outset, however, it was unclear whether the chirality of **8a** would be retained throughout the Strecker sequence. Enolization of isobutyraldehyde would cause a loss of configurational purity.[12] However, the results of two experiments indicated that enolization might be negligible under suitably mild Strecker conditions. First, glycol **7b** was treated several times with D_2O to exchange hydroxylic hydrogens. The deuterated analog with sodium metaperiodate in D_2O at 0°, then 20°, gave a mixture of aldehydes which was distilled at 20° into a cold trap. The thawed aqueous distillate, with $(ND_4)_2SO_4$, ND_4OD, and sodium cyanide in D_2O at 0°, then 20°, gave aminonitrile **9b**, purified by Kugelrohr distillation at 70° (0.5 mm). The nmr and mass spectra of this compound indicated the absence of deuterium. Similarly, [α-^{2}H]isobutyraldehyde[12] under analogous conditions but with undeuterated reagents in H_2O gave **9b** which contained one atom of deuterium, as did the D,L-valine *N*-acetate obtained after acid hydrolysis and acetylation.

Hence, glycol **7a**, with sodium metaperiodate in water at 0° for 1 hr, then 20° for 3 hr, gave a mixture containing (2*S*)-[3,3,3-$^2H_3$]isobutyraldehyde (**8a**) which was distilled nearly to dryness at 20° *in vacuo*. The distillate trapped in liquid N_2 was thawed and immediately treated with ammonium chloride, ammonium hydroxide, and sodium cyanide, at 0° for 1 hr and then for 19 hr at 20°. The crude[13] (2*RS*,3*S*)-[4,4,4-$^2H_3$]-2-amino-3-methylbutyronitrile (**9a**) isolated by continuous ether extraction was hydrolyzed with concentrated HCl at reflux for 24 hr. Evaporation gave a crude residue from which D,L-[$^2H_3$]valine (**4**) was isolated (20%) by ion-exchange chromatography on Rexyn 101 (H) cation exchange resin. Only negligible traces of glycine were obtained. Crystallization from ethanol gave pure (2*RS*,3*S*)-[4,4,4-$^2H_3$]valine (**4**): ^{1}H nmr (D_2O + ND_4OD, external TMS) δ 1.34 (d, CH_3, J = 7 Hz), 1.39 (d, CH_3, J = 7 Hz), 2.50 (1 H, m), 3.78 (1 H, d, J = 5 Hz). A portion was acetylated[11] and resolved with kidney acylase I,[11] the resultant (2*S*,3*S*)-[4,4,4-$^2H_3$]valine (**10**) ([α]D +70° (*c* 1, HoAc)) and (2*R*,3*S*)-[4,4,4-$^2H_3$]valine *N*-acetate (**11**) ([α]D −7.0 (*c* 2, HoAc)) being separated by ion exchange on Rexyn 101 (H). The ^{1}H nmr of **10** showed a single 3 H methyl doublet at 1.39 ppm indicating the stereochemical homogeneity of the isopropyl group. The acetate **11** was converted to the methyl ester: ^{1}H nmr ($CDCl_3$ with Eu(fod)$_3$, 0.30 mol) showed a single doublet, 1.98 ppm, J = 7 Hz, whereas the nmr of unlabeled (2*RS*)-valine *N*-acetate methyl ester showed doublets at 1.98 and 2.42 ppm, again indicating the stereochemical purity of **4**, estimated to be close to 100%.

Acknowledgment. We are indebted to the National Institutes of Health for Grant GM 18872 in support of this work.

(12) For extensive studies on the catalytic dedeuteration of [α-^{2}H]-isobutyraldehyde see: J. Hine and K. W. Narducy, *J. Amer. Chem. Soc.*, **95**, 3362 (1973), and earlier papers.

(13) For preparative purposes, much higher yields of valine are obtained if the aminonitrile is not purified before hydrolysis.

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Effect of Solvent on Neighboring Aryl Group Participation. Is k_Δ Enhanced?[1]

Sir:

The β-phenethyl tosylate/ethyl tosylate solvolysis rate ratio varies dramatically from 0.24 to 1770 (7500-fold!) in going from ethanol to trifluoroacetic acid (Table I, column 4). While these results indicate a solvent-induced shift of mechanism from aryl unassisted to aryl assisted,[2] the factors responsible for this extreme variation, although often discussed,[2-7] have not been quantitatively elucidated.

Solvolyses of primary and most secondary substrates are now established to proceed not by free carbocations but by strongly assisted transition states and cationoid intermediates.[2,6,8-10] Simple substrates solvolyze by the k_s (solvent assisted) route, but competition between two discrete pathways, k_s and k_Δ (or Fk_Δ,[11] anchimerically assisted), is possible when a neighboring group is present. Thus, eq 1 summarizes

$$\frac{k_t(\beta\text{-PhEtOTs})}{k_t(\text{EtOTs})} = \frac{Fk_\Delta + k_s(\beta\text{-PhEtOTs})}{k_s(\text{EtOTs})} \quad (1)$$

the β-PhEtOTs/EtOTs rate ratio. Changes in this ratio in going from one solvent to another could be caused by either of two effects (or their combination[3a]):[12] (1) by a decrease in k_s(β-PhEtOTs) and k_s(EtOTs 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. For these primary substrates, the k_s route is a simple displacement reaction which is extremely sensitive to solvent nucleophilicity, while k_Δ is an ionization process and could be more sensitive than k_s to ionizing power. The enhancement of k_Δ might be due (a) merely to a difference in response of the two dissimilar[6] pathways to solvent ionizing power ($m_\Delta > m_s$) or (b) to an increase with increased solvent ionizing power of the kinetically significant magnitude of aryl bridging in the transition state (TS_Δ) leading to the phenonium intermediate.[4,7]

Our findings indicate that a combination of effects 1 and 2a is operative and that 2b is not important.

To determine if the magnitude of assistance provided by aryl bridging in the transition state (TS_Δ) is enhanced by solvent ionizing power (effect 2b), we probed

(1) A preliminary account of this work was presented at the 7th Annual Middle Atlantic Regional Meeting of the American Chemical Society, Philadelphia, Pa., Feb 15, 1972.

(2) For a recent review, see C. J. Lancelot, D. J. Cram, and P. v. R. Schleyer in "Carbonium Ions," Vol. III, G. A. Olah and P. v. R. Schleyer, Ed., Interscience, New York, N. Y., 1972, Chapter 27, p 1347.

(3) (a) S. Winstein and H. Marshall, *J. Amer. Chem. Soc.*, **74**, 1120 (1952); (b) S. Winstein, C. R. Lindegren, H. Marshall, and L. L. Ingraham, *ibid.*, **75**, 147 (1953).

(4) H. C. Brown, R. Bernheimer, C. J. Kim, and S. E. Scheppele, *ibid.*, **89**, 370 (1967).

(5) J. E. Nordlander and W. G. Deadman, *ibid.*, **90**, 1590 (1968).

(6) A. Diaz, I. Lazdins, and S. Winstein, *ibid.*, **90**, 6546 (1968).

(7) J. A. Thompson and D. J. Cram, *ibid.*, **91**, 1778 (1969).

(8) Citations to recent work at Princeton regarding this point are listed in ref 9, footnote 11. For a review see D. J. Raber and J. M. Harris, *J. Chem. Educ.*, **49**, 60 (1972).

(9) T. W. Bentley, F. L. Schadt, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, **94**, 992 (1972).

(10) A. F. Diaz and S. Winstein, *ibid.*, **91**, 4300 (1969).

(11) F is the fraction of intimate phenonium ion pair which does not return.

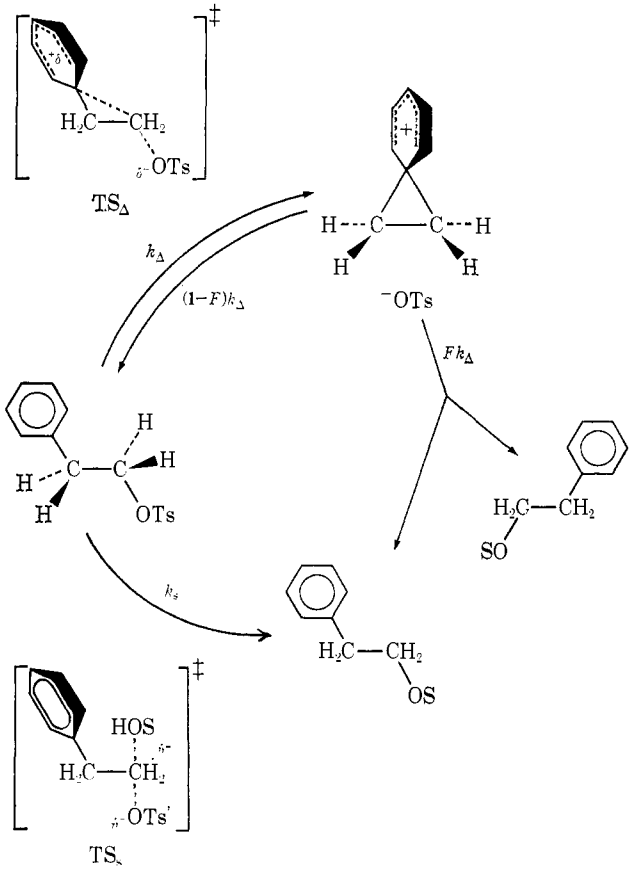
(12) More reactive leaving groups also have an effect on the competition between k_s and k_Δ.[2] See J. L. Coke, F. E. McFarlane, M. C. Mourning, and M. G. Jones, *J. Amer. Chem. Soc.*, **91**, 1154 (1969); R. J. Jablonski and E. I. Snyder, *ibid.*, **91**, 4445 (1969).

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

Solvent	$k_t \times 10^6$, sec^{-1} (75°)		$k_t(\beta\text{-PhEt})/k_t(\text{Et})$		N[b]	Y[b]
	C_2H_5OTs	$PhCH_2CH_2OTs$	Exptl	Calcd (eq 4)		
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 6 except where noted. [b] Y and N are measures of solvent ionizing power and nucleophilicity, respectively, in the general Winstein–Grunwald equation.[9,27] They were determined[9] using 2-adamantyl tosylate, a limiting substrate,[8] as a standard to measure ionizing power. [c] Extrapolated from data at 50°.[27a] [d] This work. [e] Reference 15. [f] Calculated from eq 3 using m_s and l_s (0.36, 0.82) for ethyl tosylate. [g] Extrapolated using the m value for 2-adamantyl tosylate in 70 and 97% (wt) aqueous TFE (F. Schadt, unpublished results).

Scheme I



the influence of solvent on $\rho^+(Fk_\Delta)$ and on m_Δ. Although Brown's σ^+ [2,13,14] and Yukawa–Tsuno's[2,15a,c,16] Hammett-type treatments might be employed to obtain $\rho^+(Fk_\Delta)$, the most accurate[7,17,18] method is to plot the dissected values of log Fk_Δ[13,19] for a series of substituted β-arylethyl tosylates in a given solvent against log k_t (≡ log k_Δ) for similarly substituted neophyl tosylates (acetic acid, 75°).[10,17] In effect, this approach uses the neophyl data in acetic acid to define a set of σ^+ constants more appropriate than the usual Brown values for the three-membered spiro transition state in aryl participation.[7] The observed slopes (Table II, column 2), equivalent to relative Hammett–Brown ρ^+ values, are found to be remarkably constant (1.05 ± 0.14) even when the trifluoroethanol result, based on insufficient data, is included. Delocalization of positive charge to the aryl ring is thus indicated to be quite similar for the Fk_Δ pathways in solvents of greatly differing ionizing power (see Y values, Table I). This implies that the kinetically significant degree of aryl participation in the transition state (TS$_\Delta$) is relatively constant.[20]

Table II. Plots of Log $(Fk_\Delta)_{SOH}{}^X$ β-Arylethyl Tosylates at 75° *vs.* Log $(k_t)_{AcOH}{}^X$ Substituted Neophyl Tosylates at 75° [a]

Solvent	Slope	Corr Coeff	Pts Included[a]
EtOH[b]	0.89	1.000	p-CH_3 and p-CH_3O
50% aq EtOH	0.93	0.988	All except p-Cl
AcOH	1.06	0.996	All except p-Cl
HCO_2H[c]	1.05	0.999	All except p-CH_3O[d]
CF_3CH_2OH[e]	1.27	1.000	H and p-CH_3[d]
CF_3CO_2H[f]	1.11	0.998	All except p-CH_3O[d]

[a] Substituents include p-Cl, H, m-CH_3, p-CH_3, m,p-$(CH_3)_2$, and p-CH_3O. [b] References 6, 23, and this work. [c] Includes data from ref 4. [d] p-CH_3O and p-NO_2 (see footnote *f*) are deactivated by hydrogen bonding. See R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Andersen, and G. T. Davis, *J. Amer. Chem. Soc.*, **85**, 709, 3146 (1963); G. L. Nelson, G. C. Levy, and J. D. Cargioli, *ibid.*, **94**, 3089 (1972); P. E. Peterson, D. M. Chevli, and K. A. Sipp, *J. Org. Chem.*, **33**, 972 (1968). [e] Reference 15. [f] The slope changes somewhat to 1.06 (corr coeff 0.998) 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 (see footnote *d*)). See T. Ando, N. Shimizu, S.-G. Kim, Y. Tsuno, and Y. Yukawa, *Tetrahedron Lett.*, 117 (1973).

This conclusion is supported by the determination of m_Δ values for *each* substituted β-arylethyl substrate in Table II (except p-Cl[21a] and p-CH_3O[21b]) in solvents ranging in ionizing power from either ethanol or acetic acid to trifluoroacetic acid. For each substrate, dissected log k_Δ[13,22] values were plotted against log k_t

(13) J. M. Harris, F. L. Schadt, P. v. R. Schleyer, and C. J. Lancelot, *J. Amer. Chem. Soc.*, **91**, 7508 (1969).
(14) R. Heck and S. Winstein, *ibid.*, **79**, 3432 (1957).
(15) (a) D. S. Noyce and R. L. Castenson, *ibid.*, **95**, 1247 (1973); (b) D. S. Noyce, R. L. Castenson, and D. A. Meyers, *J. Org. Chem.*, **37**, 4222 (1972); (c) R. L. Castenson, Ph.D. Thesis, University of California, Berkeley, 1971.
(16) H. Tanida, T. Tsuji, H. Ishitobi, and T. Irie, *J. Org. Chem.*, **34**, 1086 (1969).
(17) M. G. Jones and J. L. Coke, *J. Amer. Chem. Soc.*, **91**, 4284 (1969).
(18) B. G. Ramsey and N. K. Das, *ibid.*, **94**, 4233 (1972).
(19) Since F[11] is relatively constant for all participating β-arylethyl substrates in a given solvent,[17] plots of log k_Δ or log Fk_Δ will give essentially the same slope.
(20) Legitimate caution regarding the use of linear free-energy relationships in determining transition state structures has been advocated recently (C. D. Johnson and K. Schofield, *J. Amer. Chem. Soc.*, **95**, 270 (1973); see also D. S. Kemp and M. L. Casey, *ibid.*, **95**, 6670 (1973), and D. Fărcaşiu, *J. Chem. Educ.*, submitted for publication).
(21) (a) The already low k_Δ values for the parent β-phenethyl compound in the more nucleophilic solvents are decreased further by the deactivating p-Cl substituent, which makes accurate measurements difficult. (b) See Table II, footnote *d*.
(22) F[11] varies with solvent[6,15a,c,17,23] for β-arylethyl tosylates and log k_Δ must be plotted.
(23) E. F. Jenny and S. Winstein, *Helv. Chim. Acta*, **41**, 807 (1958).

($\equiv$ log k_c)[8] for the nonparticipating 2-adamantyl tosylate in the same solvents (eq 2). This modified Y treatment with 2-adamantyl as a standard for Y values appropriate to tosylate leaving groups[24] yields nicely linear correlations (correlation coefficient >0.99) with slopes: H, 0.69; *m*-CH_3, 0.74; *p*-CH_3, 0.65; *m,p*-$(CH_3)_2$, 0.74; av 0.71 ± 0.04. The lack of significant variations or trends in these values indicates that the Fk_Δ pathway does not respond selectively to changes in ionizing power.

The 7500-fold variation in the β-phenethyl tosylate/ethyl tosylate rate ratio (Table I, column 4) can be reproduced quantitatively by assuming that only effects 1 and 2a are operative. Equation 2 correlates k_Δ for β-

$$\log (k_\Delta/k_\Delta^\circ) = m_\Delta Y \qquad (2)^{26}$$

phenethyl tosylate, while eq 3 is generally applicable to

$$\log (k_s/k_s^\circ) = m_s Y + l_s N \qquad (3)$$

k_s processes.[9,27]

Combination of eq 1–3 and insertion of the appropriate m and l values[28] gives eq 4 which allows calcula-

$$\frac{k_t(\beta\text{-PhEtOTs})}{k_t(\text{EtOTs})} = \frac{Fk_\Delta^\circ[10^{0.69Y}] + k_s^\circ[10^{(0.33Y+0.78N)}]}{k_t^\circ[10^{(0.36Y+0.82N)}]} \qquad (4)^{29}$$

tion of the relative ratio (Table I, column 5). The agreement with the experimental ratios is remarkably good.

Our evidence indicates that the β-phenethyl tosylate/ethyl tosylate rate ratios are influenced by both solvent ionizing power and nucleophilicity, but that the latter is generally more important. This follows from the comparably large range of N and Y values (Table I, last two columns) and the fact that the m_s coefficients (0.3–0.4) are smaller than the l_s coefficients (0.75–0.85) in eq 4. An increase in ionizing power does favor k_Δ over k_s since $m_\Delta > m_s$, but we could detect little change in the kinetically significant magnitude of bridging of the neighboring group (effect 2b). Are these conclusions general for all k_Δ systems? The answer to this question is under investigation and will be reported subsequently.

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(30) National Institutes of Health Predoctoral Fellow, 1969–1973.

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(24) Dispersion in mY plots because of leaving group effects is well known.[25] Winstein, *et al.*, have proposed *p*-methoxyneophyl tosylate, a k_Δ substrate, as a standard to measure ionizing power for compounds with sulfonate leaving groups.[25b] 2-Adamantyl and *p*-methoxyneophyl tosylates are linear (corr coeff 0.999) in the range of solvents where common data are available.

(25) (a) A. H. Fainberg and S. Winstein, *J. Amer. Chem. Soc.*, **79**, 1608 (1957); (b) S. G. Smith, A. H. Fainberg, and S. Winstein, *ibid.*, **83**, 618 (1961).

(26) Inclusion of the solvent nucleophilicity term, lN, does not significantly improve the simple mY correlation for the k_Δ pathway.

(27) (a) S. Winstein, E. Grunwald, and H. W. Jones, *J. Amer. Chem. Soc.*, **73**, 2700 (1951); (b) S. Winstein, A. H. Fainberg, and E. Grunwald, *ibid.*, **79**, 4146 (1957).

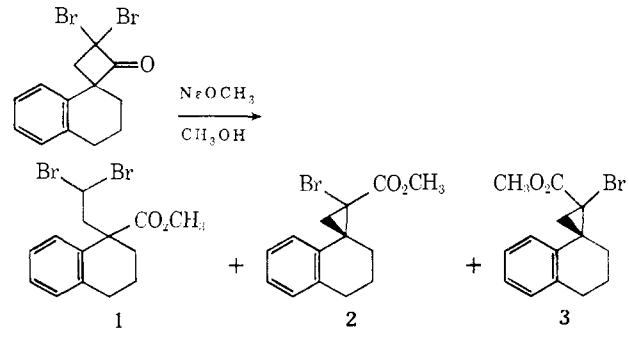
(28) m_Δ is the m value for the k_Δ pathway (β-PhEtOTs, 75°).[26] Values of (m_s, l_s) were obtained by the four-parameter Winstein–Grunwald equation[9,27] (eq 3) for the dissected k_s values of β-PhEtOTs and k_t of EtOTs at 75° in the solvents EtOH, 50% aqueous EtOH, AcOH, and HCO_2H.

(29) k_Δ°, k_s°, and k_t° are the rates for the appropriate processes in 80% aqueous EtOH calculated from literature data.[6,25b,27a] For F values[11] see ref 6, 15a, c, 17, and 23.

New Synthetic Reactions. New Approach to Geminal Alkylation

Sir:

We reported the stereoselective creation of geminal substitution from a carbonyl group based upon spiroannelation, bromination, and subsequent ring cleavage.[1] Such an approach was clearly limited to the spiroannelated products derived from ketones and to those which did not possess functionality sensitive to molecular bromine. A further limitation arose in extension of the work to the spiroannelated product of 1-tetralone. The desired ring cleaved compound (**1**) constituted only a minor product. The major products **2** and **3** arose from a modified Favorskii reaction (semi-



benzilic acid rearrangement).[2] In this communication, we report an alternative approach which does not suffer from such limitations and which results in the stereoselective creation of an α-methylcarboxylic acid unit, a common structural feature found in terpenes.

Introduction of a dithiane unit, an anion stabilizing but nonleaving group, required activation of the α-methylene unit of the spiroannelated product. An aminomethylene group, introduced by condensation of the cyclobutanone[3] (*e.g.*, **4**) with *tert*-butoxybis(dimethylamino)methane,[4] has such an activating function. The vinylogous amides are characterized by two carbonyl infrared bands at 1608–1620 (s) and 1680–1710 (m) cm^{-1} and nmr absorptions at δ 2.95–3.05 (*N*-

(1) B. M. Trost and M. J. Bogdanowicz, *J. Amer. Chem. Soc.*, **95**, 2038 (1973). For some recent aiternative approaches to geminal alkylation, see G. H. Posner and D. J. Brunelle, *Tetrahedron Lett.*, 935 (1973); D. Seebach, M. Kolb, and B.-T. Gröbel, *Angew. Chem., Int. Ed. Engl.*, **12**, 69 (1973); D. Seebach, B.-T. Gröbel, A. K. Beck, M. Braun, and K. H. Geiss, *ibid.*, **11**, 443 (1972); F. E. Ziegler and P. A. Wender, *J. Amer. Chem. Soc.*, **93**, 4318 (1971); E. J. Corey and J. I. Shulman, *ibid.*, **92**, 5522 (1970); E. Wenkert, R. A. Mueller, E. J. Reardon, Jr., S. S. Sathe, D. J. Scharf, and G. Tosi, *ibid.*, **92**, 7428 (1970).

(2) For a review of related reactions in cyclobutanes see J. M. Conia and J. R. Salaun, *Accounts Chem. Res.*, **5**, 33 (1972).

(3) Lithium fluoroborate appears to be superior to lithium perchlorate for the rearrangement of the oxospiropentanes. For preparation of this salt see I. Shapiro and H. G. Weiss, *J. Amer. Chem. Soc.*, **75**, 1753 (1953).

(4) J. Gutzwiller, G. Pizzolato, and M. Uskokovic, *ibid.*, **93**, 5907 (1971); H. Bredereck, F. Effenberger, and G. Simchen, *Chem. Ber.*, **101**, 41 (1968), and references therein.