

$$\log (k_s/k_s^0) = 0.33Y + 0.78N \quad (5)^{67}$$

$$\log (k_{\Delta}/k_{\Delta}^0) = 0.67Y \quad (6)^{67\text{-}69}$$

Secondary 1-Phenyl-2-propyl Tosylate. Values of k_s (50 °C) for 1-phenyl-2-propyl tosylate in ethanol, 80% aqueous ethanol, acetic acid, and formic acid were correlated by eq 7 (correln coeff 0.996). The *m* and *l* coefficients are similar to those used to correlate 2-propyl tosylate in these solvents, 0.60 and 0.47, respectively. Dissected k_{Δ}[68] rate constants (50 °C) in the same four solvents and trifluoroacetic acid are correlated by eq 8 (correln coeff 0.988). Comparison of eq 7 and 8 indicates that k_s and k_{Δ} for this secondary system also exhibit different sensitivities to solvent ionizing power and solvent nucleophilicity, although the relative magnitudes of m_s, m_{Δ}, and l_s vary from primary to secondary substrate.

$$\log (k_s/k_s^0) = 0.50Y + 0.46N \quad (7)$$

$$\log (k_{\Delta}/k_{\Delta}^0) = 0.82Y \quad (8)^{70}$$

Table VII. Percent Aryl Assisted Reaction as Determined by Various Methods for Secondary β-Aryl Substrates.

X	Solvent	Temp, °C	$(Fk_\Delta/k_t) \times 100$ Hammett[a]	Taft	Mult subst[b]	% yield of ester with retained config
			1-Aryl-2-propyl Tosylate			
p-H	80% aq EtOH	50	27 (24)	*c*		
	AcOH	100	47 (36)	42	28[d]	25[e]
	HCO_2H	75	91 (82)	78	72	68[e]
p-CH_3O	80% aq EtOH	50	92 (91)	87		
	AcOH	100	94 (92)	94	92	
	HCO_2H	75	100 (99)	99	99	
			threo-3-Aryl-2-butyl Brosylate[f]			
p-Cl	AcOH	75	40 (29)			39
p-H			68 (59)			59
m-CH_3			75 (67)			68
p-CH_3			89 (84)			88
p-CH_3O			99 (99)			100

[a] Values after 25 iterations. Values in parentheses after one iteration. [b] k_t was calculated from $k_0(s + \Delta)$.[13b] [c] The small magnitude of Fk_Δ in this solvent and the greater scatter of the Taft ρ^* line than for the AcOH and HCO_2H ρ^* lines did not allow an accurate calculation of Fk_Δ. [d] Reported incorrectly as 38 in ref 13b. [e] Calculated in ref 13d from data in Table IV, footnote *a*. [f] Reference 14.

Table VIII. Solvent Effects on Aryl Assisted and Solvent Assisted Pathways[a]

Solvent	$k_t \times 10^6$, s^{-1} (75 °C) C_2H_5OTs	$PhCH_2CH_2OTs$	k_t(β-PhEt)/k_t(Et) Exptl	Calcd (eq 7)	N[b]	Y[b]
EtOH	29.8	7.08	0.24	0.26	0.00	−1.75
50% aq EtOH	264.0[c]	53.9[d]	0.20	0.22	−0.09	1.29
AcOH	0.772	0.288	0.37	0.35	−2.35	−0.61
HCO_2H	18.9	39.4	2.1	2.7	−2.35	3.04
CF_3CH_2OH	0.385[e]	4.82[e]	12.5	16	−3.8[f]	1.80[g]
CF_3CO_2H	0.226	401.0	1770	1600	−5.56	4.57

[a] Taken from ref 41 except where noted. [b] Y and N are measures of solvent ionizing power and nucleophilicity, respectively, in the general Winstein-Grunwald equation.[19,57,58] They were determined[19] using 2-adamantyl tosylate, a limiting substrate,[17] as a standard to measure ionizing power. [c] Extrapolated from data at 50 °C.[57] [d] This work. [e] Reference 38. [f] Calculated from eq 3 using m_s and l_s (0.36, 0.82) for ethyl tosylate. This is probably inaccurate due to extrapolation errors[38c] and general difficulties involved in determining kinetics in anhydrous TFE.[62a,63c,66] N for the less nucleophilic, more highly ionizing solvent 97% (weight) aqueous hexafluoroisopropanol, determined directly from methyl tosylate,[18] is −4.2. Extrapolation of Raber's results[63c] for CH_3OTs in 97 (N = −2.79), 84.5, 70, and 50% (weight) aqueous TFE gives N (TFE) ~ −3.1. Extrapolation of Andrews' results for CH_3OTs in EtOH–TFE mixtures gives N(TFE) ≈ −2.1.[66] [g] Extrapolated using the m value for 2-adamantyl tosylate in 70 and 97% (weight) aqueous TFE.[18]

Discussion

The β-arylethyl (II) and 1-aryl-2-propyl (III) systems provide good illustrations of the aryl unassisted (k_s) and aryl assisted (k_Δ) pathways in primary and secondary systems, respectively. β-Arylethyl substrates, the simplest class capable of neighboring aryl group participation, solvolyze by k_Δ or k_s usually without elimination[71] or hydride shift even in trifluoroacetic acid[72] and other highly ionizing solvents,[73] while the 1-aryl-2-propyl system is less prone than other secondary substrates to these complications.[13d,74] For each system, the discrete nature of k_s and k_Δ is shown by different phenyl substituent effects[3,13,35,41] and activation parameters.[3,35,41,75] We shall examine here the different responses of the two reaction pathways to solvent properties, and consider the nature of the species for which they compete—neutral substrate or ion pair.

Primary β-Phenethyl Tosylate. The Effect of Solvent. The relative rate ratio has long been used to detect the onset of neighboring group assistance.[7,10] A prime example is the dramatic 7500-fold increase in the β-phenethyl/ethyl tosylate relative rate ratio (eq 9) in going from ethanol to trifluoroacetic acid (Table VIII, column 4).

$$\frac{k_t(PhCH_2CH_2OTs)}{k_t(EtOTs)} = \frac{Fk_\Delta + k_s(PhCH_2CH_2OTs)}{k_s(EtOTs)} \quad (9)$$

Winstein's pioneering work on neighboring group participation provides an explanation for this effect.[21] A decrease in solvent nucleophilicity, N, would lower the solvent assisted rate constants k_s(EtOTs) and k_s(β-PhEtOTs), thereby producing a relative decrease of the *denominator* in eq 9. The $k_t(\equiv k_s)$ rate constants for ethyl tosylate evidence this trend (Table VIII, columns 2 and 6). In addition, increased ionizing power, Y, might be expected to reduce somewhat the extent of bonding required of the nucleophile in the k_s pathway;[20,21] intramolecular attack (k_Δ) would then compete more favorably ($m_\Delta > m_s$), causing a preferential increase in the *numerator* of eq 9. Values of k_t for β-phenethyl tosylate, in which the k_Δ pathway is available, generally increase with increased ionizing power (Table VIII, columns 3 and 7). Also, for solvent pairs of similar nucleophilicity but different ionizing power (Table VIII, columns 6 and 7), the $100k_\Delta/(k_\Delta + k_s)$ ratio is greater in the solvent of higher Y; β-PhEtOTs (75 °C): acetic acid (53) and formic acid (91); ethanol (0.6) and 50% aqueous ethanol (8).

Recently, we employed a treatment which quantitatively reproduced the observed β-PhEtOTs/EtOTs rate ratios by assuming only these effects were operative.[1b] Incorporation of eq 5 and 6 for β-phenethyl tosylate and eq 10 for k_t of ethyl tosylate into eq 9 yields eq 11 for calculation of the relative rate ratio in a variety of solvents.

Table IX. Plots of Log (k_Δ) β-Arylalkyl Tosylates at 75 °C vs. Y[a]

Substrate[b]	Solvents	m[d]	Correln coeff
p-H	I,[c] EtOH	0.63 ± 0.01	0.999
	I,[c] EtOH, CF_3COOH	0.67 ± 0.03	0.997
m-CH_3	I[c]	0.66 ± 0.05	0.998
	I,[c] CF_3COOH	0.75 ± 0.06	0.993
p-CH_3	I,[c] EtOH	0.56 ± 0.04	0.996
	I,[c] EtOH, CF_3COOH	0.65 ± 0.06	0.989
m,p-$(CH_3)_2$	I[c]	0.64 ± 0.04	0.998
	I,[c] CF_3COOH	0.75 ± 0.07	0.991
Neophyl-OTs[b]	I, 80% aq EtOH, EtOH	0.59 ± 0.02	0.999
	I, 80% aq EtOH, EtOH, CF_3COOH	0.67 ± 0.04	0.993

[a] Based on 2-adamantyl tosylate scale.[1b,18,19] See Table VIII. [b] Designation refers to β-arylethyl tosylates except as noted. [c] Group I solvents refer to 50% aqueous ethanol, acetic acid, and formic acid. [d] Error limits indicate standard deviation of slope.

$$\log (k_t/k_t^0) = 0.36Y + 0.82N \quad (10)$$

$$\frac{k_t(\beta\text{-PhEtOTs})}{k_t(\text{EtOTs})} = \frac{Fk_\Delta^0(10^{0.67Y}) + k_s^0(10^{0.33Y+0.78N})}{k_t^0(10^{0.36Y+0.82N})} \quad (11)$$

Agreement with experimental values (Table VIII, columns 4 and 5) is remarkably good.

This approach can be applied generally to neighboring group participation, although few mechanistic studies possess the wealth of solvent data amassed for β-aryl substrates. Peterson and Kamat's data[76] for the 6-octyn-2-yl tosylate (IV)/2-pentyl tosylate (V) system in acetic, formic, and trifluoroacetic acids when correlated by eq 12

$$\frac{k_t^{IV}}{k_t^{V}} = \frac{k_s^0(10^{0.14N+0.61Y}) + k_\Delta^0 10^{0.79Y}}{k_t^0(10^{0.16N+0.70Y})} \quad (12)^{77}$$

gave the following agreement for observed (calculated) values of the relative ratio $k_t(\text{IV})/k_t(\text{V})$: acetic 2.0 (2.2), formic 1.8 (2.8), and trifluoroacetic 16 (12). Raber et al. have successfully calculated percentages of cyclized product from 5-hexen-1-yl p-nitrobenzenesulfonate in various solvents by this treatment.[63c]

The relative importance of changes in solvent ionizing power (Y) and nucleophilicity (N) on the value of $k_t(\beta\text{-PhEtOTs})/k_t(\text{EtOTs})$ can be determined from m and l coefficients (eq 11), the range of Y and N values being comparably large. The relative rate ratio does increase with increased solvent ionizing power ($m_\Delta \sim 2m_s$); however, it is more sensitive to solvent nucleophilicity since the difference between l_s (0.78, 0.82) and l_Δ (~0) coefficients is even greater. This result emphasizes the fact that neighboring aryl group and solvent are in competition to displace the leaving group. By decreasing the nucleophilicity of the latter (and the denominator of eq 11), the kinetic influence of the phenyl group becomes more noticeable, thereby increasing the magnitude of the relative ratio.[21]

Cram[5c] and Brown[22] have suggested that such relative ratios might also be enhanced by "increases in the electrophilic participation of solvent which, in turn, results in increases in the participation of aryl in the transition states leading to the bridged ion".[5c] The fact that more reactive leaving groups tend to promote the intramolecular cyclization pathway favors this interpretation. In acetic acid, slightly more rearrangement is obtained for β-phenethyl brosylate than for the tosylate (2-3%),[79,80] and a slightly greater β-PhEtX/EtX rate ratio is obtained with nosylates than tosylates (buffered media: 0.49 vs. 0.46).[71] Bergman et al. observe more cyclized product from silver catalyzed acetolysis of 3,4-pentadien-1-yl iodide than for buffered acetolysis of the tosylate.[81] "Super" leaving groups dramatically increase this trend. β-Phenethylmercury perchlorate solvolyzes 8.3 times faster than ethyl mercury perchlorate in acetic acid and 30 times faster in formic acid.[52,78] This is compared with the reduced ratios of 0.58 and 2.5 (corrected for internal return from the phenonium ion), respectively, for the tosylates. To the extent that increased ionizing power causes a specific enhancement of leaving group activity which increases the kinetically significant magnitude of aryl bridging in the transition state leading to the phenonium intermediate, the effect proposed by Cram[5c] and Brown[22] could be observed.

We find that this is of only minor importance. The β-PhEtOTs/EtOTs rate ratio can be calculated accurately (eq 11; Table VIII, columns 4 and 5) without assuming this effect. In addition, plots of log k_Δ vs. Y over a wide solvent range are fairly linear for each activated ($\sigma_{\text{neophyl}} \leq 0$) β-arylethyl substrate in Table III except p-CH_3O[82] (eq 6 for p-H, Table IX, and Figure 2). The value of m does increase (≈14%) when data for trifluoroacetic acid are included, but the degree of correlation decreases only slightly and the new value of m is generally within the combined error limits of m calculated with and without the trifluoroacetic acid point. Nevertheless, some curvature can be seen in Figure 2 plots which suggests that the k_Δ pathway might be responding modestly to changes in solvent ionizing power, as proposed by Cram[5c] and Brown.[22]

ρ^+ treatments provide a measure of transition-state positive charge development in reactions affecting the π electrons of the aromatic ring. Values of ρ_{neophyl} (Fk_Δ,β-arylethyl tosylates) relative to the value for neophyl brosylates in acetic acid (Table X) are remarkably constant (1.02 ± 0.12, omitting the CF_3CH_2OH result) with variation in solvent. The slope for anhydrous trifluoroethanol, as the Hammett ρ for deactivated k_s substrates, seems high and might result from the lack of data (only H-, and p-CH_3 are available),[82] or experimental difficulties in determining rates.[62a,63c,66] Positive charge development in the aryl ring is thus indicated to be quite similar for Fk_Δ in solvents of greatly differing ionizing power. It is difficult to make detailed comments concerning the geometry of the k_Δ transition-state complex from this ρ_{neophyl} treatment. Medium effects,[83,84] such as hydrogen bonding to the aryl ring[85] and solvation of positive charge,[86] must be considered, and might explain the increasing variation of ρ_{neophyl} (Table X) in the more acidic, less nucleophilic solvents. In addition, indiscriminate use of such linear free-energy relationships to determine the "structure of the transition state" has legitimately been criticized recently,[87] especially in conjunction with the Hammond postulate[88] which has itself been questioned at various times.[5c,87,89,90]

Isotope effects, on the other hand, should provide a more detailed measure of the structural features of the transition state[92-94] than do ρ_{neophyl} (or ρ^+) values. The data in Table XI indicate a transition state for the k_Δ pathway of primary β-aryl substrates in which the aryl ring has substantial electronic involvement with the reaction center but has migrated only slightly toward it.[95] For k_Δ of β-arylethyl substrates, α-D_2 values (in trifluoroethanol and formic and trifluoroacetic acids) are intermediate in magnitudes (1.17-1.27) relative to the

Table X. Plots of Log $(Fk_\Delta)_{SOH}$ β-Arylethyl Tosylates at 75 °C vs. σ(neophyl)

Solvent	Rel ρ[a]	Correln coeff	No. of points	Points included[b]
EtOH	0.89	(1.000)	2	p-CH_3 and p-CH_3O
50% aq EtOH	0.93	0.990	5	All except p-Cl
AcOH	1.06	0.995	5	All except p-Cl
HCO_2H[c]	1.06	0.999	5	All except p-CH_3O[d]
CF_3CO_2H[e]	1.14	0.999	5	All except p-CH_3O[d]
CF_3CH_2OH[f]	1.26	(1.000)	2	H- and p-CH_3[d]

[a] Value of ρ is relative to that of substituted neophyl brosylates in acetic acid at 75 °C, −3.96. [b] Substituents include p-Cl, H, m-CH_3, p-CH_3, m,p-$(CH_3)_2$, and p-CH_3O. [c] Includes data from ref 22. [d] Deactivated by hydrogen bonding. See Kinetics section. [e] The slope changes somewhat to 1.19 (correln coeff 0.999) when data (corrected for leaving group) for a deactivated substrate such as m-Br are included (available data for p-NO_2 were not used [d]).[43] [f] Reference 38.

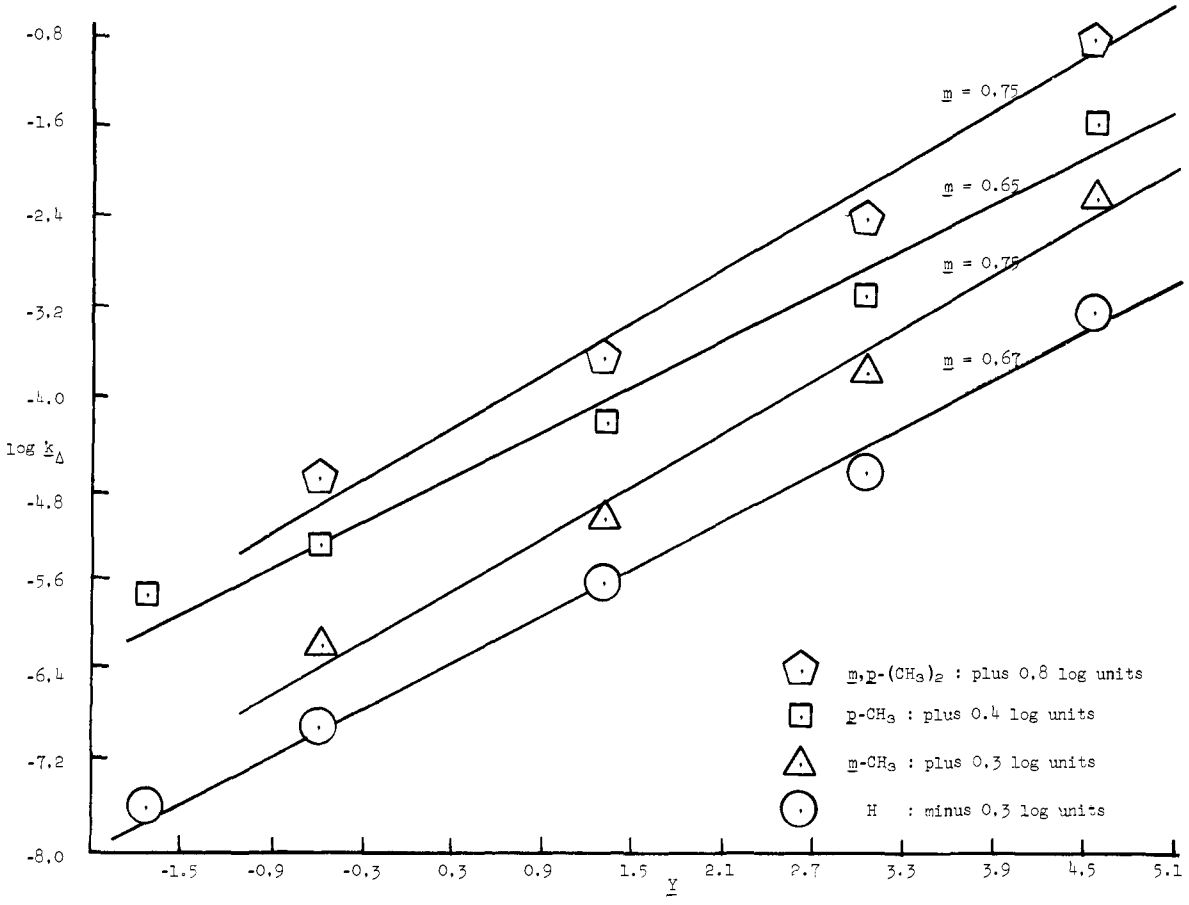


Figure 2. Plots of log k_Δ(β-arylethyl tosylates) vs. Y_{OTs}, 75 °C.

projected limiting value 1.49–1.56 (1.22–1.25 per D)[96,97] and suggest an activated complex in which the α carbon is somewhat less congested than is the solvent assisted route.[92,93] Bonding to the primary α carbon by aryl is significant as evidenced by 1-aryl-^{14}C effects for β-p-anisylethyl in all solvents, and for β-phenethyl in all solvents except acetic acid (Fk_Δ/k_t = 0.262, 75 °C);[98] small β-D_2 effects (0.97–1.00) indicate only minor transition state changes at the β carbon. For neophyl substrates, long considered to possess a strong driving force for participation,[7,10,22,33] intermediate α-D_2 (1.21–1.25) and low β-^{14}C (1.014) isotope effects indicate an early, unsymmetrical transition complex, while 1-aryl-^{14}C (1.023–1.035), α-D_2, and α-^{14}C effects[98,99] demonstrate strong perturbation at both the origin and terminus of k_Δ bonding.

When the solvent is changed to the more ionizing, less nucleophilic trifluoroacetic acid, α-D_2 isotope effects for β-phenethyl substrates increase from 1.17 (formic acid, $Fk_\Delta \approx 0.9k_t$) and 1.21 (trifluoroethanol, $Fk_\Delta \approx 0.9k_t$) to 1.27 (trifluoroacetic acid, $Fk_\Delta = k_t$), and for neophyl brosylate ($k_\Delta \equiv k_t$) from 1.21 (acetic acid) to 1.25 (trifluoroacetic acid) indicating less congestion at the α-carbon. However, electronic involvement increases somewhat[92] as shown by the increase in 1-aryl-^{14}C effects for β-phenethyl and neophyl, and α-^{14}C effects for neophyl. This coupled with the increases observed in m and $\rho_{neophyl}$ in going to the highly ionizing trifluoroacetic acid also indicates a small increase of aryl stabilization in the k_Δ pathway with increasing the solvent ionizing power, as Cram[5c] and Brown[22] have proposed.

Role of Ion Pairs. *All* of the mechanistic criteria for primary β-aryl systems indicate that solvent and neighboring aryl compete in rate determining displacement of the leaving group.[3] What is the nature of the species being attacked?

Modern solvolysis theory indicates that ion pairs, but not dissociated carbenium ions, are intermediates in some of the solvolyses of simple secondary substrates. Whether or not these ion pairs or the transition states leading to them are nucleophilically solvated and the relative magnitude of internal return to neutral substrate remain as topics of controversy.[20,26] Sneen

Table XI. Summary of H/D and $^{12}C/^{14}C$ Isotope Effects for Primary Alkyl Substrates

Substrate	Solvent	k_H/k_D (temp, °C) α	k_H/k_D (temp, °C) β	k_{12C}/k_{14C} (temp, °C) 1-Aryl-C[a]	k_{12C}/k_{14C} (temp, °C) α[a]	k_{12C}/k_{14C} (temp, °C) β[a]
β-(*p*-Nitrophenyl)ethyl[b,c]	CH_3COOH	1.044 (100)	1.061 (100)			
	CF_3COOH	1.14 (110)	1.08 (110)			
	CF_3COOH (buffered)[d]	1.11 (110)	1.09 (110)			
β-(*m*-Bromophenyl)ethyl[b,c]	CH_3COOH	1.041 (100)	1.052 (100)			
	CF_3COOH	1.19 (70)	1.01 (70)			
	CF_3COOH (buffered)[d]	1.24 (70)	0.99 (70)			
β-Phenethyl	CH_3COOH	1.03 (93.9)[e,f]	1.04 (93.9)[e,f]	1.002 (100)[b]		
	HCO_2H	1.17 (75.3)[e,f]	1.00 (75.3)[e,f]	1.023 (60)[b]		
	CF_3CH_2OH	1.21 (75)[e,g]				
	CF_3COOH	1.27 (75.0)[e,h]		1.029 (45)[b]		
	CF_3COOH (buffered)[d]			1.036 (30)[b]		
β-(*p*-Methoxyphenyl)ethyl	CH_3COOH	1.18 (75)[e,i]	1.00 (75)[e,i]	1.028 (60)[b]		
	HCO_2H	1.20 (50)[e,j]	0.97 (50)[e,j]	1.022 (30)[b]		
	CF_3COOH			1.039 (0)[b]		
Neophyl[k]	CH_3COOH	1.21 (75)[a]		1.023 (75)	1.093 (75)	1.014 (75)
	CF_3COOH	1.25 (0)[a]		1.035 (0)	1.141 (0)	1.014 (0)
Ethyl	H_2O	1.04 (54.3)[e,l]				
	CH_3OH	1.04 (56.2)[k,m]				
	CH_3COOH	1.09 (100)[k,m]	1.01 (116.8)[k,m]			
	CF_3CH_2OH	1.13 (35)[n]	1.09 (35)[n]			
	CF_3COOH	1.09 (125)[e,o]	1.16 (125)[e,o]			
	96% H_2SO_4	1.18 (30)[e,p]	1.20 (30)[e,p]			
	HSO_3F	1.30 (0)[e,q]	1.58 (0)[e,q]			

[a] References 98 and 99. [b] *p*-Nitrobenzenesulfonate leaving group. [c] Reference 43. [d] Buffered with CF_3CO_2Na. [e] Tosylate leaving group. [f] Reference 95a buffered with appropriate RCO_2Na. [g] Reference 38b,c. [h] Reference 42. Actual values of 1.08 (0.4 M), 1.17 (0.02 M), 1.23 (0.008 M), and 1.21 (0.003 M) were extrapolated to "0" ROTs concentration to obtain the tabulated value. [i] Reference 95b, 0.06 M $LiClO_4$. [j] Reference 95b, 0.055 M HCO_2Na. [k] *p*-Bromobenzenesulfonate leaving group. [l] K. T. Leffek, J. A. Llewellyn, and R. E. Robertson, *Can. J. Chem.*, **38**, 1505 (1960). [m] E. S. Lewis, J. C. Brown, and W. C. Herndon, *ibid.*, **39**, 954 (1961). [n] Triflate leaving group, CF_3SO_3. G. A. Dafforn and A. Streitwieser, Jr., *Tetrahedron Lett.*, 3159 (1970). [o] I. Lazdins Reich, A. Diaz, and S. Winstein, *J. Am. Chem. Soc.*, **91**, 5635 (1969). [p] P. C. Myhre and K. S. Brown, *ibid.*, **91**, 5639 (1969). [q] P. C. Myhre and E. Evans, *ibid.*, **91**, 5641 (1969).

has suggested "all reactions of nucleophilic substitution at a saturated carbon atom proceed via an ion pair mechanism",[27c] even methyl.[27a,c,100] Scheme II, an abbreviated version of the full ion-pair scheme,[101] is appropriate for simple primary systems where free ions and solvent separated ion pairs are not likely owing to their instability. Equation 13

$$k_t = (k_2 + Fk_p)\frac{k_1}{k_{-1} + k_2 + Fk_p} \qquad (13)^{14b,29}$$

provides the relevant kinetics expressions for Scheme II. In order to explain the fact that simple primary substrates (eq 14, no neighboring group) formally observe S_N2 kinetic behavior, Sneen postulated that $k_{-1}/k_2 \rightarrow \infty$,[27c] in which case eq 14 simplifies to eq 15.

$$k_t = k_2\frac{k_1}{k_{-1} + k_2} \qquad (14)$$

$$k_t = k_2\frac{k_1}{k_{-1}} \qquad (15)$$

We disagree with this interpretation.[19,20] Several lines of reasoning indicate that the species which is partitioned between the solvent and aryl assisted pathways does not possess a significantly different amount of positive charge than that on neutral substrate.[26c] The very low ρ's (~0 to −0.34) observed for the k_s route show this directly.

Classical primary alkyl cations are highly energetic[102] (~30 kcal less stable than typical tertiary ions[103]), and there is considerable doubt if these species can exist at all.[104] The ethyl cation is not observable directly in super acid media;[104d] the label scrambling found is probably due to intervention of intimate ion-pair intermediates.[105] Such species, or even nucleophilically solvated ion pairs, are very unlikely energetically in the less ionizing, more nucleophilic solvolysis solvents.

Sneen[27] proposes that primary ion-pair formation must occur *many* times before capture by solvent, $k_{-1} \gg k_2$. The presence of a neighboring group allows the determination of a lower limit for this inequality. According to the ion-pair interpretation, Scheme II, any rate enhancement (k_t/k_s) produced by introduction of a neighboring group generally derives not from enhancement of k_1 but from a *decrease* in internal return (k_{-1}).[23,26c,27,28] The maximum observable rate (k_t), when all ion pairs are captured by neighboring-group participation, is equal to k_1 (derived from eq 13 when $Fk_p \gg k_{-1} \gg k_2$). Under these circumstances, the maximum rate enhancement is given by eq 16.

$$(k_t/k_s)_{max} = [(k_{-1}/k_2) + 1] \qquad (16)$$

A lower limit for $(k_t/k_s)_{max}$ in the β-arylethyl system is provided by the $\approx 10^6$ difference in ethanolysis rates (25 °C) of the conjugate base of β-(*p*-hydroxyphenyl)ethyl bromide (VI), k_Δ, and β-(*p*-methoxyphenyl)ethyl bromide (VII), k_s,[106a] Correcting by a factor of ~10 for more favorable ion-pair formation in VI than VII ($\sigma_{p-O^-} - \sigma_{p-CH_3O} = -0.25$; ρ(primary ion pair) ≈ -4, ρ(solvolysis) $= -0.93$ in 80% aqueous EtOH for tertiary 1-aryl-2-methyl-2-propyl chlorides[3]), $(k_t/k_s)_{max} = k_{-1}/k_2 \approx 10^5$ is obtained. Charged aryl groups should not be excluded from Scheme II in view of the ubiquity of ion-pair intermediates proposed by advocates of this mechanism,[27,28,100] extending even to the displacement of methyl derivatives by charged nucleophiles in aqueous media.[100]

Substitution of the ratio ($k_{-1}/k_2 = 10^5$) into eq 15 for the aryl unassisted pathway of β-(*p*-anisyl)ethyl bromide yields $k_1 \sim 10^5 k_t$. Since $k_t = 2 \times 10^{-9}$, k_1 is $\sim 2 \times 10^{-4}$ (ethanol, 25 °C), 45 times *greater* than the rate of ionization of *tert*-butyl bromide (4.40×10^{-6})[106b] under the same conditions. Formation of a primary alkyl carbenium ion (k_1') should be 2.5×10^{-15} *slower* than for a tertiary ion assuming that the former

Table XII. Solvent Effects on Aryl Assisted and Solvent Assisted Pathways

Solvent	$k_t \times 10^6$, s^{-1} (50 °C)		k_t(1-Ph-2-Prop)/k_t(2-Prop)			
	$CH_3CH(OTs)CH_3$	$PhCH_2CH(OTs)CH_3$	Exptl	Calcd (eq 8)	N^a	Y^a
EtOH	8.16[b]	1.41	0.17	0.21	0.00	−1.75
80% aq EtOH	54.4[c]	9.42	0.17	0.16	0.00	0.00
AcOH	2.12[d]	0.636	0.30	0.24	−2.35	−0.61
HCO_2H	405[e]	304	0.75	2.97	−2.35	3.04
CF_3CO_2H	303[f]	5110[f,g]	16.9	17.6	−5.56	4.57

[a] Y and N are measures of solvent ionizing power and nucleophilicity, respectively, in the general Winstein-Grunwald equation.[57,58] They were determined[19] using 2-adamantyl tosylate, a limiting substrate,[17] as a standard to measure solvent ionizing power.[1b,18,19] [b] R. E. Robertson, *Can. J. Chem.*, **31**, 589 (1953). [c] Reference 20. [d] Reference 13c. [e] Calculated using the extrapolated rate constant of isopropyl brosylate at 50 °C[21] and the $(OBs/OTs)_{2\text{-prop}}^{25°}$ rate ratio of 2.57 in formic acid (ref 21 and 139). [f] Reference 74. [g] The unbuffered results of Winstein[35] were used in eq 8.

species, which is some 30 kcal/mol less stable than a tertiary cation in the gas phase,[103] is at least 20 kcal/mol less stable in solution ($\Delta G = -(1.99)\ (298)\ (2.303) \log k_1'/k_{tert} = 2 \times 10^4$). The $>10^{16}$ increase of the "observed" k_1'/k_{tert} ratio compared with the calculated value strongly implies that primary "ion-pair formation" involves very little, if any, positive charge.

There is no compelling evidence for the existence of ion-pair intermediates in the solvolyses of primary alkyl substrates.[19,20] Consideration of such stretched-bond species[27a] for primary systems only introduces needless mechanistic complications.[107] We conclude that β-arylethyl solvolysis is best interpreted in terms of concerted inter- and intramolecular displacement processes.

Secondary 1-Phenyl-2-propyl Tosylate. Effect of Solvent. The secondary 1-phenyl-2-propyl/2-propyl tosylate rate ratio (eq 1, R = CH_3), as the primary system (eq 1, R = H), varies substantially on going from ethanol to trifluoroacetic acid (100-fold). The relative rate ratio can be calculated from measures of solvent ionizing power (Y) and solvent nucleophilicity (N) with eq 18, obtained by inserting eq 7 and 8, and eq 17 for 2-propyl tosylate into eq 1 (R = CH_3).

$$\log (k/k_t^0) = 0.60Y + 0.47N \qquad (17)^{108}$$

$$\frac{k_t(1\text{-Ph-2-Prop-OTs})}{k_t(2\text{-Prop-OTs})} = \frac{Fk_\Delta^0(10^{0.82Y}) + k_s^0(10^{0.50Y+0.46N})}{k_t^0(10^{0.60Y+0.47N})} \qquad (18)$$

Agreement of calculated and observed values (Table XII, columns 4 and 5) is quite good—within a factor of 2 except for formic acid which is within a factor of 4.

For this secondary system, the sensitivities of the k_s pathway to solvent ionizing power and nucleophilicity are nearly balanced (2-Prop-OTs, $m_s = 0.60$, $l_s = 0.47$; 1-Ph-2-Prop-OTs, $m_s = 0.50$, $l_s = 0.46$). Changes in solvent ionizing power (Y) favor intramolecular displacement (k_Δ) since $m_\Delta \sim 1.3\text{-}1.5m_s$; however, solvent nucleophilicity is slightly more important in determining the overall relative rate ratio (eq 18) since the difference between l_s and l_Δ (0.46, 0.47) is greater than that between m_Δ and m_s (0.32, 0.22).

We found the effect suggested by Cram[5c] and Brown[22]—that increased ionizing power increases the degree of aryl participation in transition states (TS_Δ) leading to the bridged ion—to be of only minor importance in this secondary system, as was found for the primary β-arylethyl system. Firstly, quite good agreement of calculated and observed relative ratios is obtained *without* this assumption (Table XII). In addition, plots of log k_Δ vs. Y are linear from ethanolic solvents to formic acid for the *p*-H, *p*-CH_3, and *p*-CH_3O substituted 1-aryl-2-propyl substrates (Table XIII). Addition of trifluoroacetic acid data for the *p*-H compound does increase the m value ~19%, similar to the average 14% increase observed for the β-arylethyl substrates, as predicted by the proposed effect. However, as with the primary system, the degree of correlation is not decreased significantly and the m values calculated with and without the trifluoroacetic acid point are within the combined error limits. Finally $\rho_{neophyl}$ values (Table XIV), measuring positive charge delocalization to the aryl ring, do not increase substantially (0.87 ± 0.10) in going from ethanol to formic acid. These combined results indicate that the *kinetically significant magnitude* of aryl stabilization in the k_Δ transition state (TS_Δ) is relatively constant with variation in solvent.

Table XIII. Plots of Log (k_Δ) 1-Aryl-2-propyl Tosylates at 50 °C vs. Y^a

Substituent	Solvents	m^b	Correln coeff
p-H	I[c]	0.69 ± 0.06	0.991
	I,[c] CF_3CO_2H[d]	0.82 ± 0.07	0.988
p-CH_3	I[c]	0.67 ± 0.05	0.997
p-CH_3O	I[c]	0.63 ± 0.04	0.996

[a] Based on the 2-adamantyl tosylate scale.[1b,18,19] See Table XII and Results. [b] Error limits indicate standard deviation of slope. [c] Group I solvents refer to EtOH, 80% aqueous EtOH, AcOH, and HCO_2H. [d] Unbuffered data from ref 35.

Table XIV. Plots of Log $(Fk_\Delta)_{SOH}$ 1-Aryl-2-propyl Tosylates at 50 °C vs. σ(neophyl)

Solvent	Rel ρ^a	Correln coeff	Points included
EtOH	0.93	(1.000)	*p*-H, *p*-CH_3O
80% aq EtOH	0.78	0.999	*p*-H, *p*-CH_3, *p*-CH_3O
AcOH	0.80	0.999	*p*-H, *p*-CH_3, *p*-CH_3O
HCO_2H	0.85	0.995	*p*-Cl, *p*-H, *p*-CH_3, *p*-CH_3O
	0.97[b]	0.998	*p*-Cl, *p*-H, *p*-CH_3

[a] Value of ρ is relative to that of substituted neophyl brosylates in acetic acid at 75 °C, −3.96.[1b,36] [b] Substituents such as CH_3O might be deactivated by hydrogen bonding in certain acidic solvents. See Kinetics.

Although the wealth of isotope effect data for β-arylethyl derivatives does not exist for the 1-phenyl-2-propyl system,[91] results for the related *threo*-3-phenyl-2-butyl system are available[30,109,110] in a range of solvents (Table XV). In formic and trifluoroacetic acids, where the reaction proceeds predominantly by the k_Δ process, intermediate α-D (1.142, 1.133), low β-PhCH(D) (1.040, 1.009), and higher β-methyl (1.051, 1.054) than γ-methyl (1.005, 1.003) isotope effects provide evidence for an unsymmetrically bridged transition state, similar to the situation for primary β-arylethyl substrates.[92-95] In acetic acid and 50% aqueous ethanol, the aryl unassisted pathway is a significant component of the total rate constant: 32% (AcOH, iterative Hammett treatment, Table VII) and 22% (50% aqueous ethanol, determined from products[30]), and observed isotope effects should be a composite. α-D effects

Table XV. Summary of H/D Isotope Effects for Secondary Alkyl Substrates

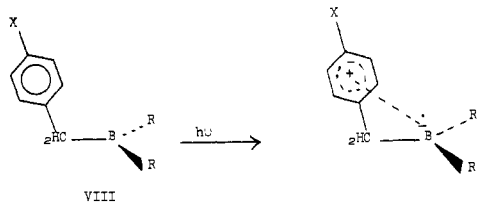
Substrate	Solvent (temp, °C)	α	β-Internal (Per D)	β-Terminal (Per D)	γ per D	$k_{p\text{-D}}/k_{p\text{-H}}$
2-Propyl brosylate[a] (25 °C)	50% aq EtOH[b]	1.114		1.059		
	CH_3CO_2H	1.14[c]				
	CF_3CO_2H	1.22				
1-Phenyl-2-propyl tosylate (25 °C)	98% aq CF_3CO_2H[d]	1.13				
threo-3-Phenyl-2-butyl aryl sulfonates	50% aq EtOH (25)[e]	1.135	1.144			0.986
	CH_3CO_2H (75.1)[f]	1.104	1.094	1.024	1.021	
	HCO_2H (25.02)[f]	1.142	1.040	1.051	1.005	
	CF_3CO_2H (−7.9)[f]	1.133	1.009	1.054	1.003	

[a] Tabulated in ref 23a. [b] Volume percent. [c] Extrapolated from value at 70 °C (1.12, K. Mislow, S. Borčic, and V. Prelog, *Helv. Chim. Acta*, **40**, 2477 (1957)) using a 0.01 increase in magnitude for every 20 °C decrease in temperature.[17f] [d] Reference 91. [e] Reference 30, brosylate leaving group. [f] References 109, 110, polarimetric rate constants, tosylate leaving group.

(1.104 and 1.135) are in the expected range for either k_s or k_Δ mechanisms in these solvents,[23a,30] while the aryl *p*-D effect (50% aqueous ethanol) evidences the major anchimeric pathway; enhanced β-PhCH(D)[15] (1.094, 1.144), and similar β-methyl (AcOH, 1.024) and γ-methyl (AcOH, 1.021) isotope effects indicate the presence of elimination and hydride shift processes[23a,30] which are included in the aryl unassisted pathway.[3,13d,14] The small change in α-D in going from formic to trifluoroacetic acid does not indicate a large change in the degree of participation by the phenyl group in transition states leading to the bridged phenonium ion.

Role of Ion Pairs. The observation of excellent rate-product correlations for acyclic secondary β-aryl system[13d,14] confirmed that the aryl unassisted (k_s) and aryl assisted (k_Δ) mechanisms are discrete processes which do not "crossover". Attack by solvent or neighboring group on neutral substrate was considered to be rate limiting,[3,14a] although it was acknowledged that formation of *intimate* ion pairs which were partitioned between k_s and Fk_Δ would be kinetically consistent with the rate–product results.[3] Several versions of the ion-pair scheme have been applied to secondary β-arylalkyl solvolysis, and these are evaluated below.

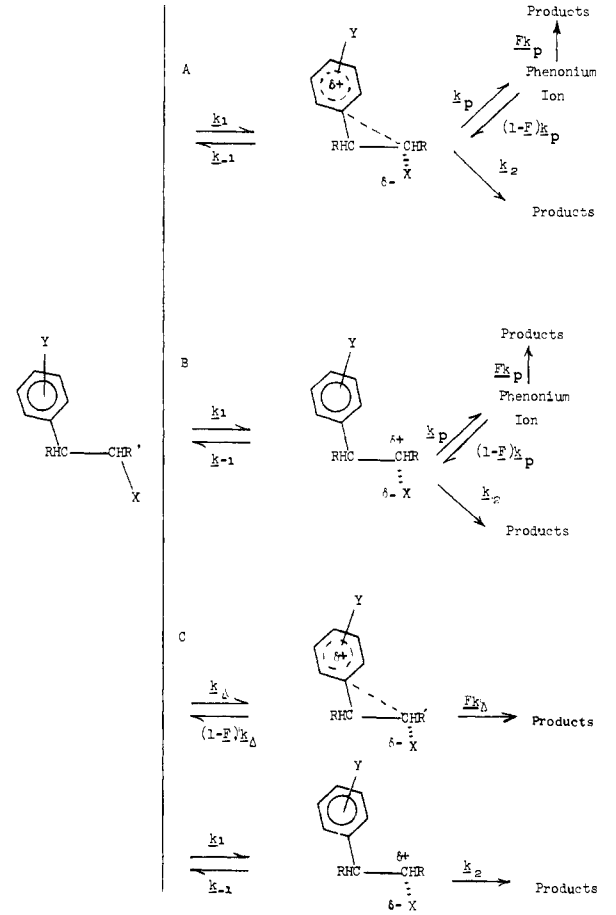
Ramsey and Das[29] have correlated rate data for primary and secondary β-arylalkyl substrates with ionization potentials of substituted benzenes, values which are related to the charge-transfer transitions in the ultraviolet spectra of aryl-substituted tribenzylboranes, VIII. The fact that better linear plots were



VIII

obtained for Fk_Δ than k_t, of β-arylethyl tosylates in acetic acid (correln coeff 0.999, 0.932, respectively), was suggested to provide additional confirmation that these primary substrates solvolyze by two totally independent pathways, k_s and k_Δ. However, very good linear correlations were obtained for the secondary systems 1-aryl-2-propyl and *threo*-3-aryl-2-butyl using total rate constants, k_t (correln coeff 0.99), even though aryl-deactivated derivatives yield almost no products from the aryl assisted pathway. It was interpreted that secondary β-aryl substrates undergo rate-limiting ionization (k_1) to an unsymmetrically π-bridged intimate ion pair, which is captured by solvent (k_2) or neighboring group (k_p) much faster than return to substrate (k_2 and $k_p > k_{-1}$), Scheme IIIA. We disagree with the latter conclusion. Firstly, although the spectral method provides an interesting treatment of β-aryl solvolysis, the ultraviolet and ionization potential data are not as precise or readily available as the preferred Hammett[13-15] and neophyl[1b,32,35] constants for correlations of k_s and Fk_Δ, respectively. Furthermore, since k_s and Fk_Δ processes have the same rate-determining step in this scheme, a satisfactory explanation for the rate-product stereochemistry correlations determined for *threo*-3-aryl-2-butyl brosylates (AcOH) cannot be provided.

Scheme III



Two other ion-pair schemes, illustrated by the 3-aryl-2-butyl system, are consistent with the implications of rate-product correlations for secondary β-aryl solvolyses. Brown and Kim,[14b] employing the basic formulation of Shiner[23] and Sneen,[27,28] propose a steady-state scheme involving formation of an intimate ion pair from neutral substrate, followed by rate-limiting attack by aryl or solvent (k_{-1}/k_2 (or k_p) $\geq$ 20, Scheme IIIB). Cramer and Jewett[30] interpret their isotope effect data (Table XV) as indicating two distinct ion-pair processes (Scheme IIIC)—rate-determining formation of a

Table XVI. Physical Constants for β-Arylethyl Alcohols[a]

	Substituent					
	m,m'-$(CF_3)_2$	*m*-Cl	*m*-F	*p*-Cl	*m*-CH_3	*p*-CH_3
Bp, °C (mm)						
Obsd	54–56[b]	79 (0.3)	90.3 (2.6)	135 (13)	70 (0.5)	82–82.5 (0.6)
Lit.				110 (0.5)[c]	87–88 (2.5)[d]	90–94 (3)[d]

	Substituent				
	m,p-$(CH_3)_2$	*p*-CH_3O	*p*-C_6H_5	2-Naphthyl[e]	2-Fluorenyl[f]
Bp, °C (mm)					
Obsd	142.5–145 (15)	127–128 (2.8)	96–97.5[b]	68.8–70.2[b]	131.1–133.1[b]
Lit.	109–110 (3)[g]	139–141 (14)[h]	94.5–95.5[b,i]	66–67[b,i]	136–137[b,j]

[a] The *p*-CF_3, *m*-CF_3, and *p*-C_6H_5O alcohols were used to prepare the tosylates (Table XVII) directly. β-Phenethyl alcohol was purchased from Aldrich. [b] Melting point, °C. [c] G. Baddeley and G. M. Bennett, *J. Chem. Soc.*, 1819 (1935). [d] Reference 22. [e] β-(2-Naphthyl)ethyl alcohol. [f] β-(2-Fluorenyl)ethyl alcohol. [g] G. W. Pope and M. T. Bogert, *J. Org. Chem.*, **2**, 276 (1937). [h] Reference 10. [i] Reference 48. [j] E. Profft and K. Steinhaus, *J. Prakt. Chem.*, **22**, 47 (1963).

phenyl bridged species (k_Δ) and rate-determining elimination from an open pair (k_2).[111]

It is difficult to experimentally distinguish these alternatives from the original Cram–Winstein description of direct aryl and solvent attack on neutral substrate. Such tight ion pairs having a slightly stretched or weakened bond[27a] to the leaving group are not very different conceptually from covalent starting material. In either formulation, concerted displacement or ion pair, substantial bonding of solvent or neighboring aryl must occur in the rate-determining step to prevent crossover of the k_s or k_Δ pathways.

We agree that ion pairs can be formed in simple secondary solvolysis[20] but suggest that the usual formulations are deficient in specifically excluding nucleophilic solvation.[19,20,26c,93] Such a "quantized" approach soon becomes kinetically complex. In describing 2-propyl solvolysis, Shiner comments "one of the classical examples of borderline solvolyses seems to be borderline in a bewildering number of ways! As many as four different steps, . . . , can be made the dominant rate controlling influence depending on the choice of solvent".[23a] Analysis of the vast amount of data at hand seems to suggest a gradual spectrum of nucleophilic attachment,[7,19–21,26c,112] ranging from limiting secondary (2-adamantyl[17]) to strongly solvent assisted primary (methyl) solvolysis.[17–20,26] In such an interpretation, unhindered secondary ion pairs, if formed, are stabilized from the rear by neighboring group or solvent.

k_s and k_Δ Pathways. Perspectives and Conclusions. Our studies of the β-arylethyl[1,13e] and 1-aryl-2-propyl[13a–d,f] systems confirm by all criteria that the solvolyses of primary and secondary β-aryl substrates are grossly similar, proceeding by discrete k_s and k_Δ pathways.[3] β-Arylethyl tosylates react via competitive displacement by nucleophiles, solvent or aryl. Secondary substrates, such as 1-aryl-2-propyl,[13a–d,f] *threo*-3-phenyl-2-butyl,[14] and *trans*- and *cis*-β-arylcyclopentyl[15] give, in some cases, significant amounts of rearranged tertiary derivatives and elimination.[13d,14,15] These products can also arise from strongly bound pathways, hydride shift, or elimination from a nucleophilically solvated ion pair.[20] Since these processes do not appear to introduce kinetic complexities (i.e., in the k_s line of Hammett plots), they are operationally included in the k_s term.[3,13d,14] This rate constant, therefore, should be designated more appropriately "aryl unassisted" for secondary systems.[113,114]

The prolonged uncertainty about the mechanism of β-arylalkyl solvolysis arose because of a lack of definition concerning the "borderline" position of the solvolysis of secondary systems in the S_N1–S_N2 spectrum of Hughes and Ingold. Cram's observations that the neighboring phenyl group in the 3-phenyl-2-butyl system predominantly controls product stereochemistry, but that solvolysis occurs more slowly than the "model", 2-butyl, posed the "dilemma"[11b] which required almost 20 years of intense effort to solve. The resultant description of simple secondary solvolysis as proceeding by substantial nucleophilic solvent participation provides a significant advance in solvolysis theory, and recent years have seen extensive efforts to refine our understanding of the implications.[3,14,23,26–28]

Experimental Section

General. All boiling points are uncorrected. Melting points, which are uncorrected, were determined using a Mettler FPI apparatus. NMR spectra were taken on Varian A60-A spectrometers using tetramethylsilane as an internal standard. Infrared spectra were determined using a Perkin-Elmer 237B grating spectrometer. Ultraviolet spectra were recorded on a Cary 14 spectrometer. Microanalyses and Karl Fischer determinations were performed by Hoffmann-La Roche, Inc., Nutley, N.J.

Materials. β-Arylethyl Derivatives. Usually the corresponding arylacetic acids, purchased from Pierce (*p*-CF_3, *m*-CF_3, *m*-F) or Aldrich (*m*-Cl, *p*-Cl, *m*-CH_3, *p*-CH_3, *p*-CH_3O, *p*-C_6H_5 (as the nitrile), and β-naphthyl), were reduced to the alcohols by lithium aluminum hydride. The following procedure for β-(*m*-chlorophenyl)ethanol illustrates the method. A solution of (10 g, 0.059 mol) of β-(*m*-chlorophenyl)acetic acid in ether was added slowly to a suspension of lithium aluminum hydride (4.85 g, 0.128 mol) in ether and refluxed overnight. Excess lithium aluminum hydride was decomposed by the normal basic procedure.[115a] The ether solution was dried and evaporated to yield 7.30 g (79%) of the alcohol. Distillation gave the pure product.

The *m,m'*-di-CF_3 and *p*-C_6H_5O alcohols were produced by reaction of the Grignard reagent of the appropriate bromobenzene (Pierce and Aldrich, respectively) with ethylene oxide. The *m,p*-di-CH_3 derivative was prepared from ethylene oxide and the Grignard prepared from *m,p*-dimethylbromobenzene (bp 104–105 °C (16 mm), lit.[116] bp 206–208 °C), obtained by diazotization of *m,p*-dimethylaniline (Aldrich, melting point from hexane 50.5–51.5 °C, lit.[117] mp 47.3–49.2 °). β-(2-Fluorenyl)ethyl alcohol was produced by lithium aluminum hydride reduction of the arylacetic acid, obtained by a Willgerodt sequence from 2-acetylfluorene[118] (Aldrich).

The corresponding tosylates were prepared by the normal pyridine method.[115b] For some derivatives it was necessary to add chloroform to the recrystallization solvent in order to effect solution at room temperature.

Physical constants and analytical data are reported in Tables XVI and XVII. IR and NMR spectra for all compounds were consistent with the structures proposed.

1-Aryl-2-propanols.[119] Commercial 1-phenylacetone (Aldrich) was reduced with lithium aluminum hydride to the alcohol, bp 96–97 °C (10 mm), lit.[120] bp 95 °C (10.5 mm). The 1-(*p*-CH_3-, *p*-Cl-, *m*-Cl-, and *m*-CF_3-) phenyl-2-propanols were prepared[119] by the base-catalyzed condensation of the corresponding benzyl cyanide[121] with ethyl acetate, followed by hydrolysis, decarboxylation,[121] and reduction

Table XVII. Physical Constants and Analytical Data for β-Arylethyl Tosylates

Substituent	Mp, °C[a] Obsd	Mp, °C[a] Lit.	Anal. Calcd, % C	Anal. Calcd, % H	Anal. Found, % C	Anal. Found, % H
m,m'-$(CF_3)_2$	72.1–73.1		49.52	3.42	49.64	3.27
p-NO_2	131.8–133.1	131.5–132.5[b]				
p-CF_3	87.5–88.7		55.81	4.39	56.12	4.40
m-CF_3	*c*				*c*	*c*
m-Cl	46.5–47.6		57.97	4.86	58.21	5.16
m-F	37–38.2		61.21	5.14	61.37	5.20
p-Cl	78.5–79.7		57.97	4.86	57.99	4.89
H	38.8–40.3	35.5–36.6[d] 38.8–39.8[e]				
m-CH_3	*c*	39–40[f]	66.18	6.25	66.32	6.38
p-CH_3	68.4–69.3	69–70[f]				
m,p-$(CH_3)_2$	40.6–42.0		67.08	6.62	67.10	6.52
p-CH_3O	57.8–58.8	57–58[d]				
p-C_6H_5	94.1–95.3	94.5–95.5[g,h]				
p-C_6H_5O	59.7–61.2		68.46	5.47	68.34	5.43
2-Naphthyl[g]	63.5–65	63–64[h] 75–76[i]				
2-Fluorenyl[j]	103.4–104.6		72.50	5.53	72.34	5.49

[a] Uncorrected. [b] Reference 5c. [c] The tosylate was a solid which melted below room temperature, even after four recrystallizations at −78 °C. Acetolysis infinity titers were within 4% of the theoretical value. [d] Reference 10. [e] Reference 72. [f] Reference 22. [g] β-(2-Naphthyl)ethyl tosylate. [h] Reference 48. [i] C. C. Lee and A. G. Forman, *Can. J. Chem.*, **44**, 841 (1966). [j] β-(2-Fluorenyl)ethyl tosylate.

with sodium borohydride:[122] *p*-CH_3, bp 99–100 °C (3 mm), lit. bp 66–67 °C[123] (0.4 mm), 97 °C[124] (2 mm); *p*-Cl, bp 94–95 °C (1.5 mm), lit.[123] bp 94–95 °C (0.1 mm); *m*-Cl, bp 109–110 °C (5 mm); *m*-CF_3, bp 66–67 °C (1.5 mm).

1-(*p*-Nitrophenyl)acetone[125,126] was reduced with sodium borohydride[122] to the alcohol, mp 70–70.6 °C, lit.[122] mp 68–69 °C.

1-(*p*-Anisyl)acetone[127] was prepared by the same procedure[125,126] and reduced with sodium borohydride[122] to the alcohol: bp 114–115 °C (4 mm), lit. bp 158–161 °C[123] (15 mm), 121 °C[128] (3 mm).

1-(*p*-Trifluoromethylphenyl)-2-propanol was prepared from the corresponding arylacetic acid by methylation with methyllithium followed by reduction, bp 73 °C (3 mm).

1,3-Di-*p*-nitrophenyl-2-propanol.[119] 1,3-Diphenyl-2-propyl acetate was nitrated;[129] hydrolysis gave the dinitro alcohol, mp 148.4–149.8 °C. Anal. Calcd for $C_{15}H_{14}O_5N_2$: C, 59.60; H, 4.64; N, 9.27. Found: C, 59.71; H, 4.56; N, 9.21.

1-*p*-Anisyl-3-*p*-nitrophenyl-2-propanol.[119] 1-*p*-Anisyl-3-*p*-nitrophenyl-2-propanone was prepared according to House and Berkowitz[130] and reduced to the alcohol with sodium borohydride, mp 83.5–85 °C. Anal. Calcd for $C_{16}H_{17}O_4N$: C, 66.87; H, 5.97; N, 4.88. Found: C, 66.14; H, 5.50; N, 4.71.

1-Phenyl-3-*p*-nitrophenyl-2-propanol.[119] 1-Phenyl-3-*p*-nitrophenyl-1-propene[131] was converted to 1-phenyl-3-*p*-nitrophenyl-2-propanone.[130] Reduction with sodium borohydride[122] gave 1-phenyl-3-*p*-nitrophenyl-2-propanol, mp 109.6–111 °C.

1-Phenyl-3-*p*-anisyl-2-propanol.[119] The precursor, 1-phenyl-3-*p*-anisyl-2-propanone[121] was reduced with sodium borohydride to the alcohol, mp 53.4–54.6 °C. Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.29; H, 7.49. Found: C, 79.06; H, 6.86.

1,3-Di-*p*-anisyl-2-propanol.[119] The alcohol, mp 81–85 °C, was prepared by lithium aluminum hydride reduction of the diaryl acetone.[132,133]

1-Aryl-2-propyl and 1,3-Diaryl-2-propyl Tosylates. Tosylates of the alcohols described above were prepared[119] in the usual manner.[115b] Spectra were consistent with the structures proposed. Physical constants and analytical data are summarized in Table XVIII.

Kinetic Procedures. Anhydrous acetic acid was distilled from a small amount of acetic anhydride.[134] Absolute ethanol was purified by the method of Lund and Bjerrum.[135] Aqueous ethanol (50% v/v) was prepared by mixing solvolytic grade ethanol with an equal volume of distilled water. Formic acid was stored over barium oxide for 2 weeks, decanted onto fresh barium oxide, and distilled under reduced pressure, bp 29.6–30 °C (46 mm).[21] Karl Fischer analyses indicated <0.02% water. Trifluoroacetic acid (Matheson Coleman and Bell) was distilled under a small positive pressure of dry nitrogen, bp 71–71.5 °C, and transferred to a storage bottle in a glove bag. Freshly distilled trifluoroacetic anhydride, bp 39–39.5 °C, (1% wt) was added[72] and the solution was stored in a desiccator. Karl Fischer analyses indicated <0.01% water.

β-Arylethyl Tosylates. Ethanolyses, acetolyses, and formolyses were performed by the usual sealed ampule technique,[134] with initial substrate concentration in the range 0.01–0.025 M. Ethanol aliquots were diluted with an equal volume of water and titrated to the phenolphthalein end point with standard aqueous NaOH. The acetolyses reported in ref 13e were determined by titration with sodium acetate in acetic acid and the indicator crystal violet;[134] data reported for the first time in this paper were determined potentiometrically using a Beckman 106502 automatic recording titrator. Formolyses were determined potentiometrically in the manner of Winstein[21,22] using sodium acetate in acetic acid as the titrant. Because of relatively high temperatures and long reaction times, the formolyses of β-(*p*-nitrophenyl)ethyl tosylate were carried out in a stoppered volumetric flask, from which aliquots were removed and pressure released periodically. Infinity titers were usually within 4% of the theoretical values. Kinetics in 50% (v/v) aqueous ethanol were followed conductimetrically using special glass cells (25-mL volume) with bright platinum electrodes and either a Wayne-Kerr Model B331 impedance bridge or a recording Wheatstone bridge.[119] Substrate concentration was $\sim 10^{-3}$ M.

All solvolyses except those in TFA displayed good first-order kinetics through at least 70% reaction. Nine titrimetric or 25–40 conductometric points were taken per kinetic run. First-order rate constants were determined using a modified version of the LSKIN computer program.[136,137]

Trifluoroacetolysis Kinetic Procedures. Trifluoroacetic acid represented the key solvent in this study. Kinetic measurements in this highly acidic medium are not possible by ordinary techniques and the UV spectrophotometric method of Swain and Morgan,[138] extended by Peterson[139] to trifluoroacetolyses, is usually employed. However, Hammett-type treatments[13e] require substituted phenyl rings, some with strongly absorbing functional groups (*p*-CH_3O, *p*-C_6H_5O, 2-fluorenyl, β-naphthyl, etc.), which would mask the spectral region of interest. Thus, a modification of the method used by Dewar and Bentley[48] to study the trifluoroacetolyses of the polynuclear β-arylethyl tosylates was developed. The following represents the final version of the procedure, having undergone slight modification in the course of the study.

A. Method. Ampules (17 cm) were constructed from 1-cm (o.d.) Pyrex glass tubing, sealed at one end. All ampules and kinetic glassware were cleaned with chromic acid and soap solutions, rinsed with distilled water, dried in an oven, and cooled to room temperature in a desiccator. Substrate sufficient for a 0.04–0.05 M solution was

Table XVIII. Physical Constants and Analytical Data for 1-Aryl-2-propyl Tosylates, $XC_6H_4CH_2CH(OTs)CH_3$, and 1,3-Diaryl-2-propyl Tosylates, $XC_6H_4CH_2CH(OTs)CH_2C_6H_4Y$

Substituent		Mp, °C		Anal. Calcd, %			Anal. Found, %		
X	Y	Obsd	Lit.	C	H	N	C	H	N
p-CH_3O		77.6-78.4	80[a] 77-78[b]	63.75	6.25		64.18	6.33	
p-CH_3		49.3-50.4	49-50[b]	67.10	6.58		66.73	6.44	
H		91.2-92.4	90.7-91.6[c]						
p-Cl		74.8-76.0	79.5-80.5[b]	59.08	5.23		59.19	5.23	
m-Cl		81.6-82.1		59.08	5.23		59.19	5.32	
m-CF_3		0 < mp < 25		56.98	4.75		56.99	4.68	
p-CF_3		75.4-76.5		56.98	4.75		56.65	4.72	
p-NO_2		115.8-117.2		57.31	5.07	4.18	57.36	5.19	4.25
p-CH_3O	*p*-NO_2	110.8-111.8		62.58	5.25	3.17	62.94	4.80	3.32
p-CH_3O	H	89.6-90.7		69.70	6.11		69.90	5.98	
p-NO_2	H	117.4-118.8		64.23	5.15	3.41	64.94	5.16	3.43
p-NO_2	*p*-NO_2	183.6-185.0 dec		57.89	4.38	6.14	58.00	4.57	6.03

[a] Reference 120. [b] Reference 123. [c] Reference 74.

Table XIX. Trifluoroacetolysis of β-Phenethyl Tosylate at 75 °C

Winstein,[a,b] 75.0 °C		Evapn technique,[c] 75.2 °C		Evapn technique,[c] 75.2 °C, 1% (wt) H_2O	
% rxn	10^4 *k*,[d] s^{-1}	% rxn	10^4 *k*,[d] s^{-1}	% rxn	10^4 *k*,[d] s^{-1}
19.4	4.28	15.3	5.68	10.7	3.89
28.6	4.16	20.7	5.56	18.1	3.84
37.3	3.93	26.7	5.06	25.3	3.77
44.7	3.79	35.1	5.52	32.0	3.38
52.4	3.64	40.6	5.40	37.0	3.16
61.9	3.54	45.7	5.34	42.1	3.12
70.3	3.40	56.7	6.15	47.2	3.00
				51.8	2.94

[a] Reference 42. [b] 8.2×10^{-3} M. [c] $(4.7\text{-}5.0) \times 10^{-2}$ M. Lower initial concentrations give rise to higher rates.[a,b] [d] Integrated first-order rate constants.

Table XX. Comparison of Various Kinetic Techniques for the Trifluoroacetolyses of β-Arylethyl Tosylates

Substituent	Temp, °C	$k_t \times 10^{+4}$	% rxn	Method	Ref
p-H	49.75[a,b]	$(7.09 \pm 0.20) \times 10^{-1}$	33	Evapn	*c*
	49.76[b,d]	$(6.63 \pm 0.36) \times 10^{-1}$	19	UV	*c*
	50.0[e,f]	$(3.83 \pm 0.01) \times 10^{-1}$ [g]	~70	UV	42
	75.11[a,b]	4.49 ± 0.38	50	Evapn	*c*
	75.24[b,d]	4.00 ± 0.13	46	UV	*c*
	75.0[e,f]	3.95 ± 0.11[g]	~70	UV	42
	75.0[d,h]	3.22	>40	UV	72
2-Naphthyl	60.0[a,b,h]	3.95	58	Evapn	*c*
	60.0[e,f]	2.1	>70	Mod UV	48

[a] Theoretical infinity used. [b] Initial [ROTs] = $(4.5\text{-}5.1) \times 10^{-2}$ M. [c] This work. [d] Prepared infinity used.[72] [e] Experimental infinity used. [f] Initial [ROTs] = $(2.1\text{-}2.5) \times 10^{-2}$ M. [g] To correct for downward drift of integrated rate constant during reaction,[42] values obtained during 70% reaction were extrapolated to $t = 0$. [h] Calculated from data at other temperatu

weighed in a 10-mL volumetric flask, and the trifluoroacetic acid–1% (wt) trifluoroacetic anhydride solution was added to the mark. Exactly 1.0 mL of this solution was delivered to each ampule with a pipet, and each ampule was snugly capped with a rubber septum until all could be sealed. Individual samples were removed from the temperature bath at appropriate times, and were cooled immediately and stored in dry ice–acetone.

The cold ampules were opened and evaporated individually, while being cooled in an ice bath, with a gentle stream of dry nitrogen by means of a small tube inserted into the ampule. The time normally required for this operation (20 min) would not have affected the kinetics of the compounds under investigation. A plug of glass wool was placed in the top of these residue-containing ampules, and the last traces of solvent removed in a vacuum desiccator.

The residue in each ampule was dissolved in anhydrous acetic acid containing 5% (vol) acetic anhydride.[140] Solution was greatly facilitated by immersing the ampule into a Beckman ultrasonic apparatus. The contents were quantitatively delivered to a 20-mL beaker, and the glass wool plug and ampule were rinsed several times with anhydrous acetic acid. Each sample was titrated potentiometrically using the Beckman instrument described above with standard sodium acetate in acetic acid. Eight or nine experimental points were determined for each kinetic run. The data were analyzed by the LSKIN computer program; theoretical infinity titers were used since experimental values were significantly low (10-30%) and showed discoloration.

B. Lyophilization Technique. A modified technique for the evaporation process was devised in expectation of fast trifluoroacetolysis rates[141] for the activated substrates. The ampule was removed from a dry ice–acetone bath and opened, a plug of glass wool was inserted, and the TFA was allowed to melt. The ampule was then inserted into a piece of rubber tubing on a high speed stirring motor. Fast rotation caused a vortex which coated the walls of the ampule with the TFA solution. While spinning, the ampule was carefully lowered into a Dewar of dry ice–acetone and the contents were frozen. The TFA was

then lyophilized by direct attachment of the ampule to a high vacuum line, while the ampule was kept cold enough to prevent melting.

C. **Control Experiments.** The following control experiment illustrates the validity of the above techniques, and the fact that CF_3COOH is not occluded in the solid residue nor is *p*-toluenesulfonic acid lost during evacuation. Exactly 1.0 mL of a 0.0520 M solution of *p*-anisylethyl tosylate in CH_2Cl_2 was delivered to a tube-type ampule and evaporated to dryness first with a stream of N_2[48] and then with high vacuum. A solution of *p*-toluenesulfonic acid monohydrate, mp 104.6–106.0 °C (lit.[142] mp 105–107 °C), in CF_3COOH was cooled in an ice bath (0.0585 M, corrected to 0 °C). This solution (1.0 mL) was added to the ampule, dissolving the tosylate residue. The lyophilization and titration procedures were performed, and the volume of titrant consumed was 97% of the theoretical value. A similar control showed that the amount of *p*-toluenesulfonic acid did not change with any reasonable length of time under high vacuum.

D. **UV Techniques.** A UV spectrophotometric technique[72] was employed for comparison rate studies of the parent β-phenethyl tosylate. Infinity values were obtained from solutions prepared with appropriate quantities of β-phenethyltrifluoroacetate, bp 56 °C (0.72 mm), lit.[72] bp 85–86 °C (12 mm), and *p*-toluenesulfonic acid.

E. **Comparison with Literature TFA Rate Constants. Effect of Water.** Since TFA is known to be very hydroscopic,[143] special precautions were undertaken in the purification (see above). In comparing our results in this solvent as well as the newly developed analytical procedure with literature values[42,72] for the parent β-phenethyl tosylate, some disagreement was observed. First-order kinetics were followed to lower percentages of reaction (especially at the lower of the two temperatures studied), rate constants were generally higher, the kinetic plot drifted upward, and slight polymer formation was observed. However, on the addition of 1% (wt) water (more than enough to react with the 1% (wt) TFA anhydride present), agreement with the previous observations[42,72] was obtained[144] (Table XIX). The presence of water in TFA has been shown to increase the rate of detritiation[145,146] and desilylation[146] of aromatic substrates and the rate of ionization of *tert*-butyl chloride.[64] Our observation of *lower* rate constants in moist TFA might result from the moderation of side reactions, thereby allowing detection of the common ion rate depression of the *p*-toluenesulfonic acid generated in the solvolysis.[42]

Some substituents (*m*-CH_3, *p*-CH_3, *m,p*-$(CH_3)_2$, and 2-naphthyl) gave substantial amounts of polymer, while others (*p*-C_6H_5, *p*-C_6H_5O, 2-fluorenyl) produced polymer and colored solutions. Dewar and Bentley showed that polymer formation did not affect the kinetic measurements.[48] Activating substituents generally increased the percentage of reaction showing good first-order kinetics, while a deactivating substituent depressed it: at 75 °C, *p*-Cl (23%), *p*-H (50%), and *p*-CH_3 (52%). Yukawa, Tsuno et al.[43] report first-order kinetics through 70% reaction for *m*-Br- and *p*-NO_2-substituted II *p*-nitrobenzenesulfonates in CF_3COOH by the Bentley-Dewar method.[48]

The results lend support to the general view that consistent solvolysis kinetics in CF_3COOH for reaction times >40%[64,72] are difficult to obtain, and are especially sensitive to medium composition. Comparison with the limited available literature (Table XX) indicates relatively good agreement, considering the variations in the three analytical methods among four different research groups.

1-Aryl-2-propyl and 1,3-Diaryl-2-propyl Tosylates. The acetolysis rate constants reported in ref 13a–c and here were detemined for the most part by the usual ampule technique,[134] titrating the liberated *p*-toluenesulfonic acid with a glacial acetic acid solution of sodium acetate. Some rate constants were also determined by a conductometric method,[119] which is shown to agree well with the titrimetric procedure for 1-(*p*-tolyl)-2-propyl tosylate.

Formolysis rate constants were determined by conductance using special glass cells (25-mL volume) with bright platinum electrodes, and a recording Wheatstone bridge.[119] Some formolysis rates were checked potentiometrically, using the method of Winstein and Marshall.[21] A Heath Model EU-20-11 recording pH meter was used for this titration. The formolysis solutions were diluted with 50 mL of glacial acetic acid and titrated to the potentiometric inflection point with an acetic acid solution of sodium acetate. The formic acid solvent was purified by storage for at least 3 days at room temperature over solid boric anhydride, followed by fractional distillation under vacuum, bp 30–33 °C (50 mm).[21]

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(68) F varies with solvent (Tables III and VI), and therefore log k_Δ instead of log Fk_Δ must be plotted.
(69) Inclusion of a solvent nucleophilicity term yields the correlation, log $(k_\Delta/k_\Delta^0) = 0.64Y - 0.05N$, with only slightly better correlation: correln coeff 0.998.
(70) Inclusion of the solvent nucleophilicity terms yielded the equation log $(k_\Delta/k_\Delta^0) = 0.65Y - 0.23N$ (correln coeff 0.996). The observation of a negative sign for l_Δ is analogous to the situation for the primary β-phenethyl system ($l_\Delta = -0.05$), although the magnitude in the present case is substantially greater. Since the degree of correlation is not greatly enhanced by including l, and because a negative value of l is somewhat difficult to interpret, we will use eq 8 in the following analysis.
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The Solution Conformation of Nicotine. A ^1H and ^2H Nuclear Magnetic Resonance Investigation

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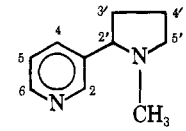
Abstract: The ^1H NMR spectrum of nicotine (1) is analyzed in detail. Selectively deuterated nicotine analogues afford considerable simplification of the pyrrolidine ^1H resonances by allowing partition of this seven-spin system into three-, four- and five-spin systems. In addition, the ^2H NMR chemical shifts of these analogues provide a means of assigning ^1H NMR chemical shifts to specific protons unambiguously. The vicinal coupling constants of the pyrrolidine ring protons suggest an envelope conformation for the five-membered ring, in which the methyl and pyridine moieties assume equatorial positions. A perpendicular spatial orientation of the pyridine and pyrrolidine rings is supported by two observations: a small long-range coupling constant (<0.05 Hz) between H(2′) and H(6), and nuclear Overhauser enhancements of 9 ± 2 and 5 ± 2% for the H(2′) resonances upon saturation of H(2) and H(4), respectively.

Introduction

Interest in describing the interactions between nicotine (**1**) and its receptors at the molecular level has prompted numerous studies concerned with facets of the conformation of nicotine.[1-9] Analogies have been drawn[4,6] between the conformational and electronic properties of acetylcholine, the naturally occurring compound which allows communication between nerve cells, and cholinergic agonists such as nicotine which also interact with nicotinic receptors. It is therefore desirable to obtain a more detailed conformational picture of nicotine to aid in the interpretation of its physiological activity in terms of structure-function relationships.

Conformational investigations of nicotine are centered on three basic aspects:

(1) Pyramidal inversion of the pyrrolidine nitrogen results in cis-trans isomerism of the methyl and pyridine moieties about the N(1′)-C(2′) bond. An earlier report[8] which suggested that the cis isomer predominated in solution was disproved in a recent study,[9] which concludes that the trans isomer is favored by 10:1. Molecular orbital calculations[6] on nicotine



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as well as x-ray crystallographic studies[1] on the dihydriodide also indicate a preference for the trans isomer.

(2) The rotational disposition of the pyridine and pyrrolidine rings about the C(2′)-C(3) bond has been the subject of x-ray studies, molecular orbital calculations,[3,6] and circular dichroism (CD) measurements.[7] These investigations suggest that the conformation is most favored in which the C(2′)-H(2′) bond and pyridine ring are coplanar, making the two rings perpendicular. Although the molecular orbital calculations and CD measurements indicate little preference for the rotamer with H(2′) and H(2) either syn or anti, nicotine dihydriodide crystallizes in the former conformation.

(3) A detailed analysis of the pyrrolidine ring geometry in solution has not as yet been presented. NMR paramagnetic

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