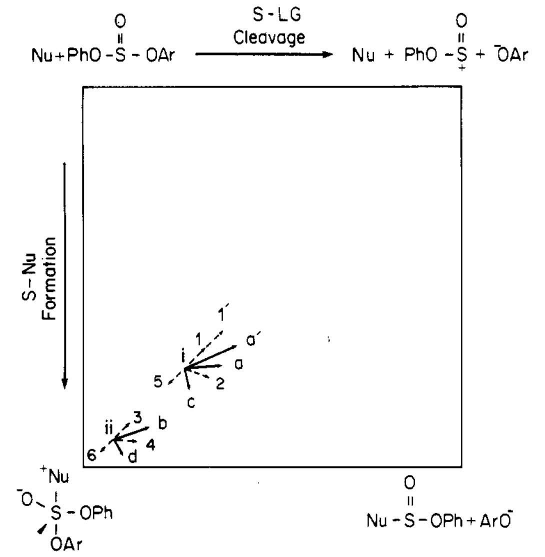

Figure 7. Energy surface diagram used in the analysis of kinetic data obtained for the nucleophilic reactions on sulfite esters.

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

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

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.

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(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

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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, μ = 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

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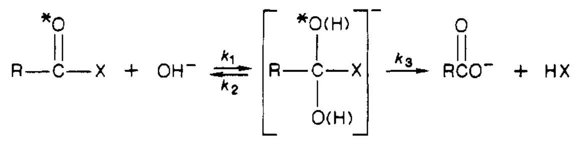
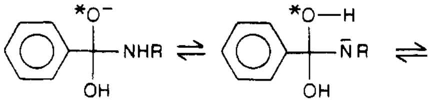


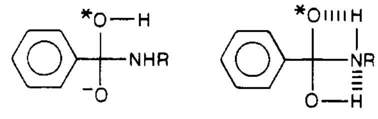
$$R\text{—}\overset{\overset{*O}{\|}}{C}\text{—}X + OH^- \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \left[R\text{—}\overset{\overset{*O(H)}{|}}{\underset{\underset{O(H)}{|}}{C}}\text{—}X\right]^- \xrightarrow{k_3} R\overset{\overset{O}{\|}}{C}O^- + HX \qquad (1)$$

I

intermediate which is symmetrical or two species in rapid equilibrium which lead to an overall symmetric system. It is reported that primary[1a–d,2] and secondary[2a] benzamides (but not tertiary[2a,b]) exhibit substantial ^{18}O exchange in unreacted amide recovered from solution at elevated temperature and $[OH^-]$. The latter observation was originally interpreted[2a,b] as implying the intermediacy of species such as II and III where an adjacent NH (but not NR_2) could facilitate the symmetrization of the ^{18}O and ^{16}O oxygens in the tetrahedral intermediate.



II

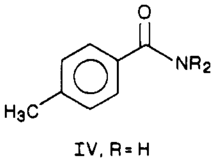


III

More recently, Deslongchamps and co-workers[3,4] have reinterpreted the original observations with *N*,*N*-dimethylbenzamide[2a,b] in support of the principle of stereoelectronic control.[4] In that interpretation, the lifetime of the tetrahedral intermediate (I, X = $N(CH_3)_2$) is too short to allow conformational changes at nitrogen which are required to assist in ejecting $^{18}O\text{–}H^-$. It was suggested, with some experimental support,[3] that "there may or may not be oxygen exchange concurrent with the basic hydrolysis of tertiary amides, and that depends upon the relative energy barriers for conformational change and fragmentation".[4]

We have recently undertaken a reinvestigation of the question of ^{18}O exchange accompanying hydrolysis of amides and have shown that in acidic media the exchange/hydrolysis ratio for acetanilide and *N*-cyclohexylacetamide unexpectedly changes as a function of $[H_3O^+]$ at constant ionic strength.[5] Therefore it was of interest that the original Bunton report[2a] contained two observations which have significant bearing on the question of ^{18}O exchange concurrent with hydrolysis. The first was an apparent change in the ratio of the exchange and hydrolysis rate constants[6] for benzamide with changing $[OH^-]$. For example, k_{ex}/k_{hyd} was observed to vary from 3.0 to 4.8 as $[OH^-]$ changes from 1.09 M to 0.07 M. It was reasonably suggested that the change resulted from nonconstant ionic strength effects,[2a] but this requires clarification in the light of our recent observations.[5]

The second question pertains to the limits of accuracy in determining the k_{ex}/k_{hyd} ratio for *N*,*N*-dimethylbenzamide which were imposed by the relatively small ^{18}O enrichment (1.4 atom % excess[2a]). This is important since the conclusion of no ^{18}O exchange[7] formed one of the bases for ideas[3,4] about conformational equilibration determining the partitioning of tetrahedral intermediates.



IV, R = H
V, R = CH_3

Herein we report results with 38% ^{18}O-enriched *p*-toluamide (IV) and *N*,*N*-dimethyl-*p*-toluamide (V) which bear on these questions. It will be seen that significant exchange is exhibited by V and furthermore that for both materials k_{ex} and k_{hyd} vary linearly with $[OH^-]$ between 0.00475 M and 1.0 M.

Experimental Section

(a) Materials. *p*-Toluamide (IV) was commercially available (Aldrich) and was purified by recrystallization from EtOH: mp 161–162 °C (lit.[8] mp 161–163 °C).

p-Toluamide (^{18}O enriched) was prepared by passing gaseous NH_3 through a solution of *p*-toluoyl chloride (38% ^{18}O enriched) in CH_2Cl_2.

N,*N*-Dimethyl-*p*-toluamide (V) was prepared by the addition of *p*-toluoyl chloride to a solution of excess dimethylamine in CH_2Cl_2. Distillation of the crude product at 100 °C (1.5 Torr) yielded amide V in 90% yield. Anal. Calcd for $C_{10}H_{13}NO$: C, 73.52; H, 8.00; N, 8.61. Found: C, 73.57; H, 8.03; N, 8.58. ^{18}O-Enriched *N*,*N*-dimethyl-*p*-toluamide was prepared similarly by adding 38% ^{18}O-enriched *p*-toluoyl chloride to a solution of excess dimethylamine in CH_2Cl_2.

^{18}O-Enriched *p*-toluoyl chloride was prepared in two steps. Firstly, commercially available *p*-toluoyl chloride (Aldrich) was hydrolyzed with a minimum amount of ~75% isotopically enriched $H_2{}^{18}O$. The resulting *p*-toluic acid was then treated with excess $SOCl_2$ at reflux for 1 h and subsequently distilled under vacuum (50 °C (1 Torr)).

(b) Kinetics. (i) Hydrolysis. Pseudo-first-order rate constants for hydrolysis (k_{hyd}) were obtained in duplicate by observing the rate of decrease (*p*-toluamide) or increase (*N*,*N*-dimethyl-*p*-toluamide) in absorbance of 2×10^{-4} M aqueous solutions (μ = 1.0 M, KCl) of the amides at the wavelength of maximum change (245 and 242 nm respectively) using a Cary 210 UV–vis spectrophotometer. Individual 5-mL aliquots of sample in the appropriate medium were thermostated in ampules at 100 °C. These were removed at various times, cooled, and the absorbance of the contents measured at 25 °C. Rate constants (k_{hyd}) were obtained from the slopes of the ln $[(A_t - A_\infty)/(A_{t0} - A_{t\infty})]$ vs time plots. $A_{t\infty}$ was evaluated independently from a solution comprising the authentic products of the hydrolysis in the particular medium. The reactions were followed to at least two half-times and in all cases exhibited clean first-order kinetics.

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(1) (a) Bender, M. L. *J. Am. Chem. Soc.* **1951**, *73*, 1626. (b) Bender, M. L.; Ginger, R. D.; Kemp, K. C. *J. Am. Chem. Soc.* **1954**, *76*, 5350. (c) Bender, M. L.; Ginger, R. D. *J. Am. Chem. Soc.* **1955**, *77*, 348. (d) Bender, M. L.; Ginger, R. D.; Unik, J. P. *J. Am. Chem. Soc.* **1958**, *80*, 1044. (e) Bender, M. L.; Thomas, R. J. *J. Am. Chem. Soc.* **1961**, *83*, 4183.

(2) (a) Bunton, C. A.; Nayak, B.; O'Connor, C. *J. Org. Chem.* **1968**, *33*, 572. (b) Bunton, C. A.; Lewis, T. A.; Llewellyn, D. R. *Chem. Ind. (London)* **1954**, 1154. (c) Bunton, C. A.; Spatcher, D. N. *J. Chem. Soc.* **1956**, 1079.

(3) (a) Deslongchamps, P.; Cheriyan, U. O.; Guida, A.; Taillefer, R. J. *Nouv. J. Chim.* **1977**, *1*, 235. (b) Deslongchamps, P.; Gerval, P.; Cheriyan, U. O.; Guida, A.; Taillefer, R. J. *Nouv. J. Chim.* **1978**, *2*, 631. (c) Deslongchamps, P.; Bartlet, R.; Taillefer, R. J. *Can. J. Chem.* **1980**, *58*, 2167.

(4) (a) Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon: Oxford, 1983. (b) See particularly pp 108–118 for discussion of this point.

(5) Ślebocka-Tilk, H.; Brown, R. S.; Olekszyk, J. *J. Am. Chem. Soc.* **1987**, *109*, 4620.

(6) Steady-state treatment of the process depicted in eq 1 yields $k_{ex} = k_2k_1[OH^-]/2(k_2 + k_3)$ and $k_{hyd} = k_3k_1[OH^-]/(k_2 + k_3)$. The factor of 2 appearing in the denominator of k_{ex} arises from the assumption that the two oxygens in I are at equilibrium with respect to proton transfer, and there is equal probability for expulsion of ^{16}OH or ^{18}OH (no kinetic or equilibrium isotope effect). It follows that $k_{ex}/k_{hyd} = k_2/2k_3$.

(7) The reported values[2a] for k_{ex}/k_{hyd} for *N*,*N*-dimethylbenzamide are 0.04, 0.07, and 0.02 at 14.7%, 24.4%, and 58% hydrolysis respectively in 0.4 M NaOH at 100 °C, but these were experimentally indistinguishable from 0.

(8) Aldrich Chemical Co. catalog 1986–1987.

Table I. Kinetic Data for Hydrolysis and ^{18}O Exchange of *p*-Toluamide in Aqueous Media at 100 °C, μ = 1.0 M (KCl)

[NaOH], M	k_{hyd}, s^{-1}	k_{ex}, s^{-1}	k_{ex}/k_{hyd}[b]	k_1,[c] s^{-1}
1.0	1.13×10^{-3}[a]	$(4.21 \pm 0.10) \times 10^{-3}$	3.7 ± 0.2	9.55×10^{-3}
0.5	5.60×10^{-4}[a]	$(1.88 \pm 0.02) \times 10^{-3}$	3.3 ± 0.1	4.32×10^{-3}
0.095	$(1.04 \pm 0.02) \times 10^{-4}$	$(4.23 \pm 0.09) \times 10^{-4}$	4.1 ± 0.2	9.50×10^{-4}
0.0475	$(4.98 \pm 0.05) \times 10^{-5}$	$(1.91 \pm 0.03) \times 10^{-4}$	3.8 ± 0.1	4.32×10^{-4}
0.0095	9.82×10^{-6}[a]	$(3.39 \pm 0.13) \times 10^{-5}$	3.5 ± 0.2	7.76×10^{-5}
0.00475	$(4.95 \pm 0.10) \times 10^{-6}$	$(1.39 \pm 0.03) \times 10^{-5}$	2.8 ± 0.1	3.28×10^{-5}

[a] Extrapolated value based on linear-least-squares fit of k_{hyd} vs $[OH^-]$: probable error ± 4% of quoted number. [b] Errors calculated from square root of the sum of the squares of the percent uncertainty in k_{ex} and k_{hyd}.[11] [c] k_1 calculated as $2k_{ex} + k_{hyd}$.

Table II. Kinetic Data for Hydrolysis and ^{18}O Exchange of *N,N*-Dimethyl-*p*-toluamide in Aqueous Media at 100 °C, μ = 1.0 M (KCl)

[NaOH], M	k_{hyd}, s^{-1}	k_{ex},[d] s^{-1}	k_{ex}/k_{hyd}[e]	k_1,[f] s^{-1}
1.0	1.02×10^{-3}[a]	$(1.07 \pm 0.07) \times 10^{-4}$	0.10	1.23×10^{-3}
0.5	5.10×10^{-4}[a]	$(4.58 \pm 0.27) \times 10^{-5}$	0.09	6.01×10^{-4}
0.1	$(9.63 \pm 0.02) \times 10^{-5}$[b]	$(1.39 \pm 0.06) \times 10^{-5}$	0.14	1.24×10^{-4}
0.0475	$(4.92 \pm 0.04) \times 10^{-5}$	$(5.66 \pm 0.23) \times 10^{-6}$	0.12	6.05×10^{-5}
0.01	$(9.53 \pm 0.07) \times 10^{-6}$[c]	$(1.09 \pm 0.05) \times 10^{-7}$	0.11	1.17×10^{-5}
0.00475	$(4.81 \pm 0.08) \times 10^{-6}$	$(5.02 \pm 0.05) \times 10^{-7}$	0.10	5.81×10^{-6}
0.005	5.10×10^{-6}[a]	$(5.37 \pm 0.27) \times 10^{-7}$	0.11	6.17×10^{-6}

[a] Extrapolated value based on linear-least-squares fit of k_{hyd} vs $[OH^-]$: probable error ± 4% of quoted number. [b] [NaOH] = 0.095 M. [c] [NaOH] = 0.0095 M. [d] Errors are standard deviations of plots of $\ln (a/(a-x))$ vs time plots where a and $(a-x)$ are percent ^{18}O content at 0 and time t. [e] Probable error ± 0.01; calculated as square root of the sum of the squares of the percent uncertainty in k_{ex} and k_{hyd}.[11] [f] k_1 calculated as $2k_{ex} + k_{hyd}$.

(ii) ^{18}O Exchange. The pseudo-first-order rate constants (k_{ex}) for loss of ^{18}O from reisolated amides IV and V were determined in duplicate by a protocol analoqous to one already described.[5] In each case a sample of enriched amide (0.0005 M–0.005 M in H_2O, μ = 1.0 M (KCl)) was split into several 10-mL portions, each being sealed in an ampule. The H_2O used was made free from dissolved CO_2[9] and stored under Ar. The ampules were then thermostated at 100 °C. Two of the ampules were removed at time 0 after thermal equilibration and worked up to determine that the extraction and analytical procedures were not producing anomalous results. The remaining ampules were subjected to the hydrolytic conditions for various times up to that of the hydrolytic $t_{1/2}$. Periodically, two or three samples were removed and extracted with CH_2Cl_2, the latter extracts being subsequently dried ($MgSO_4$) and stripped of volatiles to yield recovered amide. This was then directly analyzed with an AEI MS-12 low-resolution mass spectrometer. Percent ^{18}O content in the amide was determined as $100(I_{M^++2})/(I_{M^++2} + I_{M^+})$ where I represents the intensities of the parent and enriched parent ions. Twelve to 22 scans of the two peaks were made, and the percent values reported in Tables 1S and 2S (supplementary material) are the averages with the reported errors as standard deviations of the mean.

The k_{ex} values given in Tables I and II were obtained from the slopes of the $\ln (a/(a-x))$ vs time plots where a and $(a-x)$ represent the ^{18}O contants at 0 and time t respectively. It is important to note that for IV at low $[OH^-]$ (0.0095–0.00475 M) significant curvature in the $\ln (a/(a-x))$ plots was observed. We have no firm reason why this was so although it may have been attributable to problems in assuring pseudo-first-order conditions in the exchange experiments at low $[OH^-]$. For those two experiments, the k_{ex} values were obtained from the $\ln (a/(a-x))$ vs time plots to ~10% completion, the values being reported in Table I. Although the k_{ex} values at the two lowest hydroxide concentrations are somewhat lower than expected, we believe this is artifactual and does not alter the conclusion that k_{ex} values vary linearly with $[OH^-]$.

Results

The utilization of the *p*-toluamides IV and V as representative models for the k_{ex}/k_{hyd} phenomena in the corresponding benzamides stems from the ease of interpretation of the mass spectral data. We had originally initiated the study with *N,N*-dimethylbenzamide but encountered a severe m^+/z = 149 peak attributable to adventitious phthalate[10] which obscured the M^+ of the amide. This complication was aggravated by the small quantities of material recoverable from solutions of low concentrations of starting material required to keep the pseudo-first-order conditions of $[OH^-] \geqslant 10[\text{amide}]$. In order to circumvent the problem, we chose the *p*-methylbenzamides (IV and V) for study since neither contains an M^+ = 149.

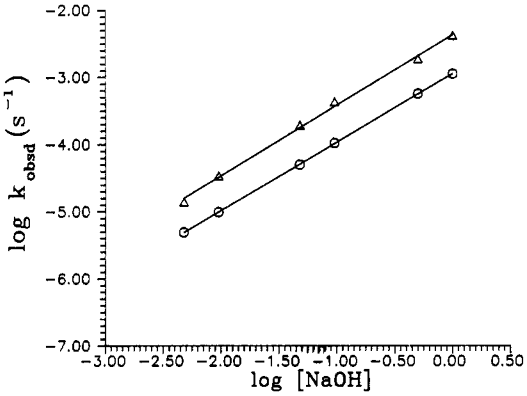

Figure 1. A plot of log k_{ex} (△) and log k_{hyd} (○) vs log [NaOH] for *p*-toluamide (T = 100 °C, μ = 1.0 M (KCl)). Straight lines through the data are linear-least-squares fits and have unit slopes.

Given in Tables I and II are the pseudo-first-order rate constants for exchange and hydrolysis of IV and V as a function of $[OH^-]$ at 100 °C, μ = 1.0 M (KCl). The k_{hyd} values presented without error limits in the tables are not experimental but are extrapolated from the linear-least-squares fits of the experimental values as a function of $[OH^-]$. For both amides, the slopes of the fits are 1.0. The k_{ex} values for both amides are also linearly dependent on $[OH^-]$.

The data supports the minimal mechanism given in eq 1. From that scheme can be derived[6] eq 2 and 3 which

$$k_{ex}/k_{hyd} = k_2/2k_3 \tag{2}$$

$$k_1 = 2k_{ex} + k_{hyd} \tag{3}$$

respectively refer to the partitioning of the tetrahedral

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(9) Rieman, W.; Neuss, J. D.; Naiman, B. *Quantitative Analysis*, *McGraw*-Hill: New York, 1951; pp 133–155.

(10) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. *Spectrometric Identification of Organic Compounds*, 4th ed.; Wiley: New York, 1981; p 30.

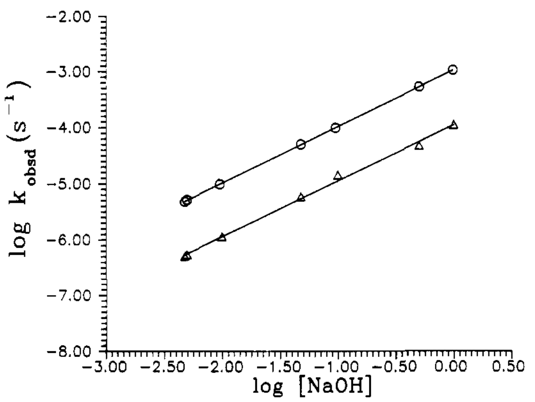

Figure 2. A plot of log k_{ex} (△) and log k_{hyd} (○) vs log [NaOH] for *N,N*-dimethyl-*p*-toluamide (T = 100 °C, μ = 1.0 M (KCl)). Straight lines through the data are linear-least-squares fits and have unit slopes.

intermediate and the pseudo-first-order rate constant for OH^- attack on the amide. These values are given in columns four and five of the tables. Finally, shown in Figures 1 and 2 are plots of log k_{ex} and log k_{hyd} for IV and V respectively as a function of log [NaOH]. The lines through each set of data are calculated best fits (slope = 1.0).

Discussion

The use of IV and V as mechanistic models for the hydrolytic process in benzamide and *N,N*-dimethylbenzamide rests upon the assumption that the p-CH_3 group does not seriously perturb the partitioning of the NH_2 and $N(CH_3)_2$ tetrahedral intermediates in one series relative to the other. Should that be the case, it would be reflected in a change in the relative ratios of the k_{hyd} values of the NH_2 and $N(CH_3)_2$ amides in both series since $k_{hyd} = k_1k_3[OH^-]/(k_2 + k_3)$. The reported second-order rate constants for benzamide and *N,N*-dimethylbenzamide at 100 °C are $16.5 \times 10^{-4}\ M^{-1}\ s^{-1}$ and $15.2 \times 10^{-4}\ M^{-1}\ s^{-1}$ respectively,[2a] while the present values for IV and V are $11.3 \times 10^{-4}\ M^{-1}\ s^{-1}$ and $10.2 \times 10^{-4}\ M^{-1}\ s^{-1}$. The fact that the ratio of the rate constants for the NH_2 and $N(CH_3)_2$ derivatives is essentially identical at 1.46 and 1.49 respectively suggests that the p-CH_3 group affects the partitioning in IV in much the same way as it does in V. This, and the fact that the average k_{ex}/k_{hyd} ratio in IV is 3.5 ± 0.2 while that for benzamide is reported to be[2a] 3.7 and 3.6 at 0.99 and 1.02 M NaOH, support the contention that the remote p-CH_3 group cannot exert a significant perturbation on the exchange processes in IV and V relative to their respective benzamides.[12]

The relatively high ^{18}O enrichment and analytical procedures adopted allow the exchange experiments to be conducted under pseudo-first-order conditions where $[NaOH] \geqslant 10[amide]$. This and an ionic strength maintained constant throughout make possible a clear-cut analysis of the data for IV and V. From the linear dependencies of the k_{ex} and k_{hyd} rate constants on [NaOH] (Figures 1 and 2), it must be concluded that in both amides the k_{ex}/k_{hyd} ratios are independent of $[OH^-]$ over the range studied. Hence, we concur with Bunton's analysis that the change in k_{ex}/k_{hyd} he observed for benzamide at changing $[OH^-]$ and ionic strength is attributable to a salt effect which changes the partitioning of the anionic tetrahedral intermediates.

The data demand that the transition states for addition and elimination of OH^- and for breakdown to products all have one OH^- incorporated. Furthermore, the observation of exchange demands a lifetime for the tetrahedral anionic intermediate long enough for the two oxygens to become (at least partially) equilibrated. The fact that V shows significant exchange suggests that it is unnecessary to postulate that structures such as II and III are required for the symmetrization of the anionic tetrahedral intermediates. Similarly, in order that this observation is to be accommodated within the original formulation of the stereoelectronic theory,[3,4] the requirement that the tetrahedral intermediate (I, X = $N(CH_3)_2$) is far from conformational equilibrium must be reassessed. We see no reason why the remote p-CH_3 group in I, X = $N(CH_3)_2$ would alter any steric arguments concerning amino rotation or inversion that might be made about the analogous intermediate from *N,N*-dimethylbenzamide. The present results indicate that the intermediate is more fully (and perhaps completely) equilibrated than was originally assumed.[3,4] In an attempt to fit the data to the theory, it might be argued that the factor of ~35 in the k_{ex}/k_{hyd} ratios of IV and V may be attributable to a less extensively equilibrated intermediate from V than IV. Although this may be so, that rationale does not consider differences in other factors such as relative steric compressions, leaving group abilities, and solvation of the forward and reverse reaction pathways which are likely to have larger effects on the partitioning of the intermediates from IV and V.

Conclusion

In summary, due to the greater accuracy currently available to determine the k_{ex}/k_{hyd} ratios in IV and V than was previously possible for the benzamides, we can determine that, for basic hydrolysis of these amides, the ratio is independent of $[OH^-]$. Furthermore, the fact that the $N(CH_3)_2$ derivative V exhibits substantial ^{18}O exchange concurrent with hydrolysis indicates that the anionic intermediate produced is more fully conformationally equilibrated than was originally assumed in formulating this aspect of the stereoelectronic theory.

Acknowledgment. We gratefully acknowledge the financial assistance of the Natural Sciences and Engineering Research Council of Canada and the University of Alberta.

Supplementary Material Available: Tables of ^{18}O content of amides IV and V reisolated from aqueous media at various times (Tables 1S and 2S) and original mass spectrometric M^+ and $M^+ + 2$ intensities for recovered IV and V (Tables 3S and 4S) (32 pages). Ordering information is given on any current masthead page.

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(11) Olson, A. R.; Orlemann, E. F.; Koch, C. *Introductory Quantitative Analysis*; W. H. Freeman: San Francisco, 1950; pp 102–113.

(12) It might be reasonably argued that even if the p-CH_3 group had the same effect on partitioning of the ionic NH_2 and $N(CH_3)_2$ intermediates, the presence of the CH_3 group induces *more* exchange in both IV and V than it does in the benzamides. In order for this to be true, the k_{ex}/k_{hyd} ratio for IV would necessarily be larger than that for benzamide. Although it is difficult to assess the error limits in the previously reported[2a] values for benzamide (and, in particular, the effects of the differing ionic strengths), to the extent that a comparison can be made, it appears as if the k_{ex}/k_{hyd} ratio for IV is greater than or equal to that for benzamide at μ = 1.0 M.