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NEIGHBORING METHOXYL PARTICIPATION IN SOLVOLYTIC NUCLEOPHILIC SUBSTITUTION*†‡§

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Abstract—In the present paper are summarized some of the results of the investigation of MeO-3,4,5,6 and 7 participation in solvolytic substitution. Among the ω-methoxy-1-alkyl bromobenzenesulfonates, solvolysis of the 4-methoxy-1-butyl and 5-methoxy-1-pentyl esters is rapid and dominated by anchimerically assisted ionization in the common solvents. While MeO-5 and 6 participation is important, MeO-3,4 and 7 is not, the corresponding esters solvolyzing with a rate constant essentially equal to the k_s value estimated from a $\rho^*\nu^*$ correlation of solvolysis rates for primary bromobenzenesulfonates solvolyzing without anchimeric assistance. On the basis of the calculated k_s values, ratios of anchimerically assisted and unassisted solvolysis rates ($k\Delta/k_s$) are derived for the MeO-5 and 6 cases.

In the case of MeO-5-assisted ionization of 4-methoxy-1-butyl bromobenzenesulfonate in acetic acid at 25°, an α- or a δ-methyl group is rate-enhancing by a factor of 6. Both the 5-methoxy-2-pentyl and 4-methoxy-1-pentyl esters give rise to an identical mixture of 5-methoxy-2-pentyl and 4-methoxy-1-pentyl acetates from methylene-O cleavage of the common cyclic oxonium ion intermediate.

The participating methoxyl group may be an *o*-methoxyl substituent in a phenyl group, as in *o*-methoxyneophyl, 3-*o*-anisyl-1-propyl, 3-methyl-3-*o*-anisyl-1-butyl and *trans*-2-*o*-anisyl*cyclo*pentyl arenesulfonates. With the compounds investigated, *o*-MeO-5, *o*-MeO-6, but not *o*-MeO-7 participation has proved to be important. Me-O cleavage of the intermediate oxonium ions formed by *o*-MeO-5 and 6 participation is important, so that benzodihydrofurans or benzodihydropyrans are produced, sometimes as the major product.

The behavior of the cyclic oxonium ion intermediates as ion pairs determines some interesting kinetic features of the acetolysis of the methoxyl-substituted alkyl arenesulfonates solvolyzing with methoxyl participation.

BECAUSE of recent interest in δ-methoxyl participation in nucleophilic substitution,[3,4,5] we are prompted to summarize some of the results of our investigation of MeO-3,4,5 and 6 participation in solvolytic substitution.¶

As in other cases of neighboring group participation in nucleophilic substitution, it is helpful to discuss methoxyl participation with the aid of: (i) k_Δ, the rate constant

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¶ The symbolism MeO-*n* is employed, where *n* is the size of the ring created in the transition state for the ionization. Analogous symbols have been employed for aryl[6–9] and complex neighboring group participations.

[1] *Chem. & Ind.* (*Rev.*) 562–563, 569–571 (1954).
[2] S. Winstein, *Experientia Supplementum* II, 137 (1955).
[3] D. S. Noyce and B. R. Thomas, *J. Amer. Chem. Soc.* **79**, 755 (1957).
[4] S. Oae, *J. Amer. Chem. Soc.* **78**, 4032 (1956).
[5] A. Kirrmann and N. Hamaide, *Bull. Soc. Chim. Fr.* **6**, 789 (1957).
[6] R. Heck and S. Winstein, *J. Amer. Chem. Soc.* **79**, 3105 (1957).
[7] R. Heck and S. Winstein, *J. Amer. Chem. Soc.* **79**, 3114 (1957).
[8] F. L. Scott, R. E. Glick and S. Winstein, *Experientia* **13**, 183 (1957).
[9] L. Goodman and S. Winstein, *J. Amer. Chem. Soc.* **79**, 4788 (1957).

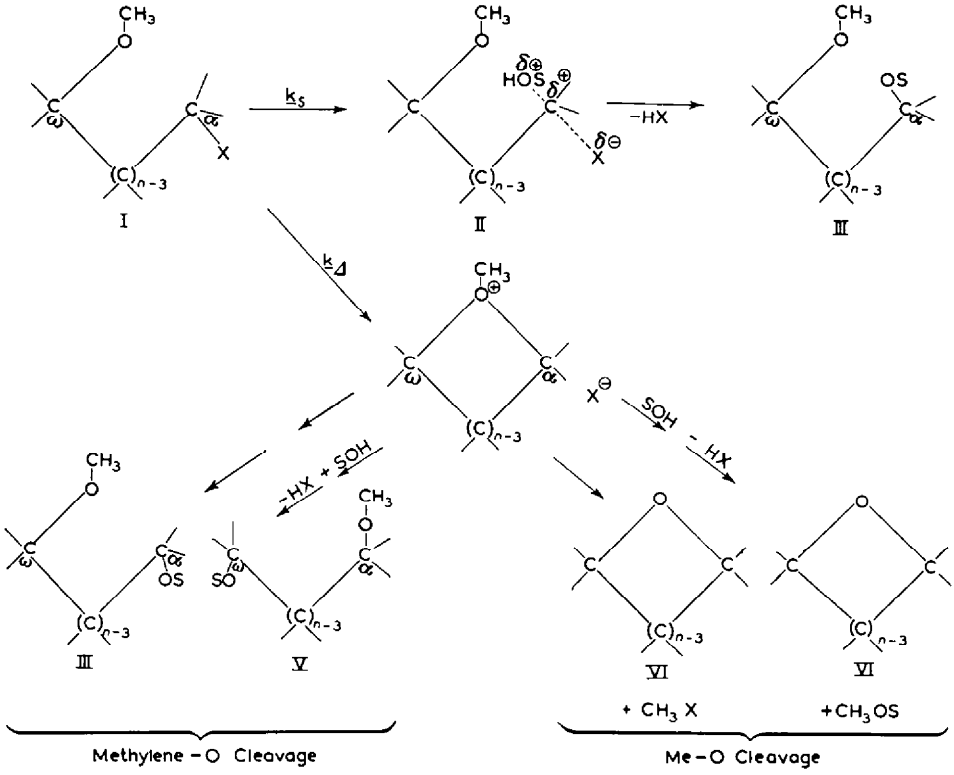
for anchimerically[10] assisted ionization; (ii) k_s, the rate constant for solvolysis not anchimerically assisted, but assisted by whatever nucleophilic solvent participation is appropriate for the substrate structure involved and the solvent being employed;[11] and (iii) k_c, the rate constant for an idealized process involving neither anchimeric assistance nor assistance from nucleophilic solvent participation. On this basis the ratio k_Δ/k_s is a measure of the competition between anchimerically assisted and anchimerically unassisted solvolysis processes. It is sometimes usefully expressed in the form of equation (1), k_Δ/k_c being

$$\frac{k_\Delta}{k_s} = \frac{k_\Delta/k_c}{k_s/k_c} = \frac{k}{k_s} - 1 \tag{1}$$

a measure of anchimeric assistance and k_s/k_c being a measure of assistance of anchimerically unassisted solvolysis by nucleophilic solvent participation.

ω-Methoxyalkyl Bromobenzenesulfonates

On examining the relative rates of solvolysis of ω-methoxylalkyl bromobenzenesulfonates summarized in Table 1, it is quite evident that solvolysis of the 4-methoxy-1-alkyl and 5-methoxy-1-alkyl bromobenzenesulfonates in the common solvolyzing solvents is rapid and dominated by anchimerically assisted ionization. On the other



[10] S. Winstein, C. R. Lindegren, H. Marshall and L. L. Ingraham, *J. Amer. Chem. Soc.* **75**, 147 (1953).
[11] S. Winstein, E. Grunwald and H. W. Jones, *J. Amer. Chem. Soc.* **73**, 2700 (1951).

TABLE 1. COMPARISON OF RATES OF SOLVOLYSIS OF ω-METHOXY-1-ALKYL *p*-BROMOBENZENESULFONATES

Compound	AcOH		Relative rates			Calculated k/k_s at 75°		
	$\Delta H\pm$ (kcal/mole)	$\Delta S\pm$ (entropy units)	EtOH 75°	AcOH 25°	HCOOH 75°	EtOH	AcOH	HCOOH
$CH_3(CH_2)_2CH_2OBs$	23·7	−17·4	1·00	1·00	1·00	0·93	0·81	1·07
$CH_3OCH_2CH_2OBs$	23·0	−22·1	0·25	0·28	0·10	1·33	1·51	0·85
$CH_3OCH_2CH_2CH_2OBs$	23·8	−17·9	0·67	0·63	0·33	1·14	1·20	0·84
$CH_3OCH_2(CH_2)_2CH_2OBs$	22·0	−10·4	20·4	657[a] (2200)[b]	461	22·2	425[a] (987)[b]	610
$CH_3OCH_2(CH_2)_3CH_2OBs$	21·6	−15·1	2·84	123	32·6	2·42	47·2	30·6
$CH_3OCH_2(CH_2)_4CH_2OBs$	23·9	−16·5	1·19	1·16	1·13	0·87	0·71	0·85

[a] Based on $k_t°$.
[b] Based on $k°_{ext}$ from special salt effect of lithium perchlorate.

hand, the rates of solvolysis of the 2-, 3- and 6-methoxy-1-alkyl esters are either lower than or nearly equal to that of the *n*-butyl analog. In fact, these rate constants are essentially equal to the k_s values, which can be estimated from a $\rho^*\sigma^*$ correlation[12,13,14] of solvolysis rates for primary bromobenzenesulfonates solvolyzing without anchimeric assistance.

$\rho^*\sigma^*$ *Correlation of* k_s *values*

In Tables 2 and 3 are summarized the application of the $\rho^*\sigma^*$ treatment, which takes account only of the polar effect of the R group of the substrate RCH_2OBs molecules, to data from these Laboratories on a number of systems. In the summarized correlation, R denotes ω-substituted alkyl, the substituent being CH_3O, Cl, Br, I, C_6H_5 and p-$CH_3OC_6H_4$. When solvolysis receives a contribution from k_Δ, the correlation is based on the k_s portion of the solvolysis rate constant.

In plots of log k for solvolysis of RCH_2OBs vs. σ^*, the point for R = Me consistently falls off the least-squares line defined by the other points.[14] Therefore, it has been omitted from the least-squares line, the data being fit to equation (2). As is clear from Tables 2 and 3, this

$$\log (k_R/k_{CH_3}) = a + \rho^*\sigma^* \qquad (2)$$

treatment fits anchimerically unassisted solvolysis of RCH_2OBs substrates in ethanol, acetic acid and formic acid solvents with a probable error in log (k_R/k_{CH_3}) of ca. 0·05. With the aid of equation (2) and the parameters summarized in Table 3, one can therefore estimate the k_s portion of the solvolysis rate constant for the RCH_2OBs substrates whose solvolysis is being examined for anchimeric assistance.

MeO-5 *and* MeO-6 *participation*

The k/k_s values for solvolysis of RCH_2OBs, based on observed k values and k_s values predicted by equation (2), are summarized in Table 1. From these it is evident that k_Δ/k_s is substantial for MeO-5 and MeO-6 participation, but essentially negligible

[12] R. W. Taft, Jr., *J. Amer. Chem. Soc.* **75**, 4231 (1953).
[13] R. W. Taft, Jr. in M. S. Newman, *Steric Effects in Organic Chemistry* Chap. 13. Wiley, New York (1956).
[14] A. Streitwieser, Jr., *J. Amer. Chem. Soc.* **78**, 4935 (1956).

TABLE 2. THE ρ^* σ^* CORRELATION OF SOLVOLYSIS RATES OF SOME PRIMARY BROMOBENZENESULFONATES (RCH_2OBs) AT 75°[c]

R of RCH_2OBs	σ^*	k_R/k_{CH_3} in EtOH		k_R/k_{CH_3} in AcOH		k_R/k_{CH_3} in HCOOH	
		obs.	calc.	obs.	calc.	obs.	calc.
CH_3	0·000						
CH_3CH_2	−0·100[a]	0·5565[f]	0·5311	0·6029[f]	0·6460		
$CH_3(CH_2)_2$	−0·115[a]	0·5213	0·5586	0·5515	0·6760	0·7807	0·7313
CH_3OCH_2	+0·520[a]	0·1315	0·1243			0·0750	0·0878
$CH_3O(CH_2)_2$	+0·140[b]	0·3472	0·3056	0·3596	0·3000	0·2610	0·3123
$CH_3O(CH_2)_5$	−0·218[b]	0·6185	0·7125	0·6691	0·9417	0·8794	1·0034
$ClCH_2$	+1·050[a]	0·0316	0·0355	0·0155[c,g]	0·0164	0·0161	0·0150
$Cl(CH_2)_2$	+0·385[a]	0·2009	0·1711	0·1636	0·1371	0·1318	0·1378
$Cl(CH_2)_3$	+0·063[b]			0·4632[d]	0·5731		
$BrCH_2$	+1·000[a]			0·0156[c,g]	0·0192		
$Br(CH_2)_2$	+0·362[b]			0·1555	0·1476		
$I(CH_2)_2$	+0·293[b]			0·1654	0·1840		
$C_6H_5CH_2$	+0·215[a]	0·2376[c,h]	0·2569	0·3118[e]	0·2361		
$C_6H_5(CH_2)_2$	+0·080[a]	0·4509[f]	0·3521	0·3933[j]	0·3626	0·4364[j]	0·3814
$C_6H_5(CH_2)_3$	+0·020[a]			0·5037[e,j]	0·4403	0·6096[e,j]	0·5326
p-$CH_3OC_6H_4CH_2$	+0·12	0·2564[c,e,h,k]	0·3199				

[a] Values quoted by Taft.[15]
[b] Calculated by using the equation:

$$\sigma^*X(CH_2)_n = -\frac{\sigma^*X(CH_2)_{n-1}}{f} + \sigma^*CH_3(CH_2)_{n-1}$$

with f equal to 2·165, the value given by the σ^* values for $ClCH_2$- and $Cl(CH_2)_2$-.
[c] Rate of toluenesulfonate relative to that of ethyl toluenesulfonate; 100° in case of acetic acid solvent.
[d] Based on $k^{\circ}_{ext.}$ value.
[e] Based on k_s value.
[f] Data of P. Magee.
[g] Data of H. Marshall.
[h] Data of Winstein *et al.*[10]
[i] Data of Winstein and Heck.[16]
[j] Data of Heck and Winstein.[6]
[k] Data of E. Jenny.

TABLE 3. SUMMARY OF LEAST-SQUARES FITS OF SOLVOLYSIS RATES OF PRIMARY ALKYL p-BROMOBENZENESULFONATES BY THE EQUATION LOG $(k_R/k_{CH_3}) = a + \rho^*\sigma^*$

Solvent	n[a]	a	ρ^*	r[b]
EtOH	10	−0·3711	−1·0275	0·044
AcOH	13	−0·3286	−1·3876	0·056
HCOOH	8	−0·3026	−1·4496	0·040

[a] n is the number of pieces of data included in the least-squares line.
[b] Probable error in log (k_R/k_{CH_3}) calculated from the equation

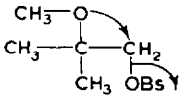
$$r = \pm 0{\cdot}6747\left(\frac{\Sigma d_i^2}{n-1}\right)^{\frac{1}{2}} \quad i = 1, \ldots n$$

where d is the difference between experimental and calculated values.

[15] R. W. Taft, Jr. in M. S. Newman, *Steric Effects in Organic Chemistry* p. 619. Wiley, New York (1956).
[16] S. Winstein and R. Heck, *J. Amer. Chem. Soc.* **78**, 4801 (1956).

for MeO-*n* participation, where *n* is 3, 4 or 7. The sequence of k_Δ values for different ring size *n* of the cyclic oxonium ions (IV) is $3,4 \ll 5 > 6 > 7$, similar to the sequence observed in formation of cyclic immonium ions.[17]

It is clear that the driving force due to neighboring methoxyl participation is very high for $n = 5$ and substantial for $n = 6$. Thus anchimerically assisted ionization dominates solvolysis of $MeO(CH_2)_4OBs$ in ethanol, acetic acid and formic acid, and that of $MeO(CH_2)_5OBs$ in the latter two solvents. For $n = 3$, 4 and 7, the driving force is sufficiently low that anchimerically assisted ionization does not compete with the anchimerically unassisted process in the case of the simple primary RCH_2OBs substrates. It should be noted, however, that k_Δ/k_s depends markedly on structure.[18] For $n = 3$, for example, MeO-assisted ionization dominates solvolytic reactions of 2-methyl-2-methoxy-1-propyl bromobenzenesulfonate (VII).[19] MeO-3-assisted ionization is also important in other cases.[20]



VII

The variation of k/k_s values with solvent in solvolysis of $MeO(CH_2)_4OBs$ and $Me(CH_2)_6OBs$ is instructive. As is clear from Table 1, k/k_s is lowest in ethanol, the most nucleophilic solvent. Thus, with $MeO(CH_2)_5OBs$, the use of ethanol as solvent makes k_s nearly as large as k_Δ. The position of alcohol in the solvent sequence of k/k_s or $(1 + k_\Delta/k_s)$ values is actually determined by two other solvent sequences, EtOH > AcOH < HCOOH for k_s and EtOH < AcOH < HCOOH for k_Δ.

It is interesting that k/k_s, and thus k_Δ/k_s, is somewhat larger in acetic acid than in formic acid in the case of MeO-5 and MeO-6 participation. This is due to the fact that k_s is more sensitive to the solvent change, AcOH → HCOOH, than is k_Δ.

α-Methyl and δ-methyl substitution

The effects of α- and δ-methyl groups on MeO-5 participation are of some interest, pertinent data being summarized in Table 4. From the rate comparisons in this table, it is clear that k_Δ/k_s is high in acetolysis for all the 4-methoxy-1-alkyl esters, whether α-, δ-, or α,δ-methyl substituted. However, α-methyl substitution does reduce k_Δ/k_s.

On scrutinizing the relative *k* values (essentially relative k_Δ values) of the 4-methoxyalkyl esters in Table 4, it is seen that a δ-methyl group increases the rate by a factor of 6. For α-methyl substitution either retardation or acceleration is conceivable on theoretical grounds.[11,18] In the present case, an α-methyl group accelerates rate by a factor of 6. This contrasts with the effect of α-methyl substitution on rate of 0–5 ring closure involving a participating benzamido group[8] but agrees with that observed in Ar_1-5 participation.[6]

The effects of σ- and δ-methyl substitution on rate of 0–5 closure by MeO-5 participation are approximately additive with the *threo*-5-methoxy-2-hexyl ester (X).

[17] G. Salomon, *Helv. Chim. Acta* **19**, 743 (1936).
[18] S. Winstein and E. Grunwald, *J. Amer. Chem. Soc.* **70**, 828 (1948).
[19] S. Winstein, C. R. Lindegren and L. L. Ingraham, *J. Amer. Chem. Soc.* **75**, 155 (1953).
[20] For example, S. Winstein *et al.*, *J. Amer. Chem. Soc.* **65**, 2196 (1943); **70**, 821 (1948); **74**, 1160 (1952).

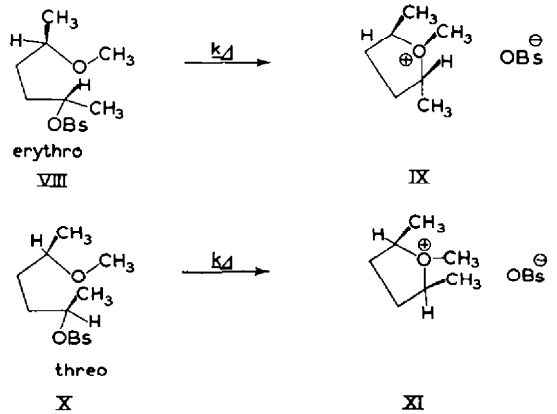
However, the *erythro*-5-methoxy-2-hexyl ester(VIII) is slower than its *threo*-isomer X by a factor of ca. 2·5, this being ascribed most plausibly to a steric retardation. In the cyclic oxonium ion, the methyl groups are *cis* in the intermediate (XI) from the *threo*-diastereomer, while they are *trans* in the intermediate (IX) from the *erythro* isomer.

TABLE 4. RELATIVE RATES OF ACETOLYSIS OF SOME METHYL-SUBSTITUTED BUTYL BROMOBENZENESULFONATES AT 25°

Compound	$\Delta H^{\pm}$ (kcal/mole)	$\Delta S^{\pm}$ (entropy units)	Relative rate	
$CH_3(CH_2)_2CH_2OBs$	23·7	−17·4	1·00	
$CH_3OCH_2(CH_2)_2CH_2OBs$	22·0	−10·4	657	1·00
			(2200)[a]	
$CH_3OCH_2(CH_2)_2CH(OBs)CH_3$	21·1	−9·4	4135[b]	6·29
			($1·23 \times 10^4$)[a]	
$CH_3OCH(CH_3)(CH_2)_2CH_2OBs$	20·8	−10·9	4111	6·26
			($1·22 \times 10^4$)[a]	
$CH_3OCH(CH_3)(CH_2)_2CH(OBs)CH_3$				
Erythro	21·0	−8·2	9447[c]	14·38
Threo			$2·28 \times 10^4$[d]	34·70
$CH_3CH_2CH(OBs)CH_3$	23·7	−7·7	140	

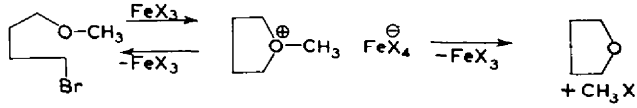
[a] Based on $k^{\circ}_{ext.}$ from special salt effect of lithium perchlorate.
[b] 30 and (ca. 80) relative to sec-BuOBs. For the bromides in 78·5% formic acid at 85°, the factor 36 is given by the data of Oae.[4]
[c] 67 relative to sec.-BuOBs.
[d] 163 relative to sec-BuOBs.

Owing to the pyramidal nature of the oxygen atom in the cyclic oxonium ion, the O-methyl group in the *cis*-intermediate XI can assume a disposition *trans* to both other methyl groups. On the other hand, in the *trans*-intermediate (IX), the O-methyl group must be *cis* to one of the other two methyl groups. This type of interaction could plausibly account for the small reactivity differential between the diastereomeric 5-methoxy-2-hexyl bromobenzenesulfonates (VIII) and (X).

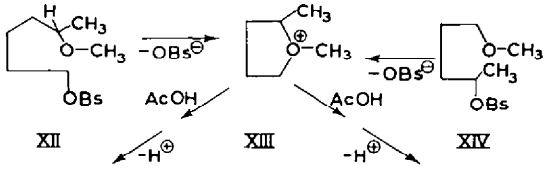


Me–O *and Methylene-O cleavage*

The products of solvolysis by way of MeO-*n* participation may conceivably involve Me–O or Methylene–O cleavage of the cyclic oxonium ion intermediate IV. In MeO-3 participation, we have not observed Me–O cleavage, the strained three-membered ring being cleaved instead.[20] In MeO-5 participation also, Me–O cleavage with resulting formation of tetrahydrofurans VI ($n = 5$) appears to be relatively unimportant.*



For example, from acetolysis of the 4-methoxy-1-pentyl and 5-methoxy-2-pentyl esters (XII) and (XIV) are obtained in very high yield identical mixtures of secondary and primary acetates (XV) and (XVI) in a 60 to 40 ratio. Some Me–O cleavage does



$CH_3OCH(CH_3)CH_2\ CH_2\ CH_2OAc$ $CH_3OCH_2CH_2\ CH_2\ CH(OAc)CH_3$

XV XVI

occur in acetolysis of 5-methoxy-1-pentyl bromobenzenesulfonate, this material giving rise to substantial amounts of tetrahydropyran, methyl acetate, methyl bromobenzenesulfonate and 5-methoxy-1-pentyl acetate.

o-MeO *participation*

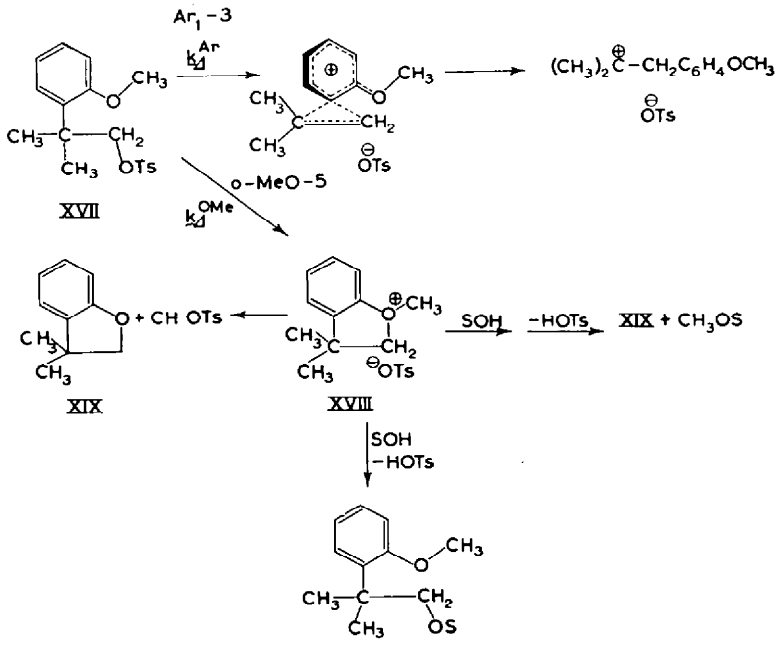
The participating methoxyl group may be an *o*-methoxyl substituent in a phenyl group, as in *o*-methoxyneophyl toluenesulfonate (XVII). As already reported elsewhere,[1,2,21,22] *o*-MeO-5 competes with Ar_1-3 participation in solvolysis of this substrate, anchimerically unassisted solvolysis being negligible. As the data summarized in Tables 5 and 6 show, *o*-MeO-assisted ionization is also important in formolysis and acetolysis of 3-*o*-anisyl-1-propyl bromobenzenesulfonate (XX) and 3-*o*-anisyl-3-methyl-1-butyl toluenesulfonate (XXIV). With these substrates, Ar_1-4 participation may be judged to be negligible by analogy with the behavior of the *p*-isomers.[6,23] Also, k_s the rate constants for anchimerically unassisted solvolysis (process S) may be approximated as equal to the values for the *p*-isomers or even the analogs without the methoxyl substituent.[6,23] On this basis, solvolysis of the 3-*o*-anisyl-1-propyl ester (XX) is largely, and that of the 3-*o*-anisyl-3-methyl-1-butyl derivative (XXIV) is exclusively *o*-MeO-6 assisted. Because of anchimeric assistance, the 3-*o*-anisyl-3-methyl-1-butyl derivative XXIV is more reactive in solvolysis than the *p*-isomer by a factor of ca. 10^4.

* It is interesting that Kirrmann and Hamaide[5] report a high yield of tetrahydrofuran from treatment of 4-methoxy-1-butyl bromide with ferric chloride. However, this result does not indicate how well Me–O competes with methylene–O cleavage, since the latter is reversible under the conditions employed.

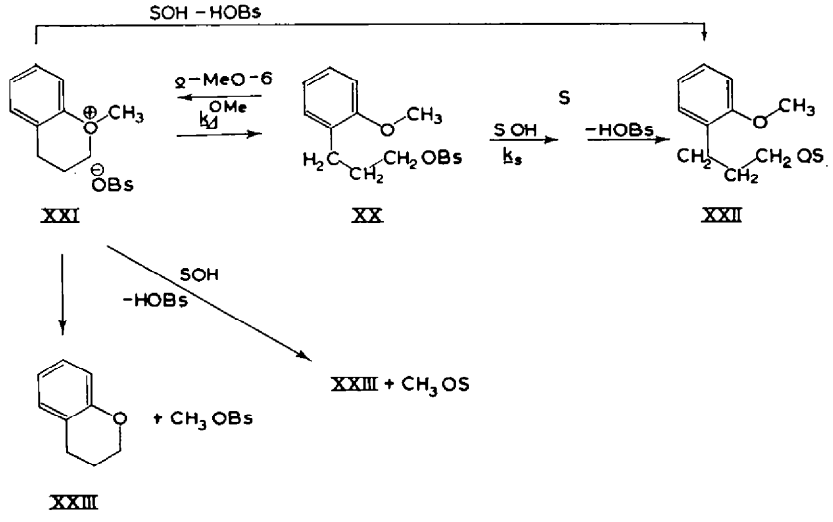
[21] R. Heck, J. Corse, E. Grunwald and S. Winstein, *J. Amer. Chem. Soc.* **79**, 3278 (1957).

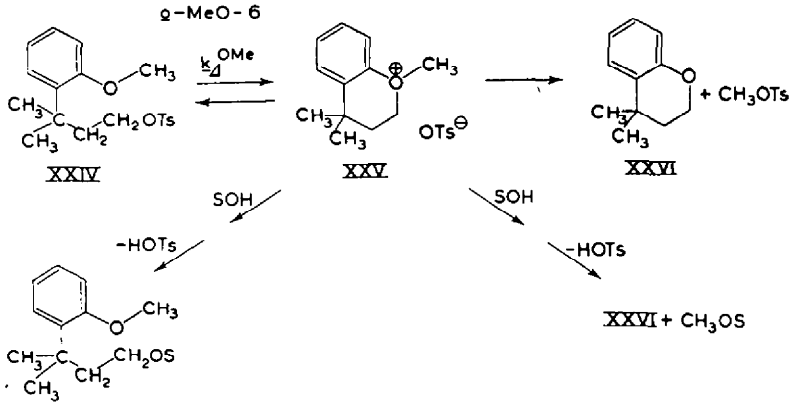
[22] S. Winstein in G. R. Robertson, *Modern Chemistry for the Engineer and Scientist* Chap. 7. McGraw-Hill, New York (1957).

[23] R. Heck, unpublished work.

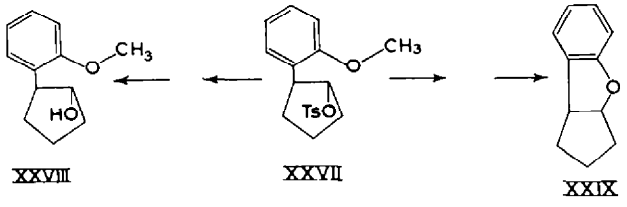


As regards the mode of cleavage of the intermediate cyclic oxonium ion intermediates from ionization of the *o*-anisyl-1-alkyl derivatives XVII, XX and XXIV, Me–O cleavage is important in all three cases. In solvolysis of the two derivatives with the *gem.*-Me_2 grouping, Me–O cleavage is almost exclusive, and this gives rise to 3,3-dimethyl-4,5-benzodihydrofuran (XIX) and 4,4-dimethyl-2,3-dihyrobenzopyran (XXVI) as products. In formolysis of the 3-*o*-anisyl-1-propyl ester XX, without the *gem.*-Me_2 grouping, methylene–O cleavage of the intermediate XXI competes nearly equally with Me–O cleavage. From the latter is obtained the benzodihydropyran XXIII.

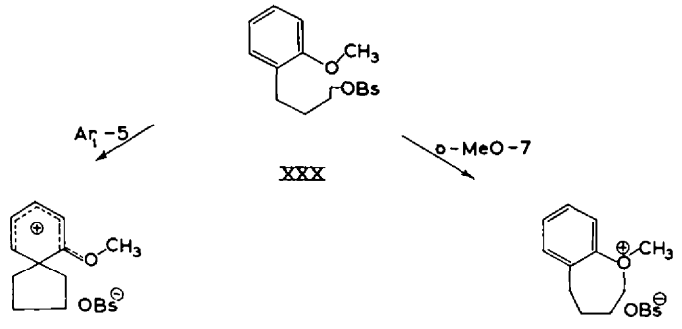




o-MeO-5 participation in solvolytic substitution may be illustrated further with the example of acetolysis of *trans*-2-*o*-anisyl*cyclo*pentyl toluenesulfonate (XXVII). This material acetolyzes[23,24] at a rate eight times that of the *p*-isomer[23,25] at 50°, even though acetolysis of the latter material is already anchimerically accelerated owing to Ar_1-3 participation.[23] At least some of the excess solvolysis rate of the *o*-isomer XXVII compared to the *p*-derivative is due to *o*-MeO-5 participation, since the cyclic ether XXIX is obtained along with *trans*-2-*o*-anisyl*cyclo*pentanol (XXVIII) in yields of 22 and 64 per cent, respectively, from acetolysis of the *o*-isomer (XXVII) and subsequent treatment of the reaction product with lithium aluminum hydride.



In solvolysis of 4-*o*-anisyl-1-butyl *p*-bromobenzenesulfonate (XXX), *o*-MeO participation would necessarily be *o*-MeO-7. However, as illustrated in Tables 5 and 6, the 4-*o*-anisyl-1-butyl ester (XXX) displays almost the same formolysis and



acetolysis rate constants as does the *p*-isomer.[6] If the k_s and k_Δ^{Ar} values are approximated as equal to those of the *p*-isomer, the k_Δ^{OMe} value turns out to be zero in acetolysis

[24] A Fainberg, unpublished work.
[25] A. H. Fainberg, G. C. Robinson and S. Winstein, *J. Amer. Chem. Soc.* **78**, 2777 (1956).

TABLE 5. *o*-MeO PARTICIPATION IN FORMOLYSIS OF *o*-ANISYLALKYL ARENESULFONATES

Compound	Temperature (°C)	Rate constants (sec^{-1})				% Reaction by				
								o-MeO		
		Total 10^5k	10^5k_s	$10^5k_\Delta^{Ar}$	$10^5k_\Delta^{OMe}$	Ar_1	*S*	Total	CH_3–O cleavage	Me–O cleavage
$(CH_3)_2C(o\text{-}CH_3OC_6H_4)CH_2OTs$	25·0	13·3	ca. 0	9·8	3·5	73	0	27	small	ca. 27
o-$CH_3OC_6H_4CH_2CH_2CH_2OBs$	75·0	39·7	2·0[a]	—	37·7	—	5	95	46	49
	50·0	3·45[b]	0·15[a]	—	3·30					
	25·0	0·20[c]	0.01[a,c]	—	0·19					
$(CH_3)_2C(o\text{-}CH_3OC_6H_4)CH_2CH_2OTs$	25·0	22·0	ca. 0	—	22·0	—	0	100	<5[d]	>95
o-$CH_3OC_6H_4CH_2CH_2CH_2CH_2OBs$	75·0	7·14	2·8[e]	3·3[e]	1·0(?)					

[a] Based on the 3-phenyl-1-propyl derivative.[6]
[b] $\Delta H\pm = 21{\cdot}2$ kcal/mole; $\Delta S\pm = -13{\cdot}6$ entropy units.
[c] Extrapolated from the data at the other temperatures.
[d] Upper limit because the liquid toluenesulfonate may have contained the alcohol as a contaminant.
[e] Based on the *p*-isomer.[6]

and a value in formolysis of about one-fortieth of that for *o*-MeO-6. In any case, *o*-MeO-7 participation does not compete substantially with anchimerically unassisted and Ar_1-5-assisted processes.

It is interesting that steric factors contrive to make the rate sequence *o*-MeO-6 > *o*-MeO-5, at least with the *o*-anisyl-1-alkyl derivatives with the *gem*.-Me_2 grouping. This is the reverse of the sequence observed in MeO-*n* participation, MeO-5 > MeO-6 The *gem*.-Me_2 grouping has a large effect on k_Δ^{OMe} for both *o*-MeO-5 and *o*-MeO-6 participation. For *o*-MeO-5 this is clear from the comparison of *o*-methoxyneophyl and 2-*o*-anisyl-1-ethyl toluenesulfonates.[21] For *o*-MeO-6, the comparison of k_Δ^{OMe} values for the 3-*o*-anisyl-1-propyl and 3-*o*-anisyl-3-methyl-1-butyl esters (XX; XXIV) shows that the *gem*.-Me_2 grouping increases k_Δ^{OMe} by a factor greater than 10^2.

It is interesting to cross-compare rates of MeO-assisted and *o*-MeO-assisted ionizations, since the *o*-anisyl derivatives have a less nucleophilic methoxyl group, but also greater conformational restrictions than their aliphatic counterparts. The k_Δ^{OMe} values for the 5-methoxy-1-pentyl and 3-*o*-anisyl-1-propyl bromobenzenesulfonates show MeO-6-assisted ionization to be faster than *o*-MeO-6 by a factor of only ca. 3 in formic acid at 75°. The rate of *o*-MeO-5-assisted ionization of the *o*-methoxyneophyl derivative XVII, with the *gem*.-Me_2 grouping, is nearly equal to that of MeO-5-assisted ionization of 4-methoxy-1-butyl toluenesulfonate.

Kinetics and ion pair return in acetolysis

The behavior of the cyclic oxonium ion intermediates as ion pairs[2,25,26–33] determines some interesting kinetic features of the acetolysis of the substrate systems solvolyzing with methoxyl participation. However, we cannot yet describe the number and nature of the various ion-pair varieties which may be involved.[26–33]

In those cases where Me–O cleavage occurs, ion-pair return[30] produces methyl

[26] W. G. Young, S. Winstein and H. L. Goering, *J. Amer. Chem. Soc.* **73**, 1958 (1951).
[27] S. Winstein and K. C. Schreiber, *J. Amer. Chem. Soc.* **74**, 2165 (1952).
[28] C. A. Grob and S. Winstein, *Helv. Chim. Acta.* **35**, 782 (1952).
[29] S. Winstein, E. Clippinger, A. H. Fainberg, R. Heck and G. C. Robinson, *J. Amer. Chem. Soc.* **76**, 2597 (1954); *Chem. & Ind. (Rev.)* 664 (1954).
[30] S. Winstein, E. Clippinger, A. H. Fainberg, R. Heck and G. C. Robinson, *J. Amer. Chem. Soc.* **78**, 328 (1956).
[31] A. H. Fainberg and S. Winstein, *J. Amer. Chem. Soc.* **78**, 2767 (1956).
[32] S. Winstein and G. C. Robinson, *J. Amer. Chem. Soc.* **80**, 169 (1958).
[33] S. Winstein and A. H. Fainberg, *J. Amer. Chem. Soc.* **80**, 459 (1958).

TABLE 6. *o*-MeO PARTICIPATION IN ACETOLYSIS OF *o*-ANISYLALKYL ARENESULFONATES

Compound	Temperature (°C)	Rate constants (sec^{-1})				Reaction (per cent) by						
						Ar_1	S	*o*-MeO				
								Total	CH_3–O Cleavage		CH_3–O Cleavage	
		Total 10^5k	10^5k_s	$10^5k_\Delta^{Ar}$	$10^5k_\Delta^{OMe}$				No ion pair return	Ion pair return	Ion pair return	No ion pair return
$(CH_3)_2C(o\text{-}CH_3OC_6H_4)CH_2OTs$	75·0[a]	48	ca. 0	11	37	25	0	75	4	ca. 0[b]	40	31
$o\text{-}CH_3OC_6H_4CH_2CH_2CH_2OBs$	75·0	0·91[c]	0·11[d]	—	0·80	—	12	88		24[b]	29	
$(CH_3)_2C(o\text{-}CH_3OC_6H_4)CH_2CH_2OTs$	75·0	56·2[e]	0·01[f]	—	56·2	—	0	100		small[b]	ca. 65	
$o\text{-}CH_3OC_6H_4CH_2CH_2CH_2CH_2OBs$	75·0	0·18	0·14[d]	0·05[d]	—							
	100·0	2·10[g]										

[a] Solvent contained 0·031 N sodium acetate.
[b] Assuming all ion pair return is eliminated by lithium perchlorate.
[c] k°_{ext} from runs with added lithium perchlorate.
[d] Based on the *p*-isomer.[6]
[e] Initial first-order rate constant for disappearance of toluenesulfonate.
[f] Based on the *p*-isomer.[33]
[g] $\Delta H^{\pm} = 24{\cdot}7$ kcal/mole; $\Delta S^{\pm} = -14{\cdot}3$ entropy units.

toluenesulfonate or bromobenzenesulfonate, as the case may be. Thus, during acetolysis of *o*-methoxyneophyl toluenesulfonate(XVII), methyl toluenesulfonate is formed.[2,21] Since the latter material is very much less reactive in acetolysis than the *o*-methoxyneophyl derivative, a relatively steady infinity acid titer, 60 per cent of theoretical, is observed, unaffected by the inclusion of lithium toluenesulfonate to the acetolysis solution.[2] By the use of this infinity acid titer, good first-order kinetics are obeyed by *o*-methoxyneophyl toluenesulfonate in the production of acid.[21] The derived first-order rate constant in this case is for disappearance of *o*-methoxyneophyl toluenesulfonate(XVII), inclusive of the reaction which produces methyl toluenesulfonate. Quite analogously, the first-order rate constant obtained for acetolysis of 5-methoxy-1-pentyl bromobenzenesulfonate includes formation of methyl bromobenzenesulfonate to the extent of 57 per cent at 50° and 54 per cent at 75°.

In the case of 3-*o*-anisyl-1-propyl bromobenzenesulfonate (XX), the methyl ester formed during acetolysis solvolyzes at a rate not far below that of the original ester. Kinetic analysis, making use of the measured rate constant for acetolysis of the methyl ester, furnishes first-order rate constants for solvolysis and formation of methyl bromobenzenesulfonate, respectively.

Formation of methyl toluenesulfonate also accompanies acetolysis of 3-*o*-anisyl-3-methyl-1-butyl toluenesulfonate (XXIV). Further, solvolysis of the methyl ester is slower than that of the original ester by a very large factor. However, the kinetics observed in this case are not as simple as those employed by the *o*-methoxyneophyl system. With the 3-*o*-anisyl-3-methyl-1-butyl system, first-order constants drift down in a run, and the 34 per cent acid infinity titer observed in acetolysis at 75° is appreciably decreased by addition of lithium toluenesulfonate to the acetolysis solution. Evidently, methyl toluenesulfonate formation involves more than ion-pair return[30] in this case.

Good first-order kinetics of acetolysis, without the complication of appreciable methyl arenesulfonate formation, are displayed by the other substrate systems solvolyzing with MeO-participation. With the exception of the 3-*o*-anisyl-3-methyl-1-butyl system XXIV, no common ion rate depression[30], is visible in acetolysis of the various substrates. The actual addition of lithium bromobenzenesulfonate in acetolysis of the 4-methoxy-1-butyl, 4-methoxy-1-pentyl and 5-methoxy-2-pentyl systems failed also to produce any common ion rate depression. Evidently, return of dissociated oxonium ion intermediate to covalent starting material is unimportant with nearly all the systems investigated.

Ion-pair return accompanying acetolysis of the methoxy-substituted alkyl arenesulfonates is very subject to added lithium perchlorate or other salts, such as lithium or sodium acetate.[26–33] While it is not yet clear whether the added salts eliminate all ion-pair return,[26–33] it is clear that the portion of ion-pair return that produces methyl arenesulfonate is essentially completely eliminated. Thus, inclusion of lithium perchlorate or acetate in acetolysis of *o*-methoxyneophyl toluenesulfonate (XVII) brings the infinity acid titer essentially up to the theoretical value. The concentration of lithium perchlorate, symbolized by $(LiClO_4)_{1/2}$, which half eliminates methyl toluenesulfonate formation is 0·003 M (Table 7). In the other acetolyses, which are accompanied by production of methyl arenesulfonate, formation of the latter is eliminated by the inclusion of lithium perchlorate. With 3-*o*-anisyl-1-propyl bromobenzenesulfonate (XX), this eliminates the downward drift in the first-order rate constant observed in acetolysis, good first-order kinetics now being observed.

TABLE 7. SUMMARY OF LITHIUM PERCHLORATE SPECIAL SALT EFFECTS IN ACETOLYSIS

Compound	Temperature (°C)	b	$(LiClO_4)_{1/2}$ 10^4M	$k^\circ_{ext.}/k^\circ_t$
$CH_3OCH_2(CH_2)_2CH_2OBs$	50·0	8·4	8	2·76
	75·0	6·8		2·32
$CH_3OCH(CH_3)(CH_2)_2CH_2OBs$	25·2	9·0	0·9	2·97
$CH_3OCH_2(CH_2)_2CH(CH_3)OBs$	25·2	12·5	0·9	2·98
erythro-$CH_3OCH(CH_3)(CH_2)_2CH(CH_3)OBs$	25·2	13		2·93
3-*o*-Anisyl-1-propyl OBs	75·0	5		2·1
o-Methoxyneophyl OTs	75·0		30[a]	
trans-2-*o*-Anisyl*cyclo*-pentyl OTs	25·0	16		2·6
	50·0	15		2·1

[a] Lithium perchlorate concentration that half eliminates formation of methyl toluenesulfonate during acetolysis.

The effect of appreciable concentrations of added lithium perchlorate on solvolysis rate sheds light on the magnitude of ion-pair return to methylene carbon atoms which is eliminated by added salt. Such ion-pair return eliminated by lithium perchlorate is not serious in the case of the two systems containing the *gem*.-Me_2 grouping, namely *o*-methoxyneophyl (XVII) and 3-*o*-anisyl-3-methyl-1-butyl (XXIV). Similarly, it is not serious with the 5-methoxy-1-pentyl derivative. It is, however, important with the 3-*o*-anisyl-1-propyl system (XX) and the other derivatives that solvolyze with methoxyl participation. The magnitude of ion-pair return at both methylene and methyl carbon atoms during acetolysis of the 3-*o*-anisyl-1-propyl derivative(XX) is summarized in Table 6.

In acetolysis of the derivatives displaying ion-pair return to the methylene position which is affected by added lithium perchlorate, the addition of this salt gives rise to the steep special[26–33] salt effects at low concentrations and the more shallow normal[26–33] linear salt effects at high concentrations. In Table 7 are listed the values of the measure of the magnitude of the special salt effects, namely k°_{ext}/k°_t. In this ratio, k°_{ext} is the solvolysis rate constant that includes the special but excludes the normal salt effects.[26–33] It is a closer approximation to $(k_s + k_\Delta)$ than is k°_t, the solvolysis rate constant in the absence of added lithium perchlorate. Also listed in Table 7 are some values of $(LiClO_4)_{1/2}$, the concentration of lithium perchlorate that produces one-half of the total special salt effect. The normal portion of the lithium perchlorate salt effects is summarized in Table 7 with the aid of the b values from the fit of the data to the linear relation given in equation (3).

$$k_t = k^\circ_{ext}[1 + b\,(LiClO_4)] \tag{3}$$

Exchange accompanying solvolysis is another aspect of the acetolysis of the present derivatives that helps to place them in the whole spectrum of systems in acetolysis of which ion pairs are important.[26–33] While lithium bromobenzenesulfonate fails to depress rate of acetolysis of the 4-methoxy-1-pentyl and 5-methoxy-2-pentyl bromobenzenesulfonates, inclusion of lithium toluenesulfonate causes relatively efficient conversion of bromobenzenesulfonate to toluenesulfonate during acetolysis. The situation here resembles that presented by the 3-*p*-anisyl-2-butyl system[30,32], exchange occurring by way of ion pairs. In other respects also (Table 7), acetolysis of the present derivatives resembles that of the 3-*p*-anisyl-2-butyl[30,32] 1-*p*-anisyl-2-propyl[30,33] or 2-*p*-anisyl-1-ethyl[31,34] systems.

[34] P. Klinedinst and E. Jenny, unpublished work.