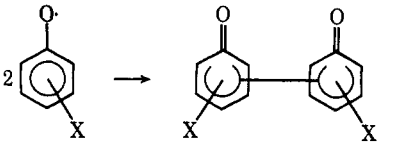
$$C \longrightarrow D + E \qquad (v)$$

heat of reaction is equal to the activation energy for the disassociation of the quinol ether in chlorobenzene, namely 25 kcal/mole.[9]

Heat of Dimerization of Phenoxyl Radicals, ΔH_8. Combining the results from the preceding section, the heats of the reactions



(vi)

are equal to $-50 + 2[(\Delta H_f)_{ArO\cdot} - (\Delta H_f)_{ArOH}]$. The values of $(\Delta H_f)_{ArO\cdot} - (\Delta H_{fArOH})$ are derived from the results of other studies from our laboratory.[9,10]

The Question of an Intermediate in a Simple Nucleophilic Substitution at Sufinyl Sulfur. The Acetate-Catalyzed Exchange of Methanol-d_3 with Methyl *p*-Toluenesulfinate[1a]

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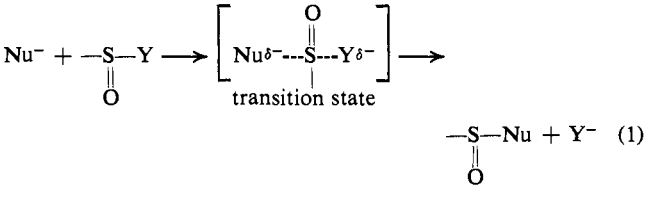
Abstract: The rate of exchange of methoxyl groups between methanol-d_3 and methyl *p*-toluenesulfinate (eq 8) has been studied in a series of acetate-acetic acid buffers in methanol-d_3 as solvent at 62°. Under these conditions the rate constant for the exchange, k_e, is the sum of two terms: $k_e = k'[AcO^-]/[AcOH] + k_{OAc}[AcO^-]$. The first of these is due to a specific methoxide ion catalyzed exchange involving reaction of CD_3O^- with the sulfinate ester. Various considerations suggest that the second term represents general base, rather than nucleophilic, catalysis by acetate. More detailed considerations, including the magnitude of the solvent isotope effect associated with k_{OAc}, argue that the general base catalysis is the result of a combination of specific methoxide ion catalysis with general acid catalysis by acetic acid and that the rate-determining step in the process is the reaction of CD_3O^- with a hydrogen-bonded complex of the sulfinate ester and acetic acid.

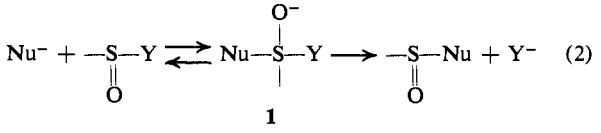
One of the most important questions to answer regarding the mechanism of representative nucleophilic substitutions at sulfinyl (>S=O) sulfur is the exact timing of the two covalency changes that occur during such a reaction. On the one hand, one can conceive of a process (eq 1), analogous to SN2 substitutions at sp^3 carbon, in which bond making and bond breaking are truly synchronous. On the other hand, the exis-



transition state

(1)

tence of stable species such as SF_4 makes it equally conceivable that substitution could follow a path (eq 2) in which an actual intermediate **1** is formed.

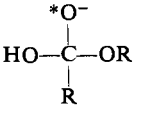


(2)

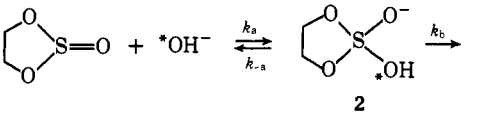
1

In the hydrolysis of an ester of a carboxylic acid the presence of an intermediate on the reaction path was first demonstrated by Bender[2] *via* the expedient of subjecting a carbonyl ^{18}O-labeled ester to partial hydrolysis and showing that the ester recovered after partial hydrolysis had undergone substantial exchange of oxygen-18. Application of this type of experiment to the hydrolysis of ethylene sulfite by Bunton and coworkers[3] led to no significant exchange of oxygen-18 between the solvent and the recovered ester.

Given the fact that in the alkaline hydrolysis of alkyl carboxylates oxygen equilibration *via* transfer of a proton between labeled and unlabeled oxygens in the tetrahedral intermediate



is competitive with the breakdown of that intermediate,[2] the results of Bunton, *et al.*, might seem at first glance to indicate that the alkaline hydrolysis of the sulfite must not be occurring by a mechanism (eq 3) involving



2

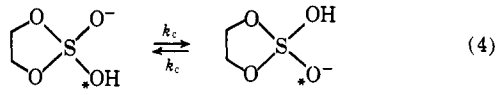
$$^-OCH_2CH_2OSO_2H \qquad (3)$$

(1) (a) This research was supported by National Science Foundation Grants GP-10732X and GP-25799; (b) to whom inquiries should be addressed at the University of Vermont; (c) NDEA Fellow, Oregon State University, 1968-1971.

(2) M. L. Bender, *J. Amer. Chem. Soc.*, 73, 1626 (1951).

(3) C. A. Bunton, P. D. B. de la Mare, P. M. Greasley, D. R. Llewellyn, N. H. Pratt, and J. G. Tillett, *J. Chem. Soc.*, 4751 (1958).

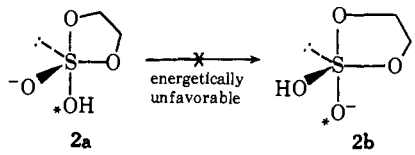
intermediate **2**. However, when the situation is considered in greater detail, one comes to realize that in the case of the sulfite there could easily be reasons why the transfer of the proton required to equilibrate the two oxygens (eq 4) might well be slow compared to the



(4)

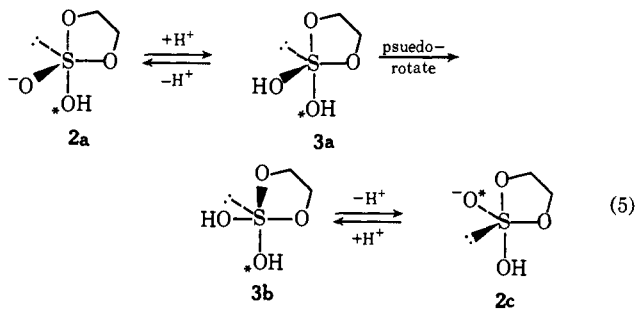
rates of breakdown of the intermediate (k_{-a} and k_b).

Thus, if **2** is a trigonal-bipyramidal intermediate formed by apical attack of hydroxide on the sulfite, the intermediate as first formed will have structure **2a**, both because the five-membered ring will presumably prefer to span an apical and an equatorial position, and because the sulfinyl oxygen and the electron pair, being less electronegative than the $-OH$ group and the other oxygen functions, will prefer to occupy equatorial rather than apical positions in the trigonal bipyramid.[4] If there is indeed a considerable energetic preference of the $-O^-$ group for an equatorial position, equilibration of the labeled and unlabeled oxygens *via* a simple proton transfer, *i.e.*, **2a** → **2b**, will be energetically unfavorable and could well be very slow compared to the break-up of **2** *via* either step k_{-a} or k_b.



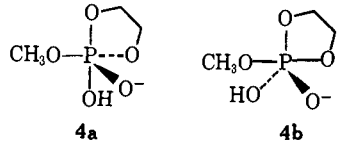
2a **2b**

An energetically more attractive route for the equilibration of the labeled and unlabeled oxygens in **2** would be *via* the sequence of steps shown in eq 5, involving first protonation of the $-O^-$ group, then pseudorotation about the electron pair as the pivot, and finally deprotonation of the *OH group, which after the pseudorotation is equatorial. However, since Westheimer and his colleagues[5] have shown that the cleavage of intermediate **4a** in the hydrolysis of methyl ethylene phosphate occurs much faster than its pseudorotation to **4b**, it is entirely possible that equilibration of the labeled and unlabeled oxygens in **2**, even *via* the process



2a **3a** **3b** **2c**

(5)

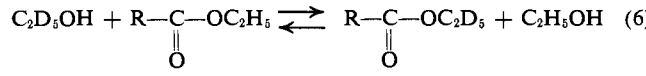


4a **4b**

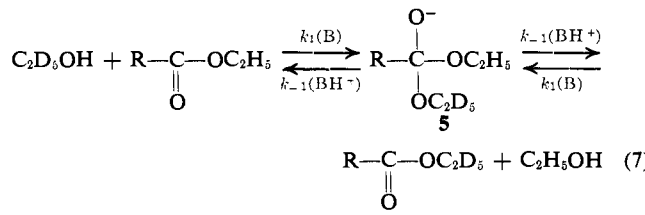
shown in eq 5, could well be much slower than the cleavage of **2** *via* steps k_{-a} or k_b of eq 3. This becomes even more likely when we remember that Mislow and Tang[6] have suggested that pseudorotation involving trigonal-bipyramidal intermediates of sulfur may well be appreciably slower than pseudorotation of analogous trigonal-bipyramidal intermediates of phosphorus.

Thus we see that the failure of oxygen-18 exchange involving the unreacted ester to accompany the hydrolysis of the sulfite does not in this case tell us anything about whether the alkaline hydrolysis of the sulfite occurs by a mechanism (eq 3) involving an intermediate (**2**), and analogous to the general scheme shown in eq 2, or, alternatively, takes place by a mechanism analogous to eq 1 in which making of the new bond to the attacking $-OH$ group and cleavage of one of the S–O bonds of the ring are synchronous. Therefore the desirability of exploring other experimental approaches that can perhaps cast some light on whether an intermediate is present on the reaction path in this and related simple nucleophilic substitutions at sulfinyl sulfur is obvious.

A few years ago Johnson[7] claimed that if a symmetrical exchange reaction of the type given in eq 6 is found to be subject to *general base catalysis* this demonstrates that the reaction must involve the mechanism shown in eq 7 where there is an intermediate **5**, on the reaction path, since Johnson felt that all the possible mechanisms that one could write for the general base catalyzed reaction that did not involve an intermediate would violate the principle of microscopic reversibility. Although it has since been pointed out[8,9] that for an exchange of the type shown in eq 6 one can indeed write mechanisms consistent with general base catalysis that do not involve an intermediate and that at the same time do not violate the principle of microscopic reversibility, it is still probably true, given the pattern of mechanistic behavior observed in most substitutions of carboxylic acid derivatives, that the mechanism proposed by Johnson (eq 7) represents the correct interpretation of general base catalysis of eq 6.



(6)



5

(7)

Darwish and Noreyko[10] have reported that the solvolysis of certain alkyl arenesulfinates can be catalyzed by added bases like acetate ion or pyridine, and they have shown that the catalyzed solvolysis involves S–O rather than alkyl–oxygen bond cleavage. They did not determine, however, whether this catalysis by added

(4) E. L. Muetterties, W. Mahler, and R. Schmutzler, *Inorg. Chem.*, 2, 613 (1961); E. L. Muetterties, W. Mahler, K. J. Packer, and R. Schmutzler, *ibid.*, 3, 1298 (1964); E. L. Muetterties and R. A. Schunn, *Quart. Rev., Chem. Soc.*, **20**, 245 (1966).

(5) R. Kluger, F. Covitz, E. Dennis, L. D. Williams, and F. H. Westheimer, *J. Amer. Chem. Soc.*, 91, 6066 (1969).

(6) R. Tang and K. Mislow, *ibid.*, **91**, 5644 (1969).

(7) S. L. Johnson, *ibid.*, **86**, 3819 (1964).

(8) T. C. Bruice and S. J. Benkovic, "Bioorganic Mechanisms," Vol. 1, W. A. Benjamin, New York, N. Y., 1966, pp 103–104.

(9) (a) R. L. Burwell, Jr., and R. G. Pearson, *J. Phys. Chem.*, **70**, 300 (1966); (b) see also M. L. Abraham, D. Dodd, M. D. Johnson, E. S. Lewis, and R. A. More O'Ferrall, *J. Chem. Soc. B*, 762 (1971), for a more extensive discussion and analysis of the type of situation in ref 9a.

(10) D. Darwish and J. Noreyko, *Can. J. Chem.*, **43**, 1366 (1965).

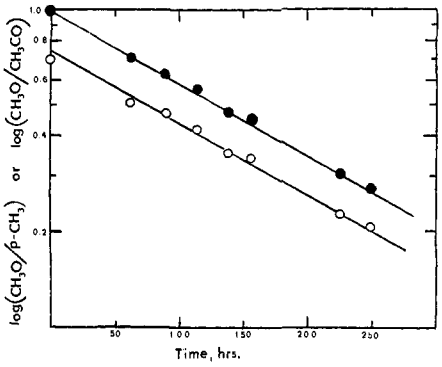
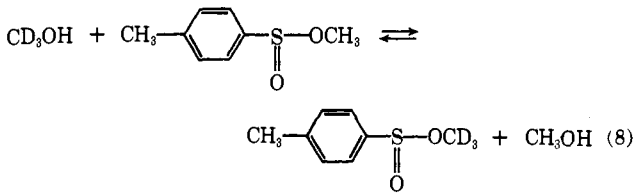


Figure 1. Kinetics of a typical exchange of methanol-d_3 with methyl *p*-toluenesulfinate (0.20 *M*) at 62°: [AcO⁻] = 0.14 *M*, [AcOH] = 0.14 *M*, [$LiClO_4$] = 0.07 *M*; ●, ratio of integral for ester CH_3O group to integral for tolyl methyl; ○, ratio of integral for ester CH_3O to integral for acetyl methyl groups for same run.

bases was due to general base catalysis, to nucleophilic catalysis, or to specific base catalysis by the lyate ion of the solvent. Nonetheless, the fact that Darwish and Noreyko[10] could observe catalysis of the solvolysis by such additives suggested to us that it would certainly be worthwhile to investigate whether or not similar catalysis could be observed for a symmetrical exchange reaction involving a *p*-toluenesulfinate ester (eq 8), and,



if it could, then to determine whether or not it was the result of general base catalysis, nucleophilic catalysis, or specific base catalysis involving methoxide ion. From what has been said earlier about eq 6, an observation of general base catalysis for eq 8 could have interesting implications regarding the existence of an intermediate on the reaction coordinate for this and related nucleophilic substitutions at sulfinyl sulfur, although, obviously, given the caveats[8,9] stated earlier, finding general base catalysis in such a situation cannot, contrary to what Johnson[7] suggested, ever constitute definitive proof of the existence of an intermediate.

The present paper describes the results of our study of the effect of added sodium acetate–acetic acid buffers on the rate of the exchange of methyl *p*-toluenesulfinate with methanol-d_3.

Results

The exchange of methanol-d_3 with methyl *p*-toluenesulfinate (eq 8) was followed by monitoring the decrease with time in the intensity of the singlet at δ 3.46 in the nmr due to the methoxyl group of the ester. Since the reactions were carried out using relatively dilute (0.20 *M*) solutions of the ester in anhydrous methanol-d_3 as solvent, equilibrium was not reached until the exchange was essentially complete and the signal at δ 3.46 had effectively disappeared completely. The amount of $CH_3OS(O)C_6H_4CH_3$-*p* remaining at a given time was determined either from the ratio of the intensity of the integral for the CH_3O group at δ 3.46 to the intensity of the integral for the tolyl methyl group at 2.41 or from the ratio of the intensity of the integral for the 3.46 signal to that of the methyl groups of the added acetate and acetic acid of the buffers used in the experiments. Use of either the tolyl methyl group or the acetate methyl as the internal standard gave equivalent results, as can be seen from Figure 1, which shows the data for a typical run plotted both as log (CH_3O/*p*-CH_3) and log ($CH_3O/CH_3C(O)$–) *vs.* time. One sees that both plots are satisfactorily linear and have the same slope. Besides the signal for the CH_3O group of the ester the only other nmr peak which changed with time during the run was that for the CH_3O group of methanol at δ 3.34 which increased with time until equilibrium was finally reached. At the end of a run a 1000-Hz sweep width spectrum of the solution was taken to check for possible appearance of any new peaks that would be indicative of the occurrence of significant amounts of side reactions accompanying the exchange. Since none were found we conclude that the only process being observed under our reaction conditions is the exchange of methanol-d_3 with the methyl sulfinate shown in eq 8.

In anhydrous methanol-d_3 in the absence of added acetate the exchange was extremely slow at 62°. In acetic acid–acetate buffers in the same solvent, the exchange, while still slow, became fast enough to be easily measurable at this temperature. For each different AcO⁻–AcOH buffer ratio, runs were carried out at a series of acetate ion concentrations using lithium perchlorate to maintain constant ionic strength. The first-order rate constants, k_e, for the exchange under the various conditions are tabulated in the first portion of Table I.

Table I. Rates of Exchange of Methanol-d_3 and -d_4 with Methyl *p*-Toluenesulfinate at 62° [a]

Solvent	AcO⁻–AcOH buffer ratio	[AcO⁻], *M*	$k_e \times 10^6$, sec^{-1}
CD_3OH	2:1	0.210	2.82
		0.158	2.38
		0.140	2.26
		0.105	1.95
		0.070	1.74
	1:1	0.210	1.87
		0.140	1.44
		0.105	1.13
	0.735:1	0.210	1.68
		0.140	1.21
		0.105	1.05
		0.070	0.85
CD_3OD	2:1	0.210	1.99
		0.158	1.70
		0.140	1.55
		0.105	1.32
		0.070	1.18
	1:1	0.210	1.20
		0.140	0.90
		0.105	0.74
		0.070	0.66

[a] All runs at constant ionic strength of 0.21 using addition of appropriate amount of lithium perchlorate.

Because a knowledge of the solvent isotope effect often provides valuable mechanistic insight, equivalent series of runs for both the 2:1 and 1:1 acetate–acetic acid buffers were also carried out in methanol-d_4 as solvent. The results of these runs are tabulated in the second portion of Table I.

Discussion

The Relative Importance of Specific Methoxide Ion and Acetate Ion Catalysis. Our first concern must be to determine to what extent the acceleration in the rate of exchange of methanol-d_3 with methyl *p*-toluenesulfinate (eq 8) brought on by acetate buffers is due to specific methoxide ion catalysis and to what extent it is due to either general base or nucleophilic catalysis by acetate ion. Figure 2A shows plots of the exchange rate constant, k_e, *vs.* acetate ion concentration for the runs in methanol-d_3 in 2:1 and 0.735:1 AcO^-–AcOH buffers. Figure 2B shows similar plots for the runs in 2:1 and 1:1 acetate–acetic acid buffers in methanol-d_4 as solvent. One sees that in each instance the plot of k_e *vs.* [AcO^-] is linear but that the intercept of the plot of the k_e axis is significantly different than zero, suggesting that a substantial portion of the observed exchange rate is due to a specific methoxide ion catalyzed term. That the observed intercepts are indeed due to such a term is confirmed by the fact that in both solvents the magnitude of the intercepts increases in a fashion directly proportional to the increase in the AcO^-–AcOH buffer ratio. Thus, for the runs in methanol-d_3 the intercept for the runs in buffers where [AcO^-]/[AcOH] = 2.0 is 1.13×10^{-6} sec^{-1}, or 2.6 times the intercept (0.43×10^{-6} sec^{-1}) for the runs in the [AcO^-]/[AcOH] = 0.735 buffers. Similarly, in methanol-d_4 the runs in the 2:1 [AcO^-]–[AcOH] buffers give an intercept (0.74×10^{-6} sec^{-1}) which is 2.1 times larger than the intercept (0.36×10^{-6} sec^{-1}) for the runs in the 1:1 AcO^-–AcOH buffers.

However, although these results clearly demonstrate that in the acetate buffers a part of the exchange rate for eq 8 is due to a specific methoxide ion catalyzed term, the obvious linear increase in k_e with [AcO^-] evident upon examination of the plots in Figure 2 shows that an acetate ion catalyzed term also makes a significant contribution to the total exchange rate. In other words, k_e appears to be given by the expression shown in eq 10, where K_{MeOH} is the autoprotolysis constant

$$k_e = k_{OMe}[MeO^-] + k_{OAc}[AcO^-] \quad (9)$$

$$k_e = k_{OMe}\left(\frac{K_{MeOH}}{K_a^{AcOH}}\right)\frac{[AcO^-]}{[AcOH]} + k_{OAc}[AcO^-] \quad (10)$$

of methanol and K_a^{AcOH} is the acid dissociation constant of acetic acid in methanol.

Table II gives the values of k_{OAc} and $k_{OMe}(K_{MeOH}/K_a^{AcOH})$ for the various reaction conditions as calculated from the slopes and intercepts of plots of the type shown in Figure 2.

Table II. Rate Constants for the Exchange of Methanol-d_3 and -d_4 with Methyl *p*-Toluenesulfinate in Acetate Buffers[a]

Solvent	[AcO^-]/[AcOH]	$k_{OMe}\left[\frac{K_{MeOH}}{K_a^{AcOH}}\right] \times 10^6$, sec^{-1}	$k_{OAc} \times 10^6$, M^{-1} sec^{-1}
CD_3OH	2.0	0.57	8.1
	1.0	0.54	6.2
	0.735	0.58	5.9
CD_3OD	2.0	0.37	5.9
	1.0	0.36	4.0

[a] All data for 62°.

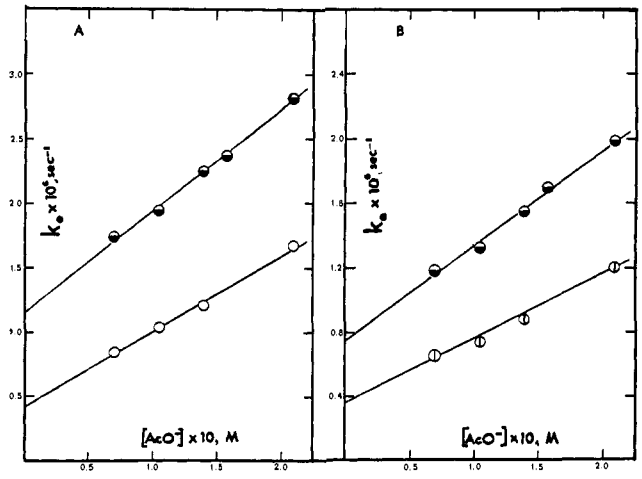
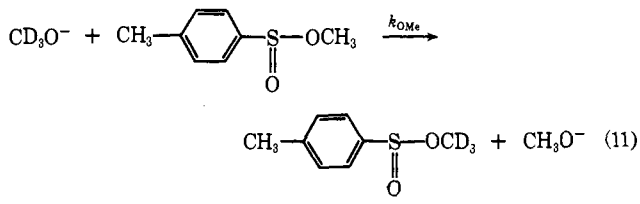
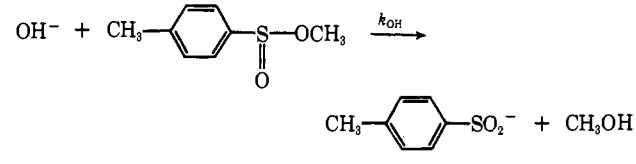


Figure 2. (A) Plot of k_e for exchange of methyl *p*-toluenesulfinate with methanol-d_3 *vs.* [AcO^-] in 2:1 (◒) and 0.735:1 (○) acetate–acetic acid buffers. (B) Plot of k_e for exchange of methyl *p*-toluenesulfinate with methanol-d_4 *vs.* [AcO^-] in 2:1 (◒) and 1:1 (◐) acetate–acetic acid buffers.

The reported[11] value of (K_{MeOH}/K_a^{HOAc}) for CH_3COOH in CH_3OH is 4×10^{-8} M. Since essentially the same value should apply for acetic acid in CD_3OH, one can calculate from the data in Table II that for the reaction



k_{OMe} has a value of 15 M^{-1} sec^{-1} at 62° in CD_3OH as solvent. Since Bunton and Hendy[12] have reported that the rate constant, k_{OH}, for reaction of hydroxide ion with the same ester in 60% dioxane at 0° is 4 M^{-1}



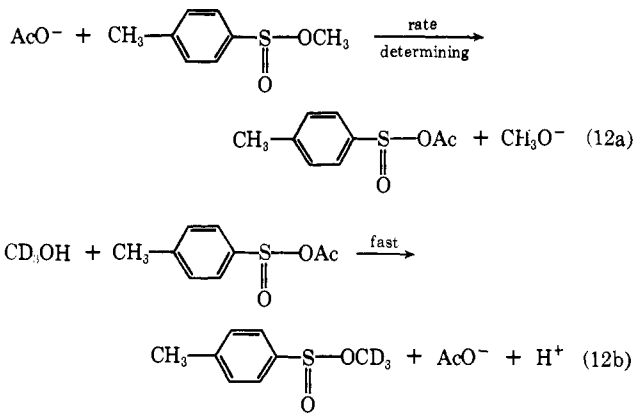
sec^{-1}, the value calculated for k_{OMe} from the data in Table II seems a most reasonable one, which further reinforces the earlier conclusion that the intercepts on the k_e axis in the plots in Figure 2 are indeed due to the specific methoxide catalyzed exchange reaction depicted in eq 11.

Catalysis by Acetate Ion. General Base or Nucleophilic? Having established that a term of the type $k_{OAc}[AcO^-]$ makes a sizable contribution to k_e, we must now determine whether this represents general base or nucleophilic catalysis by acetate ion.

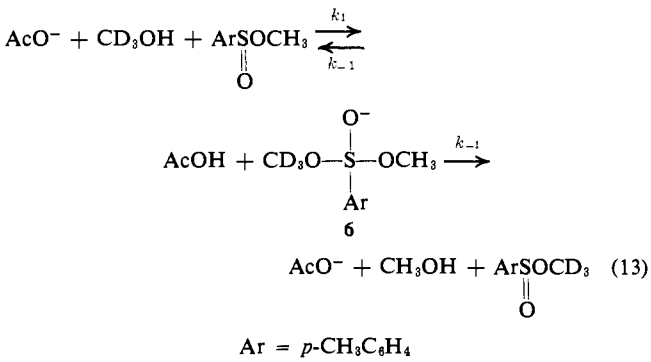
As a general rule one does not normally find that one oxygen anion can act effectively as a nucleophilic catalyst for a reaction in which in the key step it must displace another oxygen anion of much greater basicity.[13]

(11) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, p 44.
(12) C. A. Bunton and B. N. Hendy, *J. Chem. Soc.*, 2562 (1962).
(13) See, for example, W. P. Jencks, "Catalysis in Chemistry and Enzymology," McGraw-Hill, New York, N. Y., 1969, pp 510–512.

Since methoxide ion is a much stronger base than acetate it accordingly seems inherently rather unlikely that nucleophilic catalysis by acetate *via* the reaction sequence shown in eq 12 could be responsible for the catalysis of the exchange by acetate ion.



Measurement of solvent isotope effects can often provide a means of distinguishing nucleophilic from general base catalysis. Past experience indicates that reactions involving nucleophilic catalysis by carboxylate ions usually exhibit solvent isotope effects reasonably close to unity.[14] On the other hand, the solvent isotope effects which have been observed for reactions involving general base catalysis by carboxylate ions are all considerably larger, values ranging from 1.7 to 2.7 having been reported.[15a] Consequently, if the acetate-catalyzed exchange of methanol-d_3 with methyl *p*-toluenesulfinate involves the general base catalyzed mechanism shown in eq 13 one would presumably expect ($k_{OAc}^{MeOH}/k_{OAc}^{MeOD}$) to be greater than 1.7, since



a proton transfer is part of the rate-determining step. In contrast, if the acetate-catalyzed reaction involves the nucleophilic catalysis mechanism shown in eq 12, ($k_{OAc}^{MeOH}/k_{OAc}^{MeOD}$) should be much smaller, and most likely somewhere close to 1.0.

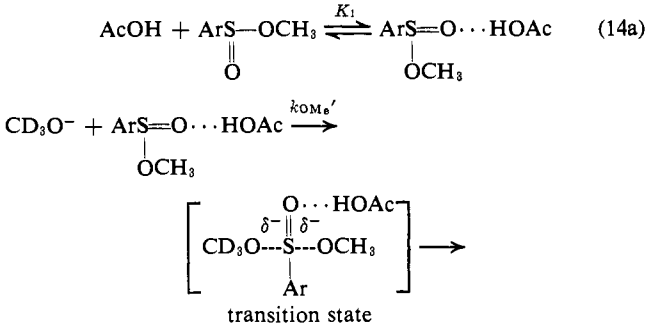
The actual measured solvent isotope effects associated with both k_{OAc} and $k_{OMe}(K_{MeOH}/K_a^{AcOH})$ in eq 10 are shown in Table III. One sees that the actual value of ($k_{OAc}^{MeOH}/k_{OAc}^{MeOD}$) = 1.4–1.5 is somewhat smaller than the minimum value one might have expected to find associated with the mechanism shown in eq 13 and somewhat larger than the most usual values observed for mechanisms involving nucleophilic catalysis by acetate, although, to be sure, one previous example believed to involve nucleophilic catalysis by acetate is known which has a solvent isotope effect of 1.5.[15a] However, as was pointed out earlier there are other fundamental considerations that make nucleophilic catalysis very unlikely as the probable mechanism for acetate catalysis in the present system.

Table III. Solvent Isotope Effects for the Rate Constants Associated with Equation 10

AcO⁻–AcOH buffer ratio	$\frac{[k_{OMe}(K_{MeOH}/K_a)]_{MeOH}}{[k_{OMe}(K_{MeOD}/K_a)]_{MeOD}}$	$\left(\frac{k_{OAc}^{MeOH}}{k_{OAc}^{MeOD}}\right)$
2:1	1.5 ± 0.1	1.4 ± 0.1
1:1	1.5 ± 0.1	1.5 ± 0.1

Where does this leave us with respect to the interpretation of the present results? One possibility, of course, is to assume that acetate catalysis does involve the general base catalyzed mechanism shown in eq 13 but that for some reason the solvent isotope effect associated with the process is smaller than those normally observed in analogous reactions involving carboxylic acid derivatives. To us this does not seem particularly attractive.[16] This is especially true since there is one further alternative which we feel seems considerably more plausible, particularly in view of the fact that the solvent isotope effects associated with k_{OAc} and $k_{OMe}\cdot(K_{MeOH}/K_a)$ have almost the same value.

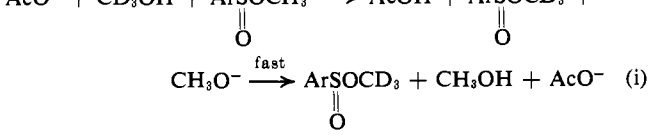
One must always remember that a process which formally exhibits general base catalysis may do so as a result of a combination of specific base catalysis accompanied by general acid catalysis. Bruice and Benkovic[8] have pointed out a mechanism of the specific base–general acid catalysis variety that could be written for a symmetrical exchange of an ester of the sort shown in eq 6 that would not involve an actual intermediate and would also not violate microscopic reversibility. For the exchange of the sulfinate ester (eq 8) this would have the form shown in eq 14. In this mechanism the rate-



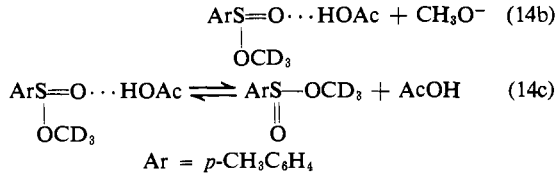
(14) The values of k_{H_2O}/k_{D_2O} which have been observed for various substitution reactions of carboxylic acid derivatives involving nucleophilic catalysis by either acetate or formate ions range from 0.80 to 1.5.[15a] For nucleophilic catalysis by acetate of a substitution at sulfonyl sulfur a k_{H_2O}/k_{D_2O} of 1.1 was observed.[15b]

(15) (a) S. L. Johnson, *Advan. Phys. Org. Chem.*, 5, 281 (1967); (b) J. L. Kice, G. J. Kasperek, and D. Patterson, *J. Amer. Chem. Soc.*, 90, 5516 (1969).

(16) We realize, in view of what Burwell and Pearson[9a] have pointed out, that a mechanism (eq i) kinetically equivalent to eq 13 but not



involving an intermediate is apparently also defensible and does not necessarily violate microscopic reversibility, as Johnson[7] had thought. However, such a mechanism would be expected to have a solvent isotope effect in the same range as eq 13, and is therefore no easier to rationalize with the observed (k_{MeOH}/k_{MeOD}) than is eq 13.



(14b)

(14c)

Ar = p-$CH_3C_6H_4$

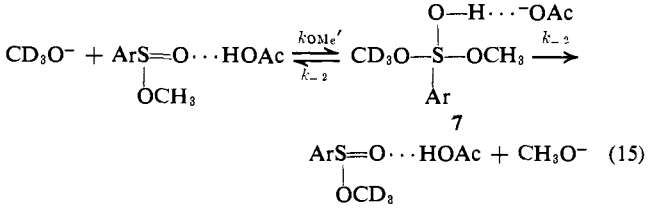
determining step of the acetate-catalyzed process is simply the attack of CD_3O^-, not on the sulfinate ester itself, but rather on the presumably more reactive hydrogen-bonded complex of the ester with a molecule of acetic acid.

If acetate catalysis involves the mechanism shown in eq 14 k_{OAc} in eq 10 would be given by $k_{OAc} = k_{OMe}'K_1(K_{MeOH}/K_a)$. Since it is unlikely that K_1 would be subject to a solvent isotope effect of any magnitude, and since k_{OMe}' for eq 14b could reasonably be expected to exhibit a solvent isotope effect very similar to that for k_{OMe} in eq 11, one can see that the mechanism in eq 14 could easily result in an overall solvent isotope effect for k_{OAc} closely similar in magnitude to that observed for the $k_{OMe}(K_{MeOH}/K_a)$ term in eq 10. This is, of course, what is observed experimentally (Table III).

We recognize the possible fallibility of mechanistic deductions based on solvent isotope effects in a solvent that is not as well understood in an isotopic sense as is water. However, we feel that the *similarity* in the solvent isotope effects for $k_{OMe}(K_{MeOH}/K_a)$ and k_{OAc} is too striking not to be given careful consideration when attempting to assign a mechanism to the acetate-catalyzed reaction, especially when a mechanism involving a rate-determining reaction of methoxide with a hydrogen-bonded complex of the ester and acetic acid would *a priori* presumably be expected to have a solvent isotope effect very close to that for $k_{OMe}(K_{MeOH}/K_a)$ and alternatives such as eq 13 would not.

It is also important to point out that given the magnitude of (K_{MeOH}/K_a), $k_{OMe}'K_1$ need have a value of only about 150 M^{-2} sec^{-1} in order to reproduce the values of k_{OAc} observed in Table II. Since K_1 is not likely[7] to have a value smaller than 0.01, and, given the strong tendency of sulfinyl groups to hydrogen bond to suitable donors, may well have a value which is significantly larger than this, k_{OMe}' is not required to have an inordinately large value for a second-order rate constant. The mechanism therefore seems a reasonable one on all counts and one which would appear, in our opinion, to be more readily compatible with all of the experimental data than the alternative shown in eq 13.

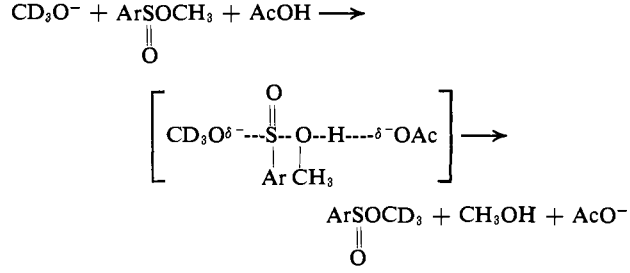
In eq 14b we have written the reaction of CD_3O^- with the hydrogen-bonded complex of the ester and acetic acid as involving synchronous formation and cleavage of the two oxygen–sulfur bonds. Actually, our data are probably also compatible with the presence of an intermediate **7** on the path for this reaction, as shown in eq 15, even though some might feel that if **7** were being



(15)

formed k_{OMe}' would exhibit a significantly larger solvent isotope effect than that for eq 14b, because an actual proton transfer occurs in forming **7**, and, therefore, that the overall solvent isotope effect for k_{OAc} would be larger than what is observed experimentally. However, as Jencks[17] has pointed out, in proton transfers of the type depicted in eq 15 one may frequently get abnormally small isotope effects.

It would also *perhaps* be legitimate, in view of what Burwell and Pearson[9a] have said, to have an unsymmetrical mechanism for the exchange involving specific base plus general acid catalysis, such as the following



Whether such a mechanism would be compatible with the observed solvent isotope effect for the acetate-catalyzed reaction is certainly open to conjecture, however.

There is one further point that merits comment. In Table II one notes that in both CD_3OH and CD_3OD as solvents the values of k_{OAc}, as determined from a plot of k_e *vs.* [AcO^-], increase somewhat with an increasing AcO^-–AcOH buffer ratio. In considering a possible reason for this it is interesting to consider the following. If the equilibrium constant, K_1, for formation of the hydrogen-bonded sulfinate ester–acetic acid complex were actually large enough so that at the higher acetic acid concentrations a significant fraction of the total sulfinate ester were to be present as the complex, and if the two important reaction pathways for exchange are eq 11 and 14, then k_e would be given, not by eq 10, but by the modified expression

$$k_e(1 + K_1[AcOH]) = k_{OMe}\left(\frac{K_{MeOH}}{K_a}\right)\frac{[AcO^-]}{[AcOH]} + k_{OMe}'K_1\left(\frac{K_{MeOH}}{K_a}\right)[AcO^-] \quad (16)$$

If one assumes, for example, a value for K_1 of 1.0 and replots the data in Table I for different buffer ratios according to eq 16, one finds adequately linear plots of $k_e(1 + K_1[AcOH])$ *vs.* [AcO^-] for all buffer ratios. While the intercepts of these plots at [AcO^-] = 0.00 M, *i.e.*, $k_{OMe}(K_{MeOH}/K_a)[AcO^-]/[AcOH]$, have essentially the same values in each case as they did when the data were plotted according to eq 10, the slopes, $k_{OAc} = k_{OMe}'K_1(K_{MeOH}/K_a)$, are larger and the effect is greater the smaller the AcO^-–AcOH buffer ratio. The net result is that k_{OAc} now shows much less variation with buffer ratio than in Table II. Since we do not know whether a value for K_1 of 1.0, or slightly larger, is realistic, we cannot really say whether this represents the proper explanation for the variation that k_{OAc} exhibits with buffer ratio when the data are plotted according to eq 10. However, given the other aspects of the data which have led us to conclude that a reaction involving the sulfinate–acetic acid complex was important in the exchange, it is certainly an intriguing possibility.

(17) W. P. Jencks, "Catalysis in Chemistry and Enzymology," McGraw-Hill, New York, N. Y., 1969, pp 231–239, 267.

The Question of an Intermediate on the Reaction Path. We have seen that the symmetrical exchange of a sulfinate ester shown in eq 8 is subject to catalysis by added acetate ion and that this almost certainly formally represents general base rather than nucleophilic catalysis.

We noted in the introductory statement that, for the reasons first enunciated by Burwell and Pearson,[9a] a finding of general base catalysis in a symmetrical exchange reaction does not necessarily constitute, as Johnson[7] had thought, definitive proof of the existence of an intermediate on the reaction coordinate. However, were the other data for the present exchange more readily compatible with a mechanism involving simple general base catalysis such as that shown in eq 13, we would at least feel that the data could be considered *suggestive* of the presence of an intermediate like **6** on the reaction path. Unfortunately, though, the results seem to accord better with the idea that the methyl *p*-toluenesulfinate–CD_3OH system is one of those where the observed general base catalysis is actually a combination of specific base–general acid catalysis. Assuming this type of mechanism, we do not feel that eq 14b accommodates the experimental data enough better than eq 15 that one can draw any firm conclusion as to whether the exchange step does or does not involve an intermediate, although those who are particularly partisan to concerted mechanisms (eq 1) for simple substitutions at sulfinyl sulfur may feel otherwise.

Experimental Section

Preparation and Purification of Materials. Methyl *p*-Toluenesulfinate was prepared by the method described by Bunton and Hendy.[12] The crude product was purified by distillation under reduced pressure. **Methanol-d_4** (99% D) was obtained from Brinkmann Instruments and rendered completely anhydrous by being distilled from magnesium methoxide-d_3 before use.[18] **Methanol-d_3**, CD_3OH, was prepared from methanol-d_4 in the following manner. Methanol-d_4, 7.5 ml (0.185 mol), was added to 56 ml (3.1 mol) of distilled water and the resulting solution was fractionally distilled using a spinning-band column. The recovered methanol, bp 63–65°, was added to a second 56-ml portion of water and the resulting solution again fractionally distilled through the spinning-band column. There was obtained 6.2 ml of methanol-d_3, bp 63–65°. Before use this was then dried by the same procedure[18] using magnesium employed for the methanol-d_4. **Acetic acid** was dried by distillation from acetyl borate using the procedure described by Wiberg,[19] bp 117–118°.

Sodium acetate was recrystallized from anhydrous methanol, dried at 125° for several hours, and stored in a desiccator until use.

Lithium perchlorate (K & K Instruments) was used without further purification.

Procedure for Kinetic Runs. Acetic acid–sodium acetate buffers were prepared in either methanol-d_3 or -d_4 by dissolving the appropriate amounts of acetic acid and sodium acetate in these solvents. Stock solutions of lithium perchlorate in each of the two solvents were also prepared. To carry out a run an appropriate amount of methyl *p*-toluenesulfinate was weighed into a 1-ml volumetric flask, dissolved in either methanol-d_3 or -d_4, as appropriate, the requisite amount of acetic acid–acetate buffer and lithium perchlorate stock solution added by micropipet, and the entire solution made up to volume with methanol-d_3 or -d_4. The final solution was transferred to several nmr tubes.

All the kinetic data were obtained using a Varian HA-100 nmr spectrometer. For the methanol-d_4 runs a benzene-filled capillary (δ 7.20) was used as an external reference; in the runs in methanol-d_3 the hydroxyl group proton of the alcohol (δ 4.81) was employed as an internal reference. Because the rates of reaction were slow in each case the reactions were followed by placing the nmr tubes containing the solution of the sulfinate ester in a constant temperature oil bath set at 62.0°, and then removing a tube at an appropriate time in order to run a series of nmr scans and integrations in the HA-100 spectrometer. Since the probe temperature of the spectrometer was appreciably lower than the bath temperature, and since the reactions were all quite slow even at 62°, no significant reaction occurred during the time that the tube was out of the bath and the measurements were being made in the spectrometer. The tube was replaced in the oil bath after a set of measurements had been made. Elapsed total reaction times were corrected for the time each tube spent out of the bath in the spectrometer.

Scans were taken over a sweep width of 250 Hz and three–five integrations were obtained on each peak of interest. The average value of the integral was then used in subsequent calculations. The important signals in the sweep range of interest were as follows: (1) a singlet at δ 3.46 due to the CH_3O group of methyl *p*-toluenesulfinate which decreased in intensity as the reaction progressed; (2) a signal centered at δ 3.34 due to incomplete deuteration of some of the methyl groups in the methanol-d_3 (or -d_4) solvent plus any CH_3OH (or CH_3OD) liberated in the course of the reaction (the intensity of this signal increased as the reaction progressed); (3) a singlet at δ 2.41 due to the para tolyl methyl group of the sulfinate ester; and (4) a signal at δ 1.92 due to the methyl groups of the acetic acid and sodium acetate. The amount of $CH_3OS(O)C_6H_4$-CH_3-*p* remaining at a given time was estimated either from (a) the ratio of the intensities of the integrals for the CH_3O group at δ 3.46 and the tolyl methyl group at δ 2.41 or from (b) the ratio of the intensities of the integrals for the CH_3O group of the sulfinate ester and the methyl groups of the acetate and acetic acid at δ 1.92. Either method gave the same result.

In several runs that were allowed to proceed to completion the final intensity of the CH_3O signal at δ 3.46 was too small to give a measurable integral. This would be expected given the initial ratios of methyl *p*-toluenesulfinate and methanol-d_3 or -d_4 used. At the beginning and end of these and the other runs 1000-Hz sweep width spectra were run to check for the appearance of new peaks which would be indicative of the occurrence of side reactions. No such peaks were noted.

(18) K. B. Wiberg, "Laboratory Technique in Organic Chemistry," McGraw-Hill, New York, N. Y., 1960, p 242.
(19) See ref 18, p 249.