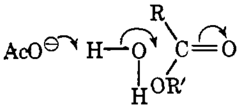
aspirin and the intramolecular reaction, are strong evidence that catalysis of ester hydrolysis by general bases actually represents classical general base catalysis of the attack of water rather than a kinetically equivalent alternative mechanism.



Finally we comment, at the request of a referee, on why aspirin hydrolysis should differ from a number of other examples of carboxyl group catalysis which do generally proceed, in the case of phenolic leaving groups, through anhydride intermediates.

It seems probable that the aspirin reaction lies close to the borderline between nucleophilic and general base catalysis; a few per cent of hydrolysis at 100° may in fact occur by the nucleophilic mechanism, and we have shown recently that the hydrolysis of the anion of 3,5-dinitroaspirin does involve the nucleophilic mechanism.[31] Thus a relatively small difference in activation enthalpy or entropy would account for the difference in mechanism.

We consider that the decisive factor is the fact that the leaving group in the case of aspirin remains attached to the anhydride produced by the nucleophilic mechanism (see Scheme I). This affects the equilibrium concentration of the anhydride III in two ways. The entropy of activation for the breakdown of the tetrahedral intermediate is less favorable because the leaving group does not gain independent translational modes, and the entropy of activation for the reverse reaction is particularly favorable, for a similar reason. In other words, rapid intramolecular acylation of the leaving group is possible, and this has a decisive effect on the partitioning of the tetrahedral intermediate.

Acknowledgments. We gratefully acknowledge a regular and valuable exchange of ideas with Professor W. P. Jencks throughout this investigation, which developed out of a study of the amine-catalyzed hydrolysis of aspirin, begun at Brandeis University in 1963 (A. J. K., unpublished work with W. P. Jencks). We acknowledge also a maintenance grant from the Science Research Council of Great Britain, and a Studentship from Gonville and Caius College (to A. R. F.).

Solvolysis Mechanisms. SN1-Like Behavior of Methyl Chloromethyl Ether. Sensitivity to Solvent Ionizing Power and α-Deuterium Isotope Effect[1,2]

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Abstract: Solvolysis of methyl chloromethyl ether in a series of solvents and solvent mixtures gives a Winstein m value (sensitivity to solvent ionizing power) of 1.02 ± 0.03, within experimental error of that (1.00) defined for t-butyl chloride and significantly different from values for typical primary and secondary compounds (m = 0.2–0.5). Moreover, methyl chloromethyl ether gives a ratio of rates in aqueous ethanol (of the same ionizing power as glacial acetic acid) *vs.* glacial acetic acid of *ca.* 9, comparable with the ratios given by primary compounds (4–100) and secondary compounds (5–90). The α-deuterium isotope effect for methyl chloromethyl-d_2 ether is $k_H/k_D = 1.24 \pm 0.08$ per deuterium atom (in 2-propanol), in the range typical of reactions involving "unimolecular" dissociation, *i.e.*, conversion of sp^3 carbon hydridization to sp^2. The solvent isotope effect in 95.2% acetone–H_2O (v/v) *vs.* 95.2% acetone–D_2O is $k_{H_2O}/k_{D_2O} = 0.93 \pm 0.05$. The evidence indicates that methyl chloromethyl ether solvolyzes by a mechanism closely resembling that of t-butyl chloride, *i.e.*, SN1-like, even though the former is sterically much like a primary halide.

Alkyl chloromethyl ethers are known to decompose with extraordinary rapidity in solvolytic *and* in SN2 reactions.[4] This behavior is found for some other compounds, *e.g.*, allyl chloride,[5] but most compounds which undergo SN reactions tend to react slowly under SN2 conditions if they react rapidly in solvolysis, and *vice versa.* Some idea of the solvent sensitivity of the rates of solvolytic reactions of chloromethyl ethers was available[4] (similar to triphenylmethyl chloride[4j]); we felt a detailed study of the features of solvolytic

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(1) Previous paper: G. J. Frisone and E. R. Thornton, *J. Am. Chem. Soc.*, in press.

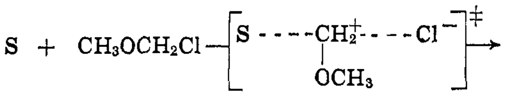
(2) For further details, *cf.* T. C. Jones, Ph.D. Dissertation in Chemistry, University of Pennsylvania, 1966; submitted to University Microfilms, Ann Arbor, Mich.

(3) National Institutes of Health Predoctoral Fellow, 1964–1966; National Science Foundation Graduate Summer Research Fellow, 1964.

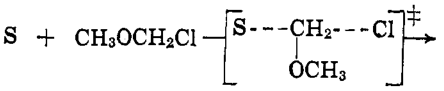
(4) (a) E. Wedekind, *Chem. Ber.*, **36**, 1383 (1903); (b) J. B. Conant, W. R. Kirner, and E. E. Hussey, *J. Am. Chem. Soc.*, 47, 488 (1925); (c) J. W. Farren, H. R. Fife, F. E. Clark, and C. E. Garland, *ibid.*, **47**, 2419 (1925); (d) W. Cocker, A. Lapworth, and A. Watson, *J. Chem. Soc.*, 446 (1930); (e) F. Straus and H. Heinze, *Ann.*, **493**, 191 (1932); (f) H. Böhme, *Chem. Ber.*, **74B**, 248 (1941); (g) R. Leimu, *Suomen Kemistilehti*, **B16**, 9 (1943); (h) R. Leimu and P. Salomaa, *Acta Chem. Scand.*, **1**, 353 (1947); (i) P. Salomaa, *Ann. Univ. Turku.* **A14**, 1 (1953); (j) P. Ballinger, P. B. D. de la Mare, G. Kohnstam, and B. M. Presst, *J. Chem. Soc.*, 3641 (1955); (k) P. Salomaa, *Acta Chem. Scand.*, **11**, 468 (1957); (l) P. Salomaa, *Suomen Kemistilehti*, **B33**, 11 (1960); (m) J. Hine, R. J. Rosscup, and D. C. Duffey, *J. Am. Chem. Soc.*, **82**, 6115, 6120 (1960).

(5) P. B. D. de la Mare and J. Vernon, *J. Chem. Soc.*, 2504 (1954).

reactions of methyl chloromethyl ether would provide evidence whether the transition state in these reactions was ion pair like (eq 1) or "tighter" and more nearly typical of the transition states thought to occur in SN2 reactions of primary halides, sulfonates, etc. (eq 2).



$$S + CH_3OCH_2Cl \longrightarrow \left[S\text{- - - -}\underset{\displaystyle OCH_3}{\underset{|}{CH_2^+}}\text{- - - -}Cl^- \right]^{\ddagger} \longrightarrow \quad (1)$$



$$S + CH_3OCH_2Cl \longrightarrow \left[S\text{- - -}\underset{\displaystyle OCH_3}{\underset{|}{CH_2}}\text{- - -}Cl \right]^{\ddagger} \longrightarrow \quad (2)$$

(S = solvent)

The nature of this solvolytic transition state seemed important in developing and testing a theory of substituent effects upon transition-state geometry in chemical reactions.[1,6] The alkyl group (CH_3OCH_2) in this case resembles *n*-propyl in size, but the methoxy group provides a very great possible stabilization of a carbonium ion through charge delocalization (eq 3). The

$$(CH_3OCH_2^+ \longleftrightarrow CH_3\overset{+}{O}{=}CH_2) \qquad (3)$$

stability of methoxymethyl cation is shown by measurements of appearance potentials and generation in sulfuric acid.[7] We present herein our evidence that the solvolysis of methyl chloromethyl ether is SN1 like, resembling *t*-butyl chloride in spite of the steric possibility of a tight, SN2-like transition state. We also show that this result is predicted by the suggested[1] theory of SN reactions.

Results

In Table I we give the rate constants for solvolysis of methyl chloromethyl ether in a series of solvents. The data were used in a Winstein mY correlation,[8] *i.e.*, a least-squares fit was made to eq 4, where k is the rate

$$\log k = m\mathrm{Y} + \log k_0 \qquad (4)$$

constant of the compound in a given solvent; k_0 is the rate constant of the compound's solvolysis in ethanol–water (80:20 v/v) at the same temperature as for k; Y is a measure of the ionizing power of the solvent obtained by defining m as 1.00 for solvolysis of *t*-butyl chloride; and m, the slope of a plot of log k *vs.* Y, is a measure of the sensitivity of the compound in question to the ionizing power of the solvent. The m value from acetone–water and dioxane–water is 1.02 ± 0.03. For acetone–water mixtures alone, m = 1.08 ± 0.03; for dioxane–water, m = 1.01 ± 0.02. As previously noted for other compounds,[9] m differs slightly from one series of solvent mixtures to another (see Figure 1). The value of m is typical of tertiary compounds, since secondary and primary compounds usually have curved plots with average slopes of *ca.* 0.2–0.5. The ratio r (eq 5), in which k_{AcOH} is the rate of solvolysis in glacial acetic acid and $k_{aq\ EtOH}$ is the rate of solvolysis in

$$r = \left(\frac{k_{aq\ EtOH}}{k_{AcOH}}\right)_{Y} \qquad (5)$$

aqueous ethanol of the same Y value as acetic acid, is thought to be a measure of nucleophilic as opposed to electrophilic sensitivity of a substrate relative to *t*-butyl chloride ($r \equiv 1$). Since r is very sensitive to the nature of the leaving group, the value of r calculated from our data, r = 9, should be compared with other chlorides, *e.g.*, α-phenylethyl chloride (5), benzyl chloride (4), and benzhydryl chloride (20).[9] In general, r values for primary compounds are considerably larger; it can be estimated that for a primary chloride r would be *ca.* 30–50. By this measure, methyl chloromethyl ether appears to utilize more nucleophilic assistance than a tertiary compound, yet have the large solvent sensitivity characteristic of a tertiary compound.

Table I. Solvolysis Rate Constants of Methyl Chloromethyl Ether at 24.87°

Solvent	$10^2(k_{obsd}$, $sec^{-1})$	Std dev	Y[a]
2-Propanol	4.791 4.90[b] 5.09[b]	0.204	−2.73
2-Propanol[c]	0.738	0.037	
2-Propanol[d]	2.486	0.313	
Glacial acetic[e] acid–0.2% acetic anhydride	2.569	0.0983	−1.639
Glacial acetic acid–water (98:2)	4.023	0.083	
95.2% acetone–H_2O	0.4198	0.083	
92% acetone–H_2O[f]	2.069	0.615	−2.11
90% acetone–H_2O	3.941	0.179	−1.856
88% acetone–H_2O[f]	7.264	0.395	−1.60
85% acetone–H_2O	19.222	2.950	−1.28
95% dioxane–H_2O[f]	0.3402	0.0290	−3.05
90% dioxane–H_2O	3.507	0.136	−2.03
85% dioxane–H_2O[f]	14.902	1.730	−1.43
80% dioxane–H_2O	30.06	15.00	−0.833
Ethanol	13.305 15.0[b]	1.53	−2.033
98% ethanol–H_2O[g]	23.47	2.51	−1.681
95% ethanol–H_2O[g]	23.4	12.0	−1.287
90% ethanol–H_2O[g]	33.3	23.0	−0.747
Methanol[h]	135		
46.7% methanol–dioxane	8.490	0.375	
43.3% methanol–dioxane	6.609	0.173	
40% methanol–dioxane	5.410	0.091	
33.3% methanol–dioxane	2.746	0.054	
32.36% methanol–dioxane[b]	2.600		
26.7% methanol–dioxane	1.372	0.027	
24.27% methanol–dioxane[b]	0.842		
23.3% methanol–dioxane	1.100	0.088	
20.0% methanol–dioxane	0.493	0.030	
16.7% methanol–dioxane	0.271	0.002	
16.18% methanol–dioxane[b]	0.197		
8.09% methanol–dioxane	0.0112		
t-Butyl alcohol	4.948	0.535	−3.26

[a] Y values obtained from ref 8. [b] See ref 4i. [c] At 0.0°. [d] At 15.1°. [e] Per cent refers to volume % before mixing. [f] Y values extrapolated from a plot of solvent composition *vs.* Y.[8] [g] The rate was too fast to measure using ordinary conductance techniques. These are lower limits of the rate. [h] This value was extrapolated from a plot of log k *vs.* mole fraction of methanol in methanol–dioxane.

The Swain–Moseley–Bown equation[10]

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(6) E. R. Thornton, *J. Am. Chem. Soc.*, **89**, 2915 (1967).

(7) R. W. Taft, R. H. Martin, and F. W. Lampe, *ibid.*, **87**, 2490 (1965); B. G. Ramsay and R. W. Taft, *ibid.*, **88**, 3058 (1966); R. H. Martin, F. W. Lampe, and R. W. Taft, *ibid.*, **88**, 1353 (1966).

(8) E. Grunwald and S. Winstein, *ibid.*, **70**, 846 (1948); S. Winstein and A. H. Fainberg, *ibid.*, **78**, 2770 (1956); for a theoretical discussion of such equations, see J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963, Chapters 6 and 8.

(9) A. H. Fainberg and S. Winstein, *J. Am. Chem. Soc.*, **79**, 1597 1602, 1608 (1957); S. Winstein, A. H. Fainberg, and E. Grunwald, *ibid.*, **79**, 4146 (1957).

(10) C. G. Swain, R. B. Moseley, and D. E. Bown, *ibid.*, **77**, 373 (1955).

$$\log (k/k_0) = c_1 d_1 + c_2 d_2 \qquad (6)$$

where k and k_0 are the same as those in eq 4, but d_1 is supposed to measure solvent nucleophilicity; d_2, solvent electrophilicity; c_1, sensitivity of the substrate to d_1; and c_2, sensitivity of the substrate to d_2, is a useful means of correlating solvolysis reactions. The ratio c_1/c_2 should be a measure of relative sensitivity to nucleophilic and electrophilic assistance. For methyl chloromethyl ether, $c_1 = 1.21 \pm 0.15$, $c_2 = 1.08 \pm 0.13$,[2] giving a ratio of 1.12 ± 0.19. This ratio may be compared with values of 0.84, 0.99, 1.00, and 1.7 for α-phenylethyl, benzhydryl, *t*-butyl, and benzyl chlorides, respectively.

To give further information about transition-state structure, the rates of solvolysis of methyl chloromethyl ether and methyl chloromethyl-d_2 ether in 2-propanol at 0.0° were measured, giving an isotope effect k_H/k_D of 1.24 ± 0.08 per deuterium atom. α-Deuterium isotope effects close to 1.0 are observed in S_N2 reactions, while values of 1.15 per deuterium atom are typical of "unimolecular" bond-breaking reactions of several types.[11] In order to obtain a hopefully more reliable isotope effect, kinetic runs with methyl chloromethyl ether and methyl chloromethyl-d_2 ether were carried out alternately in rapid succession; the mean rate constants so obtained were 7.870 and 5.124×10^{-3} sec^{-1}, respectively, in 2-propanol at 0.0°. In comparison with Table I, the former is several per cent higher, but further experiments were not carried out, because we feel the result is clear and because the deuterated ether is very expensive to prepare.

The solvent isotope effect was measured in acetone–H_2O (95.2:4.8) *vs.* acetone–D_2O (95.2:4.8) at 25°, giving rate constants of 4.198 and 4.505×10^{-2} sec^{-1}, respectively, and $k_{H_2O}/k_{D_2O} = 0.932 \pm 0.05$. This inverse isotope effect is unusual, but is very close to 1.0. Though such isotope effects in pure H_2O *vs.* D_2O are usually *ca.* 1.2–1.4 for hydrolysis of akyl halides,[12] a value of only 1.05 at 20.1° has been reported for solvolysis of *t*-butyl chloride in dioxane–H_2O (60:40) *vs.* dioxane–D_2O (60:40) (1.35 in the pure waters).[13]

The solvolysis of methyl chloromethyl ether has unusually low enthalpy of activation, $\Delta H_0^{\ddagger}$, and entropy of activation, $\Delta S_0^{\ddagger}$, values of $\Delta H_0^{\ddagger}$ from 8.6 to 13.9 kcal mole^{-1} and of $\Delta S_0^{\ddagger}$ from −43.7 to −15.6 cal mole^{-1} deg^{-1} having been reported in various solvents.[4i] Our data in 2-propanol at 0, 15.1, and 25° give $\Delta H_0^{\ddagger} = 10.7 \pm 0.6$, $\Delta S_0^{\ddagger} = -28.8 \pm 1.6$ (lit.[4i] 13.8 and −18.2, respectively). Since $\Delta H_0^{\ddagger}$ for solvolysis of alkyl chlorides is typically *ca.* 20 to 25 kcal mole^{-1}, and $\Delta S_0^{\ddagger}$, typically *ca.* −4 to −12 cal mole^{-1} deg^{-1}, it is obvious that there is some very substantial difference between the activation processes involved. Even though methyl chloromethyl ether is similar to *t*-butyl chloride in many aspects of its solvolysis reactions, these activation parameters differ widely for the two substrates. Tentatively, we conclude that the difference is not directly associated with the S_N reaction site, but rather with double-bond character in the incipient cation of the methyl chloromethyl ether transition state (eq 3). Double-bond character could substantially lower the energy (and concomitantly the enthalpy) of activation, while also restricting rotation of the CH_3O group with respect to the CH_2 group, producing a substantial reduction in entropy of activation; additional reduction in entropy of activation might arise from solvation of the positive oxygen atom of the transition state.

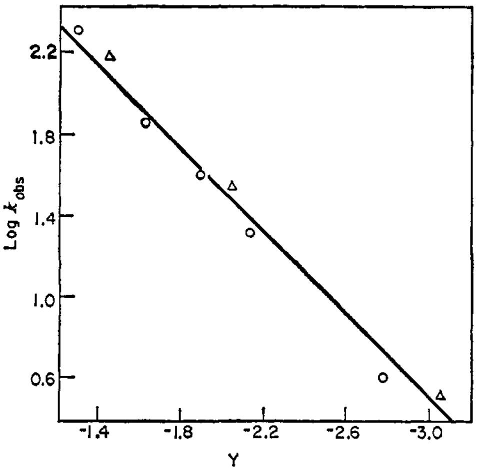

Figure 1. Plot of log k_{obsd} *vs.* Y for solvolysis of methyl chloromethyl ether at 24.87° (this work) in dioxane–water, Δ; and acetone–water, O. Line is least-squares line for all points; slope $m = 1.02 \pm 0.03$.

Discussion

The conclusion of the previous section, that the solvolysis transition state for methyl chloromethyl ether is very much like that of *t*-butyl chloride and not like that of, say, *n*-propyl chloride, is in accord with predictions for solvolytic mechanisms[1] based on a theory of substituent effects upon transition-state geometry.[6] It was suggested[1] that the experimental evidence on S_N reactions is explained by assuming that S_N2 and S_N1 reactions differ only in the tightness of their transition states (with respect to both bond making and bond breaking), the tighter transition states being more selective among nucleophiles and therefore capable of undergoing S_N2 reactions. Steric and electronic effects in the R group of an alkyl halide RX would have very little effect on reactant-like:product-like character, *i.e.*, ratio of bond making to bond breaking, but would have a "perpendicular" effect: if substitution in R makes stretching of the bonds to nucleophile and leaving group easier, these bonds will both be longer in the transition state. Though methyl chloromethyl ether could easily allow strong nucleophilic participation without steric interference, the electronic effect, associated with stretching the two bonds, of partial CO double bond formation (eq 3) should make stretching of these bonds much easier than in the case of a primary alkyl chloride. Therefore, both bonds are expected to be a good deal longer for methyl chloromethyl ether than for the corresponding alkyl chloride (which presumably would give a tight, S_N2-like transition state), *i.e.*, the former is expected to have a transition state with a great deal of carbonium ion character.

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(11) J. A. Llewellyn, R. E. Robertson, and J. M. W. Scott, *Can. J. Chem.*, **38**, 222 (1960); A. Streitwieser, Jr., R. H. Jagow, R. C. Fahey, and S. Suzuki, *J. Am. Chem. Soc.*, **80**, 2326 (1958); A. A. Zavitsas and S. Seltzer, *ibid.*, **86**, 3836 (1964); S. Seltzer, *ibid.*, **83**, 2625 (1961).

(12) P. M. Laughton and R. E. Robertson, *Can. J. Chem.*, **34**, 1714 (1956); R. E. Robertson and P. M. Laughton, *ibid.*, **35**, 1319 (1957); **37**, 1491 (1959).

(13) W. G. Craig, L. Hakka, P. M. Laughton, and R. E. Robertson, *ibid.*, **41**, 2118 (1963).

The suggested theory would predict that, in the absence of strong stabilization of the nucleophile and leaving group by solvation, methyl chloromethyl ether would form a tight, SN2 transition state, whereas this process would be sterically unfeasible for *t*-butyl chloride. It would be of great interest to explore the transition states for SN2 reactions of methyl chloromethyl ether to see if they really are tight rather than carbonium ion like, *i.e.*, whether the above prediction is the correct explanation of the compound's great reactivity in both SN1 and SN2 processes.[4] Acylmethyl halides, very reactive under SN2 conditions but relatively unreactive under SN1 conditions, are predicted to have looser transition states resulting from the delocalization effect but tighter transition states resulting from the inductive effect. Apparently, the inductive effect is more important, requiring a relatively tight transition state, since tight geometry would be expected to produce the observed reactivities.

Experimental Section

Boiling points are uncorrected. Indexes of refraction were taken on a Bausch and Lomb refractometer. A Wayne-Kerr Universal Bridge B221 was used for all conductance readings.

A 25-amp dc power supply was used with a Whirlpool thermoelectric immersion cooler for cooling, and a 150-w infrared lamp was used for intermittent heating, in the constant temperature bath. A mercury contact thermoregulator was used with an Aminco supersensitive relay for temperature control. Constant temperature was maintained in a vigorously stirred oil bath at 24.87 ± 0.01° and then at 15.1 ± 0.1°. The temperature was checked against a Beckmann thermometer standardized with NBS thermometer Princo 558370. Studies at 0.0° used a distilled water-ice bath.

Conductance cells[2] were constructed with shiny platinum electrodes and with space for a glass-enclosed magnetic stirring bar. Test runs showed no dependence of rate constant on the type of cell used.

The cells were normally rinsed with distilled water, then acetone, dried by blowing nitrogen through them, and stored in a desiccator. Before each run, they were always first rinsed twice with small amounts of the solvent to be used.

A magnetic stirrer, immersible in the oil bath, was used to stir each run at least 0.08 min; stirring for longer times or for the whole course of the reaction did not affect rate constants.

At the beginning of each run, methyl chloromethyl ether was distilled from the main bulb on the vacuum line to a small 0.5-ml capacity bulb cooled with Dry Ice-acetone. After the distillate had reached room temperature, 0.05 to 0.10 ml was withdrawn with a syringe and immediately injected into the stirred, equilibrated solvent in the conductance cell. The timer was started upon injection, and the cell was stoppered and sealed with vacuum grease. In the case of slow runs, paraffin wax was also painted over the connection. The cleaned syringe was stored in a 200° oven and cooled by blowing nitrogen through it before each run.

For fast runs with a half-life of 1 to 10 min the conductance readings were anticipated and preset.

To check internal consistency and possible salt effects, additional methyl chloromethyl ether was injected at the end of the first runs and the kinetics was studied. As many as four injections were made this way in any one solvent and all showed no discernible salt effects. The rate constants always agreed to within the experimental error of the first run.

Dioxane. Dioxane (Eastman) was purified by treatment with hydrochloric acid and potassium hydroxide, then refluxed over sodium in the method described by Fieser.[14] It was fractionated through a 60-cm silvered column packed with 30-mm glass helices, bp 100.5°, n^{25}D 1.430 (lit.[14] bp 101.3°).

Methanol. Absolute methanol was dried further by refluxing over magnesium using the same method employed by Winstein and Fainberg.[8] It was then fractionated through a 30-cm glass column packed with 6-mm i.d. glass helices, bp 64.5°, n^{25}D 1.330 (lit.[15] bp 64.65°, n^{25}D 1.33118).

Ethanol. Absolute ethanol was dried and purified using the same methods as for methanol,[8] bp 78.5°, n^{25}D 1.360 (lit.[15] bp 78.5°, n^{20}D 1.3611).

2-Propanol. 2-Propanol was purified by refluxing with sodium and then fractionating through a 30-cm glass column packed with 6-mm i.d. glass helices, immediately before use. Alternately, it was purified by refluxing and distillation from Drierite. No effect of method of purification on rate of solvolysis of methyl chloromethyl ether was noted. All runs at 0 and 15.1° and all runs using methyl chloromethyl-d_2 ether used solvent purified over sodium, bp 82.5°, n^{25}D 1.38 (lit.[15] bp 82.3°, n^{25}D 1.3776).

Water. Laboratory distilled water was refluxed and distilled from potassium permanganate before use.

Deuterium oxide, obtained in 99.5% purity from Liquid Carbonic Company, was stored in a Teflon stopcocked vial in a nitrogen-filled drybox. All solutions were prepared in the drybox and all glassware rinsed with the solution before use.

Acetone. Reagent grade acetone was purified by the method of Winstein and Fainberg,[8] bp 56.8°, n^{25}D 1.359 (lit.[15] bp 58.5°, n^{19}D 1.35886).

Glacial Acetic Acid. The Baker Analyzed reagent was equilibrated with 0.2% acetic anhydride at room temperature under a nitrogen cover and used directly. A fresh bottle was opened for every run. The resulting kinetic data was checked against runs where the acetic anhydride was allowed to equilibrate for 24 hr before use and no significant differences were found between them.

Preparation of Binary Solvent Mixtures. All binary solvent mixtures were prepared by mixing the required volumes of the components at room temperature (25°). Pipets were used for volume measurement and the final volume of the mixture was never less than 150 ml.

Individual solvents were always fractionally distilled immediately before use in each run. A new solvent mixture was always prepared for each run and a minimum of three such runs were performed for each solvent composition. All solvents were equilibrated in the constant temperature bath before each run.

Checks of solvent purity were performed also by doing reference runs with *t*-butyl chloride in the most ionizing solvent of each series. Since *t*-butyl chloride reacted very slowly even in these solvents, the reactions were only carried to about 10% completion, and the infinity points were obtained by sealing the solution in a glass ampoule and heating 1-2 weeks on a steam bath and then taking the final conductance values. The rate constants were obtained graphically; observed conductances were considered directly proportional to the concentration of the hydrogen chloride formed. The rate constants were found to agree within 1.5% of those obtained by Winstein and Fainberg.[8]

Preparation of Methyl Chloromethyl Ether.[16] A 40% aqueous formaldehyde solution (122 g, 1.2 moles) was added to absolute methanol (58.3 g, 1.8 moles) in a round-bottomed flask equipped with a dropping funnel, thermometer, and condenser. The mixture was stirred by a magnetic stirring bar and cooled in an ice-water bath. Chlorosulfonic acid (196 g, 1.68 moles) was added dropwise in 4 hr while maintaining the temperature at 10-15°. The yellowish organic layer was separated, fractionated under atmospheric pressure, purified by vacuum-line distillation, and stored in a stopcocked ampoule on the vacuum line, bp 58.5° (lit.[17] bp 58.5°), yield 21 g (25%) of pure product. The nmr spectrum indicated the compound was pure; however, no effect on rate constant was detected using crude *vs.* purified material.

Preparation of Methyl Chloromethyl-d_2 Ether. Formaldehyde-d_2 (99% isotopic purity) in a 30% aqueous solution with 10% methanol as a stabilizer was purchased from Merck Sharpe and Dohme of Canada.

Formaldehyde solution (2.4 ml, 0.01 mole) was added to absolute methanol (1 ml, 0.014 mole) in a 6-in. test tube and stirred with a small Teflon-covered magnetic stirring bar. An ice-water bath was used for cooling. Precooled chlorosulfonic acid (1.5 ml, 0.007 mole) was added dropwise until the organic layer was visible, and large frothy bubbles were observed upon the addition of an extra drop. The organic layer was immediately separated and added to the 2-propanol for a kinetic run. Total time elapsed from synthesis to injection was about 2 min.

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(14) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 1957, pp 284, 285, 287, 307.

(15) "Handbook of Chemistry and Physics," C. D. Hodgman, Ed., 39th ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1958.

(16) A. H. Greer, U. S. Patent 3,086,060 (April 16, 1963).

(17) R. G. Jones and W. J. Orville-Thomas, *J. Chem. Soc.*, 692 (1964).

The undeuterated compound was synthesized and injected in exactly the same manner within the same hour for proper comparison between it and the deuterated ether. Freshly fractionated 2-propanol was used for each run.

Calculation of Rate Constants. The nonlinear least-squares computer program of Lietzke[18] was used to fit the data to the equation

$$y = a_0\{1 - \exp[-k(t + b)]\}$$

where y is the concentration (conductivity), t is the time, and the following three parameters were adjusted by the program to give the best least-squares fit to the equation: k, the rate constant; a_0, the infinity point; and b, the "time error." Use of this program has been discussed by Collins.[19] The assumption of a linear relationship between conductance (as read from the bridge) and HCl concentration was shown to be valid within our experimental error over the concentration range used (*ca.* 10^{-13} *M*) by comparison with the literature[2] and by construction of a calibration line[2] for the very poorly ionizing solvent, dioxane–methanol (83.3:16.7).

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Medium Effects. I. Solvolysis of 5-Hexenyl *p*-Nitrobenzenesulfonate in Acetic Acid–Nonhydroxylic Solvent (20:80) Mixtures[1a,b]

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Abstract: Acetolysis of 5-hexenyl *p*-nitrobenzenesulfonate in the presence of the base urea has been previously shown to lead to open (55%) and cyclic (45%) products. These two sets of products may be considered to be the result of (a) external nucleophilic attack by the solvent, acetic acid, to give open product and (b) internal nucleophilic attack by the olefin to give cyclic products. Products of the solvolysis of 5-hexenyl *p*-nitrobenzenesulfonate in media composed of acetic acid–nonhydroxylic solvent (20:80) and urea were determined. Yields of cyclic materials from the solvolysis of other 5-hexenyl sulfonates in some of these media were also determined. These results are analyzed and discussed with respect to solvent nucleophilicity.

One of the most important and least understood ways to influence a chemical reaction is by solvent variation. Physical organic chemists have paid much attention to the empirical correlation of solvent effects on rates and equilibria through linear free energy relationships.[2,3] Numerous parameters such as Y values and Z values have been developed. All of these parameters with the exception of Swain's equation, eq 1,[4]

$$\log (k/k^0) = c_1d_1 + c_2d_2 \tag{1}$$

measure "solvent polarity" exclusively. Swain's equation when applied to the reaction of nucleophiles with neutral substrates contains nucleophilic and electrophilic terms and the notation given by eq 2 is used. However,

$$\log (k/k^0) = sn + s'e \tag{2}$$

when applied to solvolysis reactions, Swain points out that these terms may not measure nucleophilic and electrophilic reactivity of the solvent and in order to avoid the implication that it does, he changes the notation to that of eq 1.

Nucleophilicity is concerned with the rate that a given substrate undergoes a certain nucleophilic reaction.[4] Thus if substance A is more nucleophilic than substance B, A will undergo a nucleophilic reaction faster than B will undergo this reaction.

The term "solvent nucleophilicity" is a rather vague term, and its meaning is complicated by the fact that a change of solvent changes the medium. It is therefore impossible to talk about "solvent nucleophilicity" in a given medium as one can do with "anion nucleophilicity." Nevertheless, the term "solvent nucleophilicity" should have some meaning since many of the characteristics of anions, such as basicity and solvation, which affect "anion nucleophilicity" are also present in solvents.

In order to discuss "solvent nucleophilicity," we propose the following definition: "solvent nucleophilicity"

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