Methoxonium Ions in Solvolysis. Neighboring Acetal Participation

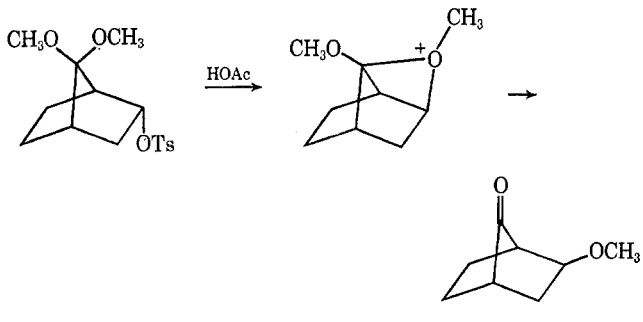
J. R. HAZEN[1]

Department of Chemistry, Vanderbilt University, Nashville, Tennessee 37203

Received September 26, 1969

The dimethoxy-1 alcohols **1** (n = 2–4) were synthesized and the corresponding tosylates **2** (n = 2–4) were solvolyzed in both methanol and trifluoroethanol to examine the possibility of methoxyl participation by the dimethyl acetal functional group. The solvolysis rates were measured and compared with that of n-octyl tosylate as a model compound and with that of 5-methoxy-1-pentyl tosylate, which is known to solvolyze with methoxyl participation. The 4,4- and 5,5-dimethoxy compounds **2** (n = 2 and 3) showed rate enhancement of *ca.* 3900 and 245, respectively, relative to n-octyl tosylate in trifluoroethanol, indicating that acetal methoxyl participation dominates the solvolysis in both cases. Comparison of 5,5-dimethoxy-1-pentyl tosylate and 5-methoxy-1-pentyl tosylate showed that the acetal methoxyl group is a much poorer intramolecular nucleophile than the simple methyl ether group in both solvents. Product studies of the trifluoroethanolysis of 4,4-dimethoxy-1-butyl and 5,5-dimethoxy-1-pentyl tosylate confirmed the neighboring-group phenomenon in both cases in that the major products were the mixed acetals **8** and **9** resulting from 1,4 and 1,5 migration, respectively, of an acetal methoxyl group. The kinetic features of the trifluoroethanolysis reactions of 5-methoxy-1-pentyl tosylate and 5,5-dimethoxy-1-pentyl tosylate are discussed in terms of the ion-pair chemistry of the solvolysis intermediates.

Although a large number of functional groups have been examined for their ability to serve as intramolecular nucleophiles in solvolytic displacement reactions,[2] conspicuous by its absence is a systematic study of the neighboring acetal or ketal group. Since participation by the methyl ether oxygen has been exhaustively studied,[3,4] an examination of the dimethyl acetal or ketal group participation would allow an instructive comparison of the relative nucleophilicities of the methoxy group in the two functional groups. To date only one example of neighboring ketal participation has been reported. Thus backside MeO-4[5] participation has been invoked in the acetolysis of *endo*-7,7-dimethoxy-2-norbornyl tosylate to account for the migration of the methoxyl group to the 2-*exo* position and concomitant ketone formation. The corresponding *exo*



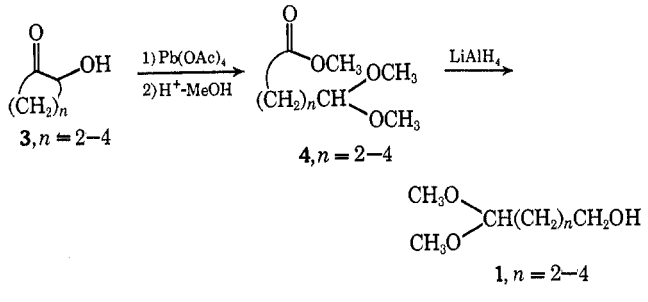
tosylate, in which methoxyl participation cannot occur, gives only unrearranged substitution products (the corresponding *exo* and *endo* acetates), the ketal function remaining intact.[6] Several examples of acetal participation have previously been noted in the carbohydrate field.[7]

It was therefore of interest to examine a series of homologous dimethoxy tosylates for evidence for the generality of acetal participation, for elucidation of mechanism, and for a direct comparison with the structurally related methoxyalkyl tosylates studied previously.

Results

Syntheses.—The required dimethoxy-1 alcohols **1** (n = 2–4) were prepared from the appropriate cyclic acyloins essentially by the method of Saunders and Hurd,[8] as outlined in Scheme I. The acyloins were

SCHEME I



treated first with lead tetraacetate in methanol and then with methanolic sulfuric acid. The resulting acetal esters **4** were then reduced with lithium aluminum hydride to yield the dimethoxy alcohols **1**.

The precursor acyloins were synthesized by known methods. Adipoin (**3**, n = 4) was readily prepared by the hydrolysis of 2-chlorocyclohexanone, which in turn was synthesized by the chlorination of cyclohexanone.[9] The remaining acyloins (**3**, n = 2, 3) were prepared by the acyloin condensation with diethyl succinate and diethyl glutarate, respectively, employing the recent modification with chlorotrimethylsilane.[10–12] With this modification the acyloins were isolated as the 1,2-bistrimethylsiloxy-1-cyclo alkenes **6**, (see Scheme II). The acyloins **3** (n = 2, 3) were then generated simply by

(1) Address correspondence to Division of Natural Science, University of California, Santa Cruz, Calif. 95060.

(2) B. Capon, *Quart. Rev.* (London), **18**, 45 (1964).

(3) S. Winstein, E. Allred, R. Heck, and R. Glick, *Tetrahedron*, **3**, 1 (1958).

(4) (a) E. Allred and S. Winstein, *J. Amer. Chem. Soc.*, **89**, 3991 (1967); (b) E. Allred and S. Winstein, *ibid.*, **89**, 3998 (1967); (c) E. Allred and S. Winstein, *ibid.*, **89**, 4008 (1967); (d) E. Allred and S. Winstein, *ibid.*, **89**, 4012 (1967).

(5) This terminology is explained in ref 3.

(6) P. G. Gassman and J. L. Marshall, *Tetrahedron Lett.*, 2429, 2433 (1968).

(7) See *e.g.*, (a) R. U. Lemieux and B. Fraser-Reid, *Can. J. Chem.*, **42**, 539 (1964); (b) N. A. Hughes and P. R. H. Speakman, *J. Chem. Soc., C*, 1182 (1967); (c) C. L. Stevens, R. P. Glinski, K. G. Taylor, P. Blumbergs, and F. Sirokman, *J. Amer. Chem. Soc.*, **88**, 2073 (1966); (d) J. G. Buchanan, A. R. Edgar, and D. G. Large, *Chem. Commun.*, 558 (1969).

(8) C. L. Hurd and W. H. Saunders, Jr., *J. Amer. Chem. Soc.*, **74**, 5324 (1952).

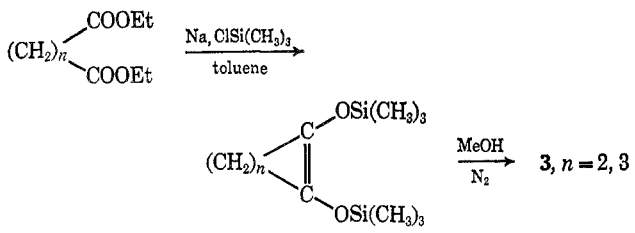
(9) M. S. Newman, M. D. Farbman, and H. Hipsher, "Organic Syntheses," Coll. Vol. III, John Wiley & Sons, Inc., New York, N. Y., 1955, p 188.

(10) U. Schrapler and K. Ruhlmann, *Chem. Ber.*, **97**, 1383 (1964).

(11) J. J. Bloomfield, *Tetrahedron Lett.*, 587 (1968).

(12) G. E. Gream and S. Worthley, *ibid.*, 3319 (1968).

SCHEME II



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stirring in absolute methanol under a nitrogen atmosphere.

The tosylates 2 were prepared from the alcohols by the sodium hydride method.[13] None of the tosylates was crystalline; since they proved to be moderately unstable even in the cold, they were prepared as needed.

Kinetic and Product Studies.—The tosylates were solvolyzed in absolute methanol and in buffered trifluoroethanol, and their rate constants were determined titrimetrically. Methanol was a suitable choice, since its use obviated the problem of acetal exchange and the need to neutralize the acid liberated in the solvolysis. Trifluoroethanol, being considerably more ionizing and less nucleophilic than methanol,[14] is an ideal nonacidic solvent, since it allows neighboring-group participation to predominate over direct solvent displacement. The first-order rate data are summarized in Tables I and II.

TABLE I
SUMMARY OF KINETIC DATA IN METHANOL AT 59.86 ± 0.05°

Compd	10^5k, sec^{-1}	Rel rate	Fk_Δ,[a] %
$CH_3(CH_2)_6CH_2OTs$	0.765	1.0	...
$(CH_3O)_2CH(CH_2)_2CH_2OTs$	5.73 ± 0.05	7.49	87
$(CH_3O)_2CH(CH_2)_3CH_2OTs$	1.49 ± 0.02	1.95	49
$(CH_3O)_2CH(CH_2)_4CH_2OTs$	~1.1	~1.4	~30
$CH_3OCH_2(CH_2)_3CH_2OTs$	2.08 ± 0.02	2.72	63

[a] Calculated from the kinetic data.

The application of the kinetic rate-enhancement criterion for neighboring-group participation requires a means of estimating the expected value of the rate constant in the absence of participation, the observed rate constant (k_{obsd}) being the sum of the assisted (k_Δ) and unassisted (k_s) rate constants.

$$k_{obsd} = Fk_\Delta + k_s$$

A measure of the unassisted portion of the solvolysis rates of the dimethoxy-1-alkyl tosylates was taken to be the rate of solvolysis of *n*-octyl tosylate.[15] No attempt was made to assess the extent of internal return (1 − *F*) to covalent starting material.

The solvolysis of 5-methoxy-1-pentyl tosylate, which is dominated by methoxyl participation,[4d] was also examined to provide a comparison with the corresponding 5,5-dimethoxy-1-pentyl system (Tables I and II).

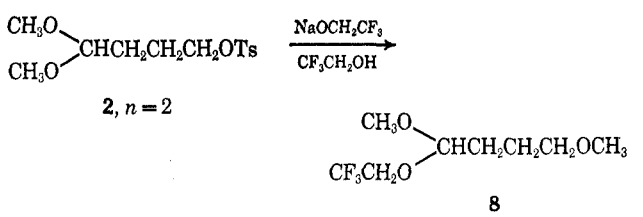
(13) J. K. Kochi and G. S. Hammond, *J. Amer. Chem. Soc.*, **75**, 3443 (1953).

(14) F. L. Scott, *Chem. Ind.* (London), 224 (1959); V. J. Shiner, Jr., W. Dowd, R. D. Fisher, S. R. Hartshorn, M. A. Kessick, L. Milakofsky, and M. W. Rapp, *J. Amer. Chem. Soc.*, **91**, 4838 (1969).

(15) The actual choice of which primary alkyl tosylate (*n*-butyl, *n*-pentyl, or *n*-hexyl) to use as a model compound is relatively unimportant, since they all solvolyze at very nearly the same rate (in ethanol and in water); see P. M. Laughton and R. E. Robertson, *Can. J. Chem.*, **33**, 1207 (1955).

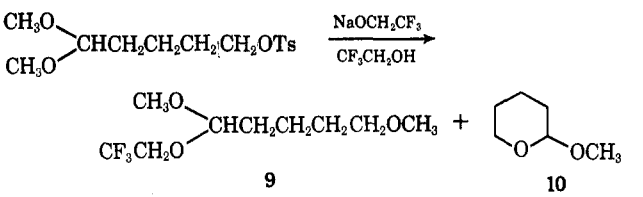
The 5-methoxy-1-pentyl derivative solvolyzes with first-order behavior in methanol, but in trifluoroethanol exhibits behavior typical of the internal return rearrangement to methyl tosylate (and tetrahydropyran) *via* the cyclic methoxonium ion observed previously for this system in acetic acid.[4d] The rearrangement is kinetically detectable as a downward-drifting rate constant and a low acid infinity titer in unbuffered solvent, and as an upward-drifting rate constant (and a theoretical infinity titer) in sodium trifluoroethoxide buffered trifluoroethanol.[16] However, similar rearrangement to methyl tosylate does not accompany the trifluoroethanolysis of 5,5-dimethoxy-1-pentyl tosylate, since there was observed no drift in the first-order rate constant through at least 80% reaction.

The products from the trifluoroethanolysis of 4,4-dimethoxy-1-butyl (**2**, $n = 2$) and 5,5-dimethoxy-1-pentyl (**2**, $n = 3$) tosylates were examined to substantiate the kinetic evidence for the neighboring-group phenomenon. From the trifluoroethanolysis of **2** ($n = 2$) was detected a single major product, formed in 70% yield, as estimated by gas chromatography using internal standards. This material was isolated by distillation, purified by preparative gas chromatography, and identified as the mixed acetal 1,4-dimethoxy-1-trifluoroethoxybutane (**8**) on the basis of elemental analysis and infrared, nmr, and mass spectra. In particular, the nmr spectrum showed two singlets corresponding to the nonequivalent methoxyl groups. Also the base-peak ion in the mass spectrum occurred at *m/e* 143 and was assigned structure a, a typical fragment ion in the mass spectra of acetals.[17]



a, *m/e* 143

Similarly, the trifluoroethanolysis of 5,5-dimethoxy-1-pentyl tosylate (**2**, $n = 3$) gave 1,5-dimethoxy-1-trifluoroethoxypentane (**9**) in *ca.* 25% yield. The structure assignment was again based on the fact that the material showed two distinctly nonequivalent methoxyl singlets in the nmr, and had a base-peak ion at *m/e* 143 owing to ion a in its mass spectrum. The



(16) The interesting kinetic features of this system in trifluoroethanol have been reported elsewhere; see J. R. Hazen, *Tetrahedron Lett.*, 1897 (1969).

(17) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1964, pp 52–54.

TABLE II

SUMMARY OF KINETIC DATA IN TRIFLUOROETHANOL AT 69.90 ± 0.05°

Compd	CF_3CH_2ONa, M	k, sec^{-1}	Rel rate	Fk_Δ,[a] %
$CH_3(CH_2)_6CH_2OTs$	...	3×10^{-7}	1.0	...
$(CH_3O)_2CH(CH_2)_2CH_2OTs$	0.0505	$1.18 \pm 0.02 \times 10^{-3}$	3.9×10^3	100
$(CH_3O)_2CH(CH_2)_3CH_2OTs$	0.0560	$7.35 \pm 0.10 \times 10^{-5}$	2.45×10^2	>99
$CH_3OCH_2(CH_2)_3CH_2OTs$	0.0560	$2.04 \pm 0.02 \times 10^{-4}$	6.80×10^2	>99
	...	$1.59 \pm 0.03 \times 10^{-4}$	5.30×10^2	

[a] Calculated from the kinetic data.

major product in the trifluoroethanolysis of **2** ($n = 3$) is 2-methoxytetrahydropyran (**10**), identified by comparison of its gas chromatography retention time with that of an authentic sample.

Discussion

There are several *a priori* considerations with regard to a comparison of MeO-*n* participation in the dimethoxy and simple methoxy compounds. First, a statistical factor of two must be recognized, since either of the two methoxyl groups of the acetal function can serve as the neighboring group. Second, it is well known that alkyl substituents on the aliphatic chain serve to enhance cyclization reactions. For example, 5-methoxy-1-hexyl brosylate solvolyzes about six times more rapidly than 5-methoxy-1-pentyl brosylate in acetic acid.[4a] It is reasonable to assume that the methoxyl group has a steric bulk which is intermediate between that of methyl and an ethyl group. The presence of the second methoxyl group may therefore be estimated to increase the rate of a ring-closure reaction by a factor of roughly 10–15.[2,4a,18] On the basis of this factor and the statistical factor, it might be estimated that the dimethoxy compounds would solvolyze some 20–30 times faster than the methoxyl compounds. A third factor, however, should counterbalance these first two. The electron-withdrawing inductive effect of each methoxyl group on the other in the dimethoxy compounds should significantly reduce the ability of the methoxyl oxygen atoms to donate their nonbonded electrons to a neighboring electron-deficient carbon atom in the solvolysis transition state. That is, the methoxyl groups of the acetal are expected to be much less nucleophilic in intramolecular displacements than the methyl ether group. The relative importance of these factors will become apparent from the discussion below.

It is clear from the data in Table I that the rate enhancement owing to acetal participation is quite modest in methanol, being only a factor of 7.5 in the case of 4,4-dimethoxy-1-butyl tosylate.[19] However, the magnitude of the neighboring-group effect in the series of tosylates is in the expected order in that **2** ($n = 2$) is more reactive than **2** ($n = 3$), which in turn is more reactive than **2** ($n = 4$). This observation is in accordance with the expectation that formation of the five-membered-ring transition state is the most favorable and formation of the seven-membered-ring transition state is the least favorable.[2,3] It is significant to note that 5-methoxy-1-pentyl tosylate solvolyzes 40% faster than 5,5-dimethoxy-1-pentyl tosylate, indicating that acetal methoxyl participation is less favorable than simple methoxyl participation. This observation reflects the overriding importance of the inductive or electronic factor on the nucleophilicity of the acetal methoxyl groups.

The fact that the k_s route represents a large portion of the solvolysis pathway in methanol is undoubtedly due to its relatively high nucleophilicity. An ionizing but weakly nucleophilic solvent would make any participation effects more apparent, since k_s for primary tosylates is reduced in a less nucleophilic solvent. Since the usual acidic solvents are unsuitable, the tosylates were solvolyzed in trifluoroethanol in the presence of sodium trifluoroethoxide as a buffer to prevent acetal exchange.

The large rate accelerations for the tosylates **2** in the cases where $n = 2$ and 3 relative to *n*-octyl tosylate (Table II) clearly indicate that methoxyl-assisted ionization completely dominates the solvolysis in both cases. Furthermore, both compounds solvolyze with good first-order behavior, indicating the absence of any SN2 displacement by sodium trifluoroethoxide. On the other hand, both *n*-octyl tosylate and 6,6-dimethoxy-1-hexyl tosylate (**2**, $n = 4$) undergo predominant bimolecular displacement by the alkoxide and do not follow first-order kinetics. The solvolysis rate of *n*-octyl tosylate was therefore determined in unbuffered solvent. The observation of a substantial contribution from the second-order displacement by alkoxide with 6,6-dimethoxy-1-hexyl tosylate in competition with the methoxyl-assisted displacement is consistent with the long-recognized fact that participation *via* seven-membered ring intermediates is a relatively minor pathway.[2,3] It is also pertinent to note that the solvolysis rate of 4,4-dimethoxy-1-butyl tosylate is 16 times faster than that of 5,5-dimethoxy-1-pentyl tosylate (Table II). This result compares favorably with the observation that the corresponding 4-methoxy-1-butyl system solvolyzes 14 times more rapidly than the 5-methoxy-1-pentyl system at 75° in formic acid, in which solvent both compounds solvolyze exclusively *via* methoxyl participation.[3]

It should again be noted that the apparent neighboring-group rate accelerations of 3900 for **2** ($n = 2$)

(18) See, for example, T. C. Bruice and W. C. Bradbury, *J. Amer. Chem. Soc.*, **87**, 4846 (1965); D. S. Bailey, "The Gem-Dialkyl Effect," Organic Chemistry Seminar, University of Rochester, Rochester, N. Y., 1967, pp 60–68.

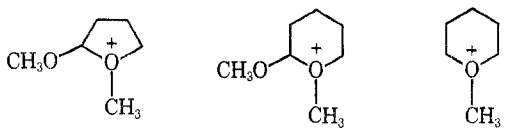
(19) Corrections for the inductive effect of the $(CH_3O)_2CH$ group have not been applied to any of the data. The inductive effect, though small, is not negligible. The σ^* value for $(CH_3O)_2CH$ has recently been determined to be +1.14,[20] about twice that of the CH_3OCH_2 substituent. Using the reaction constant $\rho^* = 1.03$ (the value for ethanol[3]) and σ^* $[CH_3(CH_2)_nCH_2] = -0.10$,[3] the inductive rate *retardation* for the 4,4-dimethoxy compound (**2**, $n = 2$) relative to the unsubstituted compound may be calculated to be a factor of *ca.* 1.80. Thus the actual rate enhancement due to MeO-5 participation would be 7.5 × 1.80 or 13.5. Similarly, the inductive effect in the 5,5-dimethoxy analog will produce a rate retardation factor of *ca.* 1.4, indicating that the true neighboring-group rate acceleration for **2** ($n = 3$) amounts to a factor of 1.95 × 1.4 or 2.8.

The inductive effects in trifluoroethanol are probably even somewhat larger, since the reaction constant ρ^* is probably larger in this more ionizing solvent.

(20) T. Minamida, Y. Ikeda, K. Uneyama, and S. Oae, *Tetrahedron*, **24**, 5293 (1968).

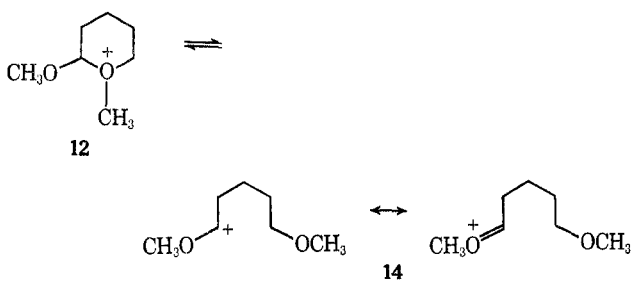
and 245 for 2 (n = 3) (Table II) are approximations, since no corrections have been applied to allow for the differences in the inductive effect in n-octyl tosylate and the substrates of interest.[19] Also no allowance has been made for the fact that the solvolyses of n-octyl tosylate and the dimethoxy tosylates were not conducted under conditions of identical ionic strength, since the latter compounds were solvolyzed in the presence of sodium trifluoroethoxide buffer. However, these effects are relatively small (and tend to counterbalance one another), compared with the magnitude of the rate accelerations, and may be neglected without affecting the validity of the kinetic conclusions.

The domination of the trifluoroethanolyses by methoxyl participation indicates that the initially formed intermediates from 2 (n = 2) and 2 (n = 3) are the methoxonium ions **11** and **12**, respectively.



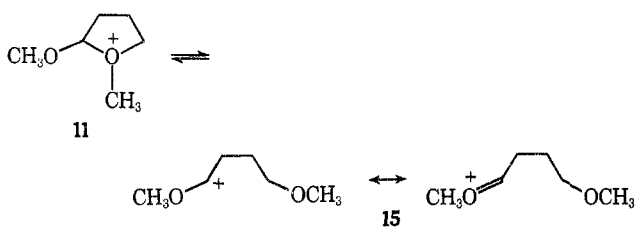
11 **12** **13**

A comparison of the kinetic behavior of 5-methoxy-1-pentyl and 5,5-dimethoxy-1-pentyl systems allows further mechanistic insight. It is again clear that the acetal methoxyl groups are considerably less nucleophilic than the simple methyl ether group, since the dimethoxy tosylate reacts nearly three times more slowly than 5-methoxy-1-pentyl tosylate. Especially interesting is the observation that, while the solvolysis of 5-methoxy-1-pentyl tosylate in buffered trifluoroethanol is accompanied by internal return rearrangement to methyl tosylate (*via* the methoxonium ion **13**),[16] no such rearrangement occurs from methoxonium ion **12**. The absence of O-methyl cleavage by the tosylate anion in the solvolysis of the 5,5-dimethoxy system may reasonably be interpreted as being indicative of a rapid equilibrium between the cylic oxonium ion **12** and the highly resonance-stabilized α-methoxycarbonium ion **14**. Since such an equilibrium would involve a rapid



12 **14**

change in the geometries of the intermediates as well as a rapid shifting of the site of the electron deficiency, it seems unlikely that the tosylate anion would often



11 **15**

be in a proper position to collapse with either of the O-methyl groups. Hence, solvent capture of the intermediates **12** and **14** is the favored process, with little or no methyl tosylate formation. The cyclic ion **11** is similarly postulated to give rise to the α-methoxycarbonium ion **15** prior to solvent capture.

The kinetic evidence for the neighboring-group effect was substantiated by the product study. The formation of the rearranged, mixed acetals **8** and **9**, respectively, from 2 (n = 2) and 2 (n = 3) requires the migration of a methoxyl group to the carbon initially bearing the leaving group in both cases. No unrearranged dimethyl acetal product was detected in the solvolysis of either substrate.[21] The formation of the mixed acetals is also consistent with (but does not prove) the intermediacy of the α-methoxycarbonium ions **14** and **15**.

While it is obvious that methoxyl participation in the acetals is important, it is less so than in the simple methyl ether analogs. The lesser reactivity of the dimethoxy compounds relative to the methoxy compounds clearly indicates that the most important factor in determining their relative reactivities is the electronic factor. Thus although the statistical and steric factors should make the dimethoxy compounds roughly 20–30 times more reactive than the corresponding methoxy compounds (*vide supra*), the electron-withdrawing inductive effect exerted by each methoxyl group on the other in the acetals more than counterbalances these factors. The fact that 5-methoxy-1-pentyl tosylate is nearly three times *more* reactive than 5,5-dimethoxy-1-pentyl tosylate indicates that the intrinsic nucleophilicity of the acetal methoxyl group is roughly 3 × 20–30 or *ca.* 10^2 less than that of the simple methoxyl group. It is interesting that this factor is also about the same as the magnitude of the inductive effect found for the generation of positive charge on a *carbon* atom with a β-methoxyl group (as in the solvolysis of 2-methoxycyclohexyl brosylate).[22]

Experimental Section

1,2-Bistrimethylsiloxy-1-cyclobutane (**6**, n = 2).—In a 500-ml, three-necked flask equipped with mechanical stirrer, condenser and drying tube, and a dropping funnel with a nitrogen inlet tube was placed 180 ml of dry toluene and 14.0 g (0.61 mol) of freshly cut cubes of sodium. The mixture was heated to reflux under nitrogen with vigorous stirring to disperse the globules of melted sodium. Then a solution of 26.2 g (0.15 mol) of diethyl succinate and 70 g (0.644 mol) of chlorotrimethylsilane plus 25 ml of dry toluene was added dropwise to the refluxing, vigorously stirred mixture under nitrogen at such a rate as to maintain refluxing. After the addition of the diester solution (*ca.* 1.5 hr), refluxing the stirring were continued for an additional 19 hr. The mixture was cooled and filtered, and the filtered salts were washed with ether. The solvent was removed from the filtrate under reduced pressure and the residue was distilled to give 23 g (67% yield) of product, bp 103–107° (25–30 mm), n^{28}D 1.4292. The nmr spectrum (neat) showed a singlet at τ 7.90 (4 H, methylene protons) and a singlet at τ 9.82 (18 H, trimethylsiloxy protons).

4,4-Dimethoxy-1-butanol (**1**, n = 2).—To 90 ml of absolute methanol was added dropwise 22.0 g (0.096 mol) of 1,2-bistrimethylsiloxy-1-cyclobutene under a nitrogen atmosphere.[11] After the addition was complete, the solution was stirred for an

(21) The possibility of acetal participation suggested by J. P. Ward [*Tetrahedron Lett.*, 3905 (1965)] for 4,4-diethoxy-1-butyl chloride in potassium hydroxide–ethylene glycol was not confirmed by the reported product study, since only the unrearranged product 4,4-diethoxy-1-butanol was formed.

(22) S. Winstein, E. Grunwald, and L. L. Ingraham, *J. Amer. Chem. Soc.*, **70**, 821 (1948).

additional 0.5 hr, followed by the portionwise addition of *ca.* 50 g of lead tetraacetate with occasional external cooling (ice bath).[8] About 0.5 hr after the lead tetraacetate addition was complete, a solution of 18 g of concentrated sulfuric acid in 45 ml of absolute methanol was added dropwise with vigorous stirring and, when the mixture became thick, with manual agitation. The reaction mass was allowed to stand for 3 days, after which it was filtered. The filtrate was poured into 150 ml of 30% potassium carbonate solution, and the resulting mixture was immediately extracted with a total of 400 ml of ether. The combined extracts were washed with 75 ml of water, dried over sodium sulfate and then 3A molecular sieves, and distilled. The product, methyl 4,4-dimethoxybutyrate (**4**, $n = 2$), was collected at 84° (12 mm), $n^{25.5}$D 1.4140–1.4144 [lit.[23] bp 85.5–86° (13 mm), n^{20}D 1.4171]. The infrared spectrum (liquid film) showed a strong carbonyl absorption at 1735 cm^{-1}. The yield was 6.6 g (42%). The acetal ester was then reduced with lithium aluminum hydride in ether to yield, after base hydrolysis, a 61% yield of 4,4-dimethoxy-1-butanol (**1**, $n = 2$), bp 97.5–99.5° (12 mm), n^{25}D 1.4246. The infrared spectrum (liquid film) showed a hydroxyl at 3450 cm^{-1}, but no carbonyl absorption.

Anal. Calcd for $C_6H_{14}O_3$: C, 53.71; H, 10.52. Found: C, 53.70; H, 10.67.

4,4-Dimethoxy-1-butyl Tosylate (**2**, $n = 2$).[13]—4,4-Dimethoxy-1-butanol (4.75 g, 0.0355 mol) was stirred and refluxed under nitrogen with an equivalent amount of oil-free sodium hydride in ether for 18 hr. Then, after cooling, 6.6 g (0.0346 mol) of freshly recrystallized tosyl chloride in ether was added over 0.5 hr. After 9.5 hr in the cold the mixture was centrifuged (3000 rpm, 20 min) and the supernatant solution was filtered through a sintered glass disk. The solvent was removed under reduced pressure (the final traces with a vacuum pump) to give 6.8 g (68%) of a clear, pale yellow oil, n^{25}D 1.4911. All attempts to induce crystallization failed. However, the infrared spectrum showed no hydroxyl absorption, and the material contained no tosyl chloride (as determined by treatment with 0.0516 *M* sodium trifluoroethoxide in trifluoroethanol and back titration with perchloric acid in 95% ethanol). The tosylate showed good first-order kinetics and had a 96% infinity titer in both methanol and trifluoroethanol.

Anal. Calcd for $C_{13}H_{20}O_5S$: C, 54.14; H, 6.99. Found: C, 54.14; H, 7.11.

1,2-Bistrimethylsiloxy-1-cyclopentene (**6**, $n = 3$).—This compound was prepared as described above for bistrimethylsiloxycyclobutene, bp 65° (2 mm) and 88° (9–10 mm), n^{25}D 1.4390 [lit.[10] bp 93–94° (10–12 mm), n^{20}D 1.4426].

Methyl 5,5-Dimethoxyvalerate (**4**, $n = 3$).—The above-prepared bistrimethylsiloxycyclopentene (34.6 g) was added dropwise over 0.5 hr to 160 ml of stirred absolute methanol. After 4 hr the reaction solution was treated with *ca.* 80 g of lead tetraacetate, portionwise over a 0.5-hr period. After an additional 1.5 hr, 29.5 g of concentrated sulfuric acid in 75 ml of methanol was added dropwise with cooling and vigorous agitation. After 2 days the reaction mixture was filtered, poured into 30% potassium carbonate solution (from 150 g in 350 ml of water), extracted with 800 ml of ether, washed with a total of 150 ml of water, and dried over sodium sulfate and molecular sieves. The solvent was then removed and the product was distilled to give 14.5 g (58%) of pure material, bp 70–72° (2.3 mm), n^{26}D 1.4206.

Anal. Calcd for $C_8H_{16}O_4$: C, 54.53; H, 9.15. Found: C, 54.36; H, 9.06.

5,5-Dimethoxy-1-pentanol (**1**, $n = 3$).—A solution of 14.5 g of the acetal ester (**4**, $n = 3$) in 20 ml of ether was added cautiously, dropwise, to a stirred suspension of 2.2 g of lithium aluminum hydride in 100 ml of ether over the course of 45 min. After several hours the mixture was hydrolyzed with 2 ml of water, 2 ml of 15% aqueous sodium hydroxide, and 6 ml of water. After filtration and drying over 3A molecular sieves, the solvent was removed and the product was distilled to give 7.9 g (66%) of the dimethoxy alcohol, bp 67–69° (0.2 mm), $n^{25.5}$D 1.4315 [lit.[24] bp 57–63° (0.07 mm), n^{20}D 1.4344].

Anal. Calcd for $C_6H_{14}O_3$: C, 56.73; H, 10.88. Found: C, 57.07; H, 10.88.

5,5-Dimethoxy-1-pentyl Tosylate (**2**, $n = 3$).—The tosylate was prepared from the alcohol (**1**, $n = 3$) by the sodium hydride method as described above. Several preparations of varying reaction time, temperature, etc., all gave the tosylate as a pale yellow oil containing 8.5–10.4% by weight of tosyl chloride as estimated by quantitatively diluting the impure ester in standardized sodium trifluoroethoxide in trifluoroethanol and back-titrating the excess trifluoroethoxide with standardized perchloric acid in ethanol to the bromphenol blue end point. Control experiments showed that this assay method is accurate. The refractive indices of the various preparations varied from n^{25}D 1.4979 to n^{25}D 1.5008. After correction for the tosyl chloride impurity, the tosylate exhibited good first-order kinetic behavior and a 99% infinity titer.

6,6-Dimethoxy-1-hexanol (**1**, $n = 4$).—This alcohol was prepared as described by Saunders and Hurd, bp 65–67° (0.2 mm), n^{25}D 1.4336 [lit.[8] bp 84° (1.0 mm), n^{20}D 1.4358]. The tosylate (**2**, $n = 4$) was prepared as described above and was isolated as an impure, pale yellow oil containing tosyl chloride. Repeated sodium bicarbonate washings of an ethereal solution of the ester failed to remove the tosyl chloride completely. A sample of material, n^{25}D 1.5002, contained 8.0% tosyl chloride. The presence of tosyl chloride precluded an accurate determination in Table I.

5-Methoxy-1-pentyl Tosylate (**7**).—The tosylate was prepared from 5-methoxy-1-pentanol by the usual low-temperature method and was isolated as a clear, colorless oil, $n^{27.5}$D 1.4990. This material solvolyzed with well-defined kinetics and liberated the theoretical amount of *p*-toluenesulfonic acid in both methanol and trifluoroethanol. The nmr and infrared spectra were consistent with the expected structure.

1-Octyl Tosylate.—The ester, prepared in 67% yield from *n*-octanol (Eastman) by the usual low-temperature method in pyridine, had n^{27}D 1.4878 (lit.[25] n^{20}D 1.4946) and solvolyzed with steady, first-order kinetics.

Kinetics.—The kinetic runs were followed titrimetrically by standard techniques, and the rate constants were calculated from the first-order rate law. Commercial absolute methanol containing *ca.* 0.04% water was used without further purification. The titrations for the methanolyses were performed with standard aqueous ethanolic sodium carbonate using bromphenol blue as the indicator. Trifluoroethanol was used as received from Matheson Coleman and Bell. Sodium trifluoroethoxide–trifluoroethanol solutions were standardized by titration with perchloric acid in 95% ethanol, which in turn was standardized against aqueous ethanolic primary standard sodium carbonate. The trifluoroethanolysis kinetics were followed by titration with standardized perchloric acid in ethanol to the bromphenol blue end point. A typical rate run is given in Table III.

TABLE III

SOLVOLYSIS OF 0.0374 *M* 5,5-DIMETHOXY-1-PENTYL TOSYLATE IN 0.0507 *M* SODIUM TRIFLUOROETHOXIDE IN TRIFLUOROETHANOL AT 69.88 ± 0.02°

Time, sec	0.0254 *M* $HClO_4$–EtOH,[a] ml	[ROTs], *M*	10^5k,[b] sec^{-1}
0	3.76	0.0352	...
1,472	3.495	0.0318	6.95
3,255	3.195	0.0279	7.42
5,170	2.90	0.0241	7.22
7,450	2.60	0.0202	7.46
9,280	2.40	0.0176	7.47
12,550	2.12	0.01040	7.35
15,400	1.915	0.01135	7.36
∞	1.035	...	...

[a] Per 1.98 ml of aliquot. [b] Average $k = 7.32 \pm 0.13$.

Trifluoroethanolysis Products from 4,4-Dimethoxy-1-butyl Tosylate (**2**, $n = 2$).—The tosylate (3.0 g) was diluted with 50 ml of 0.25 *M* sodium trifluoroethoxide–trifluoroethanol and heated at 70° for 115 min. The mixture was cooled, filtered, concentrated, and distilled. A single fraction was collected (1.15 g, 51%), bp 84–87° (20 mm), n^{26}D 1.3715. This material consisted of a single component with trace amounts of several other products as determined by gas chromatography (10 ft × 0.25 in. 20% FFAP on Chromosorb P column at 125°). An analytical sample was obtained by preparative gas chromatography and identified as 1,4-dimethoxy-1-trifluoroethoxybutane (**8**): n^{26}D 1.3703; nmr ($CDCl_3$) τ 5.40 [t, 1, $(CH_3O)_2CH$], 6.32

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(q, 2, J = 9 Hz, CF_3CH_2), 6.65 (s, 3, CH_3OCH), 6.68 (s, 3, CH_3OCH_2), and *ca.* 8.3 (m, 4, methylene); mass spectrum (70 eV) *m/e* 143 (base peak); ir (neat) 1280 cm^{-1} (CF_3).

Anal. Calcd for $C_8H_{15}F_3O_3$: C, 44.44; H, 6.99; F, 26.36. Found: C, 44.14; H, 7.04; F, 26.48.

A better estimate of the yield of **8** was obtained by gas chromatographic analysis using internal standards. In a typical experiment the accurately weighed ester (*ca.* 0.4 g) was solvolyzed as above, the reaction mixture was cooled, and cyclohexyl acetate and *n*-octyl alcohol were accurately weighed into the reaction mixture. The mixture was vigorously shaken and analyzed directly on a 20% FFAP on Chromosorb P column. The yield of **8**, determined from the relative peak areas suitably corrected for minor differences in detector response, was 70%.

Trifluoroethanolysis Products from 5,5-Dimethoxy-1-pentyl Tosylate (2, *n* = 3).—The tosylate (2.82 g) was diluted with 95 ml of 0.130 *M* sodium trifluoroethoxide–trifluoroethanol and heated at 70° for 14 hr. The mixture was cooled, filtered, and concentrated. Ether (*ca.* 35 ml) was added to precipitate the remaining salts. The mixture was filtered, concentrated, and distilled. A single high-boiling component was isolated (0.5 g), bp 95° (17 mm), $n^{27}D$ 1.3816. This material was further purified by preparative gas chromatography and identified as 1,5-dimethoxy-1-trifluoroethoxypentane (**9**): nmr (CCl_4) 5.50 [t, 1, J = *ca.* 5 Hz, $(CH_3O)_2CH$], 6.23 (q, 2, J = 9 Hz, CF_3CH_2); 6.70 (s, 3, CH_3OCH), 6.75 (s, 3, CH_3OCH_2–), and *ca.* 8.5 (m, 6, methylene); mass spectrum (70 eV) *m/e* 143 (base peak); ir (neat) 1280 cm^{-1} (CF_3).

Anal. Calcd for $C_9H_{17}F_3O_3$: C, 46.95; H, 7.44; F, 24.76. Found: C, 46.85; J, 7.51; F, 24.79.

The yield of **9**, determined by gas chromatography using an internal standard, was *ca.* 25%. Although no attempt was made to recover the major solvolysis product, it was identified as 2-methoxytetrahydropyran on the basis of its identical gas chromatography retention time with that of an authentic sample.

Registry No.—**1** (*n* = 2), 23068-87-3; **2** (*n* = 2), 23068-88-4; **2** (*n* = 3), 23068-89-5; **2** (*n* = 4), 23068-90-8; **4** (*n* = 3), 23068-91-9; **6** (*n* = 2), 17082-61-0; **7**, 23074-20-6; **8**, 23074-21-7; **9**, 23074-22-8; 1-octyl tosylate, 3386-35-4.

Acknowledgment.—The author gratefully acknowledges the interest of Professor D. S. Tarbell and financial support by the National Institutes of Health (Grant AI-08424) and the Petroleum Research Fund of the American Chemical Society (Grant 2252-C). The author is also indebted to Mr. Charles Wetter and Miss Betty Lankford for their skillful assistance in obtaining the mass spectra.

Cyclopropylcarbinyl *p*-Toluenesulfonate Solvolysis. IV. Correlation with Cholesteryl Tosylate Solvolysis Rates

DONALD D. ROBERTS AND THOMAS M. WATSON[1]

Department of Chemistry, Louisiana Polytechnic Institute, Ruston, Louisiana 71270

Received September 15, 1969

The solvolysis rates of cholesteryl and cyclopropylcarbinyl (**3**-H) tosylate have been determined in a series of solvents of varying ionizing strength. The correlation of the cholesteryl tosylate solvolysis rates with those of **3**-H reflects a mechanistic similarity between the two substrates. The solvolysis rates of 1-*p*-nitrophenylcyclopropylcarbinyl tosylate (**3**-NPh) have been determined in acetic acid and ethyl alcohol. The solvolysis of **3**-NPh relative to **3**-H is retarded by a factor of 10^{-1}. Comparison of the substituent effect upon the solvolytic reactivity of **3**-H with related compounds supports a transition state with little charge localized at the methinyl carbon.

The rates of ionization of *p*-methoxyneophyl tosylate, log k_{ion}, in several solvents provide a useful scale of solvent polarity for measuring the response of an anchimerically assisted reaction to solvent variation.[2] Earlier work[3] revealed that solvolysis rates of cyclopropylcarbinyl arenesulfonates, although obeying a limiting SN1 mechanism, are poorly correlated by such a scale.

This finding, coupled with more recent observations,[4,5] suggests that a substrate subject to homoallylic rather than phenyl anchimeric assistance would be a more suitable model reaction for correlating cyclopropylcarbinyl arenesulfonate solvolysis rates.

That cholesteryl tosylate solvolyses are assisted by homoallylic interaction[6] has been well established.[6,7] Accordingly, reaction rates of cholesteryl tosylate have been measured in a solvent series of varying ionizing and nucleophilic strength.[8]

The kinetic data are given in Table I. The course of each reaction was followed by titrating the liberated *p*-toluenesulfonic acid. The solvolysis reactions of cyclopropylcarbinyl tosylate (**3**-H) in the aqueous binary solvents demonstrated the previously reported "internal return" rearrangement,[9,10] which accounted for 5–15% of the starting material. The purities of the starting materials were, therefore, checked by methanolysis, where a rearrangement to less reactive tosylates does not occur.[10] The solvolysis rates of cholesteryl tosylate in aqueous dioxane solvents obeyed first-order kinetics up to 85% conversion, with the exception that the first 5% of reaction was accelerated.

All other reactions were strictly first order in *p*-toluenesulfonate and furnished, within experimental error, 100% of the theoretical amount of acid present.

Discussion

The correlation of the cholesteryl tosylate solvolysis rates with those of cyclopropylcarbinyl tosylate results in a dispersion of points into two accurately straight lines (*cf.* Figure 1) in contrast to scatter diagrams

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