Reactions of Quinuclidines and Oxyanions with Substituted Diphenyl Sulfites. Inductive Effects Mutually Exerted between Entering and Leaving Groups in Transition States

Junghun Suh,* Dongsoo Koh, and Changhee Min

Department of Chemistry, Seoul National University, Seoul 151-742, Korea

Received July 31, 1987

Nucleophilic reactions of quinuclidine derivatives and various oxyanions with substituted diphenyl sulfite esters were kinetically studied. A linear plot was obtained for the dependence of the logarithmic value of the second-order rate constant on the pK_a of the oxyanion in the reaction of *m*-nitrophenyl phenyl sulfite. Since the pK_a range (2.8–15.8) of the oxyanions employed was very wide and the pK_a of *m*-nitrophenol (8.42) lies in the middle of the pK_a range, the linearity is consistent either with the concerted mechanism or with the associative mechanism in which the addition intermediate lies on a shallow energy well. Values of β_{LG} and β_{Nu} were obtained for the nucleophilic reactions. Effective charges on the entering and the leaving atoms in the reactants, products, and transition states were assigned on the basis of the β values. In the transition states of the nucleophilic reactions, the bond orders of the sulfur–nucleophile bond and the sulfur-leaving group bond were at least 0.65–0.74, in marked contrast with the transition states for sulfuryl or phosphoryl transfer reactions. The value of parameters $\partial\beta_{Nu}/\partial pK_{LG}$ and $\partial\beta_{LG}/\partial pK_{Nu}$ was −0.058 for the reaction of quinuclidines and about 0 for the reaction of oxyanions. These values were anomalous since the positive values of $\partial\beta_{Nu}/\partial pK_{LG}$ and $\partial\beta_{LG}/\partial pK_{Nu}$ correspond to normal "Hammond" effects. The nonpositive values of $\partial\beta_{Nu}/\partial pK_{LG}$ and $\partial\beta_{LG}/\partial pK_{Nu}$ observed in the present study were explained in terms of inductive effects mutually exerted between the entering and leaving groups in the transition states and the consequent modification of the "effective" charges on the entering and leaving atoms. It was further suggested that the inductive effects mutually exerted by the polar groups of transition states could be a general phenomenon.

Mechanisms of the nucleophilic reactions on the derivatives of oxyacids of sulfur have been the subject of extensive investigation.[1] The studies are aimed at the elucidation of the reaction paths and the structures of the transition states unique to the reactions of the derivatives of sulfenic (RSOH), sulfinic (RSOOH), and sulfonic (RSO_2OH) acids. The mechanistic information obtained with the sulfur compounds can be compared with that disclosed by the studies with the derivatives of oxyacids of phosphorus and carbon. This comparison is especially meaningful in view of the significance of the derivatives of the carbon, phosphorus, and sulfur oxyacids in biological systems.[2]

The sulfinyl sulfur atom contains a nonbonding electron pair and its configuration is tetrahedral.[3] Whether the nucleophilic reaction on a sulfinyl derivative proceeds through a stepwise (associative or addition–elimination) mechanism involving a discrete addition intermediate or through a concerted mechanism is not clear.[1] In either case, the configuration of the central sulfur atom in the transition state is trigonal bipyramidal and the entering and leaving groups occupy the apical positions of the bipyramid. Although several lines of evidence have been presented in support of each mechanism, the mechanistic ambiguity has not been resolved yet.[1] The failure to detect the incorporation of ^{18}O into the unreacted substrate in the hydrolysis of sulfinyl esters in ^{18}O-enriched water[4,5] does not necessarily indicate the absence of addition intermediates.[1] The slopes (Hammett ρ, β_{LG}, β_{Nu}) obtained in the linear free-energy relationships measured for the nucleophilic reactions on arenesulfinamides or aryl methanesulfinates also did not provide any decisive information concerning the two mechanisms.[1,6,7]

It is highly probable that the two mechanisms (concerted and associative mechanisms) represent extremes of a mechanistic spectrum and that the actual mechanism depends on the structures of the leaving group and the sulfinyl portion of the substrate and on the nature of the nucleophile. In this regard, another extreme similar to S_N1 (dissociative mechanism) involving the formation of sulfinylium cations is possible.[8]

Diphenyl sulfite esters undergo nucleophilic reactions even with weak bases such as carboxylates.[9] Sulfite esters (ROSOOR) contain sulfinyl groups and are structurally related to carbonate esters (ROCOOR), for which intensive mechanistic analysis has been performed.[10] Thus, the structure–reactivity relationships in the aminolysis by quinuclidine derivatives of substituted diphenyl carbonate esters led to various β_{Nu} and β_{LG} values. Based on these β values, Gresser and Jencks were able to determine the magnitude of "effective" charges developed on the leaving and entering atoms as well as the carbonyl oxygen atom in reactants, products, tetrahedral intermediates, and transition states.[10]

In the present study, several structure–reactivity relationships were investigated in order to obtain information on the existence of a discrete intermediate and on the structure of the transition state. Thus, the kinetics of nucleophilic reactions of various oxyanions and quinuclidine derivatives on substituted diphenyl sulfites **1a–e** have been studied. In this paper, the values of β_{Nu} and β_{LG} for various combinations of nucleophiles and leaving groups are reported and the elucidation of the structures of the transition states based on these values are discussed. In particular, examination of the dependence of β_{Nu} and β_{LG}

---

[1] Kice, J. L. *Adv. Phys. Org. Chem.* **1980**, *17*, 65 and references therein.

[2] Spector, L. B. *Covalent Catalysis by Enzymes*; Springer-Verlag: New York, 1982.

[3] Mislow, K.; Greene, M. M.; Laur, P.; Mellilo, J. T.; Simmons, T.; Ternay, A. L., Jr. *J. Am. Chem. Soc.* **1965**, *87*, 1958.

[4] Najam, A. A.; Tillett, J. G. *J. Chem. Soc., Perkin Trans. 2* **1975**, 858.

[5] Bunton, C. A.; de la Mare, P. D. B.; Greaseley, P. M.; Llewellyn, D. R.; Pratt, N. H.; Tillett, J. G. *J. Chem. Soc.* **1958**, 4751.

[6] Biasotti, J. B.; Andersen, K. K. *J. Am. Chem. Soc.* **1972**, *93*, 1178.

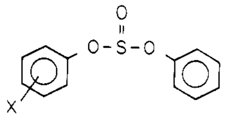
[7] Senatore, L.; Ciuffarin, E.; Fava, A.; Levita, G. *J. Am. Chem. Soc.* **1973**, *95*, 2918.

[8] Suh, J.; Lee, J. C., to be published.

[9] King, L.-H.; Kaiser, E. T. *J. Am. Chem. Soc.* **1974**, *96*, 1410.

[10] Gresser, M. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 6963.

0022-3263/88/1953-1147$01.50/0



1a: X = *p*-NO_2
b: X = *p*-CN
c: X = *m*-NO_2
d: X = *m*-Cl
e: X = H

on pK_{LG} and pK_{Nu}, respectively, reveals that inductive effects are mutually exerted between the entering and leaving groups in the transition states.

Experimental Section

Sulfite Esters. Phenyl chlorosulfinate was prepared by refluxing an excess of thionyl chloride with phenol according to the literature,[1] bp 75 °C (5 Torr) [lit.[11] bp 95 °C (10 Torr)]. Diphenyl sulfite (**1e**) was prepared by reacting phenyl chlorosulfinate with phenol in the presence of triethylamine,[12] mp 13–14 °C (lit.[12] mp 13–16 °C). Unsymmetrical diaryl sulfites **1a–d** were not separated as pure materials by this method because of decomposition in the purification steps. This is attributable to the relative instability of these esters compared with **1e**. Thus, the stock solutions of these esters were generated in situ. A solution of phenyl chlorosulfinate in acetonitrile was added to an acetonitrile solution containing equivalent amounts of substituted phenol and triethylamine at 0 °C. Examination by UV–vis spectra (based on initial absorbance values and the absorbance changes during the nucleophilic reactions) and TLC indicated that the yields of the sulfite esters were at least 60–70%. Reaction rates were measured with $(0.5–2) \times 10^{-4}$ M total concentration ($[S]_0$) of the sulfur derivatives (the sulfite ester, unreacted phenyl chlorosulfinate, and decomposition products). In order to assure that the unwanted compounds (hydrolysis products and triethylamine) existing in the stock solutions do not alter the kinetic results appreciably, the pseudo-first-order rate constants (k_0) were measured with the amount of the stock solutions taken into the reaction media being varied by 2–3-fold for each reaction. The k_0 values were not affected noticeably by this change in the amount of the unwanted materials. In some reactions, hydrolysis products and triethylamine were externally added in the concentration of $(1–2) \times 10^{-4}$ M, but the rate data were not altered. In addition, no differences in the kinetic data for **1e** were observed when the purified substrate was used or when the substrate generated in situ was employed in the kinetic measurements.

Other Materials. The nucleophiles examined in this study (quinuclidine derivatives, carboxylic acids, phenols, and alcohols) were obtained from commercial sources and were purified by either recrystallization or distillation. Water was redistilled and deionized prior to use in the kinetic studies. Triethylamine and acetonitrile were purified according to the literature.[13]

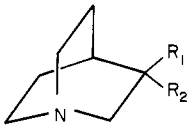
Kinetic Measurements. Rates of the reactions were measured with a Beckman 5260 UV–vis spectrophotometer. Temperature was controlled at 25 ± 0.1 °C with a Lauda/Brinkman E2 circulator. Kinetic data were obtained in the presence of 9.1% (v/v) acetonitrile. pH measurements were performed with a Fisher Accumet Model 525 pH meter. Buffers (0.01 M) used were 4-morpholinoethanesulfonic acid (pH 5.5–7) or *N*-(2-hydroxyethyl)piperazine-*N*′-2-ethanesulfonic acid (pH 7–8). These buffers were used when the nucleophiles added had insufficient buffer capacity over the pH range in which kinetic measurements were made. Ionic strength was maintained at 1.0 M with sodium chloride. The values of k_0 were obtained with the measured values of infinity absorbance readings. The k_0 values measured at a fixed pH consisted of contribution of the attack by hydroxide ion and that by added buffer or nucleophile. Thus, the attack by water or chloride ion was negligible under the experimental conditions.

Ionization Constants of Nucleophiles. Calculation of the bimolecular rate constants for the reactions by various nucleophiles from the measured k_0 values required the correct pK_a values of the nucleophiles. Therefore, the pK_a values[14] were measured in the presence of 9.1% (v/v) acetonitrile at ionic strength 1.0 M and 25 °C by titrating the solutions of the nucleophiles with a Syringe Microburet Model No. SB2 of MicroMetric Instrument Co. From the pH values measured at partial neutralization stages, the pK_a values were calculated.

Results

Kinetic data were obtained under the pseudo-first-order conditions($[Nu]_{total} \gg [S]_0$). For most of the nucleophiles, however, the reactivity of the nucleophiles was very high and reaction rates at pHs comparable to the respective pK_as were too fast to measure without the stopped-flow technique. For some nucleophiles, therefore, it was necessary to lower the concentration of the basic form of the nucleophile while the total concentration of the nucleophile should be kept in great excess of $[S]_0$. For this purpose, kinetic measurements were performed at pHs significantly lower than the pK_a of the nucleophile, and the rate data were normalized to 1 M of the basic form of the nucleophile to calculate the bimolecular rate constant (k_2). In order to raise the reliability of k_2, rate data were collected at at least two pHs and the average of the normalized rate constants calculated at these pHs was taken as the k_2 value. The normalized rate constants calculated at different pHs usually agreed within 10%.

As amine nucleophiles, quinuclidine derivatives (quinuclidine (**2a**), 3-hydroxyquinuclidine (**2b**), 3-chloroquinuclidine (**2c**), 3-quinuclidinone (**2d**)) were employed.



2a: R_1 = H, R_2 = H
b: R_1 = OH, R_2 = H
c: R_1 = Cl, R_2 = H
d: R_1, R_2 = =O

Since quinuclidines are tertiary amines, complications due to the transfer of protons from the amine nitrogens can be avoided. In addition, ambiguities from variable steric effects in the series of substituted amines can be avoided with the quinuclidine derivatives. For these reasons, quinuclidine derivatives have been intensively used in the elucidation of the structure of transition states in transacylation reactions.[10,15,16] The log k_2 values for the aminolysis of **1a–e** by quinuclidine derivatives are plotted against the pK_a of the nucleophiles (pK_{Nu}) in Figure 1. The same log k_2 values are plotted against pK_a of the leaving phenols (pK_{LG}) for each quinuclidine derivative in Figure 2.

The oxyanion nucleophiles employed in the present study are carboxylate (cyanoacetate, chloroacetate, formate, acetate, and dianionic succinate), phenolate (2,3,5,6-tetrafluorophenolate, *p*-cyanophenolate, *p*-chlorophenolate, and phenolate), alkoxide (2,2,2-trifluoroethoxide, 2,2-dichloroethoxide, and 2-chloroethoxide), and hydroxide ions, in the order of increasing basicity.

For **1c**, nucleophilic reactions were kinetically examined with all of the oxyanions listed above. The plot of log k_2 for the reactions of the oxyanions against pK_{Nu} of the

---

(11) Bissinger, W. E.; Kung, F. E. *J. Am. Chem. Soc.* **1948**, *70*, 2664.

(12) Van Woerden, H. F. *Chem. Rev.* **1963**, *63*, 557.

(13) Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. *Purification of Laboratory Chemicals*; Pergamon: London, 1966.

(14) The pK_a values measured under other conditions are given in ref 10 and: Jencks, W. P.; Regenstein, J. *Handbook of Biochemistry and Molecular Biology*, 3rd ed.; Fasman, G. D., Ed.; CRC Press: Cleveland, 1976; Vol. 1, pp 305–351.

(15) Gresser, M. J., Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 6970.

(16) Suh, J.; Lee, B. H. *J. Org. Chem.* **1980**, *45*, 3103.

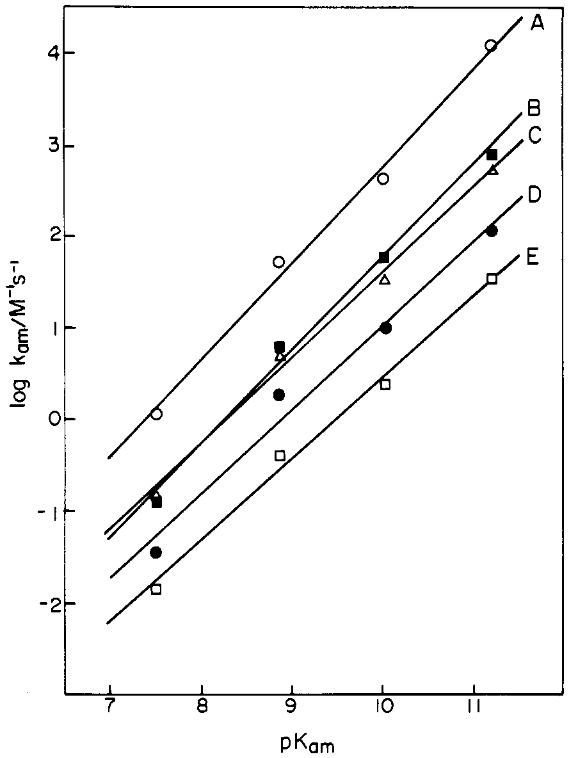


Figure 1. Plots of log k_2 against pK_{Nu} for the reactions of quinuclidines **2a–d** with sulfite ester substrates **1a–e**. Line A (○) is for **1a**, line B (■) for **1b**, line C (△) for **1c**, line D (●) for **1d**, and line E (□) for **1e**. Slopes of the linear lines are summarized in Table II.

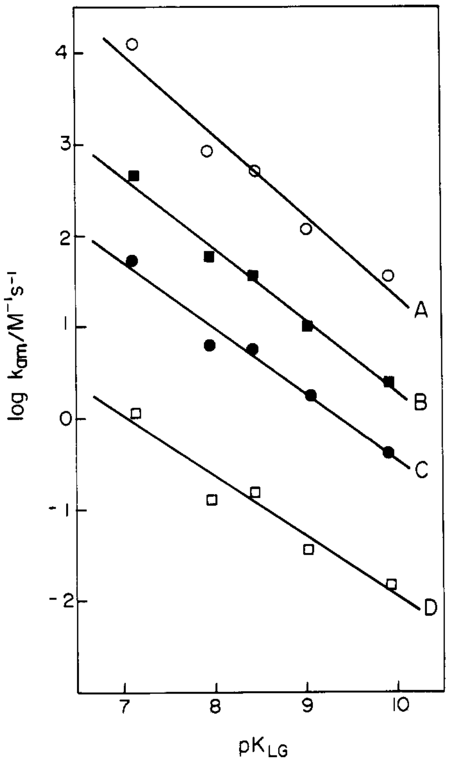


Figure 2. Plots of log k_2 against pK_{LG} for the reactions of quinuclidines **2a–d** with sulfite ester substrates **1a–e**. Line A is for **2a**, line B for **2b**, line C for **2c**, and line D for **2d**. Slopes of the linear lines are summarized in Table III.

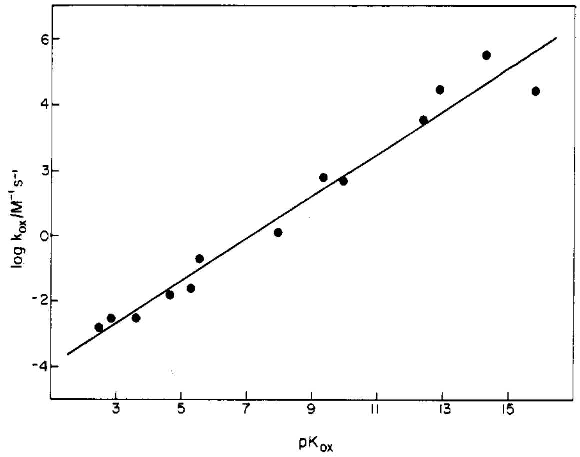


Figure 3. Plot of log k_2 against pK_{Nu} for the reactions of various oxyanions with sulfite ester substrate **1c**. Slope of the straight line drawn in the figure is 0.65 ± 0.04.

Table I. β_{Nu} Values for the Reactions of the Quinuclidine Derivatives with 1a–e[a,b]

substrate	pK_{LG}[c]	β_{Nu}
1a	7.12	1.05 ± 0.06
1b	7.95	1.01 ± 0.06
1c	8.42	0.94 ± 0.06
1d	9.03	0.92 ± 0.08
1e	9.92	0.89 ± 0.05

[a] Quinuclidine derivatives used are **2a–d**. [b] Weighted linear regression of β_{Nu} against pK_{LG} leads to a slope of −0.056 ± 0.009. [c] Measured under the conditions of the present study.

Table II β_{LG} Values for the Reactions of Quinuclidine Derivatives with 1a–e[a]

quinuclidine derivative	pK_{Nu}[b]	β_{LG}
2a	11.20	−0.89 ± 0.09
2b	10.02	−0.79 ± 0.04
2c	8.86	−0.72 ● 0.07
2d	7.50	−0.66 ± 0.09

[a] Weighted linear regression of β_{LG} against pK_{Nu} leads to a slope of −0.060 ± 0.008. [b] Measured under the conditions of the present study.

oxyanions is illustrated in Figure 3 for **1c**. For other substrates, kinetics of the nucleophilic reactions by oxyanions were measured only with cyanoacetate, acetate, dianionic succinate, 2,2,2-trifluoroethoxide, and hydroxide ions. The plot of log k_2 against pK_{Nu} of these oxyanions are illustrated for each substrate in Figure 4. The plot of log k_2 against pK_{LG} is illustrated in Figure 5 for each of these oxyanions. The plots of Figure 4 would provide more accurate mechanistic information if data points were also collected over the pK_{Nu} range of 7–10, which corresponds to the ionization of phenols. Because nucleophiles should be added in great excess of $[S]_0$ and the absorbances of the phenols are very large at <300 nm, the spectrophotometric kinetic measurements were not possible for the substrates that contain no nitro substituents. The standard deviations of the logarithmic values of the bimolecular rate constants indicated in Figures 1–5 are smaller than the size of the symbols used for the data points.

The attack of nucleophiles at the sulfite esters should displace[9] the better leaving phenol group. For **1a–d**, therefore, only the substituted phenolates are cleaved during the nucleophilic attack while both of the leaving groups are subjected to expulsion in this process for the reaction of **1e**. Thus, statistical corrections were made by dividing the observed values of bimolecular rate constants by two for the reactions of **1e**.

The straight lines drawn in Figures 1–5 represent various linear free-energy relationships, and the slopes of the lines provide various β values. In Table I, the β_{Nu} values for the aminolysis by the quinuclidine derivatives (the slopes of

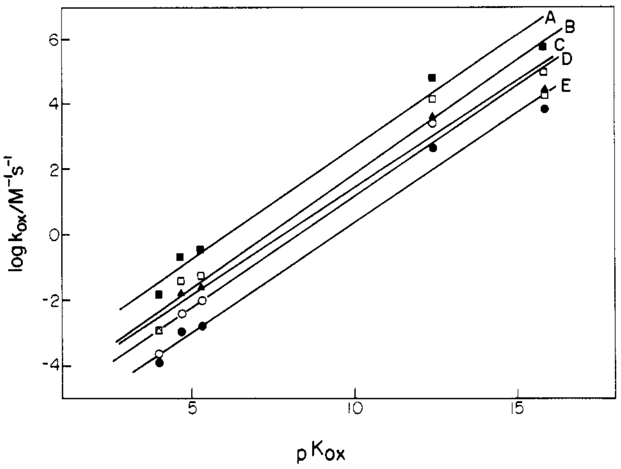


Figure 4. Plots of log k_2 against pK_{Nu} for the reactions of hydroxide ion, 2,2,2-trifluoroethoxide ion, succinate dianion, acetate ion, and cyanoacetate ion with sulfite ester substrates **1a–e**. Line A (■) is for **1a**, line B (□) for **1b**, line C (▲) for **1c**, line D (○) for **1d**, and line E (●) for **1e**. Slopes of the linear lines are summarized in Table IV.

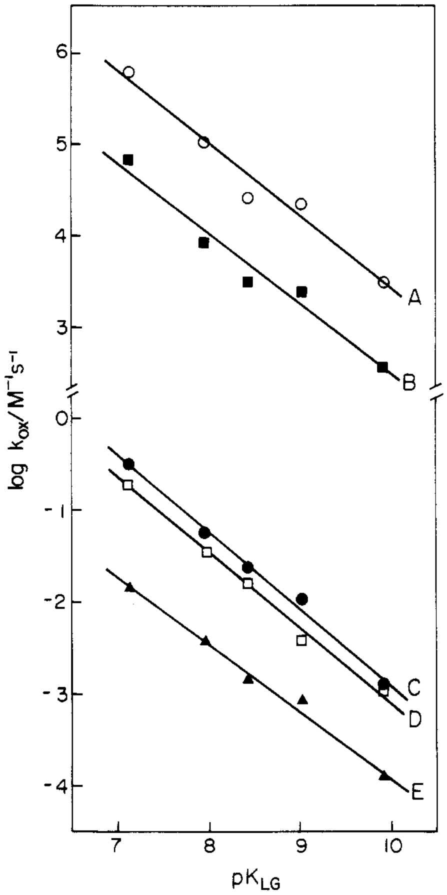


Figure 5. Plots of log k_2 against pK_{LG} for the reactions of oxyanion nucleophiles included in Figure 4 with sulfite ester substrates **1a–e**. Line A is for hydroxide ion, line B for 2,2,2-trifluoroethoxide ion, line C for succinate dianion, line D for acetate ion, and line E for cyanoacetate ion. Slopes of the linear lines are summarized in Table V.

linear lines drawn in Figure 1) are summarized for each substrate. In Table II, the β_{LG} values for the aminolysis reactions (the slopes of linear lines drawn in Figure 2) are listed for each quinuclidine derivative. In Table III, the β_{Nu} values for the attack by oxyanions (the slopes of linear lines drawn in Figure 4) are listed for each substrate. The slope (β_{Nu}) of the straight line drawn in Figure 3 is 0.65 ± 0.04. In Table IV, the β_{LG} values for the reactions by oxyanions (the slopes of linear lines drawn in Figure 5) are summarized for each nucleophile. In Figure 6, the plots of β_{Nu} against pK_{LG} and β_{LG} against pK_{Nu} are illustrated for the aminolysis reactions.

Table III. β_{Nu} Values for the Reactions of Oxyanions with 1a–d[a,b]

substrate	pK_{LG}[c]	β_{Nu}
1a	7.12	0.61 ± 0.04
1b	7.95	0.62 ± 0.04
1c	8.42	0.59 ± 0.04
1d	9.03	0.61 ± 0.05
1e	9.92	0.61 ± 0.05

[a] Oxyanion nucleophiles used are hydroxide ion, 2,2,2-trifluoroethoxide ion, succinate dianion, acetate ion, and cyanoacetate ion. [b] Weighted linear regression of β_{Nu} against pK_{LG} leads to a slope of −0.002 ± 0.007. [c] Measured under the conditions of the present study.

Table IV. β_{LG} Values for the Reactions of Oxyanions with 1a–e[a]

oxyanion	pK_{Nu}[b]	β_{LG}
hydroxide	15.80[c]	−0.79 ● 0.08
2,2,2-trifluoroethoxide	12.40	−0.77 ± 0.08
succinate dianion	5.30	−0.83 ± 0.03
acetate	4.66	−0.81 ± 0.04
cyanoacetate	2.49	−0.73 ± 0.05

[a] Weighted linear regression of β_{LG} against pK_{Nu} leads to a slope of −0.001 ± 0.006. [b] Measured under the conditions of the present study. The pK_{Nu} of the other oxyanions employed in the present study are 2.84 for chloroacetate, 3.60 for formate, 5.52 for 2,3,5,6-tetrafluorophenolate, 9.35 for *p*-chlorophenolate, 12.90 for 2,2-dichloroethoxide, and 14.30 for 2-chloroethoxide. [c] This value was calculated by examining the effects of the addition of 1.0 M sodium chloride and 9.1% (v/v) acetonitrile on the pH values of aqueous solutions containing 0.01–0.05 M sodium hydroxide.

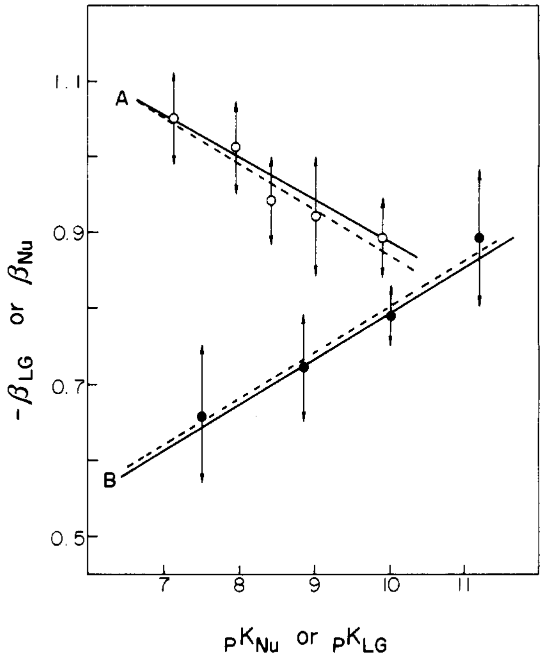


Figure 6. Plot (line A) of β_{Nu} against pK_{LG} and plot (line B) of $-\beta_{LG}$ against pK_{Nu} for the reactions of quinuclidine derivatives **2a–d** with sulfite ester substrates **1a–e**. The solid theoretical lines are obtained by weighted linear regression and the dotted ones by unweighted linear regression.

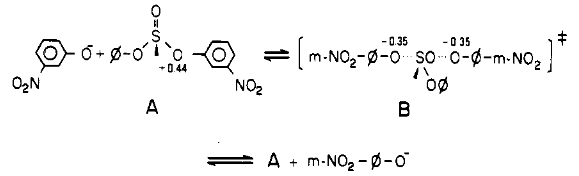
Discussion

Structures of Transition States. The pK_a values of the oxyanion nucleophiles involved in the linear correlation illustrated in Figure 3 are 2.8–15.8, while that of the leaving *m*-nitrophenol of the substrate is 8.4. The observation of linear or slightly curved Brønsted plot of log k_2 against pK_{Nu} similar to that of Figure 3 has been taken as evidence for the concerted mechanism in the transfer of phosphoryl, sulfuryl, or sulfonyl groups between various nucleophiles.[17-25] If a discrete intermediate is formed by the addition of the nucleophile to the sulfinyl group, a change in the rate-determining step would occur as the pK_a of the nucleophile is changed in this wide range and a break would be observed in the Brønsted plot at pK_a of the nucleophile similar to that of the leaving group.

The linear relationship of Figure 3, however, is also compatible with the associative mechanism, if it is assumed that the addition intermediate lies on a shallow energy well. In this case, the transition states for the formation and for the breakdown of the addition intermediate should resemble the intermediate very closely.

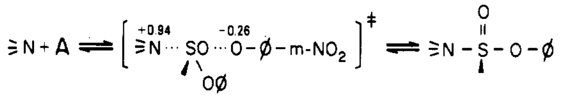
The values of β_{Nu} and β_{LG} provide valuable information on the structure of transition state, especially when they are obtained systematically.[7] The values of β_{Nu} and β_{LG} may be regarded as the effective charges on the nucleophile and the leaving group atoms, respectively, in the transition state relative to the ground state.[10,16] In addition, the effective charge on the nucleophile atom in the product relative to the reactant can be represented by β_{eq}, which is obtained from the relationship $\beta_{eq} = \beta_{Nu} - \beta_{LG}$.[23] It has been emphasized that this equation must be applied to the same molecule or group of the same chemical reaction in both directions ("identity reactions").[23,24] The β_{eq} value also represents the dependence of the equilibrium constants on the basicity of the nucleophile.

In the nucleophilic reactions of various oxyanions with **1c** (Figure 3), a β_{Nu} value of 0.65 was observed. This value can be assigned for the attack of *m*-nitrophenolate on **1c**, in which both the entering and leaving groups are *m*-nitrophenolate. As summarized in Table IV, the β_{LG} values for various oxyanions are independent of the pK_{Nu} values. Thus, a β_{LG} value of −0.79 can be assigned for the nucleophilic attack by *m*-nitrophenolate on the substrates. From these β values, β_{eq} of 1.44 is obtained as the magnitude of charge (A) in the ester relative to the nucleophile for the attacking phenolate oxygen (the numbers in A–K indicate the effective charges on the entering or leaving oxygen or nitrogen atoms attached to the central atoms). When the values of β_{eq}, β_{Nu}, and β_{LG} are combined, the effective charges on the leaving and entering oxygen atoms in the transition state can be represented as in B.



A B (1)

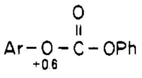
The plot of $-\beta_{LG}$ against pK_{Nu} for the reactions of quinuclidines is linear as illustrated in Figure 6. For a hypothetical quinuclidine whose pK_a is the same as that (8.42) of *m*-nitrophenol, β_{LG} of −0.70 is expected. By using this value and the β_{Nu} of 0.94 observed for **1c** (Table I), the charge distribution on the entering and leaving atoms in the transition state may be assigned as C.



$$\equiv N + A \rightleftharpoons \left[\overset{+0.94}{\equiv N}\cdots \underset{\diagup\diagdown O\phi}{SO}\cdots\overset{-0.26}{O}-\phi-m\text{-}NO_2\right]^{\ddagger} \rightleftharpoons \equiv N-\overset{O}{\overset{\|}{S}}-O-\phi \qquad (2)$$

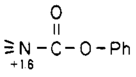
C D

The presence of a positive charge on the phenolic oxygen in A is attributable to the inductive and resonance effects of the sulfinyl group. In the case of aminolysis by quinuclidines of substituted diphenyl carbonate esters, similar effects of the carbonyl group led to the charge distribution depicted in E and F.[10] Comparison of the charge distribution in A, E, and F suggests that the effects of the carbonyl and sulfinyl groups are comparable in this matter and that the charge on the nitrogen atom of D would be significantly greater than +1.



$$\mathrm{Ar-\underset{+0.6}{O}-\overset{O}{\overset{\|}{C}}-OPh}$$

E

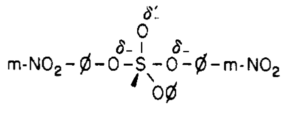


$$\mathrm{\underset{+1.6}{\equiv N}-\overset{O}{\overset{\|}{C}}-O-Ph}$$

F

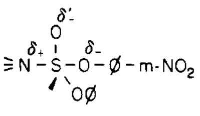
For an identity reaction in which the entering and leaving groups are the same, the transition state is located on the diagonal line connecting the upper right and lower left corners of the energy surface diagram of Figure 7, unless a discrete intermediate corresponding to each of the corners is present.[24] Degrees of formation of the sulfur-nucleophile (S–Nu) bond and cleavage of the sulfur–leaving group (S–LG) bond in the transition state are indicated by the position of the transition state on the diagonal line. The position of the transition state in turn can be calculated from the effective charges on the entering and leaving atoms in the transition state. For this calculation, however, the effective charges on the entering and leaving atoms in the addition intermediate should be known. This intermediate is a hypothetical one in case of the concerted mechanism whereas it lies on a shallow energy well if the associative mechanism is operative.

It has been reported that apical S–O bond lengths in pentacoordinate analogues of the addition intermediate are substantially increased over the lengths in the tetrahedral structures.[26-28] Then, the atoms occupying the apical positions of the hypervalent intermediate might bear extra negative charges,[1] and, thus, the oxygen ligands in G and H could possess partial negative charges while the positive charge on the nitrogen atom in H could be smaller than 1.0.



$$m\text{-}NO_2-\phi-\overset{\delta-}{O}-\underset{\diagup\diagdown O\phi}{\overset{\overset{\delta-}{O}}{\overset{|}{S}}}-\overset{\delta-}{O}-\phi-m\text{-}NO_2$$

G



$$\overset{\delta+}{\equiv N}-\underset{\diagup\diagdown O\phi}{\overset{\overset{\delta-}{O}}{\overset{|}{S}}}-\overset{\delta-}{O}-\phi-m\text{-}NO_2$$

H

When δ_- of G and H is taken as 0 and δ_+ of H as 1, the bond orders of the S–Nu and S–LG bonds in B are 0.65, whereas that of the S–Nu bond in C is 0.94 and that of the

---

[17] Skoog, M. T.; Jencks, W. P. *J. Am. Chem. Soc.* **1983**, *105*, 3357.

[18] Bourne, N.; Williams, A. *J. Am. Chem. Soc.* **1983**, *105*, 3357.

[19] Hopkins, A.; Bourne, N.; Williams, A. *J. Am. Chem. Soc.* **1983**, *105*, 3358.

[20] Hopkins, A.; Day, R. A.; Williams, A. *J. Am. Chem. Soc.* **1983**, *105*, 6062.

[21] D'Rozario, P.; Smyth, R. L.; Williams, A. *J. Am. Chem. Soc.* **1984**, *106*, 5027.

[22] Bourne, N.; Williams, A. *J. Am. Chem. Soc.* **1984**, *106*, 7591.

[23] Skoog, M. T.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 7597.

[24] Williams, A. *J. Am. Chem. Soc.* **1985**, *107*, 6335.

[25] Jencks, W. P.; Haber, M. T.; Herschlag, D.; Nazaretian, K. L. *J. Am. Chem. Soc.* **1986**, *108*, 479.

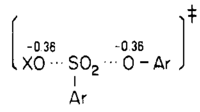
[26] Paul, I. C.; Martin, J. C.; Perozzi, E. F. *J. Am. Chem. Soc.* **1972**, *94*, 5010.

[27] Perozzi, E. F.; Martin, J. C.; Paul, I. C. *J. Am. Chem. Soc.* **1974**, *96*, 6735.

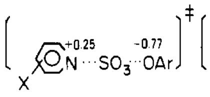
[28] Perkins, C. W.; Wilson, S. R.; Martin, J. C. *J. Am. Chem. Soc.* **1985**, *107*, 3209.

S–LG bond in C is 0.74. The actual bond orders would be greater than these. Therefore, even if a concerted mechanism is assumed, the bond orders of the S–Nu and S–LG bonds may be greater than 0.65 in B, the transition state of an identity reaction. Then, B and, similarly, C resemble the addition intermediate even in the case of the concerted mechanism. If the associative mechanism is operative, B and D should resemble the addition intermediate very closely and the charge distribution indicated in B and C may be taken as that in the addition intermediate.

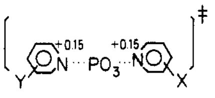
The effective charges on the entering and leaving atoms in the transition states for sulfonyl, sulfuryl, and phosphoryl transfer reactions are indicated in I–K.[20–22] The effective charges in I are similar to those in B. However, those in J and K indicate that the bond orders of the S–Nu and S–LG bonds in these transition states are much smaller compared with those of the sulfinyl- or sulfonyl-transfer reactions illustrated by B, C, or I. The transition states for the sulfuryl- or phosphoryl-transfer reactions has been described as being open "exploded".[20]



I



J



K

Inductive Effects in Transition States. The β_{Nu} and β_{LG} values for the reactions of quinuclidines with **1a–e** manifest linear dependence on pK_{LG} and pK_{Nu}, respectively, as illustrated in Figure 6, respectively. On the other hand, the corresponding β values are independent of pK_{LG} or pK_{Nu} for the reactions of oxyanions as summarized in Tables III and IV. The β_{Nu} values calculated from the linear lines of Figure 4 are not as reliable as that of Figure 3, since the data points for pK_a 7–10 were not obtained for the plots of Figure 4 as pointed out in the Results section. However, the β_{Nu} values calculated for **1c** based on the data of these two figures agree well and β_{Nu} for the reactions of the oxyanions (Table III) can be taken as being independent of pK_{LG}.

The mechanistic significances of the dependence of β_{Nu} and β_{LG} on pK_{LG} and pK_{Nu}, respectively, can be analyzed with Figure 7. Thus, effects on the structure of the transition state exerted by the structural changes in reactant molecules may be predicted according to the postulates proposed by Hammond and Thornton.[29,30] The analysis presented above indicates that the transition states resembles the addition intermediate and that the transition state may be put on point i of Figure 7 in case of the concerted mechanism or on point ii in case of the associative mechanism.

When the nucleophile becomes weaker, the structures on the upper horizontal edge of Figure 7 are stabilized, and, consequently, the transition state would be shifted toward a or b, the sum of vectors 1 and 2 or vectors 3 and 4. The actual shapes of vector a or b depends on the magnitude of vectors 1 and 2 or vectors 3 and 4 as exemplified by vectors a and a′. When vectors 1–4 are small, the structure of the transition state would not be affected significantly as pK_{Nu} is varied. The analysis made with this diagram, however, does indicate that the cleavage of the S–LG bond in the transition state should not proceed to a lesser extent as the nucleophile becomes weaker. In the present study, $-\beta_{LG}$ decreases for the reactions of quinuclidines as pK_{Nu} is lowered (Table II). If $-\beta_{LG}$ represents the degree of the cleavage of the S–LG bond, this stands in sharp contrast with the prediction made in Figure 7.

If the leaving ability of the leaving phenolate is decreased, the structures on the left vertical edge of Figure 7 are stabilized and the transition state would move toward *c* or *d*, the sum of vectors 2 and 5 and vectors 4 and 6. Again the actual shapes of vectors *c* and *d* depend on the magnitude of vectors 2 and 5 or vectors 4 and 6. The analysis made in Figure 7, however, does indicate that the formation of the S–Nu bond in the transition state should not proceed to a lesser degree when pK_{LG} is raised. The observed β_{Nu} values decreases in the reactions of the quinuclidines (Table I) as pK_{LG} is increased, on the contrary to the prediction made here.

The values of β_{LG} and β_{Nu} represent $\partial \log k_2/\partial pK_{LG}$ and $\partial \log k_2/\partial pK_{Nu}$, respectively, being related to $\partial \Delta G^{\ddagger}/\partial pK_{LG}$ and $\partial \Delta G^{\ddagger}/\partial pK_{Nu}$. A simple approximation to a description of the Gibbs free energy of a point (x, y) on the energy surface diagram such as Figure 7 has been given[23,31] by eq 3. When the coordinates of the transition state in the

$$\Delta G/2.303RT = ax^2 + by^2 + cxy + dx + ey + f \quad (3)$$

saddle point can be represented by β_x and β_y, respectively, eq 3 is transformed into eq 4.[23,31,32] The $\beta_x{}^0$ and $\beta_y{}^0$ values

$$-\log k = \tfrac{1}{2}p_x pK_{LG}{}^2 + \tfrac{1}{2}p_y pK_{Nu}{}^2 - p_{xy}pK_{Nu}pK_{LG} - \beta_x{}^0 pK_{LG} - \beta_y{}^0 pK_{Nu} + F \quad (4)$$

are the β_x and β_y values when $pK_{LG} = pK_{Nu} = 0$. Parameter p_x, p_y, and p_{xy} are defined as shown in eq 5–7.

$$p_x = \partial\beta_x/\partial pK_{LG} \quad (5)$$

$$p_y = \partial\beta_y/-\partial pK_{Nu} \quad (6)$$

$$p_{xy} = \partial\beta_y/\partial pK_{LG} = \partial\beta_x/-\partial pK_{Nu} \quad (7)$$

In the phosphoryl transfer between pyridine and primary amines or in the general acid-catalyzed addition of thiol anions to acetaldehyde,[31,33] the *p* parameter values were calculated by assuming that $\beta_x = -\beta_{LG}$ and $\beta_y = \beta_{Nu}$. The cross-coefficient p_{xy} describes the interaction between the entering and leaving groups.[23] The positive sign of p_{xy}, as has been observed in the transfer of phosphoryl groups (0.142) and the addition of thiol anions (0.026), corresponds to a normal "Hammond" effect.[23] However, it has been noted that the negative sign of p_{xy} is expected for "a direct electrostatic interaction between dipoles of the attacking and leaving groups".[23] The nonpositive values (−0.058 ± 0.006 for quinuclidines and −0.001 ± 0.004 for oxyanions) of p_{xy} calculated as $\partial\beta_{LG}/\partial pK_{Nu}$ or $\partial\beta_{Nu}/\partial pK_{LG}$ for the reactions of sulfite esters, therefore, suggest that inductive effects are mutually exerted between the entering and leaving groups in the transition states.

The results obtained with the reactions of quinuclidine derivatives on the sulfite esters can be explained in terms of the inductive effects in the transition states as follows. When the basicity of the quinuclidine is lowered, the electron-withdrawing property of a less basic nucleophile could be transmitted to the leaving phenol oxygen, decreasing the effective negative charge ($|\beta_{LG}|$) on the leaving oxygen atom (Table II) although the S–LG bond is cleaved

---

(29) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334.

(30) Thornton, E. R. *J. Am. Chem. Soc.* **1967**, *89*, 2915.

(31) Jencks, D. A.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 7948.

(32) If $-\beta_{LG}$ and β_{Nu} represent the changes in the effective charges only due to the bond cleavage or formation, they can be taken as the scales of β_x and β_y, respectively, which has been assumed in ref 17. In ref 17, the *x* and *y* axes used in the derivation of eq 2 are reversed compared to those of the present study.

(33) Gilbert, H. F.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 7931.

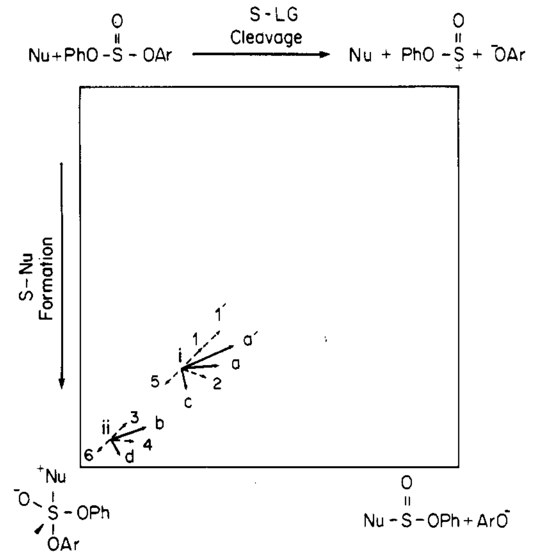


Figure 7. Energy surface diagram used in the analysis of kinetic data obtained for the nucleophilic reactions on sulfite esters.

to a greater extent in the transition state. As pK_{LG} is increased by the introduction of an electron-donating group in the leaving phenol, the inductive effect of the leaving phenol might decrease the effective positive charge (β_{Nu}) on the nucleophile nitrogen atom although S–Nu bond is formed to a greater extent (Table I).[34]

The smaller values of $\partial\beta_{LG}/\partial pK_{Nu}$ and $\partial\beta_{Nu}/\partial pK_{LG}$ (–0.058) for the reactions of quinuclidines compared to those (ca. 0) for the reactions of oxyanions indicate that inductive effects exerted between the entering and leaving groups in the transition states are more effective in the attack of quinuclidines. This may be attributed to the zwitterionic character of the transition states and, consequently, to the more effective electrostatic interactions in the transition states for the aminolysis reactions.[35]

After the present study was complete, Bordwell and Hughes reported kinetic results of S_N2 reactions by anionic nucleophiles in dimethyl sulfoxide which indicated that there was no direct relationship between the size of β_{Nu} and the extent of bond making or bond breaking in the transition states of the reactions.[36] It was suggested that the S_N2 reactions occur in two stages (eq 8) and that the size of β_{Nu} is determined in the first stage where an ion–dipole complex (L) is formed. The lack of correlation

$$\mathrm{Nu}^- + \mathrm{R-X} \rightleftharpoons \underset{\mathrm{L}}{\mathrm{Nu\cdots R-X}} \rightleftharpoons \underset{\mathrm{M}}{[\mathrm{Nu\cdots R\cdots X}]^{\ddagger}} \rightleftharpoons \mathrm{Nu-R} + \mathrm{X}^- \qquad (8)$$

between β_{Nu} and the extent of bond formation between the nucleophile and the electrophilic carbon, however, may be also ascribed to the electrostatic interaction between the two groups in the transition state (M) of the rate-determining step. The effective charge (β_{Nu}) on the nucleophile atom in M would be decided not only by the degree of bond formation but also by the inductive effects mutually exerted by the entering and central atoms.

The inductive effects mutually exerted by the polar groups (the entering group, the central atom, and the leaving group) of the transition state can be a very general phenomenon. Slopes of various linear free-energy relationships are among the most frequently used tools in the elucidation of reaction mechanisms. In the mechanistic analysis, it is generally assumed that many of the slopes of the linear free-energy relationships, e.g., Brønsted α and β for general acid or base catalysis in addition to β_{LG} and β_{Nu} discussed in this study, are the scales of bond formation or cleavage in the transition state. This can be oversimplified and interpretation of the slopes should be performed carefully.

Acknowledgment. This study was supported by a grant from the Korea Science and Engineering Foundation.

---

[34] When both the leaving group and the nucleophile are *m*-nitrophenolates (eq 1), the electron density on the phenolic oxygen atom of a *m*-nitrophenolate in the transition state would be lowered by the inductive effect of the other *m*-nitrophenolate. On the other hand, the same inductive effect by the *m*-nitrophenolate would increase the electron density on its own phenolic oxygen atom. Consequently, the effective charges on the leaving and entering oxygen atoms of this identity reaction might not be affected significantly by the inductive effects. In this regard, the charge distribution in B can be correlated with bond orders.

[35] Inductive effects exerted between the entering and leaving groups in the transition states were not observed in the kinetic studies of the transfer of sulfuryl or phosphoryl groups in contrast to the present reaction.[17–20,22–25] This may be partially attributed to the smaller bond orders between the entering group and the central atom or between the leaving group and the central atom in the transition states for sulfuryl- or phosphoryl-transfer reactions compared with those in the present reaction. The greater bond orders in the present reaction, therefore, are related to the closer distance between the entering and the leaving groups in the transition state, which in turn would result in more effective electrostatic interaction between the two groups.

[36] Bordwell, F. G.; Hughes, D. L. *J. Am. Chem. Soc.* 1986, *108*, 7300.

Determination of ^{18}O Exchange Accompanying Basic Hydrolysis of *p*-Toluamide and *N*,*N*-Dimethyl-*p*-toluamide

H. Šlebocka-Tilk and R. S. Brown*

Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada T6G 2G2

Received August 28, 1987

The base-catalyzed hydrolysis and ^{18}O-exchange rate constants for *p*-toluamide (IV) and *N*,*N*-dimethyl-*p*-toluamide (V) have been determined under pseudo-first-order conditions as a function of $[OH^-]$ at $T = 100$ °C, $\mu = 1.0$ M. Both sets of rate constants are linearly dependent on $[OH^-]$, and therefore the ratio of k_{ex}/k_{hyd} for IV and V does not change as a function of $[OH^-]$. For IV and V the ratios are 3.5 ± 0.2 and 0.11 ± 0.007 respectively. The fact that V shows substantial exchange suggests that the original formulation of the Deslongchamps stereoelectronic theory needs to be reassessed with respect to the conformational equilibration of the anionic tetrahedral addition intermediate produced from *N*,*N*-dimethylbenzamide and OH^-.

Carbonyl ^{18}O exchange concurrent with basic hydrolysis has been demonstrated for a variety of carboxylic esters and amides.[1–3] The mechanistic analysis (as in the minimum scheme given in eq 1) requires a reversibly formed

0022-3263/88/1953-1153$01.50/0 © 1988 American Chemical Society