Table II. Rate and Relaxation Parameters Obtained Fitting Inversion–Transfer Data on Anomeric Resonances of D-Fructose at pH 8.4 (27 °C)

experiment[a]	$k_{\beta f,\alpha f}$	$k_{\beta p,\beta f}$	$k_{\beta p,\alpha f}$	$R_{\alpha f}$	$R_{\beta f}$	$R_{\beta p}$
invert $M_{\alpha f}$	1.9	$<10^{-2}$	<0.1	5.2	2.8	0.3
invert $M_{\beta f}$	1.7	<0.1	$<10^{-2}$	6.1	2.1	0.2
invert $M_{\beta p}$	1.8	$<10^{-2}$	<0.1	4.7	3.2	0.2

[a] $M_{\alpha f}$, $M_{\beta f}$, $M_{\beta p}$ are magnetizations associated with the anomeric carbon of the α-furanose, β-furanose, and β-pyranose forms of D-fructose.

in Figure 10. Rate parameters describing variations of resonance intensities were determined by fitting experimental data to eq 1–3 (as described in the Experimental Section) and are summarized in Table II. Considering the complexity of the fitting procedure, values for $k_{\beta f,\alpha f}$, $R_{\alpha f}$, $R_{\beta f}$, and $R_{\beta p}$ are remarkably consistent, irrespective of which type of inversion experiment is carried out. The mean value of 1.8 for $k_{\beta f,\alpha f}$ is also consistent with rate constants determined by resonance line broadenings. For example, using the measured equilibrium constant $K^{eq}_{\beta f,\alpha f}$ at pH 8.4 and 27 °C and $k_{\beta f,\alpha f}$ determined by the inversion–transfer method, one calculates a $k_{\alpha f,\beta f}$ of 7.3 s^{-1}. This value compares favorably with the rate constant for ring-opening of the α-furanose isomer determined from line-broadening measurements ($k_{\alpha f,a.c.}$ = 6.6 ± 1.3 s^{-1} at pH 8.4 and 26.5 °C). The close agreement between $k_{\alpha f,\beta f}$ and $k_{\alpha f,a.c.}$ also indicates that the ring-closing rate to the β-furanose form must be much faster than ring-closing to either the α-furanose or β-pyranose forms, a finding consistent with ring-closing rate constants calculated from line-broadening data and measured equilibrium constants (Figure 7). On the other hand, the rate measured by the inversion–transfer method for conversion of the β-furanose form to the α-furanose form ($k_{\beta f,\alpha f}$) is only 18% of the ring-opening rate from β-furanose to the acyclic form, as determined by line-width measurement ($k_{\beta f,a.c.}$ = 10.1 s^{-1} at pH 8.4 and 26.5 °C). However, this lower value is consistent with the ratio of rates determined from line widths for the conversion of acyclic intermediate to α-furanose and β-furanose forms (80 s^{-1}/500 s^{-1} × 100 = 16%). This result implies that once the β-furanose is converted to the acyclic form, roughly 20% of the acyclic form is converted to α-furanose while 80% returns to β-furanose. A negligible amount is converted to β-pyranose.

Interconversion rate constants listed in Table II from the β-pyranose form ($k_{\beta p,\beta f}$, $k_{\beta p,\alpha f}$) are certainly of less significance than $k_{\beta f,\alpha f}$ values, and they may arise as artifacts of the complex fitting routine. However, the magnitude of the values is certainly consistent with very slow ring-opening rates from the β-pyranose form and somewhat larger ring-closing rates to the β-pyranose form. For example, if 0.1 s^{-1} is taken as an upper limit for the β-pyranose–β-furanose conversion rate, then $k_{\beta p,a.c.}$ is also on the order of 0.1 s^{-1} and $k_{a.c.,\beta p}$ is less than 20 s^{-1}, a rate much slower than ring-closing to either the β-furanose or α-furanose forms (500 and 80 s^{-1}, respectively). Hence, dynamically only about 3% of the acyclic keto form is converted to the β-pyranose form. However, this form dominates the isomeric equilibrium due to its much smaller ring-opening rate.

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Registry No. D-Fructose, 57-48-7; β-fractopyranose, 7660-25-5; α-fructofuranose, 10489-79-9; β-fructofuranose, 470-23-5.

Single Transition State for Sulfuryl Group ($-SO_3^-$) Transfer between Pyridine Nucleophiles

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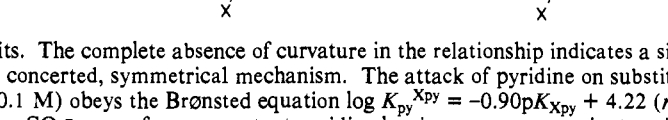
Abstract: The second order rate constants for the nucleophilic attack of pyridines on isoquinoline-*N*-sulfonate (25 °C, 0.1 M ionic strength) obey an excellent linear relation, $\log k_{Xpy}^{isq} = 0.23pK_{Xpy} - 1.91$ (r = 0.995), with the pK of the attacking



pyridine over eight pK units. The complete absence of curvature in the relationship indicates a single transition state for the reaction consistent with a concerted, symmetrical mechanism. The attack of pyridine on substituted pyridine-*N*-sulfonates (25 °C, ionic strength at 0.1 M) obeys the Brønsted equation $\log K_{py}^{Xpy} = -0.90pK_{Xpy} + 4.22$ (r = 0.998). The β_{EQ} for the equilibrium transfer of the $-SO_3^-$ group from a constant pyridine leaving group to a variant pyridine nucleophile (+1.13) is close to that predicted from a previous study. The electronic structure of the transition state possesses considerable sulfur trioxide character as deduced from the changes in effective charge on the entering and leaving pyridine nitrogen atoms.

There is much interest in the existence of preassociation stepwise mechanisms where an intermediate is not stable enough to diffuse outside an encounter complex containing a product-yielding reagent molecule.[1] Such processes have been considered in carbonyl addition,[2] $-PO_3^{2-}$ group transfer,[3,4] ligand exchange, and aromatic electrophilic substitution;[4] the following scheme (eq 1) summarizes the possibilities for a nucleophilic substitution reaction

(1) Jencks, W. P. *Chem. Soc. Rev.* **1981**, *10*, 345.
(2) Ortiz, J. J.; Cordes, E. H. *J. Am. Chem. Soc.* **1978**, *100*, 7080.
(3) (a) Skoog, M. T.; Jencks, W. P. *J. Am. Chem. Soc.* **1983**, *105*, 3356. (b) Bourne, N.; Williams, A. *Ibid.* **1983**, *105*, 3357. (c) Buchwald, S. L.; Knowles, J. R. *Ibid.* **1982**, *104*, 1438. (d) Westheimer, F. H. *Chem. Rev.* **1981**, *81*, 313.
(4) Hartshorn, S. R.; Ridd, J. H. *J. Chem. Soc. B* **1968**, 1068.

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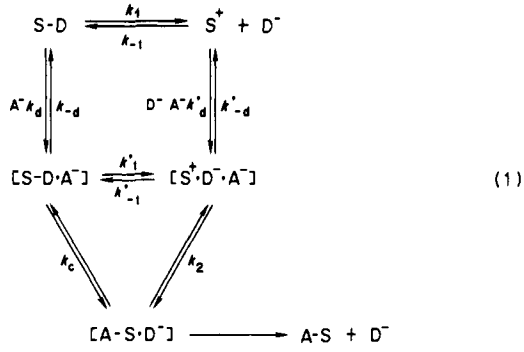
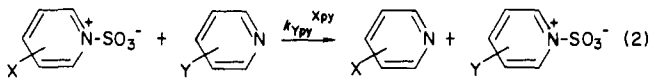
where D^- and A^- are leaving group and nucleophile, respectively, and S^+ is an unsaturated intermediate analogous to PO_3^-, SO_3^-, or carbenium ion. The preassociation pathway is where the



(1)

reaction flux passes through the ternary encounter complex ($S^+ \cdot D^- \cdot A^-$) and is taken when k'_{-1} is larger than the diffusion rate constant k'_{-d}. No particular ordering of S^+, D^-, and A^- is implied in the encounter complex, and we use the representation ($S^+ \cdot D^- \cdot A^-$) rather than ($S^+ \cdot D^- \cdot A^-$) to register this. A special concerted mechanism could be enforced if the lifetime of S^+ in the ternary encounter complex became less than that of a vibration period. A regular concerted mechanism could take the reaction flux if k_c was greater than k'_1. The demonstration of preassociation stepwise mechanisms is normally difficult and usually relies heavily on the interpretation of secondary kinetic evidence.[1]

The transfer of the sulfuryl group ($-SO_3^-$)[5] between elecronegative atoms is the basis of many important biochemical reactions; it is involved in the initial steps of inorganic sulfate utilization, in steroid metabolism, in detoxification processes, and in sulfate ester hydrolyses.[6] The distinction between a concerted bimolecular path and the preassociation stepwise mechanism is important to our understanding of these biochemical processes; it is conceivable that a reactive intermediate could be formed in an active site yet not diffuse out into the solvent. The latter possibility is a real and general problem in enzyme mechanism studies. The present paper[7] is a study of the transfer of $-SO_3^-$ between pyridine donors and acceptors (eq 2) where a simple, clear-cut distinction is possible between the mechanism. When



(2)

the donor (Xpy) and acceptor (Ypy) pyridines (eq 2) have the same basicity, the reaction is symmetrical and the preassociation stepwise mechanism (eq 3) predicts a change in the rate-limiting step; this results in a nonlinear Brønsted plot for the bimolecular rate constant for attack of acceptor pyridine. On the other hand,

$$Xpy^+\text{–}SO_3^- \overset{+Ypy}{\rightleftharpoons} [Xpy^+\text{–}SO_3^- \cdot Ypy] \rightleftarrows [Xpy \cdot Ypy \cdot SO_3] \rightleftarrows [Ypy^+\text{–}SO_3^- \cdot Xpy] \overset{-Xpy}{\rightleftharpoons} Ypy^+\text{–}SO_3^- \quad (3)$$

a linear Brønsted equation holding for pK values of the acceptor well above and below that of the donor indicates a single transition state consistent with a regular concerted process.

Recent work has inferred that imidazole-N-sulfonate intermediates, of which the present substrates are analogues, participate in sulfatase mechanisms.[8]

Experimental Section

Materials. Pyridine-N-sulfonates were prepared as described in a previous paper[9] by bubbling a stream of nitrogen carrying sulfur trioxide through a dichloromethane solution of the pyridine. The sulfur trioxide was prepared by passing a stream of dry nitrogen over a quantity of oleum (40%) which was gently warmed on an oil bath. Pyridines were obtained commercially and were purified by vacuum distillation from the material dried over KOH pellets. We are grateful to Dr. R. B. Moodie for a kind gift of 4-morpholinopyridine. Acetonitrile was purified by the method of Lewis and Smyth[10] and then redistilled from calcium hydride. Water used throughout the investigation was doubly distilled from glass.

Methods. The kinetics of reaction of pyridine-N-sulfonates were typically followed by adding a solution of the substrate (20–50 μL of a stock solution in dry acetonitrile) to 2.5 mL of aqueous buffer in a 1 cm path length silica cell. The spectrum was scanned repetitively to determine the optimum wavelength for the kinetic study. We employed either a Unicam SP 800 or a Perkin-Elmer 554 spectrometer fitted with external recorders. The pseudo-first-order rate constant for decay of the pyridine-N-sulfonate was obtained from the slopes of the linear plots of $A_t - A_\infty$ against time on two cycle semilogarithmic graph paper.

Buffer solutions containing increasing amounts of added pyridine (ranging from 0 to 0.025 M) were prepared by mixing two stock solutions, adjusted to the same pH, one containing the pyridine and background buffer and the other containing only the background buffer. For pH's near 8 and 10, respectively, tris(hydroxymethyl)aminomethane (Tris) and carbonate buffers were employed.

The temperature of the buffers was maintained at 25 ± 0.1 °C during the kinetics by the use of external water circulating thermostats for each spectrometer. The pH of the reaction solution was measured before and after each run with a Radiometer PHM 26 pH meter. Ionization constants were determined by potentiometric titration of the species with either standard NaOH or HCl with a Radiometer pH titration set comprising pH meter PHM 26, titrator TTT60, REC servograph, REA titratigraph, and autoburette ABU 11. The Henderson Hasselbalch equation (pH = pK + log [B]/[HB]) was employed to estimate the pK values. Brønsted correlations and statistical treatments of the various kinetic parameters were made with a Texas TI-51 III calculator.

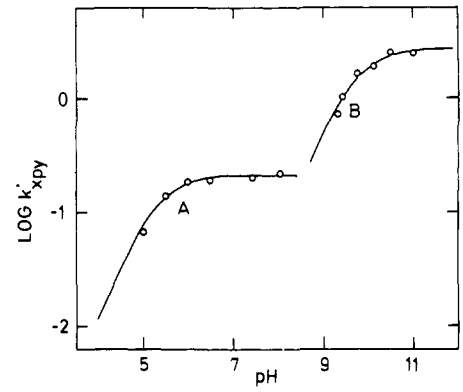


Figure 1. Dependence on pH of the pseudo-second-order rate constant for attack of (A) pyridine and (B) 4-(dimethylamino)pyridine on isoquinoline-N-sulfonate. Conditions: 25 °C, ionic strength maintained at 0.1 M with KCl, buffers at 0.01 M (pH_5, acetate; 5.5–7, phosphate; 7–8.5, Tris; 9–12, borate and carbonate). The lines are calculated from eq 4 and parameters from Table I. Each point represents the slope obtained from a line possessing at least three points spaced over a concentration range of 0–0.025 M in the pyridine.

Results

The products of the reactions of pyridine-N-sulfonates in buffers containing no pyridines or nucleophilic species were pyridines and the sulfate ion.[9] It was possible to choose a wavelength, for most of the reactions of pyridine-N-sulfonates in pyridine buffers, which yielded simple first-order kinetics over at least 90% of the total reaction. The pseudo-first-order rate constants were linear in total pyridine concentration (see supplementary Figure 1). Values of k_{obsd} at the higher concentrations sometimes showed a little curvature; this was not investigated, and slopes were taken from the values for lower concentrations where strict linearity occurs. The pH dependence of the slope k_{Xpy}' for two selected pyridines was determined (Figure 1), and this obeys the rate law (eq 4)

(5) The IUPAC name for the $-SO_3^-$ group is sulfonato, but we prefer sulfuryl as this term has been commonly employed in the past (note, however, the use of sulfuryl for $>SO_2$).

(6) Roy, A. B. "The Enzymes", 3rd ed.; Academic Press: New York, 1971; Vol. 5, p 1.

(7) A preliminary account of this work has appeared: Hopkins, A.; Bourne, N.; Williams, A. *J. Am. Chem. Soc.* **1983**, *105*, 3358.

(8) Lee, G. D.; Van Etten, R. L. *Arch. Bioch. Biophys.* **1975**, *171*, 424.

(9) Hopkins, A.; Day, R. A.; Williams, A. *J. Am. Chem. Soc.* **1983**, *105*, 6062.

(10) Lewis, G. L.; Smyth, C. P. *J. Chem. Phys.* **1939**, *7*, 1085.

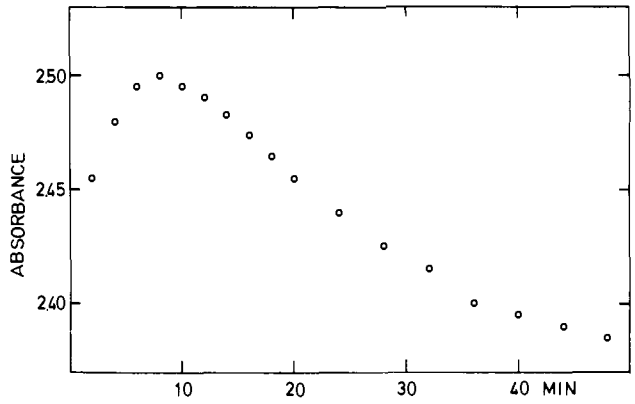


Figure 2. Decomposition of 4-picoline-*N*-sulfonate (4.96×10^{-4} M) in Tris buffer (0.01 M) containing pyridine (0.01 M) at pH 7.67 and 25 °C; ionic strength maintained at 0.1 M with KCl. Absorption measured at 270 nm.

Table I. Reaction of Pyridines with Isoquinoline-*N*-sulfonate[a]

pyridine	pK	Δ^b	$k_{Xpy}^{isq} \times 10^{2e}$	N[c]	pH[f]
4-formyl	4.71	−0.148	10.7	8	8.06
parent	5.31	0.003	20.7	d	5–8
3-cyanomethyl	4.09	−0.005	10.6	8	8.05
3-picoline	5.82	0.055	31.0	8	7.75
3,4-lutidine	6.45	0.020	39.5	9	8.00
methyl isonicotinate	3.27	−0.015	6.75	8	8.07
4-dimethylamino	9.61	0.033	221	d	9–11
3,5-lutidine	6.14	0.061	37.0	8	8.03
4-amino	9.15	−0.005	160	7	8.05
3-cyano	1.44	−0.022	2.5	9	8.00
4-morpholino	8.71	−0.070	108	8	8.83
4-picoline	6.14	−0.009	31.3	8	7.67
3-formyl	3.71	0.063	10.2	8	7.36
3-bromo	2.83	0.037	5.98	9	8.00
isoquinoline	5.46		0.52	4	8.17
2,6-lutidine	5.78		0.32	4	8.12

[a] Ionic strength maintained at 0.1 with KCl, $\lambda_{kinetic}$ = 339 nm, Tris buffer at 0.01 M total concentration, 25 °C. [b] The "residual" (log k_{Xpy} − log k_{Xpy}(calcd)). [c] Number of data points. [d] See Figure 1. [e] Units L mol^{-1} s^{-1}; errors are less than 5%. [f] Average pH of the reactions (variation ±0.01 pH units).

where k_{int} is the pseudo-first-order rate constant at zero buffer concentration, $[Xpy]_t$ is the total concentration of the pyridine species, and K_a^{Xpy} is the ionization constant of the conjugate acid of the pyridine. It is assumed that the rate law is the same for

$$k_{Xpy}' = (k_{obsd} - k_{int})/[Xpy]_t = k_{Xpy}/(1 + [H^+]/K_a^{Xpy}) \quad (4)$$

all the species, and k_{Xpy} was obtained from the slope of the linear plot of k_{obsd} vs. the free pyridine concentration. The latter was calculated from the pK of the pyridine and the pH in question. The values of k_{Xpy} are recorded in Tables I and II.

We were able to observe the formation and decay of an intermediate species (Figure 2) in the hydrolysis of some pyridine-*N*-sulfonates in pyridine buffers by careful choice of the wavelength. In the example chosen, we reacted 4-picoline-*N*-sulfonate in pyridine buffers (see Figure 2 for conditions) and followed the reaction at 270 nm. The decay of the intermediate obeyed a pseudo-first-order rate constant (1.20×10^{-3} s^{-1}) which

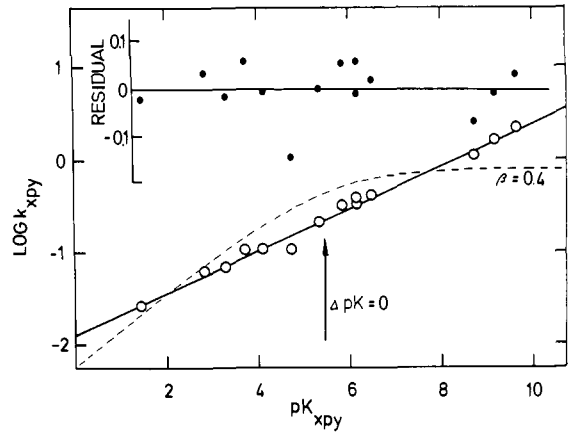


Figure 3. Reactivity of isoquinoline-*N*-sulfonate against pyridines (○) in increasing order of pK_{Xpy}: 3-CN, 3-Br, 4-MeOCO-, 3-CHO, 3-CH_2CN, 4-CHO, parent, 3-Me, 3,5-Me_2, 4-Me, 3,4-Me_2, 4-morpholino, 4-NH_2, 4-Me_2N). Conditions and values are from Table I, and the line is calculated from eq 5. The arrow indicates the pK_{Xpy} corresponding to a change in rate-limiting step for the putative mechanism of eq 3. The error "residuals" (●) are plotted on an inset scale (see text for details). The dotted line is calculated from eq 7 with β = 0.4.

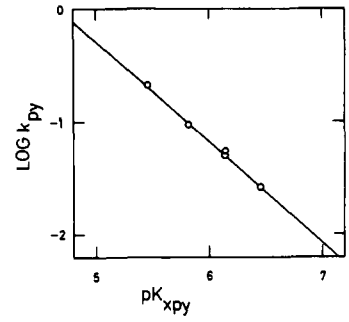


Figure 4. Variation of the reactivity of pyridine-*N*-sulfonates against pyridine as a function of pK_{Xpy}. The data are from Table II, and the line is calculated from eq 6. Conditions are recorded in Table II.

agrees very well with that found for the decomposition of pyridine-*N*-sulfonate in a buffer of the same composition (1.18×10^{-3} s^{-1}); the rate constant for decay was found to be independent of the buffer concentration. The reaction of pyridine-*N*-sulfonate in 3-picoline buffers at pH 8 (270 nm) also exhibited an intermediate. The pseudo-first-order rate constants for formation of the intermediate were determined by back-extrapolating the decay portion of the trace and employing the extrapolated absorption, at a given time, as an "infinity"; the rate constants were treated as in eq 4 to obtain k_{Xpy}.

The rate constants, k_{Xpy}^{isq}, for reaction of isoquinoline-*N*-sulfonate in pyridine buffers obey an excellent linear Brønsted-type relationship (Figure 3 and eq 5). The rate constants for de-

$$\log k_{Xpy}^{isq} = 0.23 \pm 0.01 pK_{Xpy} - 1.91 \pm 0.04 \quad (r = 0.995) \quad (5)$$

composition of substituted pyridine-*N*-sulfonates in buffers containing pyridine also obey a linear Brønsted-type relationship (Figure 4 and eq 6). The theoretical rate expression for the

Table II. Reaction of Pyridine with Substituted Pyridine-*N*-sulfonates[a]

pyridine-*N*-sulfonate	pK_{Xpy}	λ_k[c]	$\Delta\epsilon_k$[g]	$k_{py}^{Xpy} \times 10^{2d}$	N[b]	pH[f]	λ_m[j]	ϵ_m[h]
3,4-lutidine	6.45	270	1.64	2.55	12	8.01	263	2.81
3,5-lutidine	6.14	273	1.70	5.35	10	7.95	274	5.36
4-picoline	6.14	270	0.21	5.26	13	8.05	253	4.05
3-picoline	5.82	273	1.83	9.40	11	7.98	262	3.66
isoquinoline[e]	5.46	339	1.29	20.7			333	3.42

[a] Ionic strength maintained at 0.1 M with KCl, 25 °C, Tris buffer at 0.01 M total concentration. [b] Number of data points. [c] Wavelength for kinetics (nm). [d] Units are L mol^{-1} s^{-1}; errors are less than 5%. [e] Data from Table I. [f] Average pH of the reactions (±0.01). [g] Extinction coefficient $\times 10^{-3}$; the value for pyridine-*N*-sulfonate is λ_k = 270 nm with $\Delta\epsilon_k$ = 105. The units are for molar extinction coefficient. [h] Molar extinction coefficient $\times 10^{-3}$; λ_m for the pyridine-*N*-sulfonate is 256 nm with ϵ_m = 1290. [j] Wavelength for maximal absorption.

$$\log k_{py}^{Xpy} = -0.90 \pm 0.03pK_{Xpy} + 4.22 \pm 0.19 \quad (r = 0.998) \tag{6}$$

mechanism of eq 3 derived previously[11] is shown in eq 7 where ΔpK is $pK_{Xpy} - pK_{Ypy}$. The parameter β refers to the Brønsted

$$k/k_0 = 1/(1 + 10^{\Delta pK\beta}) \tag{7}$$

selectivity for attack of pyridines on sulfur trioxide in the ternary encounter complex and will be the same for the forward reaction as for the return. If the donor pyridine, in our case isoquinoline, is kept constant, the value of k_0 will be the combined rate constant for formation of the ternary complex when the acceptor pyridine (Ypy) is much more basic than the donor (Xpy). It is assumed in this mechanism that the rate-limiting steps are independent of the structure of the respective "spectator" nucleophiles. For example, the attack of the acceptor pyridine in the ternary encounter complex is assumed not to be influenced by the structure of the donor pyridine. Equation 7 is a normalized function which gives rise to a family of curves (see Figure 2 in the supplementary material of the previous work[11]). There is no fit of any of the normalized curves to the Brønsted plot of Figure 3; the only nearly linear theoretical line has a slope less than 0.1, and the best forced fit is for $\beta = 0.4$. There is no evidence of any curvature in either of the Brønsted plots of Figures 3 and 4, and we would expect a significant break in the line of Figure 3 where the ΔpK varies from −4 to +4. A plot of the error "residuals" to eq 5 (Δ = log k_{Xpy} − log k_{Xpy}(calcd)) vs. pK_{Xpy} obviously shows no trend; the distribution is random about zero (see Figure 3).

There is no effect of varying the concentration of isoquinoline (isq) on the decomposition of isoquinoline-*N*-sulfonate in buffers, confirming the absence of general base catalysis as a contributor to k_{Xpy}; nucleophilic attack of isoquinoline on isoquinoline-*N*-sulfonate, although it exists, does not contribute to the nucleophilic rate constant. The rate constants for buffer containing Tris (0.1 M) at 0.1 M ionic strength (made up with KCl), 25 °C, 20% ethanol, and pH 8.17 were as follows: 1.69×10^{-3} s^{-1} (0.01 M isq); 1.68×10^{-3} s^{-1} (0.03 M isq); 1.73×10^{-3} (0.05 M isq); 1.68×10^{-3} s^{-1} (zero isq). We can calculate an upper limit for the general base catalysis term for isoquinoline by using the variation in rate constant (error limits): k_{isq}(general base) $< 5 \times 10^{-3}$ L mol^{-1} s^{-1}. This value is some 40-fold smaller than the value calculated from eq 5 for k_{isq}. The calculated value for $k_{2,6\text{-lutidine}}$ (0.26 L mol^{-1} s^{-1}) is about 80-fold larger than the observed value.

Discussion

We can safely assume that the species formed in the second-order reaction of pyridine with 4-picoline-*N*-sulfonate is the nucleophilic product pyridine-*N*-sulfonate; the observed intermediate decomposes with the same rate constant as a known sample of pyridine-*N*-sulfonate in buffers of the same composition. A general base catalysis mechanism is excluded by the absence of any effect of isoquinoline concentration on the rate constant for decomposition of isoquinoline-*N*-sulfonate. The very low reactivity of 2,6-lutidine toward isoquinoline-*N*-sulfonate compared with that calculated for this species from the Brønsted eq 5 is also inconsistent with a general base catalysis mechanism. Since excellent linear Brønsted relationships fit all the second-order rate constants for nonhindered pyridines, we can assume that the nucleophilic mechanism is taken for all the reactions of pyridines with pyridine-*N*-sulfonates even though a detailed distinction has not been carried out for each reaction.

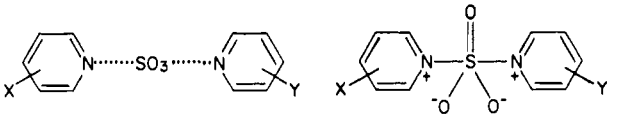
The linearity of the Brønsted plot for attack of pyridines on isoquinoline-*N*-sulfonate over a very wide p*K* range indicates a constant effective charge on the nucleophile in the transition state of the rate-limiting step. This result is consistent with a single transition state over the p*K* range. We can predict exactly that a change in the rate-limiting step should occur for the preassociation stepwise mechanism (eq 3) at a p*K* for the nucleophile corresponding to that of isoquinoline. A change in rate-limiting step would give rise to a different observed transition state and hence to a nonlinear Brønsted plot. The form of the Brønsted plot for eq 3 has been discussed previously[11] and is governed by eq 7 which does not fit the linear plot (Figure 3) of slope 0.23. The simplest conclusion is that the displacement reaction possesses a regular concerted mechanism corresponding to k_c of eq 1. An "enforced" concerted process does not satisfy the dependence of k_{Xpy} on the basicity of the nucleophilic pyridine; such a mechanism would involve rate-limiting formation of the ternary encounter complex from the binary one.

The change in effective charge[12] on the nitrogen of the nucleophilic pyridine may be estimated from the β_{EQ} ($\beta_{EQ} = \beta_N - \beta_L$) for the reaction with isoquinoline-*N*-sulfonate (eq 8). The

$$isq^+\text{–}SO_3^- + Xpy \underset{\beta_L}{\overset{\beta_N}{\rightleftharpoons}} isq + Xpy^+\text{–}SO_3^- \tag{8}$$

value of β_L is estimated to be close to that for the value for the attack of pyridine on substituted pyridine-*N*-sulfonates (−0.9) because there is only a small difference in p*K* between pyridine and isoquinoline. The value of β_{EQ} (+1.13) is close to that found for transfer of the sulfuryl ($-SO_3^-$) group from pyridine-*N*-sulfonates to a common phenolate ion.[9] Theory indicates that the β_{EQ} should be the same for the two reactions, indicating consistency between the two results.

The existence of a single transition state for the symmetrical reaction of pyridines with pyridine-*N*-sulfonates requires that the S–N bonds must have the same bond order in that transition state. There should also be the same effective charge on the donor and acceptor nitrogens; this is illustrated in structure **1** where ϵ is the effective charge defined on the scale +1 to 0 for the ionization of protonated pyridines[12] and $\Delta\epsilon$ is the change in effective charge defined on the same scale. The net change in effective charge



1

$\Delta\epsilon$ +0.23 +0.66 −0.89
ϵ +0.23 −0.34 +0.23
(observed values)

2

$\Delta\epsilon$ 0.0 −1.0 +1.0
ϵ +1.0 −2.0 +1.0
(values expected for a transition state close to a pentacoordinate intermediate)

on the donor and acceptor nitrogens could be supplied (in order to retain the original charge) from the SO_3 group of atoms. This group thus becomes more neutral, starting from a negative charge in the ground state, and therefore approximates in charge to monomeric sulfur trioxide. The charge pattern is not consistent with a transition state close to a pentacoordinate intermediate **2** where large positive effective charges should exist on the nitrogen, and the SO_3 group of atoms should become more negative than in the ground state.

In the present system, the change in effective charge on the acceptor nitrogen (0.23) as a function of the overall change in effective charge (1.13) is probably a good measure of bond order (0.19 of a full single bond). The approach in this case is subject to the conditions discussed previously[12-14] but does not suffer from the ambiguity confirmed by Pross and Shaik for substituent effects which could arise from more than one bond change.[15] In terms of the valence bond configuration mixing model,[15] a major contributor to the transition-state structure is Xpy:SO_3:Ypy.

Recent work has indicated that sulfonyl group transfer (RSO_2–) between phenolate nucleophiles is also characterized by a single transition state.[16] The S–O bond order for the sulfonyl group transfer is relatively high in the transition state. The sum of the bond orders for entering and leaving phenolate groups approaches

(11) Bourne, N.; Williams, A. *J. Am. Chem. Soc.* **1984**, *106*, 7591.

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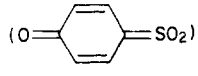
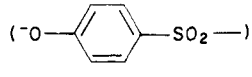
unity, unlike the present case, indicating the existence of a "closed" concerted transition state; this is in direct contrast to the sulfuryl group transfer which is characterized by an "open" or "exploded"[1] transition state. The simplest explanation of this difference is that sulfur(VI) requires six valence pairs which can only be satisfied in the "sulfonyl" transition state by using the "reacting bond" electrons. In sulfuryl group transfer, the lone pair on the oxy anion (an "internal nucleophile")[17] can be utilized to satisfy the sulfur, leaving a much less important role to the "reacting bond" electrons in bonding in the transition state. When the transferred group is either aminosulfonyl ($R\bar{N}-SO_2-$)[18] or arylmethanesulfonyl anion ($ArC\bar{H}-SO_2-$)[19,20] the adjacent anion is sufficiently powerful as an internal nucleophile to completely satisfy the sulfur and remove the need for reacting bond electrons; there is no bonding from the acceptor nucleophile to sulfur in the rate-limiting transition state in these cases.[18-20] Discrete intermediates are formed ($RN{=}SO_2$ and $ArCH{=}SO_2$). A sulfoquinone



intermediate[21] is formed for similar reasons in the transfer of the



group.

Compared with the corresponding $-PO_3^{2-}$ group transfer reactions the β_{EQ}, β_N, and β_L are very similar, indicating that the mechanisms have similar electronic requirements. Although both PO_3^- and SO_3 are known in the gas phase, they are reluctant to form in solution, and "exploded" transition states result for displacement reactions. Reactivity in $-PO_3^-$ group transfers is greater than in the corresponding sulfuryl ones. Isoquinoline-*N*-phosphonate has a rate constant 1.02 L mol^{-1} s^{-1} [11] for reaction with pyridine some 5-fold larger than the sulfuryl rate constant (Table I). Whereas pyridine-*N*-sulfonates react readily with oxy anions,[9] the corresponding phosphonates do not give measurable reaction except with hydroxide ion where the reactivity[22] is some 16-fold less than that for the sulfate (for the 4-picoline species). It would appear that the phosphorus is intrinsically more reactive than the sulfur but the extra negative charge on the phosphorus equalizes the affinities of the atoms for nucleophiles. The reactivity of phosphorus and sulfur cannot be easily compared because of valence differences, but, for example, 4-nitrophenyl diphenylphosphinate is about 450-fold more reactive[23] than 4-nitrophenyl benzenesulfonate[19] toward hydroxide ion.

The intimate processes by which a bimolecular reaction occurs in solution have been discussed fully by Ridd.[24] We wish to repeat the distinction, made by Hassid, Kreevoy, and Liang,[25] between encounter complexes (analogous to solvent separated ion pairs) and reaction complexes (analogous to intimate ion pairs) where the two reactants have interpenetrating solvent shells and are generally more organized than in the encounter complex. If the ternary complex in eq 3 was a reaction complex, then it would be safe to assume that the outgoing pyridine would be affected by the nucleophile. In other words, the decomposition to products of the ternary complex would not be independent of the donor pyridine. We cannot therefore distinguish between such a mechanism and a regular concerted one. The conceptual difference between a regular concerted mechanism with an "exploded" transition state and a mechanism with a ternary *reaction* complex seems to us to be very small as in both cases there should be a small influence of acceptor on the donor reaction.

The results for the analogous $-PO_3^-$ transfer mechanisms are well complemented by stereochemical studies with isotopically labeled oxygens;[26] the stereochemical probe would be very useful in biological sulfate studies where substrate variation is difficult. Enantiomeric chiral ^{16}O, ^{17}O, ^{18}O sulfate esters have been synthesized recently.[27]

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Registry No. Isoquinoline-*N*-sulfonate, 53854-50-5; 4-formylpyridine, 872-85-5; pyridine, 110-86-1; 3-cyanomethylpyridine, 6443-85-2; 3-picoline, 108-99-6; 3,4-lutidine, 583-58-4; methyl isonicotinate, 2459-09-8; 4-(dimethylamino)pyridine, 1122-58-3; 3,5-lutidine, 591-22-0; 4-aminopyridine, 504-24-5; 3-cyanopyridine, 100-54-9; 4-morpholinopyridine, 2767-91-1; 4-picoline, 108-89-4; 3-formylpyridine, 500-22-1; 3-bromopyridine, 626-55-1; isoquinoline, 119-65-3; 2,6-lutidine, 108-48-5; 3,4-lutidine-*N*-sulfonate, 86260-31-3; 3,5-lutidine-*N*-sulfonate, 86260-32-4; 4-picoline-*N*-sulfonate, 86260-30-2; 3-picoline-*N*-sulfonate, 55546-46-8.

Supplementary Material Available: Two figures showing the reactivity of 3,4-lutidine-*N*-sulfonate as a concentration of pyridine and log k/k_0 vs. ΔpK (3 pages). Ordering information is given on any current masthead page.

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