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Using $^{11}C/^{14}C$ Incoming Group and Secondary α-Deuterium KIEs To Determine How a Change in Leaving Group Alters the Structure of the Transition State of the S_N2 Reactions between *m*-Chlorobenzyl *para*-Substituted Benzenesulfonates and Cyanide Ion

Kenneth C. Westaway,*,† Yao-ren Fang,† Jonas Persson,‡ and Olle Matsson*,‡

Contribution from the Department of Chemistry and Biochemistry, Laurentian University, Sudbury, Ontario, Canada P3E 2C6, and the Institute of Chemistry, Department of Organic Chemistry, Uppsala University, Box 531, S-75121, Uppsala, Sweden

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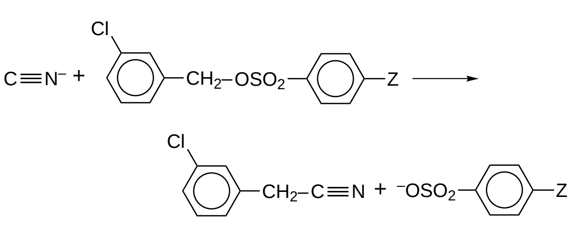
Abstract: The $^{11}C/^{14}C$ incoming group and secondary α-deuterium KIEs and Hammett ρ value found by changing the substituent in the leaving group of the S_N2 reactions between *meta*-chlorobenzyl *para*-substituted benzenesulfonates and cyanide ion in 0.5% aqueous acetonitrile at 0 °C suggest that these reactions occur via an unsymmetrical, product-like transition state. Changing to a better leaving group leads to a transition state with a slightly shorter nucleophile−α-carbon bond and a longer α-carbon−leaving group bond. The changes in transition state structure are consistent with the Bond Strength Hypothesis.

Introduction

Physical organic chemists have been trying to determine how changes in the structure of the substrate, the leaving group, and the nucleophile affect the structure of the transition state for an S_N2 reaction for some time.[1−5] This has been difficult because chemists have not had a reliable technique for determining the length of the nucleophile−α-carbon bond in the S_N2 transition state. This problem was partially overcome recently when Matsson, Westaway, and co-workers[6] reported large primary $^{11}C/^{14}C$ incoming group kinetic isotope effects (KIEs) for the S_N2 reactions between a series of *para*-substituted benzyl chlorides and labeled cyanide ion. This work demonstrated that this new type of KIE can be used to determine how the α-carbon−nucleophile bond changes when a substituent in the substrate is altered. In this study, these new isotope effects are used to determine how a change in substituent in the leaving group affects the structure of the S_N2 transition state.

Results and Discussion

The system chosen for this investigation is the S_N2 reactions between a series of *m*-chlorobenzyl *para*-substituted benzenesulfonates with cyanide ion in 0.5% aqueous acetonitrile, eq 1.



(1)

These substrates were chosen because (i) the *para* substituent on the leaving group could be changed easily and (ii) benzylbenzenesulfonates with an electron-withdrawing substituent on the benzene ring of the benzyl group are more stable than the unsubstituted benzylbenzenesulfonates. For example, Ando, Tanabe, and Yamataka[7] used a *m*-bromo substituent to stabilize the benzylbenzenesufonates for their studies of the S_N2 reactions between *para*-substituted *N*,*N*-dimethylanilines and benzyl *para*-substituted benzenesulfonates.

Primary $^{11}C/^{14}C$ Incoming Group KIEs. The primary $^{11}C/^{14}C$ incoming group KIEs found when isotopically labeled cyanide ion was reacted with *m*-chlorobenzyl *para*-substituted benzenesulfonates are presented in Table 1. An examination of the data indicates that all of the isotope effects are real, i.e., they are much larger than the experimental error in the method. The second observation is that the k^{11}/k^{14} decrease slightly as a more electron-withdrawing substituent is added to the leaving group, i.e., they decrease from 1.0119 for the *p*-methylbenzenesulfonate leaving group to 1.0096 for the *p*-chlorobenzenesulfonate leaving group. However, the change in the isotope effect with substituent is small. In fact, it only decreases by 0.0023 when the *para* substituent in the leaving group is changed from the electron-donating methyl to the electron-withdrawing chloro substituent. This small change was expected because the change in structure was made several atoms away from the α-carbon and because the rate of reaction only changed 4.6 times (Table 1) when the *para* substituent on the benzene ring was altered from methyl to chloro. It is important to note, however, that the change in the KIE with substituent is greater than the error in the individual KIEs, i.e., the KIE for the reaction with the *p*-chlorobenzenesulfonate leaving group is clearly smaller than the KIE for the *p*-methylbenzenesulfonate leaving group.

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* To whom correspondence should be addressed.
† Laurentian University.
‡ Uppsala University.

(1) Hudson, R. F.; Klopman, G. *J. Chem. Soc.* **1962**, 1062.
(2) Koshy, K. M.; Robertson, R. E. *J. Am. Chem. Soc.* **1974**, *96*, 914.
(3) Westaway, K. C.; Ali, S. F. *Can. J. Chem.* **1979**, *57*, 1354.
(4) Westaway, K. C.; Waszczylo, Z. *Can. J. Chem.* **1982**, *60*, 2500.
(5) Persson, J.; Berg, U.; Matsson, O. *J. Org. Chem.* **1995**, *60*, 5037.
(6) Matsson, O.; Persson, J.; Axelsson, B. S.; Långström, B.; Fang, Y.; Westaway, K. C. *J. Am. Chem. Soc.* **1996**, *118*, 6350.
(7) Ando, T.; Tanabe, H.; Yamataka, H. *J. Am. Chem. Soc.* **1984**, *106*, 2084.

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Table 1. The Rate Constants, the Incoming Group $^{11}C/^{14}C$ KIEs, and the Secondary α-Deuterium KIEs for the S_N2 Reactions between a Series of *m*-Chlorobenzyl *para*-Substituted Benzenesulfonates and Cyanide Ion in 0.5% Aqueous Acetonitrile at 0 °C

para substituent	10^3k_H (L/(mol·s))	k^{11}/k^{14}	$(k_H/k_D)_\alpha$
CH_3O	4.840 ± 0.022^a		1.025 ± 0.008^c
CH_3	7.694 ± 0.007	1.0119 ± 0.0010^b	1.028 ± 0.005
H	13.29 ± 0.032	1.0111 ± 0.0020	1.012 ± 0.008
Cl	36.17 ± 0.25	1.0096 ± 0.0005	1.009 ± 0.012

[a] The standard deviation of the mean of between three and five different measurements. [b] The standard deviation for three independent measurements of the isotope effect. [c] The error in the isotope effect = $1/k_D[(\Delta k_H)^2 + (k_H/k_D)^2(\Delta k_D)^2]^{1/2}$ where Δk_H and Δk_D are the standard deviations for the rate constants for the undeuterated and deuterated substrates, respectively.

The magnitude of an incoming group KIE is determined by two terms, a temperature-independent (TI) term and a temperature-dependent (TD) term,[8] eq 2,

$$k_L/k_H = \underbrace{(\nu_L^\ddagger/\nu_H^\ddagger)}_{\text{TI}}\ \underbrace{[1 - \sum G(u_i^\ddagger)\Delta u_i^\ddagger + \sum G(u_i)\Delta u_i]}_{\text{TD}} \quad (2)$$

where $G(u_i) = [^1/_2 - 1/u_i + 1/(e^{u_i} - 1)]$ and $\Delta u_i = hc/kT(\Delta\nu_i)$. The terms h, c, k, and T are Planck's constant, the speed of light, Boltzmann's constant, and the absolute temperature, respectively. $\Delta\nu_i$ is the change in the frequency of a vibration caused by isotopic substitution. The temperature-independent term, $(\nu_L^\ddagger/\nu_H^\ddagger)$, is always greater than unity since the imaginary frequency is always larger for the reaction with the lighter isotope. The value of the temperature-independent term cannot be determined. However, Melander and Saunders[9] have suggested equations that allow one to estimate this term. On the basis of their equations and the masses of the reacting atoms, the temperature-independent term for an incoming group k^{11}/k^{14} on these reactions should be approximately 1.018.

The temperature-dependent term, on the other hand, is determined by the changes that occur in the vibrational energy of the normal modes involving the isotopically labeled atom when the reactants are converted into the transition state. The bonding to the labeled carbon atom of the cyanide ion will be greater in the transition state than in the reactants because the new cyanide carbon−α-carbon (nucleophile−α-carbon) bond is forming in the S_N2 transition state. As a result, the vibrational energy of the labeled carbon will be greater in the transition state and the temperature-dependent term, eq 2, will be less than one. The magnitude of the temperature-dependent term depends on transition state structure. Since the vibrational energy of the nucleophile−α-carbon bond increases with increasing nucleophile−α-carbon bond formation, the magnitude of the temperature-dependent term decreases as the nucleophile−α-carbon bond formation becomes more complete in the S_N2 transition state. This means the KIE, which is the product of the temperature-independent and the temperature-dependent term, will be less than the magnitude of the temperature-independent term, i.e., <1.018.[10] In fact, a simple calculation using the observed vibrational frequencies for the reactant (the cyanide ion in various aqueous solutions and the product (benzyl cyanide)[6,11] and assuming complete cyanide ion−α-carbon bond formation in the transition state, shows that the minimum value for the temperature-dependent term is 0.85. This means that these KIEs should be between 1.02 and 0.87. The actual value will, of course, be determined by the amount of nucleophile−α-carbon bonding in the S_N2 transition state. Since the magnitude of these isotope effects decreases as the amount of nucleophile−α-carbon bond formation increases in the transition state, these isotope effects suggest that the amount of $N{\equiv}C{-}C_\alpha$ bond formation increases slightly as a more electron-withdrawing substituent is added to the leaving group.

These incoming group $^{11}C/^{14}C$ isotope effects can be examined in the light of the other $^{11}C/^{14}C$ incoming group KIEs that have been measured for cyanide ion S_N2 reactions. The incoming group k^{11}/k^{14} for the S_N2 reactions between labeled cyanide ion and *para*-substituted benzyl chlorides[6] ranged from 1.0105 to 1.0070. The isotope effects found in the reactions between labeled cyanide ion and *m*-chlorobenzyl *para*-substituted benzenesulfonates are slightly larger than those found for the benzyl chlorides indicating that there is less cyanide−α-carbon bond formation (the nucleophile−α-carbon bond is slightly longer) in the arenesulfonate S_N2 transition states.

Secondary α-Deuterium KIEs. The secondary α-deuterium $[(k_H/k_D)_\alpha]$ KIEs were also determined for the *m*-chlorobenzyl *para*-substituted benzenesulfonate S_N2 reactions in order to learn how a change in leaving group affects the total transition state structure. The $(k_H/k_D)_\alpha$ for these reactions, Table 1, are all small[12] and normal. Clearly, these KIEs are much smaller than the secondary α-deuterium KIEs of 1.10 ± 0.04[14] found for many of the S_N2 reactions of *para*-substituted benzyl chlorides. Since the magnitude of the secondary α-deuterium KIE for an S_N2 reaction normally varies with the nucleophile-leaving group (the $N{\equiv}C$- -O distance) in the transition state,[15] the usual explanation would be that the small $(k_H/k_D)_\alpha$s found for these reactions indicate that the transition states for these S_N2 reactions are tight with short $N{\equiv}C$- -O distances.

The second observation is that the change in the secondary α-deuterium KIEs with substitutent is very small, i.e., they only decrease slightly from 1.025 to 1.009 when the *para* substituent on the leaving group changes from the strongly electron-donating methoxy group to the electron-withdrawing chloro group. Recently, it has been suggested[16] that the secondary α-deuterium KIE for an S_N2 reaction with an unsymmetrical transition state is determined by the length of only the shorter, and stronger, reacting bond rather than by the nucleophile−leaving group distance and will not change significantly with a change in substituent. Therefore, the almost constant secondary α-deuterium KIEs found for these benzenesulfonate reactions suggest that the transition state is unsymmetrical with either a short $N{\equiv}C{-}C_\alpha$ and a long $C_\alpha{-}O$ bond *or* a long $N{\equiv}C{-}C_\alpha$ and a short $C_\alpha{-}O$ bond. Both these alternatives are discussed below.

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[8] Melander L.; Saunders: W. H., Jr. *Reaction Rates of Isotopic Molecules*; Wiley-Interscience: New York, 1980; pp 48 and 49.

[9] Melander, L.; Saunders, W. H., Jr. *Reaction Rates of Isotopic Molecules*; Wiley-Interscience: New York, 1980; pp 46 and 47.

[10] The change in the TI term with transition state structure is small with respect to the change in the TD term.[6]

[11] Jobe D. J.; Westaway, K. C. *Can. J. Chem.* **1993**, *71*, 1353.

[12] Willi and co-workers[13] found an almost identical secondary α-deuterium KIE of 1.025 for the S_N2 reaction between cyanide ion and benzyl chloride in 55% (v/v) methyl cellusolve.

[13] Willi, A. V.; Ho, C.; Ghanbarpour, A. *J. Org. Chem.* **1972**, *37*, 1185.

[14] Westaway, K. C. Secondary hydrogen−deuterium kinetic isotope effects and transition state structure in S_N2 processes. In *Isotopes in organic chemistry*; Buncel, E., Lee, C. C., Eds.; Elsevier: Amsterdam, 1987; Vol. 7, pp 275−392.

[15] Poirier, R. A.; Wang, Y.; Westaway, K. C. *J. Am. Chem. Soc.* **1994**, *116*, 2526.

[16] Westaway, K. C.; Pham, T. V.; Fang, Y. *J. Am. Chem. Soc.* **1997**, *119*, 3670.

The first suggestion, i.e., that the transition states are unsymmetrical and have short $N{\equiv}C{-}C_\alpha$ and long $C_\alpha{-}O$ bonds, is preferred for several reasons. First, in all the other S_N2 reactions where the secondary α-deuterium KIEs are almost independent of substituent and the reactions have been investigated in sufficient detail so one knows how the substituent affects transition state structure,[16] the stronger reacting bond is short and the weaker reacting bond is long. Since the $C{-}C_\alpha$ bond is stronger than the $C_\alpha{-}O$ reacting bond[17] in this system, one would expect the $N{\equiv}C{-}C_\alpha$ bond to be short in these S_N2 transition states. A second reason this alternative is favored is because the secondary α-deuterium KIEs mimic the k^{11}/k^{14}, Table 1, i.e., both the k^{11}/k^{14} and the $(k_H/k_D)_\alpha$ decrease slightly when a more electron-withdrawing substituent is added to the leaving group. Thus, it appears that these two isotope effects are controlled by the same factor(s). One obvious explanation for the similar changes in the primary k^{11}/k^{14} and secondary $(k_H/k_D)_\alpha$ isotope effects is that the transition states for these reactions are unsymmetrical with a short $N{\equiv}C{-}C_\alpha$ bond and a long $C_\alpha{-}O$ bond. If this is the case, the short $N{\equiv}C{-}C_\alpha$ bond, rather than the $N{\equiv}C$- -O distance in the unsymmetrical transition state, would determine the magnitude of the secondary α-deuterium KIEs.[16] This happens because the changes that occur in the transition state $C_\alpha{-}H(D)$ out-of-plane bending vibrations as the substituent in the leaving group is altered are only affected by the change in the short $N{\equiv}C{-}C_\alpha$ bond and not by the changes in the weaker (longer) $C_\alpha{-}O$ bond to the leaving group. This is because the changes that occur in the weaker $C_\alpha{-}O$ bond are too far from the α-carbon in the transition state to affect the $C_\alpha{-}H(D)$ out-of-plane bending vibrations that determine the magnitude of these KIEs.[16] As a result, the magnitude of the secondary α-deuterium KIEs should decrease in the same way as the primary incoming group k^{11}/k^{14}. This is, in fact, what is observed.

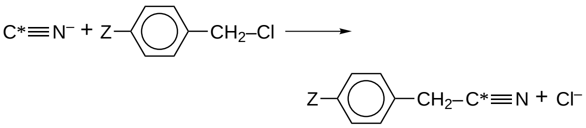
Hammett ρ Value. The preferred interpretation of the incoming group k^{11}/k^{14} and secondary α-deuterium KIEs is based on the fact that the $N{\equiv}C{-}C_\alpha$ bond is short and the $C_\alpha{-}O$ bond is long in these benzenesulfonate transition states. The Hammett ρ value, obtained by changing the substituent in the leaving group, has been determined to learn if this explanation is tenable. The Hammett ρ value, calculated from the second-order rate constants for the S_N2 reactions between the *m*-chlorobenzyl *para*-substituted benzenesulfonates, Table 1, is 1.71 ± 0.08 and the Hammett ρ plot has a correlation coefficient of 0.996. Although the ρ value is reasonably large, it does not *prove* that the $C_\alpha{-}O$ bond is long in these S_N2 transition states. However, the Hammett ρ values found for other S_N2 reactions of benzyl *para*-substituted benzenesulfonates range from 0.76 for the S_N2 reactions with a poor nucleophile, *N*,*N*-dimethyl-*m*-nitroaniline in acetonitrile at 30 °C,[18] to a ρ of 2.13 in the S_N2 reactions with a good nucleophile, *N*,*N*-dimethyl-*p*-methoxyaniline in acetone at 35 °C.[18] Thus, the Hammett ρ value of 1.71 found in this reaction is close to the largest ρ value found for S_N2 reactions with *para*-substituted benzenesulfonate leaving groups and it supports the contention that $C_\alpha{-}O$ bond rupture is well advanced and that these cyanide ion−*m*-chlorobenzyl *para*-substituted benzenesulfonate S_N2 transition states are unsymmetrical with short $N{\equiv}C{-}C_\alpha$ and long $C_\alpha{-}O$ bonds.

Another reason this unusual interpretation of the secondary α-deuterium and primary $^{11}C/^{14}C$ incoming group KIEs has been suggested is because this same behavior was found in the S_N2 reactions between cyanide ion and *para*-substituted benzyl chlorides in 20% aqueous DMSO at 30 °C, eq 3.

Table 2. The Incoming Group $^{11}C/^{14}C$, the Secondary α-Deuterium, and the Chlorine Leaving Group KIEs for the S_N2 Reactions between *para*-Substituted Benzyl Chlorides and Cyanide Ion in 20% Aqueous DMSO at 30 °C

para substituent	k^{11}/k^{14}	$(k_H/k_D)_\alpha$	$k^{35}/k^{37\,a}$
CH_3	1.0104 ± 0.0001	1.008 ± 0.003	1.0079 ± 0.0004
H	1.0105 ± 0.002	1.011 ± 0.001	1.0072 ± 0.0003
Cl	1.0070 ± 0.001	1.002 ± 0.003	1.0060 ± 0.0002

[a] Measured in 20% aqueous dioxane at 20 °C, see ref 6.

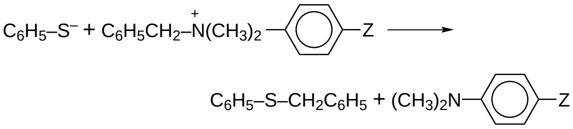


(3)

In this system,[6] the carbon $^{11}C/^{14}C$ incoming group and the secondary α-deuterium KIEs also change in the same way, Table 2, and it was concluded that the transition state was unsymmetrical with a short $N{\equiv}C{-}C_\alpha$ bond and a long α $C_\alpha{-}Cl$ bond. Since the same behavior is observed in this series of reactions, it seems likely that these transition states are also related in a similar fashion.

Finally, if the S_N2 transition states in these benzenesulfonate reactions are unsymmetrical with short $N{\equiv}C{-}C_\alpha$ and long $C_\alpha{-}O$ bonds, the incoming group $^{11}C/^{14}C$ and secondary α-deuterium KIEs, Table 1, both suggest and that the short $N{\equiv}C{-}C_\alpha$ bond shortens slightly when a better leaving group is used, i.e., adding a more electron-withdrawing substituent to the leaving group leads to a transition state with a slightly shorter nucleophile−α-carbon transition state bond. Unfortunately, one does not know how the longer $C_\alpha{-}O$ transition state bond changes when a more electron withdrawing substituent is added to the leaving group. It is interesting to note that the substituent effect suggested by these isotope effects is consistent with the predictions of the Bond Strength Hypothesis,[17] which suggests that the major change in transition state structure will be in the weakest (the $C_\alpha{-}O$) reacting bond and that very little change will occur in the stronger (the $N{\equiv}C{-}C_\alpha$) reacting bond when a substituent in the leaving group is altered.

The only other study where the effect of a change in leaving group has been determined in some detail was published by Westaway and Ali.[3] Adding a more electron-withdrawing substituent to the leaving group in their system, eq 4,



(4)

caused a significant shortening of the nucleophile−α-carbon bond and a very slight lengthening of the α-carbon−leaving group bond in the S_N2 transition state. These results were interpreted in terms of the Bond Strength Hypothesis,[17] which suggests that the change in transition state structure observed when a substituent in the leaving group is altered will occur at the weaker $S{-}C_\alpha$ bond and that little or no change will occur at the stronger $C_\alpha{-}N$ bond. If the Bond Strength Hypothesis is applied to the benzenesulfonate reactions, the major change would be expected in the weaker $C_\alpha{-}O$ bond and little or no change would be expected in the stronger $N{\equiv}C{-}C_\alpha$ bond. As a result, only the small change that is observed in the primary

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(17) Westaway, K. C. *Can. J. Chem.* **1993**, *71*, 2084.

(18) Lee, I.; Koh, H. J.; Lee, B.-S.; Sohn, D. S.; Lee, B. C. *J. Chem. Soc., Perkin Trans. 2* **1991**, 1741.

$^{11}C/^{14}C$ incoming group and the secondary α-deuterium KIEs would be expected while a significant change would be anticipated in the weaker C_α−O bond. Adding an electron-withdrawing group in this series of reactions causes a slight decrease in the nucleophile−α-carbon bond in agreement with the results published by Westaway and Ali.[3] If the behavior found by Westaway and Ali for the α-carbon−leaving group bond is observed in this system, one would predict a significantly longer C_α−O bond when a more electron-withdrawing substituent is on the leaving group. Thus, these results suggest that changing to a better leaving group in the S_N2 reactions between cyanide ion and *m*-chlorobenzyl *para* substituted benzenesulfonates leads to a transition state with a slightly shorter $N{\equiv}C{-}C_\alpha$ bond and a significantly longer C_α−O bond. This means the leaving group oxygen KIE would increase and the α-carbon KIE would decrease (the transition state would become less symmetrical) when a more electron-withdrawing substituent is on the leaving group.

An alternative to the product-like transition states suggested above is that the transition states are early with a long $N{\equiv}C{-}C_\alpha$ bond and a short C_α−O bond. This is consistent with the large primary incoming group k^{11}/k^{14} and the small secondary $(k_H/k_D)_\alpha$ values found for this series of reactions. However, it is not consistent with (i) the large Hammett ρ value, (ii) the transition states found for the other S_N2 reactions of *para*-substituted benzyl substrates with unsymmetrical transition states, i.e., that the stronger reacting bond is always short,[16] or (iii) the transition states found for the closely related S_N2 reactions between cyanide ion and *para*-substituted benzyl chlorides.[6] In fact, the only data that require a reactant-like transition state are the large k^{11}/k^{14} isotope effects. Although the authors are unable to explain why large k^{11}/k^{14} isotope effects are observed in this system where the best explanation of the data is a product-like transition state, it is important to note that all of the incoming group KIEs that have been reported[19−25] are normal or only very slightly inverse. In fact, the most inverse incoming group KIE was reported by Kurz et al.,[21] who found a slightly inverse nitrogen incoming group KIE of 0.9937 ± 0.0002 for the Menshutkin reaction between 4-methylpyridine and methyl triflate in acetonitrile at 25 °C. The failure to find large inverse incoming group KIEs in the benzenesulfonate reactions suggests that the relationship between transition state geometry and the magnitude of the KIEs is not as simple as currently believed. In fact, Schrøder Glad and Jensen[26,27] have suggested on the basis of theoretical calculations of E2 transition states that the magnitude of an isotope effect is not always related to transition state structure (geometry).

The Form of the Reacting Nucleophile. Finally, it was of interest to try to determine the form of the reacting nucleophile in these S_N2 reactions. Westaway and co-workers[28−30] have shown that ion pairing can affect the structure of an S_N2 transition state markedly. Since Jobe and Westaway had examined the infrared spectrum of cyanide salts in dipolar aprotic solvents,[11] the form of the reacting nucleophile could be determined in these S_N2 reactions. The FTIR spectra of the tetraethylammonium cyanide in 0.50% aqueous acetonitrile at concentrations close to those used in the isotope effect experiments had two cyanide ion absorbances, one at 2058 cm^{-1} and the other at 2071 cm^{-1}. In aqueous DMF solutions, the DMF-solvated cyanide ion absorbed at 2055 cm^{-1} and the water-solvated cyanide ion absorbed at 2069 cm^{-1}. The close agreement between the DMF and acetonitrile spectra suggests that an acetonitrile-solvated cyanide ion which absorbs at 2058 cm^{-1} and a water-solvated cyanide ion that absorbs at 2071 cm^{-1} are present in the reaction mixture. A kinetic run was carried out in the FTIR at 22 °C to learn which cyanide ion reacted in the benzenesulfonate reactions. The results showed that the ratio of the two cyanide ion absorbances remained constant throughout the reaction. This indicates that the equilibrium between the two solvated forms of cyanide ion is very much faster than the rate of the S_N2 reaction. As a result, one cannot determine whether the reaction occurs via the acetonitrile-solvated or the water-solvated cyanide ion although it would seem likely that the acetonitrile-solvated cyanide ion is the reactant because (i) this form of the reacting ion is present in higher concentration and (ii) Jobe and Westaway found that the DMF-solvated cyanide ion was much more reactive than the water-solvated cyanide ion in the reaction with benzyl chloride in DMF.[11]

Experimental Section

Preparation of Reagents. (a) Tetraethylammonium Cyanide. Tetraethylammonium cyanide (Aldrich) was used as purchased although it was stored in a vacuum desiccator once it had been opened.

(b) *m*-Chloro(1,1-$^2H_2$)benzyl Alcohol. Lithium aluminum deuteride (5.0 g, 0.11 mol) was suspended in 250 mL of dry diethyl ether[31] in a three-necked 1-L round-bottomed flask fitted with a condenser sealed with a calcium chloride drying tube and a 500 mL dropping funnel. A solution of 34 g (0.199 mol) of methyl 3-chlorobenzoate (Aldrich) in 250 mL of dry ether was added dropwise with stirring and the resulting mixture was refluxed for 3 h. Then, the unreacted deuteride was hydrolyzed by the careful addition of a 10% sulfuric acid solution. The ether layer was separated and the aqueous layer was extracted with three 50 mL portions of ether. The ether layers were combined and extracted once with 200 mL of water, and then the ether was removed on the rotary evaporator. The remaining liquid was mixed with 100 mL of a 20% sodium hydroxide solution in 50% aqueous methanol and refluxed for 4 h to hydrolyze any unreduced ester. After the methanol had been removed on a rotary evaporator, the product was extracted with three 40 mL portions of ether. The ether layers were combined and dried over anhydrous magnesium sulfate. Finally, the drying agent was removed, the ether was removed on the rotary evaporator, and the product was distilled. The bp was 100 °C at 4 mm. and the yield was 22 g (64%).

(c) *m*-Chlorobenzyl *para*-Substituted Benzenesulfonates. A solution of 7.1 g (0.05 mol) of *m*-chlorobenzyl alcohol (Aldrich) in 50 mL of ether was added slowly (so the temperature stayed at 0 °C) with stirring to a solution of 8.8 g (0.05 mol) of benzenesulfonyl chloride (Aldrich) in 160 mL of ether that had been cooled in an ice−salt bath. A 1.5 g portion of potassium hydroxide was added slowly to the mixture at 15 min intervals until 6 g of potassium hydroxide had been added. The reaction mixture was kept at 0 °C for 12 h, then allowed to warm to room temperature in 1 h. The reaction mixture was filtered and the ether was removed on a rotary evaporator. The crude solid was recrystalized twice from hexane and stored under dry nitrogen in a

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(19) Ando, T.; Yamataka, H.; Wada, E. *Isr. J. Chem.* **1985**, *26*, 354.

(20) Smith, P. J.; Westaway, K. C. *The Chemistry of the Functional Groups, Supplement F: The Chemistry of Amino, Nitroso and Nitro Compounds and Their Derivatives*; Patai, S., Ed.; J. Wiley and Sons: London, 1982; p 1277.

(21) Kurz, J. L.; Daniels, M. W.; Cook, K. S.; Nasr, M. M. *J. Phys. Chem.* **1986**, *90*, 5357.

(22) Kurz, J. L.; Pantano, J. E.; Wright, D. R.; Nasr, M. M. *J. Phys. Chem.* **1986**, *90*, 5360.

(23) Paneth, P.; O'Leary, M. H. *J. Am. Chem. Soc.* **1991**, *113*, 1691.

(24) Szylhabel-Godala, A.; Madhavan, S.; Rudzinski, J.; O'Leary, M. H.; Paneth, P. *J. Phys. Org. Chem.* **1996**, *9*, 35.

(25) Lynn, K. R.; Yankwich, P. E. *J. Am. Chem. Soc.* **1961**, *83*, 53.

(26) Schrøder Glad, S.; Jensen, F. *J. Am. Chem. Soc.* **1994**, *116*, 9302.

(27) Schrøder Glad, S.; Jensen, F. *J. Org. Chem.* **1997**, *62*, 253.

(28) Westaway, K. C.; Lai, Z.-G. *Can. J. Chem.* **1988**, *66*, 1263.

(29) Lai, Z.-G.; Westaway, K. C. *Can. J. Chem.* **1989**, *67*, 21.

(30) Fang, Y.-R.; Westaway, K. C. *Can. J. Chem.* **1991**, *69*, 1017.

(31) The dry ether was prepared by distilling anhydrous diethyl ether from a lithium aluminum hydride−ether suspension.

Table 3. The Percent Yields and Melting Points for the *m*-Chlorobenzyl *para*-Substituted Benzenesulfonates

	m-chlorobenzyl *para*-substituted benzenesulfonates		*m*-chloro(1,1-$^2H_2$)benzyl *para*-substituted benzenesulfonates	
para substituent	% yield (purified)	MP (°C)	% yield (purified)	MP (°C)
CH_3O	58	50−51	57	50−51
CH_3	60	81−82	58	81−82
H	56	45.5−46.5	60	45.5−46.5
Cl	49	59.0−59.5	51	59−60

freezer until it was required. The purified yield of *m*-chlorobenzylbenzenesulfonate was 7.9 g (56%) and the mp was 45.5−46.5 °C.

Identical syntheses with *p*-methoxybenzenesulfonyl chloride (Aldrich), *p*-toluenesulfonyl chloride (Aldrich), and *p*-chlorobenzenesulfonyl chloride (Aldrich) gave the other *m*-chlorobenzyl *para*-substituted benzenesulfonates used in this study. The corresponding *m*-chloro(1,1-$^2H_2$)benzyl *para*-substituted benzenesulfonates were also synthesized with this procedure. The percent yield and melting points of the undeuterated and deuterated *m*-chlorobenzyl *para*-substituted benzenesulfonates are given in Table 3.

KIEs. (a) $^{11}C/^{14}C$ KIEs. The procedure used to measure the incoming group $^{11}C/^{14}C$ KIEs has been described previously.[6]

(b) Secondary α-Deuterium KIEs. The rate constants required for measuring the secondary α-deuterium KIEs were determined by dissolving approximately 0.88 g (weighed accurately) of tetraethylammonium cyanide (Aldrich) and approximately 0.002 g (accurately weighed) of *p*-nitrotoluene in 200 mL of a 0.54% (v/v) solution of aqueous acetonitrile.[32] Then, 2.5 mL of this solution was pipetted into the reaction vessel in a 37 × 37 I^{2}R glovebag filled with extra-dry nitrogen (Praxair), and this solution was temperature equilibrated for at least 45 min at 0 °C in a distilled water−ice constant-temperature bath. A second solution containing approximately 0.025 g of the substrate (weighed accurately) in approximately 0.397 g (weighed accurately) of acetonitrile was prepared and the kinetic run was begun by injecting approximately 0.16 g (accurately weighed) of this solution into the 2.5 mL solution in the constant-temperature bath. At least twelve 10 μL samples were withdrawn at various times throughout the kinetic run and injected onto an HPLC consisting of a Waters 600 Multisolvent Delivery System, a 3.9 mm × 15 cm, 3 μm Nova-Pak C18 column, a Waters Programmable Multiwavelength UV detector, and an HP 3396A Integrator. The eluting solvent was 45% aqueous acetonitrile, and the flow rate was 1.3 mL/min. The Waters 600 ultraviolet detector was set at 270 nm. The concentration of the product, *m*-chlorobenzyl cyanide, was calculated from the area ratio of the *m*-chlorobenzyl cyanide/internal standard (*p*-nitrotoluene) and the known concentration of *p*-nitrotoluene, with a calibration curve.[33] Several experiments showed that the internal standard did not affect either the products or the rate of the reaction. The second-order rate constants were calculated in the usual way.[34]

FTIR Study of Tetraethylammonium Cyanide Solutions. The tetraethylammonium cyanide spectra were recorded on a Michelson 100 FTIR with use of calcium fluoride cells with a 0.1 mm path length in 0.50% aqueous acetonitrile at 22 °C. The peaks at 2058 and 2071 cm^{-1} have been ascribed to an acetonitrile-solvated cyanide ion and a water-solvated cyanide ion, respectively.[11] A reaction with *m*-chlorobenzyl tosylate and tetraethylammonium cyanide showed that the ratio of the absorbances for the two types of cyanide ion remained constant throughout the kinetic run.

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Supporting Information Available: Tables of the individual incoming group $^{11}C/^{14}C$ KIEs and the average rate constants used to calculate the secondary α-deuterium KIEs for the S_N2 reactions between several *meta*-chlorobenzyl *para*-substituted benzenesulfonates and cyanide ion in 0.5% aqueous acetonitrile at 0 °C (2 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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(32) The 0.54% aqueous acetonitrile was prepared by diluting 5.40 mL of double-distilled water to 1 L in a volumetric flask with dry acetonitrile (Caledon Laboratories Ltd. HPLC grade). Different batches of the "dry" acetonitrile obtained from the supplier gave different rate constants. This was undoubtedly due to the small, but different, amounts of water in the dry acetonitrile. Adding a small amount of water gave a reproducible solvent and reproducible rate constants and isotope effects.

(33) Snyder, L. R.; Kirkland, J. J. *Introduction to Modern Liquid Chromatography*, 2nd ed.; Wiley-Interscience: New York, 1979; pp 549−555.

(34) Laidler, K. J. *Chemical Kinetics*; McGraw-Hill: Toronto, Canada, 1965; p 8.