Transition-State Structure for the Methoxide-Promoted Dechlorination of 1-Chloro-2,4-dinitrobenzene in Methanol[1]

Ganesa Gopalakrishnan[2] and John L. Hogg*

Department of Chemistry, Texas A&M University, College Station, Texas 77843

Received August 31, 1983

The transition-state structure for the methoxide-promoted dechlorination of 1-chloro-2,4-dinitrobenzene is suggested to involve methoxide-catalyzed attack of one of the three methanol molecules solvating the methoxide ion. Support for this transition state is presented in the form of proton inventory data. The observed inverse solvent deuterium isotope effect ($k_{CH_3OD}/k_{CH_3OH} = 2.01$) is suggested to arise from three reactant-state contributions and three transition-state contributions. The downwardly curved proton inventory is reproduced by $k_n = 2800 (1 - n + 0.89n)^3/(1 - n + 0.70n)^3$. Activation parameters and the variation of the isotope effect in methanol and methanol–acetonitrile mixtures are reported and also support a transition state involving methoxide-promoted attack of a solvating methanol molecule.

The general understanding at present is that most or all nucleophilic substitutions at activated aromatic rings proceed through an intermediate tetrahedral complex so that at least two transition states (for the formation and decomposition of the intermediate) occur along the reaction path and either of the two transition states may be rate limiting.[3-12] The first (TS_1) and the second (TS_2) transition states are alike in general structure and more nearly resemble the intermediate complex in energy than either initial or final states.[13,14] The great majority of S_NAr reactions involving good leaving groups follow the addition–elimination path with TS_1 as the rate-limiting transition state rather than TS_2, and a large body of evidence has been accumulated in favor of this. However, the ion-pair reactivities observed recently in ethoxy dechlorination of certain activated aromatic compounds with good leaving groups paint a different picture and favor TS_2 as the rate-limiting transition state.[15]

If TS_1 is rate limiting, kinetic nucleophilicity involves bond formation by the nucleophile without rupture of the bond to the leaving group. Thus, factors consequent on the latter process have no influence. If the formation of TS_2 is rate limiting, however, factors influencing bond rupture will be directly involved. This situation resembles that in reactions passing through a single transition state.[12]

A considerable kinetic solvent isotope effect is observed in almost all S_NAr reactions involving alkoxide ions. However, it has neither been studied extensively nor been used to delineate the structure of the rate-limiting transition state or to decide between the two possible transition states. Since the solvation requirements of the two transition states are different, we felt that proton inventory studies could help us in pinpointing the nature and structure of the rate-limiting transition state.

Table I. Comparison of the Observed Rate Constants k_2^n for the Methoxy Dechlorination of 1-Chloro-2,4-dinitrobenzene in CH_3OH-CH_3OD Mixtures of Atom Fraction of Deuterium (n) at 30 ± 0.05 °C with Rate Constants k_2^n Calculated from eq 6, 9, and 13

	$10^5k_2^n$, M^{-1} s^{-1}	$10^5k_2^n$, M^{-1} s^{-1} (calcd)		
n	(obsd)[a]	eq 6[b]	eq 9[c]	eq 13[d]
0.000	2800 ± 6	2800	2800	2800
0.248	3237 ± 16	3261	3246	3239
0.495	3786 ± 13	3862	3821	3811
0.743	4548 ± 12	4635	4585	4578
0.990[e]	5630 ± 19	5665	5631	5631

[a] Each value is the average of five runs and errors are standard deviations. [b] Calculated by using $\phi_{RS} = 0.70$ in eq 6. [c] Calculated by using $\phi_{RS} = 0.70$ and $\phi_{TS} = 0.83$ in eq 9. [d] Calculated by using $\phi_{RS} = 0.70$ and $\phi_b = 0.89$ in eq 13. [e] Atom fraction of deuterium in "100%" deuterated methanol as determined by Josef Nemeth.[42]

Table II. Solvent Composition Dependence of the First-Order Rate Constants and of the Kinetic Solvent Isotope Effect for the Methoxy Dechlorination of 1-Chloro-2,4-dinitrobenzene at 25 ± 0.05 °C

solvent composition[a] CH_3OL-CH_3CN (L = H or D)	$10^6k_1^H$, s^{-1}	$10^6k_1^D$, s^{-1}	k_1^D/k_1^H
100-0	844 ± 5[b]	1743 ± 7	2.07 ± 0.01
80-20	1462 ± 4	2886 ± 39	1.97 ± 0.03
60-40	2665 ± 10	5014 ± 9	1.88 ± 0.01
40-60	5846 ± 23	8116 ± 7	1.39 ± 0.01
20-80[c]	11163 ± 34	13620 ± 12	1.22 ± 0.01

[a] Solvent composition is reported as the volume percentage before mixing. [b] Average of two runs for each solvent system. [c] Concentration of methoxide was 0.025 M. In all other runs it is 0.05 M.

Results

Pseudo-first-order rate constants k_{obsd} for the nucleophilic substitution of methoxide ion on 1-chloro-2,4-dinitrobenzene (CDNB) have been measured by using different concentrations of sodium methoxide in several CH_3OH-CH_3OD mixtures at 30 °C. In each case the reaction exhibited a first-order dependence on methoxide ion concentration and a neglible (or zero) rate at zero concentration of methoxide. This is revealed by the linear least-square fit of k_{obsd} to eq 1 with k_{spon} (i.e., the rate

$$k_{obsd} = k_{spon} + k_{MeO^-}[MeO^-] \qquad (1)$$

constant of the spontaneous reaction) equal to zero. Values of k_{MeO^-} (hence forth known as k_2^n) at different atom

---

[1] This research was supported by the Robert A. Welch Foundation.

[2] On leave from the Department of Chemistry, Presidency College, Madras, India.

[3] Bunnett, J. F.; Zahler, R. E. *Chem. Rev.* **1951**, *49*, 273.

[4] Bunnett, J. F. *Q. Rev. Chem. Soc.* **1958**, *12*, 1.

[5] Bunnett, J. F.; Randall, J. J. *J. Am. Chem. Soc.* **1958**, *80*, 6020.

[6] Ross, S. D. *Progr. Phys. Org. Chem.* **1963**, *1*, 31.

[7] Ross, S. D. In "Comprehensive Chemical Kinetics"; Bamford, C. H., Tipper, C. F. H., Ed.; Elsevier: New York, 1972, Vol. 13.

[8] Bunnett, J. F.; Garst, R. H. *J. Am. Chem. Soc.* **1965**, *87*, 3879.

[9] Bunnett, J. F.; Bernasconi, C. F. *J. Am. Chem. Soc.* **1965**, *87*, 5209.

[10] Hart, C. R.; Bourns, A. N. *Tetrahedron Lett.* **1966**, 2995.

[11] Coniglio, B. O.; Giles, D. E.; McDonald, W. R.; Parker, A. J. *J. Chem. Soc. B* **1966**, 152.

[12] Miller, J. "Aromatic Nucleophilic Substitution"; Elsevier: New York, 1968.

[13] Miller, J. *J. Am. Chem. Soc.* **1963**, *85*, 1628.

[14] Hill, D. L.; Ho, K. C.; Miller, J. *J. Chem. Soc. B* **1966**, 299.

[15] Jones, P.; Harrison, R.; Wynne-Jones, L. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1679.

0022-3263/84/1949-1191$01.50/0

Table III. Activation Parameters for Methoxy Dechlorination of 1-Chloro-2,4-dinitrobenzene in Methanol and in Mixtures of Methanol and Acetonitrile[a]

solvent composition,[b] CH_3OH-CH_3CN	$\Delta H^\ddagger$, kcal mol^{-1}	$-\Delta S^\ddagger$, eu
100-0	15.6	18.7
80-20	16.1	17.7
60-40	15.5	16.7
40-60	16.1	12.2
20-80	16.9	10.8

[a] Determined over the range 15.0-40.3 °C at six different temperatures. [b] Solvent mixtures in volume percentage before mixing.

fractions of deuterium (n) in a given CH_3OH-CH_3OD mixture are reported in Table I.

The first-order rate constants k_{obsd} have also been measured at 25 °C in several mixtures of $CH_3OH(D)$–acetonitrile by using a constant concentration of MeO^-. The data (Table II) reveal a large increase in rate constant with the increase in acetonitrile concentration in the solvent mixture. Further, they reveal a decrease in the solvent isotope effect with the increase in acetonitrile concentration in the solvent mixture.

The temperature dependence of the reaction has been studied within the range 15.0–40.3 °C. The various activation parameters have been evaluated by using Arrhenius and Eyring equations by the least-squares technique.[16] The results are summarized in Table III.

Discussion

The proton inventory technique has been used successfully in recent years to delineate the transition-state structures for a number of chemical and biochemical reactions. Details of the theory and method of application have been discussed in detail in many of the recent publications and reviews[17-19] so we give only a brief treatment below.

This technique involves the measurement of reaction rate constants in protiated solvent, deuterated solvent, and mixtures of the two. The observed rate constant, k_n, in a solvent mixture of atom fraction of deuterium, n, is related to the rate constant, k_0, in protiated solvent by eq 2. TS refers to transition state and RS refers to reactant

$$k_n = k_0 \prod_i^{TS} (1 - n + n\phi_i) / \prod_j^{RS} (1 - n + n\phi_j) \qquad (2)$$

state. All exchangeable transition-state hydrogenic sites, i, that contribute to the observed solvent isotope effect constitute the numerator of eq 2, while exchangeable reactant-state sites, j, constitute a similar term in the denominator. The fractionation factor ϕ is an expression of the preference for deuterium over protium at an exchangeable site relative to the deuterium preference in the average solvent site, i.e.,

$$\phi_k = [(D)/(H)]_k / [(D)/(H)]_{solvent} \qquad (3)$$

The curvature exhibited by the plot of k_n vs. n depends on the magnitude of the observed solvent isotope effect and the number of transition-state and reactant-state contributions to the measured effect. It can be seen in eq 2 that only sites which change fractionation factor on going from the reactant state to the transition state will be important in determining the solvent isotope effect.

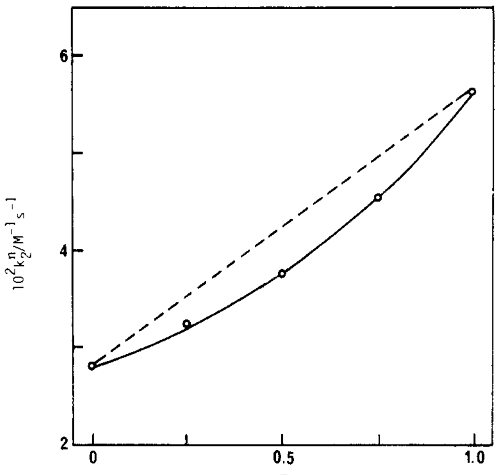


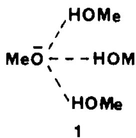
Figure 1. Proton inventory plot of the second-order rate constants for the methoxide-promoted dechlorination of 1-chloro-2,4-dinitrobenzene vs. the atom fraction of deuterium (n) in the MeOH–MeOD solvent system. The solid line through the data points is based on eq 13 with $\phi_{RS} = 0.70$ and $\phi_b = 0.89$. The data are presented in Table I. The dashed line is present to emphasize the nonlinearity.

Albery has proposed a procedure to analyze the proton inventory data.[20,21] This is based on a quantity γ which is related by eq 4 to the overall solvent isotope effect, k_1/k_0, and the solvent isotope effect at $n = 0.5$, $k_{0.5}/k_0$.

$$\gamma = 8 \ln [(k_{0.5}/k_0)/(k_1/k_0)^{1/2}]/[\ln (k_1/k_0)] \qquad (4)$$

Any positive value of γ gives us information about the role of protons that have been singled out from the crowd in the solvent. It also helps to decide how much of the isotope effect is caused by those special protons and how much by the medium effect. Any negative value of γ gives us the information that the reaction involves reactant–state fractionation on individual sites or that the reaction proceeds through parallel transition states.

In the present work the proton inventory curve (i.e., the plot of k_2^n vs. n) for the methoxide-promoted dechlorination exhibits a deep downward bowing (Figure 1). The curvature parameter γ calculated from the data in Table I has a negative value (i.e., $\gamma = -0.83 \pm 0.03$). This coupled with the observed inverse kinetic solvent isotope effect of $(k_{MeOD})/(k_{MeOH}) = 2.01$ suggests the involvement of reactant-state fractionation on some individual sites.



1

The methoxide ion in methanol is known to exist as a triply solvated species (1) with three chemically equivalent fractionation sites. The fractionation factor of methoxide ion in methanol was determined by Gold and Grist to be 0.74.[22] In a recent study, More O'Ferrall et al. redetermined it to be 0.70.[23] The difference in the value is es-

---

[16] Laidler, K. J. "Chemical Kinetics"; McGraw-Hill: New York, 1965; p 53, 89.

[17] Schowen, K. B. J. In "Transition States of Biochemical Processes"; Gandour, R. D., Schowen, R. L., Eds.; Plenum: New York, 1978.

[18] Schowen, R. L. In "Isotope Effects on Enzyme-Catalyzed Reactions"; Cleland, W. W., O'Leary, M. H., Northrop, D. B., Eds.; University Park Press: Baltimore, MD, 1977.

[19] Schowen, R. L. In "Progress in Physical Organic Chemistry"; Streitwieser, Jr., A., Taft, R. W., Eds.; Wiley-Interscience: New York, 1972; Vol. 9.

[20] Albery, W. J.; Davies, M. H. *J. Chem. Soc., Faraday Trans. 1* **1972**, 167.

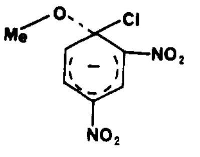
[21] Albery, W. J. In "Proton Transfer Reactions"; Caldin, E., Gold, V., Eds.; Chapman and Hall: London, 1975.

[22] Gold, V.; Grist, S. *J. Chem. Soc. B* **1971**, 1665.

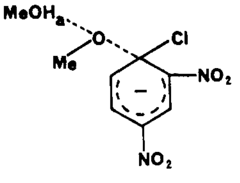
sentially due to the elimination of certain assumptions entertained by Gold and Grist.[22] The latter value has been used in our analysis.

Proton inventory curves of the shape of Figure 1 arise only if any one of the following multiproton possibilities, each with a greater contribution from the reactant state than from the transition state to the solvent isotope effect, exists:[17] (1) the entire contribution comes only from one or more reactant-state proton(s), (2) there are opposing reactant- and transition-state contributions with both ϕ_{TS} and ϕ_{RS} greater than unity, or (3) there are large inverse isotope effect(s) partially offset by smaller normal effect(s).

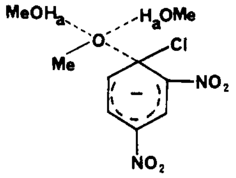
The most reasonable transition states consistent with the first possibility are those with zero, one, or two solvent molecules (**2**, **3**, and **4**) with each remaining proton (H_a) having the same fractionation factor as those in the solvation shell of the methoxide ion (i.e., $\phi_{TS} = \phi_{RS}$). These can be formed by the nucleophilic attack of the completely or partially desolvated methoxide ion on the activated aromatic ring of the substrate.



2



3



4

Of these transition states, **2** and **3** can accommodate the sodium ion within the cradle of the oxygen atoms of MeO^- and $-NO_2$ and the chlorine atom of the π complex.[15,24] These transition states **2**, **3**, and **4** would be consistent with the eq 5–7 with $\phi_{RS} = 0.70$, respectively, assuming the

$$k_n = k_0/(1 - n + n\phi_{RS})^3 \qquad (5)$$

$$k_n = k_0/(1 - n + n\phi_{RS})^2 \qquad (6)$$

$$k_n = k_0/(1 - n + n\phi_{RS}) \qquad (7)$$

exchangeable protons of the freed methanols now have unit fractionation factors as would be expected. The assumption is also necessary that the remaining solvating methanol molecule retains the same fractionation factor of 0.70.

Equations 5 and 7 badly fail to reproduce the observed proton inventory curve and the solvent kinetic isotope effect. Equation 6, however, generates moderately acceptable but less than satisfactory k_n values and solvent isotope effects as evident from the k_n values calculated in Table I.

The fractionation factor of the exchangeable protons of the solvent cage of methoxide ion is 0.70 and that of the protons in the bulk solvent is 1.0. Hence, neither in the solvation cage of the nucleophile nor in that of the transition state is it likely the protons have a fractionation factor greater than unity since we expect a smooth progression from reactants to transition state. Thus, the second possibility of opposing reactant- and transition-state contributions with both ϕ_{TS} and ϕ_{RS} greater than unity is ruled out in this case.

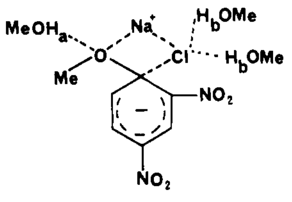
The most reasonable transition states consistent with the third possibility of large inverse isotope effect(s) partially offset by smaller normal effect(s) are **3** and **4** with fractionation factors for the transition-state protons being different than those for the reactant state. These possibilities are consistent with eq 8 and 9, respectively. Again the assumption is made that the freed methanol molecules have unit fractionation factors.

$$k_n = k_0(1 - n + n\phi_{TS})/(1 - n + n\phi_{RS})^3 \qquad (8)$$

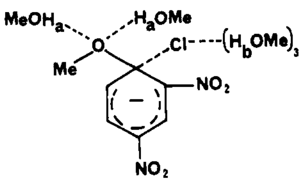
$$k_n = k_0(1 - n + n\phi_{TS})^2/(1 - n + n\phi_{RS})^3 \qquad (9)$$

The substitution of $\phi_{RS} = 0.70$, the experimentally determined values of rate constants in protium oxide and deuterium oxide, and the value of n for "pure" deuterium oxide in eq 8 and 9 gives 0.70 and 0.83 for ϕ_{TS} in eq 8 and 9, respectively. Thus, eq 8 reduces to eq 6 since ϕ_{TS} equals ϕ_{RS} and the model becomes identical with that considered earlier. Substitution of various values of n and $\phi_{TS} = 0.83$ in eq 9 allows one to calculate a theoretical proton inventory for this model. The values of k_n thus calculated are included in Table I. A comparison of the k_n values calculated by using eq 6 and 9 and collected in Table I reveals that eq 9 does a better job of generating acceptable but less than satisfactory k_n values and of reproducing for the observed kinetic solvent isotope effect. This transition-state model is analogous to that suggested by Cattania and Beltrame for ethoxy dechlorination of CDNB.[25]

On the other hand, if we assume that breakdown of the intermediate complex is rate limiting and TS_2 is the rate-limiting transition state,[15] we have to include the fractionation of the exchangeable solvent protons in the developing solvent cage of the departing chloride ion. It is pertinent at this point to note that chloride ion in water has a fractionation factor of 0.71 as calculated on the basis of the free energy of transfer.[26,27] Therefore, depending on the degree of C–Cl bond cleavage, the protons of the solvent cage can have fractionation factors between 1.0 and 0.71. Then one can envision two possible transition states, **5** and **6**. Transition state **5** is similar to the one proposed by Jones et al.[15] Both **5** and **6** have two kinds of protons, H_a and H_b, in the transition state. These would be consistent with eq 10 and 11, respectively, with $\phi_{RS} = 0.70$.



5



6

$$k_n = k_0(1 - n + n\phi_a)(1 - n + n\phi_b)^2/(1 - n + n\phi_{RS})^3 \qquad (10)$$

$$k_n = k_0(1 - n + n\phi_a)^2(1 - n + n\phi_b)^3/(1 - n + n\phi_{RS})^3 \qquad (11)$$

Since in these transition states the bond between CH_3O^-

---

[23] Al-Rawi, 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] Gold, V.; Toullec, J. *J. Chem. Soc., Perkin Trans. 2* **1979**, 596.

[25] Cattania, M. G.; Beltrame, P. *Int. J. Chem. Kinet.* **1973**, *5*, 911–917.

[26] Salomaa, P. *Acta Chem. Scand.* **1971**, *25*, 365.

[27] Salomaa, P.; Aalto, V. *Acta Chem. Scand.* **1966**, *20*, 2035.

and the benzene ring is fully developed, the H_a protons should have unit fractionation factors (i.e., $\phi_a = 1.0$). If this is so, eq 10 and 11 reduce to eq 12 and 13, respectively.

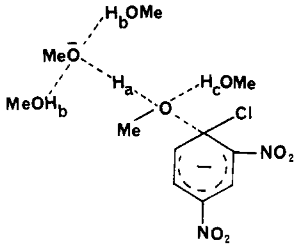
$$k_n = k_0(1 - n + n\phi_b)^2/(1 - n + n\phi_{RS})^3 \qquad (12)$$

$$k_n = k_0(1 - n + n\phi_b)^3/(1 - n + n\phi_{RS})^3 \qquad (13)$$

Equation 12 is identical with eq 9, and although it generates acceptable but less than satisfactory values of k_n we must be cautious in associating it with **5**. In **5** the metal ion is assumed to catalyze the cleavage of the carbon–halogen bond.[15] The association constant of metal and halide ions should be in the order MI > MBr > MCl since the weaker the ionic solvation the less the stability of free ions and the shorter the distance between oppositely charged ions in the ion pair. Hence, halogen mobility in the Ar–X bond cleavage should be in the order I > Br > Cl > F. The reverse order is observed, however.[28]

Equation 13 with $\phi_b = 0.89$ in fact generates k_n values that agree very well with the experimental k_n values (Table I). The solid line of Figure 1 is based on this equation. In spite of this, we must observe caution in accepting the corresponding transition state **6** for the following reasons. In acetonitrile the cyano nitrogens have a partial negative charge, but the positive part of the dipole is diffused in the methyl group as well as being quenched by dimer formation.[29,30] If acetonitrile can solvate the developing chloride ion in Ar–Cl bond cleavage at all it will be only through the very weak partial positive charge on the methyl hydrogens.[31] Thus, the rate of the reaction should either decrease or show a very slight increase (because of the destabilization of the methoxide in acetonitrile) with the increase in acetonile concentration in the solvent mixture. However, an impressive rate acceleration is observed as can be seen from the data in Table II.

The best alternative is to consider a different rate-determining transition state in the formation of the intermediate that is consistent with eq 13. In this context we shall consider the methoxide-assisted attack of methanol on the electrophilic carbon center in the rate-determining step. The transition state for this process would be **7**,



7

where $MeOH_c$ could be substituted for by a metal ion. The fractionation factor of the H_c proton will be unity since it is a part of the hydrogen-bonded solvent network. Thus, transition state **7** would be consistent with eq 14. If ϕ_a

$$k_n = k_0(1 - n + n\phi_a)(1 - n + n\phi_b)^2/(1 - n + n\phi_{RS})^3 \qquad (14)$$

$= \phi_b$, then eq 14 becomes identical with eq 13. This equivalence is possible only if the H_a proton in **7** is caught in a strong unsymmetrical hydrogen bond at the transition state and the H_b protons are proportionally moved away from the methoxide ion. Such situations have been predicted by Schowen[32,33] and Thornton[34] in the general-base-catalyzed hydrolysis of certain acyl compounds. The reaction-coordinate motion of this transition state would then be the nucleophilic attack of the methanol on the electrophilic site of the aromatic ring.

The maximum inverse kinetic solvent isotope effect expected from the loss of the three solvating methanols of the methoxide ion is 2.92 [i.e., $(1/0.7)^3$]. The observed inverse effect in the present investigation is 2.01. This means the transition-state contribution to the solvent isotope effect that opposes the reactant-state contribution is 1.45. This value is too low to be considered as a primary solvent isotope effect. Thus, proton transfer cannot be a part of the reaction coordinate motion in transition state **7**. If this is so then transition state **7** would be followed by another transition state resulting directly from the reaction coordinate motion of **7**, giving a structure with a fully formed O–C bond and with proton H_a still bound between methoxide and the methoxide portion of the solvent molecule by a hydrogen bond with the same strength as that in **7**. The reaction coordinate motion of the latter would be the methoxide-assisted H_a transfer. Thus, the general base (i.e., methoxide) catalyzed nucleophilic attack by the solvent involves two consecutive transition states with the first (i.e., **7**) being that of the rate-determining step. This type of general-base-catalyzed nucleophilic attack of the solvent on arenes has been observed in many cases.[35-37] Richie has suggested a similar general-base catalysis by hydroxide ion of the addition of water to an electrophile because of the unfavorable free energy change that would be associated with a process in which free hydroxide is generated from the water molecule formerly solvating the electrophile.[38]

Direct nucleophilic attack of the methoxide on the substrate as in **6** requires the removal of one molecule of a solvating methanol in order to have contact occur between the nucleophile and the substrate. The observed reaction rate and activation energy for such a mechanism should reflect the energy required for this loss and the extent to which it is made up by interaction with the substrate in the transition state. A gradual increase in the concentration of acetonitrile in the solvent mixture will cause a gradual desolvation of the methoxide ion. Hence, at sufficiently high concentrations of acetonitrile the methoxide becomes desolvated in the reactant state. At higher concentrations of acetonitrile the desolvation of methoxide ion during activation will not be required if direct methoxide attack is the correct mechanism. This situation should result in a drastic decrease in the enthalpy of activation. However, a slight increase in ΔH^* is observed with increasing acetonitrile content (Table III). This argues against such a mechanism.

Transition state **7** requires no desolvation but only the cleavage of the O–H bond of the nucleophilic solvent. The energy required for this is partly compensated by the energy change due to interaction of the solvent with the substrate. The gradual desolvation of the methoxide

---

[28] Bunnett, J. F.; Garbisch, E. N.; Pruitt, K. M. *J. Am. Chem. Soc.* **1957**, *79*, 385.

[29] Lambert, J. D.; Roberts, G. A. H.; Raulinson, J. S.; Wilkinson, V. J. *Proc. R. Soc. London Ser. A* **1949**, *A196*, 113.

[30] Murray, F. E.; Schneider, W. G. *Can. J. Chem.* **1955**, *33*, 797.

[31] Swain, C. G.; Kuhn, D. A.; Schowen, R. L. *J. Am. Chem. Soc.* **1965**, *87*, 1553.

[32] Minor, S. S.; Schowen, R. L. *J. Am. Chem. Soc.* **1973**, *95*, 2279.

[33] Hegazi, M.; Mata-Segreda, J. F.; Schowen, R. L. *J. Org. Chem.* **1980**, *45*, 307.

[34] Choi, M.; Thornton, E. R. *J. Am. Chem. Soc.* **1974**, *96*, 1428.

[35] Miller, J.; Parker, A. J. *J. Am. Chem. Soc.* **1961**, *83*, 117.

[36] Caudri, J. F. M. *Recl. Trav. Chim. Pays-Bas* **1929**, *47*, 422, 589, 778.

[37] Murto, J. *Suom. Kemistil. B* **1962**, *B35*, 157.

[38] Ritchie, C. D. *J. Am. Chem. Soc.* **1975**, *97*, 1170.

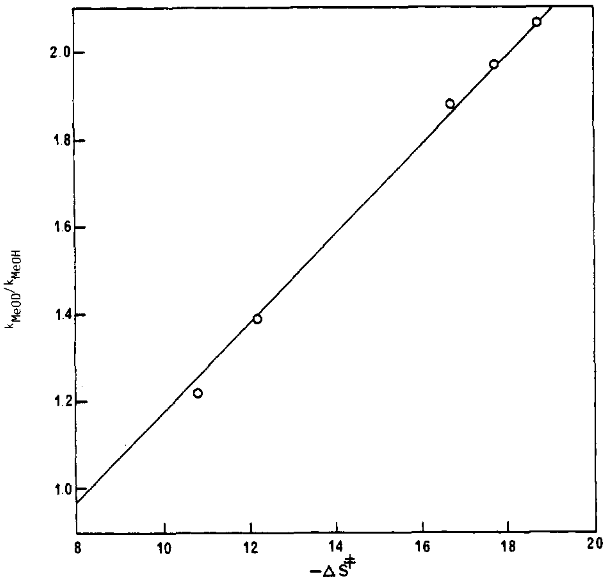


Figure 2. Plot of the solvent deuterium isotope effect, k_{MeOD}/k_{MeOH}, for the methoxide-promoted dechlorination of 1-chloro-2,4-dinitrobenzene vs. the entropy of activation.

caused by the gradual increase of acetonitrile leads to more symmetric hydrogen bonds for those methanol molecules that are still in a hydrogen-bonded position. This in turn decreases the strength of the O–H bonds and increases the nucleophilicity of the solvent molecule. In such a process, although there is a decrease in the energy required to break the O–H bond the fact that this requirement is less compensated for by interaction of the nucleophile with the substrate results in a slight net increase in the enthalpy of activation on changing from methanol-rich solvent to acetonitrile-rich solvent. This is observed.

The observed decrease of the inverse solvent isotope effect with the increase in acetonitrile concentration in the solvent mixture parallels the increase in entropy of activation as revealed by the plot of k_{MeOD}/k_{MeOH} vs. $-\Delta S^*$ (Figure 2). The isotope effect vanishes at $\Delta S^* = -8$ eu. This is the entropy loss due to the simple loss of translational and rotational degrees of freedom in bringing two reactants together in a bimolecular reaction.[39] The maximum inverse isotope effect of 2.07 is observed at $\Delta S^* = -18.7$ eu. Note that the isotope effect calculated on the basis of the ratio of pseudo-first-order rate constants is slightly higher than the 2.01 value quoted earlier for the data of Table I. This means the maximum inverse isotope effect is caused by a decrease of about 11 eu. This decrease in ΔS^* probably is due to the loss of translational and rotational degrees of freedom of solvent molecules. We can ascribe the observed inverse solvent isotope effect to an increase in the librational frequencies of solvent molecules[40] rather than to an increase in the internal frequencies of the solvent molecules.[41] The increase in the rate of the reaction observed with the increase of acetonitrile in the solvent mixture does not arise from a lower value of ΔH^*, partly counteracted by a lower value of ΔS^*, in the methanol-rich solvent than in the acetonitrile-rich solvent. Instead it arises due to a higher value of ΔS^* partly counteracted by a higher value of ΔH^*. Although the activation of the reactants to transition states **4** and **7** leads to a decrease of charge on methoxide, it occurs to a larger extent in **4** than in **7** because the negative charge is dispersed over a larger area in **7** than in **4**. Thus, it is possible to have more solvent molecules constrained in transition state **7** than in **4** compared to that in the initial state, with a concomitant decrease in entropy.

In conclusion, an analysis of the proton inventory data, the solvent influence of added acetonitrile, and the activation parameters support transition state **7** for the methoxide-promoted dechlorination of 1-chloro-2,4-dinitrobenzene.

Experimental Section

Materials. 1-Chloro-2,4-dinitrobenzene (Aldrich) was used after repeated recrystallization from benzene. Sodium methoxide (Matheson, Coleman and Bell) was used as such. Methanol (Aldrich Gold Label) and methanol-*d* (99.5+ atom % D, Gold Label, Aldrich) were used as such by storing them over molecular sieves. Acetonitrile was distilled from phosphorus pentoxide and stored under nitrogen.

The stock solutions of sodium methoxide in methanol and methanol-*d* were prepared by dissolving exactly equal amounts of sodium methoxide in each. Solvent mixtures of different atom fraction of deuterium were prepared by mixing appropriate volumes of the two stock solutions. Deuterium analyses were performed by Mr. Josef Nemeth.[42]

Kinetics. The methoxy dechlorination of 1-chloro-2,4-dinitrobenzene was monitored by following the increase in absorbance at 300 nm with a Cary 118C ultraviolet-visible spectrophotometer equipped with a constant-temperature cell compartment and interfaced with a computerized data acquisition system. The absorbance values at 1- 10-s intervals were collected and analyzed by using a nonlinear least-squares computer program. Plots of log $(A_\infty - A_t)$ vs. time were used in a confirmatory fashion.

Reactions were initiated by injecting 50 μL of a stock solution that was 7.4×10^{-3} M in 1-chloro-2,4-dinitrobenzene in acetonitrile into 3.00 mL of the appropriate sodium methoxide solutions. Reactions were followed for well over 3 half-lives.

Registry No. 1-Chloro-2,4-dinitrobenzene, 97-00-7; methoxide, 3315-60-4; deuterium, 7782-39-0.

---

[39] Gerstein, J.; Jencks, W. P. *J. Am. Chem. Soc.* **1964**, *86*, 4655.

[40] (a) Swain, C. G.; Bader, R. F. W. *Tetrahedron* **1960**, *10*, 182. (b) Swain, C. G.; Bader, R. F. W.; Thornton, E. R. *Ibid.* **1960**, *10*, 200. (c) Swain, C. G.; Thornton, E. R. *J. Am. Chem. Soc.* **1961**, *83*, 3884, 3890.

[41] Bunton, C. A.; Shiner, V. J. *J. Am. Chem. Soc.* **1961**, *83*, 42, 3207, 3214.

[42] Urbana, IL 61801.