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Simultaneous Occurrence of Solvent Reorganization and Heavy-Atom Reorganization in a Transmethylation Transition State[1]

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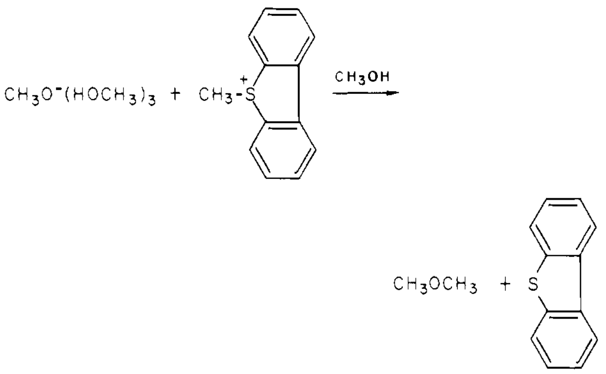
Abstract: The methylation of methoxide anion by *S*-methyldibenzothiophenium cation in methanol solution from 10 to 25°C (ionic strength 0.100), and in binary mixtures of methanol-*h* and methanol-*d* at 25 °C, exhibits (a) a carbon isotope effect at transferring methyl, $k_{12}/k_{13} = 1.072 \pm 0.006$ (10 °C), 1.072 ± 0.007 (20 °C), 1.080 ± 0.011 (25 °C), (b) an α-deuterium secondary isotope effect at transferring methyl, $k_{3H}/k_{3D} = 0.996 \pm 0.006$ (10 °C), 0.994 ± 0.008 (20 °C), 0.972 ± 0.012 (25 °C), and (c) a solvent isotope effect, $k_{CH_3OD}/k_{CH_3OH} = 2.04$, with the data in mixtures being consistent with transition-state solvation models involving any number of solvent hydrogen bonds to transition-state sites. The results require a transition state with substantial amounts of both C–S bond fission and C–O bond formation and with reorganization of the initial-state solvation structure being considerably advanced but still incomplete. Specific salt effects are observable and are treated by a modified Setschenow formulation.

The transfer of an intact methyl group,[2-4] exemplified by the reaction of eq 1, is an interesting process for two different kinds



(1)

of reasons. First, transmethylation is one of the simplest heavy-atom (i.e., non-hydrogen) group-transfer reactions and is therefore a sort of paradigm for mechanistic studies of such reactions.[5-15] Although the transferring group is itself of simple structure and the bonding features less complicated than for groups containing elements like silicon, phosphorus, or sulfur, the overall reaction nevertheless involves a number of changes in bonding, geometric structure, and solvation. The degree of coordination, if any, among these changes during the course of the displacement is a difficult current question in solution chemical dynamics.[2] Second, in biochemistry, transmethylation appears to hold a place of profound importance in the regulation of a number of processes of varied character.[3,4] The enzymes that catalyze the corresponding transmethylation reactions are highly effective (catalytic acceleration factors around 10^{16}), and the origins of their catalytic power are currently under study.[3,4,16-20] Here the two fields of interest converge, for the enzymes must derive their catalytic power by taking advantage of the *chemical opportunities for catalysis* that are presented by the mechanistic features of the substrate reaction.[20] An understanding of these features, in rather complete detail, is therefore a prerequisite for development of an adequate account of the catalysis of transmethylation.

In the reaction of eq 1, which is the subject of this paper, we select several of the changes that occur in the overall reaction and then determine as well as possible what the status of each change is in the rate-determining transition state(s). These changes are (1) the fission of the C–S bond, (2) the formation of the C–O bond, and (3) the loss of the three methanol molecules that solvate the methoxide ion as it is transformed to dimethyl ether. We will make use of the $^{12}CH_3/^{13}CH_3$, or "C-13", and CH_3/CD_3, or "α-3D", kinetic isotope effects to illuminate the degrees of C–S fission and C–O formation.[16-19]

The C-13 isotope effect tends to measure the importance of concerted fission of the C–S bond and formation of the C–O bond. If these two processes occur concertedly so that the carbon has considerable amplitude in the reaction coordinate, substantial normal C-13 effects should be seen (see Figures 4c and 5d in Rodgers, Femec, and Schowen[19]). For example, even "asymmetric" transition states with a strong bond to either sulfur or oxygen but not to the other should generate C-13 effects around 1.01–1.04. More "symmetric" transition states should produce effects of 1.06–1.09, depending on total bond order at carbon. If the carbon is not involved in reaction-coordinate motion, effects near 1.00 or the equilibrium effect[19] (~0.98) should be observed.

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[2] Albery, W. J.; Kreevoy, M. M. *Adv. Phys. Org. Chem.* **1978**, *16*, 87-147.

[3] Borchardt, R. T., Creveling, C. R., Usdin, E., Eds., "Transmethylation"; Elsevier: New York, 1978.

[4] Borchardt, R. T., Creveling, C. R., Usdin, E., Eds. "Biochemistry of *S*-Adenosylmethionine and Related Compounds"; MacMillan: New York, 1982.

[5] Abraham, M. H.; Nasehzadeh, A. *J. Chem. Soc., Chem. Commun.* **1981**, 905.

[6] Arnett, E. M.; Reich, R. *J. Am. Chem. Soc.* **1980**, *102*, 5892.

[7] Blandamer, M. J.; Robertson, R. E.; Golding, P. D.; MacNeil, J. M.; Scott, J. M. V. *J. Am. Chem. Soc.* **1981**, *103*, 2415.

[8] Harris, J. M.; Paley, M. S.; Prasthofer, T. W. *J. Am. Chem. Soc.* **1981**, *103*, 5915.

[9] Kevill, D. N. *J. Chem. Soc., Chem. Commun.* **1981**, 421.

[10] Knier, B. L.; Jencks, W. P. *J. Am. Chem. Soc.* **1980**, *102*, 6789.

[11] Kurz, J. L.; Lee, J. *J. Am. Chem. Soc.* **1980**, *102*, 5427.

[12] Kurz, J. L.; Lee, J.; Rhodes, S. *J. Am. Chem. Soc.* **1981**, *103*, 7651.

[13] McKenna, J.; Sims, L. B.; Williams, I. H. *J. Am. Chem. Soc.* **1981**, *103*, 268.

[14] Viers, J. W.; Schug, J. C.; Seeman, J. I. *J. Am. Chem. Soc.* **1982**, *104*, 85.

[15] Yamataka, H.; Ando, T. *J. Am. Chem. Soc.* **1979**, *101*, 266.

[16] Mihel, I.; Knipe, J. O.; Coward, J. K.; Schowen, R. L. *J. Am. Chem. Soc.* **1979**, *101*, 4349-51.

[17] Gray, C. H.; Coward, J. K.; Schowen, K. B.; Schowen, R. L. *J. Am. Chem. Soc.* **1979**, *101*, 4351-58.

[18] Hegazi, M. F.; Borchardt, R. T.; Schowen, R. L. *J. Am. Chem. Soc.* **1979**, *101*, 4359-65.

[19] Rodgers, J.; Femec, D. A.; Schowen, R. L. *J. Am. Chem. Soc.* **1982**, *104*, 3263-68.

[20] Stein, R. L.; Quinn, D. M.; Schowen, R. L. *Proc. Symp. Mol. Cell. Reg. Enz. Act.* in press.

0002-7863/83/1505-1951$01.50/0

The α-3D effect measures the overall "tightness" of the transition state. If both C–O and C–S bonds are long and weak, $k_{3H}/k_{3D} > 1$; if both bonds are short and strong, $k_{3H}/k_{3D} < 1$; if the total bonding to the methyl is about equal to that in the reactant, $k_{3H}/k_{3D} \sim 1$.

The solvent isotope effect (k_{CH_3OH}/k_{CH_3OD}) should measure the degree of solvent reorganization at the transition state. The average fractionation factor for a methanol molecule solvating a methoxide ion ("reactant", R) is known from NMR studies[21-24] to be 0.74 ± 0.02 ($= \phi_R \equiv \{([CH_3OD]_R/[CH_3OH]_R)/([CH_3OD]bulk/[CH_3OH]bulk)\}$). This means[25,26] that the complete liberation of one molecule of solvation from a methoxide ion back to the bulk solvent will produce a contribution to the solvent isotope effect of k_{ROD}/k_{ROH} of 1.35 ± 0.04. Furthermore, the equilibrium solvent isotope effect for addition of methoxide ion[27] or ethoxide ion[28] to nitroaromatic compounds to produce Meisenheimer complexes (which have delocalized charge and are probably not strongly and specifically solvated) are just the cube of 1.35: 2.63 for methoxide ion,[27] 2.53 for ethoxide ion.[28] This demonstrates that the (k_{CH_3OH}/k_{CH_3OD}) solvation number of the methoxide ion is 3.

Thus, for eq 1, we expect a kinetic solvent isotope effect k_{ROD}/k_{ROH} between 1.00 (no change in solvation between reactants and transition state) and 2.47 (complete release of all three reactant molecules of solvation, with no compensatory resolvation of the transition state). For the intermediate cases of partial desolvation, the proton-inventory approach, in which mixtures of CH_3OH and CH_3OD are used, may help in discerning the detailed character of the residual transition-state solvation.[26] For the reaction of eq 1, the appropriate Gross-Butler equation is that of eq 2 (n is the mole fraction of CH_3OD in binary isotopic

$$k_n = k_0[\prod_i^{TS}(1 - n + n\phi_{Ti})]/[(1 - n + n[0.74])^3] \quad (2a)$$

$$k_n[(1 - n + n[0.74])^3] = k_0[\prod_i^{TS}(1 - n + n\phi_{Ti})] \quad (2b)$$

$$k_n{\cdot}RSC(n) = k_0{\cdot}TSC(n) \quad (2c)$$

mixtures; RSC and TSC are the reactant-state and transition-state contributions, respectively). Because $k_n{\cdot}RSC(n)$ is known once $k_n(n)$ is determined, it can be used, as eq 2b and 2c suggest, in order to form an idea of the number of factors $(1 - n + n\phi_{Ti})$ that contribute to TSC(n). If this function is linear, one site contributes to TSC(n); more sites are indicated by increasing nonlinearity with an exponential form corresponding to a very large number of sites (generalized solvation).[26]

Results

General Kinetics and Salt Effects. First-order rate constants were determined by an automated spectrophotometric procedure[16,17,29] for the reaction of eq 1, sodium methoxide or lithium methoxide always being present in 38- to 144-fold excess over the sulfonium tetrafluoroborate salt concentration. The total salt concentration was maintained at a constant value of 0.100 M by addition of lithium perchlorate. Under such conditions, k_0 is not a linear function of the methoxide salt concentration, [$MOCH_3$] (Figure 1). Instead, the slope of the plot of k_0 vs. [$MOCH_3$] increases with [$MOCH_3$] so that if a linear dependence is forced upon the data small but definite negative intercepts at [$MOCH_3$] = 0 are calculated.[17]

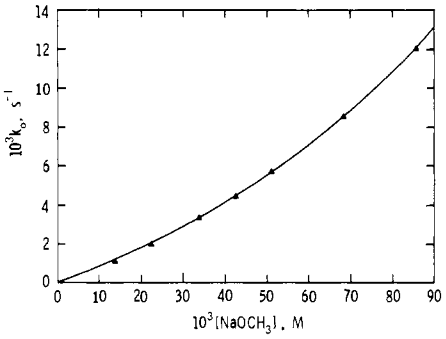

Figure 1. First-order rate constants for reaction of sodium methoxide and **1** as a function of sodium methoxide concentration in methanol solution at 10.00 ± 0.04 °C, with total salt concentration maintained at 0.100 M with added lithium perchlorate. The solid line is a plot of eq 7 with $I = 1 \pm 3 \times 10^{-3}$ s^{-1}, $k_2°A = 0.077 \pm 0.003$ M^{-1} s^{-1} and $B = 7.0$ M^{-1}. The parameters were obtained by a nonlinear least-squares fit.

A reasonable model for this behavior is one in which the activity coefficients of any or all of the reactant and transition states are taken to respond differentially to the concentrations of particular cations and anions.[30] Equation 3 gives the expected form of the

$$k_2 = k_2°\gamma_S\gamma_M/\gamma_T \quad (3)$$

second-order rate constant k_2, where γ_T, γ_S, and γ_M are the activity coefficients of the transition state, the sulfonium cation, and the methoxide anion, respectively, and $k_2°$ is the second-order rate constant at unit activity for all species. The simplest, completely empirical form for the γ's is that of Setschenow,[31] here modified as in eq 4 to make ln γ linear in the concentrations of the individual

$$\ln \gamma_X = \sum \alpha_{Xi} C_i \quad (4)$$

ions C_i, over all of which the sum is taken. The α_{Xi} are empirical coefficients that express the effect of ion i on species X (*negative* α_{Xi}: ion i "salts in" species X; *positive* α_{Xi}: ion i "salts out" species X). From electroneutrality and the constancy of the total salt concentration C_T, we obtain eq 5, where C_m is the concentration

$$\ln(\gamma_S\gamma_M/\gamma_T) = \ln A + BC_m \quad (5)$$

$$A = \exp[(\alpha_{Sr} + \alpha_{Su} + \alpha_{Mr} + \alpha_{Mu} - \alpha_{Tr} - \alpha_{Tu})C_T] \quad (5a)$$

$$B = (\alpha_{Sp} + \alpha_{Sm} - \alpha_{Sr} - \alpha_{Su}) + (\alpha_{Mp} + \alpha_{Mm} - \alpha_{Mr} - \alpha_{Mu}) + (\alpha_{Tr} + \alpha_{Tu} - \alpha_{Tp} - \alpha_{Tm}) \quad (5b)$$

of methoxide ion and A and B are constants. If the subscripts m and p denote methoxide ion and its counterion and the subscripts r and u the ions of the added salt, A and B are defined by eq 5a and 5b. This suggests the form of eq 6 for the dependence of the

$$k_0 = (k_2°A)[\exp(BC_m)]C_m \quad (6)$$

first-order rate constant k_0 on C_m. More generally, allowing for some reaction at $C_m = 0$, we write eq 7. The data were then fitted

$$k_0 = I + k_2°A[\exp(BC_m)]C_m \quad (7)$$

to eq 7 by a nonlinear least-squares technique[32] with each value of k_0 weighted by its variance ($w = \sigma^{-2}$). Values of I, $k_2°A$, and B were obtained with small standard deviations and small residual variances, suggesting an acceptable account of the data by eq 7.

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(21) More O'Ferrall, R. A. *J. Chem. Soc. D* **1969**, 114.

(22) Gold, V.; Grist, S. J. *J. Chem. Soc. B* **1971**, 1165.

(23) Al-Rarvi, J. M. A.; Bloxsidge, J. P.; Elvidge, J. A.; Jones, J. R.; More O'Ferrall, R. A. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1593.

(24) The value of the methoxide anion fractionation factor has also been determined by L. Baltzer (Doctoral Dissertation, University of Göteborg, 1981; see: Baltzer, L.; Bergman, N. A.; *J. Chem. Soc., Perkin Trans. 2* **1982**, 313.), who has also given a critical discussion of the preceding work. We shall use the value of 0.74 arrived at by Baltzer, although a more complex model is suggested by the results in ref 23. See also the recent work of Gold and Morris: Gold, V.; Morris, K. P. *J. Chem. Soc., Perkin Trans. 2* **1982**, 1615.

(25) Schowen, R. L. *Prog. Phys. Org. Chem.* **1972**, *9*, 275.

(26) Schowen, K. B. In "Transition States of Biochemical Processes"; Gandour, R. D., Schowen, R. L., Eds.; Plenum: New York, 1978.

(27) Bernasconi, C. F. *J. Am. Chem. Soc.* **1968**, *90*, 4982–88.

(28) Gold, B.; Toullec, J. *J. Chem. Soc., Perkin* Trans. *2* **1979**, 596–602.

(29) Rosenberg, S.; Kirsch, J. F. *Anal. Chem.* **1979**, *51*, 1379–83.

(30) Hammett, L. P. "Physical Organic Chemistry", 2nd ed.; McGraw-Hill: New York, 1970; p 187 ff.

(31) Setschenow, J. *Z. Phys. Chem.* (*Leipzig*) **1889**, *4*, 116. Cf.; Graze, G.; Osborne, R.; Kirby, A. J. *J. Chem. Soc., Perkin Trans. 2* **1978**, 357–68. Clark, G. A.; Taft, R. W. *J. Am. Chem. Soc.* **1962**, *84*, 2295.

(32) BMDPAR: "BMDP-79, Biomedical Computer Programs, P-Series"; Dixon, W. J., Brown, M. B., Eds.; University of California Press: Berkeley and Los Angeles, 1979.

Table I. Rate Constants[a] and Isotope Effects for Reaction of Methoxide Anion in Methanol with *S*-Methyldibenzothiophenium Cation ($\mu = 0.100$)

temp, °C	$10^4 k_2°A$, $M^{-1}\,s^{-1}$	methyl label	$10^5 I$, s^{-1}	isotope effects
10	769 ± 3	$[^{12}C(^1H)_3]^b$	1 ± 3	k_{12}/k_{13} = 1.072 ± 0.006
	772 ± 4	$[^{12}C(^2H)_3]^b$	1 ± 3	k_{3H}/k_{3D} = 0.996 ± 0.006
	717 ± 3	$[^{13}C(^1H)_3]^b$	1.4 ± 2.2	
20	2449 ± 10	$[^{12}C(^1H)_3]^c$	0.6 ± 0.4	k_{12}/k_{13} = 1.072 ± 0.007
	2465 ± 16	$[^{12}C(^2H)_3]^c$	0.6 ± 0.7	k_{3H}/k_{3D} = 0.994 ± 0.008
	2285 ± 12	$[^{13}C(^1H)_3]^c$	0.4 ± 0.5	
25	5252 ± 33	$[^{12}C(^1H)_3]^d$	9 ± 17	k_{12}/k_{13} = 1.080 ± 0.011
	5405 ± 59	$[^{12}C(^2H)_3]^d$	−45 ± 29	k_{3H}/k_{3D} = 0.972 ± 0.012
	4862 ± 40	$[^{13}C(^1H)_3]^d$	19 ± 20	

[a] See eq 7. Tabulated errors are standard deviations. [b] B = 7.00. [c] B = 6.00. [d] B = 4.00. The data used in these calculations are those of ref 6.

Best-fit values of B ranged from 5.3 to 7.2 M^{-1} with no systematic relationship to controlled variables for data sets including lithium and sodium as cations, methoxide, nitrate, and perchlorate as anions, $^{12}CH_3$-, $^{13}CH_3$-, and $^{12}C(^2H)_3$-labeled sulfonium substrates, binary mixtures of CH_3OH and CH_3OD as solvents with mole fractions of CH_3OD from 0.00 to 0.95, and temperatures from 10 to 25 °C. A value of $B = 6.00$ M^{-1} was therefore chosen and used as a constant in nearly all calculations. In a few cases, other values gave improved fits and were used; these are noted in the tables of results.

The resulting values of I are small, either positive or negative, and commonly within two standard deviations of zero. The relative standard deviations for $k_2°A$ range from 0.4 to 1.1%, with the average around 0.7%. The parameters I and $k_2°A$ also generally have a substantial covariance.

Substrate Isotope Effects. Table I gives the effect of ^{13}C and deuterium substitution in the transferring methyl group. The C-13 isotope effect is very substantial, around 7–8%. The α-3D effect is very close to unity, perhaps slightly inverse. No trend with temperature over this small range is discernible.

Activation Parameters. A fit of $k_2°A$ from Table I to the Eyring equation gives $\Delta H^* = 20.5 \pm 1.8$ kcal mol^{-1} and $\Delta S^* = +8.9 \pm 1.0$ eu for the ideal solution at 1 M concentrations as the standard state.

Solvent Isotope Effects. Rate constants for reactions in binary mixtures of CH_3OH and CH_3OD are shown in Table II. The reactions proceed slightly more than twice as fast in CH_3OD than in CH_3OH, the extrapolated value from the data of Table II being $k_{CH_3OD}/k_{CH_3OH} = 2.04$.

Discussion

Substrate Isotope Effects. The large C-13 isotope effect of 7–8% is close to the maximum expected for complete loss of the stretching vibration of the C–S bond at the transition state. Qualitatively this suggests a transition state with nearly equal bond orders to the entering oxygen and departing sulfur, a supposition that is confirmed by detailed model calculations.[19]

The absence or near absence of an α-deuterium secondary isotope effect indicates that the softening of the vibrational potential at the methyl hydrogens, expected from deparature of the sulfur and flattening of the methyl group, has been almost exactly compensated by the approach of the nucleophilic oxygen. This qualitative argument is also confirmed by the model calculations.[19]

The substrate isotope effects therefore show that (a) substantial C–S bond fission and (b) substantial C–O bond formation are definite features of this transmethylation transition-state structure. The results are not consistent with a model in which the activation process is generation of an appropriate reactant-like structure by reorganization of solvent molecules, with this process being followed by a rapid transfer of the methyl group.

Table II. Rate Constants[a] and Partial Solvent Isotope Effects for Reaction of Methoxide Anion with *S*-Methyldibenzothiophenium Cation in Binary Mixtures of Methanol-*h* and Methanol-*d* ($\mu = 0.100$) at 25.00 ± 0.04 °C

n^b	$10^4 k_2°A$, $M^{-1}\,s^{-1}$	$10^5 I$, s^{-1}	$[(k_2°A)_n/(k_2°A)_0]^c$
0.000	4685 ± 17	−11 ± 9	1.00
0.15_5	5025 ± 22	+1 ± 8	1.07
0.23_8	5573 ± 52	−65 ± 19	1.19
0.30_2	5813 ± 34	−63 ± 15	1.24
0.38_5	5914 ± 36	−9 ± 13	1.26
0.48_1	6461 ± 44	−31 ± 21	1.38
0.57_7	6792 ± 77	−21 ± 28	1.45
0.71_2	7429 ± 55	+28 ± 19	1.59
0.83_9	8427 ± 64	−12 ± 20	1.80
0.95_2	9393 ± 76	−77 ± 28	2.00

[a] See eq 7. B = 6.00 throughout. Tabulated errors are standard deviations. [b] Mole fraction of CH_3OD. [c] Relative standard deviations around ±1.5%.

Solvent Isotope Effects. The solvent isotope effect of $k_{CH_3OD}/k_{CH_3OH} \sim 2$ should be interpreted in the light of the expectation of an effect of around 1.4 for removal of each of the three solvating methanol molecules from the reactant methoxide ion (see introductory section). The observed effect roughly indicates that, in some sense, an average of two molecules of solvation have been lost at the transition state.

Proceeding from eq 2, we first used the factor $(1 - n + n[0.74])^3$ as RSC(n) and considered various models for TSC(n). Later we allowed the reactant fractionation factor to be different from 0.74. Unfortunately the magnitude of TSC(1) is too small (1/1.21) to allow a detailed delineation of transition-state structure with respect to solvation. The midpoint value of TSC(n), TSC(0.5), is predicted to be 1/1.11 if a single proton in the transition state produces the entire effect and 1/1.10 if a very large number of protons contribute. The experimental value is of course completely consistent with either model.

What is clear is that there is some residual solvation in the transition state that produces a normal isotope effect. Among the models that suggest themselves are the following:

(a) A generalized-solvation model in which the apparent TSC(1) = 1/1.21 is simply the resultant of reactant-state and transition-state solvation isotope effects or relative solubilities in CH_3OD/CH_3OH, while all three inner-shell molecules of solvation initially present about methoxide anion have been completely released in the transition state. This release would contribute an isotope effect $k_{CH_3OD}/k_{CH_3OH} = 2.47$ and the relative solubilities 1/1.21, for a resultant effect of 2.04. This model cannot be rigorously excluded, but it seems very doubtful. Isotopic solubility ratios[33] in HOH and DOD, for most compounds that do not interact by strong inner-shell forces with solvent, are very rarely as large as 1.2. Similar behavior is expected in methanol. This model would require the transition-state effect to *exceed* the reactant-state effect by a factor of 1.2, which seem unlikely. Certainly, if correct, it would require an unusual character of transition-state solvation.

(b) One molecule of solvation of the initial methoxide anion has departed completely (liberating a lone pair of electrons to accept the methyl group), and two molecules remain in the transition state, solvating the nucleophilic oxygen. Such a model generates TSC(n) = $(1 - n + n\phi_T)^2$ in eq 2. The best-fit value of ϕ_T is then 0.91. If one assumed a linear change with O--C bond order B_{OC} of the isotopic free-energy difference for molecules solvating the oxygen, i.e., $\ln \phi_T = (1 - B_{OC}) \ln (0.74)$ since the product ϕ value should be unity, then one would estimate from ϕ_T a transition-state C--O bond order $B_{OC} = 0.69$. This is not inconsistent with the carbon and hydrogen isotope effects. An argument favoring the model is that $\ln \phi_T$ may well *not* change

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(33) Jancso, G.; Van Hook, W. A. *Chem. Rev.* **1974**, *74*, 689. Spiegel, G. W. Ph.D. Thesis in Chemistry, Washington University, 1980 (courtesy of Professor J. L. Kurz).

in the indicated linear manner. Large fractionation factors for hydrogen bonds are observed only for quite strong bases such as hydroxide and methoxide anions. At a pK for the conjugate acid of about 9–10, unit factors are already observed.[34] This suggests a very quick fall-off of the isotope effect for solvation as basicity decreases. The estimate $B_{OC} = 0.69$ is thus a maximum estimate, and many reasonable transition-state structures with $B_{OC} < 0.69$ are consistent with the findings.

(c) Nucleophilic attack at methyl by one of the molecules of solvation, rather than by the methoxide anion itself:

$$CH_3O{\sim}{\sim}H{\sim}{\sim}O(CH_3){-}{-}{-}CH_3{-}{-}{-}S{<}$$

By the argument given above (probable nonlinear dependence on ln ϕ on pK for solvating molecules), ϕ_T could well be about unity for two of the initial molecules of solvation. The third hydrogen bond might well remain intact, however, serving in effect as a connecting link for transfer of negative charge to the nucleophilic oxygen. Such a model produces $\phi_T = 0.82$. Isotope effects substantially larger than this ($1/0.82 = 1.21$) are commonly observed for bridging protons in general acid–base catalyzed reactions[25,26] (note that this model corresponds to general base catalysis by methoxide ion of methanol attack at the methyl carbon). For this reason, we consider this model also to be relatively improbable.

Conclusions

The C-13 isotope effect of 1.07–1.08 shows that substantial C–S bond fission has occurred at the transition state. The absence or near absence of an α-3D secondary isotope effect shows that substantial C–O bond formation has occurred. The solvent isotope effect k_{CH_3OD}/k_{CH_3OH} of about 2 is large enough to show that very considerable desolvation of methoxide anion has been completed at the transition state, but the effect is short of the expected equilibrium effect of 2.47 for complete desolvation. Therefore solvent reorganization has proceeded to a large, but still quite incomplete, extent.

Models that can be excluded on the basis of these findings include (i) models in which solvent reorganization is the major activation step, with no C–O bond formation or C–S bond fission at the transition state, (ii) models in which C–S bond fission precedes C–O bond formation, in a separate reaction step, with either step rate determining, and (iii) models in which the initial-state solvation of the methoxide anion is maintained intact at the transition state.

Experimental Section

Materials. Methanol (Mallinckrodt analytical reagent grade) and methanol-O-d (Stohler Isotope Chemicals, 99% D) were dried with magnesium and distilled. Basic materials in these solvents, titratable by sulfuric acid, were present at ca. 10^{-4} M. These solvents were stored in sealed glass containers and kept in desiccators over calcium sulfate. The deuterium contents of the deuterated methanol solutions were determined by an NMR method. Sodium methoxide solutions were prepared by dissolution of clean sodium in cold methanol under nitrogen. These stock solutions were standardized with potassium hydrogen phthalate (Mallinckrodt analytical grade, dried at 120 °C). Lithium perchlorate (G. Frederic Smith, anhydrous reagent grade) was dried under vacuum and kept in a desiccator. S-Methyldibenzothiophenium tetrafluoroborate and its isotopic isomers were prepared as described originally by Acheson and Harrison[35] and later by Gray et al.[17] (treatment of CH_3I or its isotopic isomers with dibenzothiophene and silver tetrafluoroborate). Isotopic mixtures of methanol solvents were prepared gravimetrically. Sodium methoxide–lithium perchlorate reaction solutions were prepared by mixing appropriate weights of lithium perchlorate with known volumes of sodium methoxide stock solution in 50-mL volumetric flasks, followed by dilution. Total salt concentration was maintained at 0.100_0 M.

Kinetics. The data acquisition system, consisting of a Cary-118 spectrophotometer interfaced to a microcomputer, has been described elsewhere.[16-18,29] Stock solutions of substrate (7.5–7.8×10^{-2} M) were prepared fresh and kept cold on ice. Cuvettes containing 3.50 mL of the reaction solution were allowed to reach thermal equilibrium in the thermostated cell holder of the Cary-118. The reaction was initiated by injection of 20 μL of the substrate solution into the cuvette, and the increase in absorbance at 322 nm was monitored. First-order rate constants were obtained by a weighted, nonlinear least-squares fit of the data to an exponential function.

Registry No. Methoxide, 3315-60-4; S-methyldibenzothiophenium tetrafluoroborate, 29829-22-9; carbon-13, 14762-74-4; deuterium, 7782-39-0.

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[34] Schowen, K. B.; Schowen, R. L. *Methods Enzymol.* **1982**, *87*, 551.

[35] Acheson, R. M.; Harrison, D. R. *J. Chem. Soc.* **1970**, 1764.

Competition between Modes of Solvolytic Participation in Cyclopent-3-enyl Tosylate

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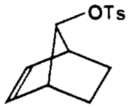
Abstract: Cyclopent-3-enyl tosylate has been prepared with a stereochemical proton label in order to distinguish the solvolytic pathways of double bond participation (substitution with retention) and solvent displacement (inversion). The product in either case has the same carbon skeleton as starting material. The modes may be distinguished by examination of the single 5-proton resonance in cyclopent-3-enyl-*1,2,2,3,4,(cis-5)*-d_6 tosylate. The reaction was found to proceed with inversion (solvent displacement) in acetic acid and in 70% 1,4-dioxane/water. In formic acid, however, the reaction occurs entirely with retention (double bond participation). The low nucleophilicity and high ionizing power of this solvent promote the retention pathway, previously thought not to occur in this structure. Participation by the double bond in this five-membered ring is slightly stronger than that in the analogous six-membered ring in formolysis.

The most spectacular example of intramolecular participation by double bonds[2] in solvolysis may be the 10^{11} acceleration found in the *anti*-7-norborn-2-enyl system **1**, which produces a bishomocyclopropenyl ion through symmetrical interaction of both ends of the double bond with the developing positive charge.[3] In contrast, the *exo*-2-norborn-5-enyl system **2** shows a slight rate



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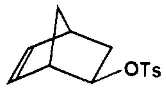

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[2] Hanack, M.; Schneider, H.-J. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 666–667.

0002-7863/83/1505-1954$01.50/0