Hz, 1 H), 3.14 (dd, J = 8.7 Hz, 7.9 Hz, 1 H), 3.25 (d, J = 4.6 Hz, 2 H), 3.99 (d, J = 11.7 Hz, 1 H), 4.05 (d, J = 5.3 Hz, 2 H), 4.10 (d, J = 11.7 Hz, 1 H), 4.64 (d, J = 7.2 Hz, 1 H), 4.74 (dt, J = 7.2 Hz, 2.4 Hz, 1 H), 4.86 (d, J = 5.3 Hz, 1 H), 7.0–7.6 (m, 15 H); IR (neat) 2120 (ν_{N_3}), 1765 ($\nu_{C=O}$) cm^{-1}. Anal. Calcd for $C_{31}H_{35}N_5O_2$: C, 73.05; H, 6.92; N, 13.74. Found: C, 72.98; H, 7.02; N, 13.50.

X-ray Structure Determination of the *cis*-3-Imino-β-lactam 3a. The structure was solved by using the MULTAN program package and refined by full-matrix least-squares methods and difference fourier syntheses. The positions of the hydrogen atoms were calculated by the program HYDRO.[18]

(18) (a) Okaya, Y. In *Computing in Crystallography*; Schenk, H., Olthof-Hazekamp, R., van Koningsveld, H., Bassi, G. C., Eds.; Delft University Press: 1978; pp 153–165. (b) Frenz, B. A. In *Computing in Crystallography*; Schenk, H.; Olthof-Hazekamp, R., van Koningsveld, H., Bassi, G. C., Eds.; Delft University Press: 1978; pp 64–71.

Acknowledgment. This work was mainly supported by a grant from the Center for Biotechnology, SUNY at Stony Brook, which is sponsored by the New York State Science and Technology Foundation. Generous support from National Institute of Health (NIGMS), Ajinomoto Co., Inc., and Fuji Chemical Ind. is also gratefully acknowledged. We thank Professor Joseph W. Lauher for his valuable advice for X-ray analysis and ROTOCHEM programs. We also thank Dr. Takehiko Yamato for his technical assistance.

Supplementary Material Available: The summary of crystal parameters, data collection, and refinement and tables of positional and thermal parameters, bond lengths, and angles for 3a, and general experimental methods (38 pages). Ordering information is given on any current masthead page.

Iodide Reduction of Sulfilimines. 2. Evidence for Concurrent Stepwise and Concerted Mechanisms for the Decomposition of Sulfurane Intermediates

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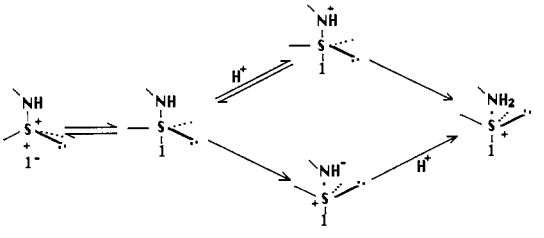
Abstract: The iodide reduction of *N*-(substituted ethyl or phenyl)-*S*,*S*-dimethylsulfilimmonium salts (aqueous solution, 25 °C, μ = 1.0 with KCl) is first order in proton activity and iodide concentration in the pH range 0.5–5. The solvent deuterium isotope effects for the reduction reaction vary in the range k_H/k_D = 0.26–0.48 as the nitrogen substituent is changed from ethyl- to trifluoroethylamine. Electron-withdrawing groups in the leaving group decrease the rate of the reaction and give β_{lg} values of ≈0.7 for cyanoethyl- and trifluoroethylamine leaving groups and ≈0.1 for the more basic ethylamine derivatives; a β_{lg} of 0.58 is observed for aniline derivatives. General acid catalysis is observed in the reduction of the acidic ethylamine and aniline derivatives with Brønsted α values of 0.59 and 0.39 for cyanoethyl- and trifluoroethylamine leaving groups, respectively; for anilines, the Brønsted α values decreased from 0.67 to 0.50 as the leaving group is changed from 4-methyl- to 3-nitroaniline. The value of β_{lg} decreases with decreasing strength of the catalyzing acid and the term $p_{xy} = (\partial\beta_{lg}/\partial pK_a^{HA}) = (\partial\alpha/\partial pK_a^{lg})$ ≈ −0.06 to −0.1. The solvent deuterium isotope effect on the general catalyzed reduction reaction increases with increasing acid strength; for the cyanoethylamine derivative, k_{BH}/k_{BD} = 1.47–2.32 for acetic and chloroacetic acids, respectively. A mechanism is suggested involving concurrent stepwise and concerted mechanisms for the reduction reaction; the mechanism observed seems to depend on the nature of the catalyzing acid.

For complex reaction mechanisms in solution where several possible parallel pathways exist for the conversion of starting materials to products, it is important to understand the factors that dictate which of the possible pathways will be observed for a given class of reactants and under a given set of conditions.[1,2] The iodide reduction of sulfilimine salts[3–7] is an example of a substitution reaction in which an initially formed addition product, a tetracoordinate sulfurane,[7,8] can partition by a variety of mechanisms to give an iodosulfonium ion, which rapidly undergoes

Scheme I



a second reduction step to give the final products, the amine, the sulfide, and iodine (Scheme I). In previous work,[7] we have reported that the value of the Brønsted β_{lg} underwent a transition from a small positive value to a larger value (≈0.6) as the leaving group was changed from basic primary amines to less basic anilines. Further, the reaction of basic amine derivative was not subject to general-acid catalysis while a Brønsted α value of about 0.7 was observed for aniline derivatives. These data suggested that a change in the rate-limiting step or in the nature of the mechanism may be occurring as a consequence of the change in leaving group pK_a. In order to define more clearly the nature of

(1) Jencks, W. P. *Acc. Chem. Res.* **1980**, *13*, 161–169.
(2) Richard, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1982**, *104*, 4689–4691.
(3) Tillett, J. G. *Chem. Rev.* **1976**, *76*, 747–772. Gilchrest, T. L.; Moody, C. J. *Ibid.* **1977**, *77*, 409–435. Oae, S.; Furukawa, N. In *Sulfilimines and Related Derivatives*; ACS Monograph 179, American Chemical Society: Washington, D.C., 1983.
(4) Doi, J. T.; Goodrow, M. H.; Musker, W. K. *J. Org. Chem.* **1986**, *51*, 1026–1029.
(5) Dell'Erba, C.; Guanti, G.; Leandir, G.; Corrallo, G. P. *Int. J. Sulfur Chem.* **1973**, *8*, 261–265.
(6) Gensch, K.-H.; Higuchi, T. *J. Pharm. Sci.* **1969**, *56*, 177–184.
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the observed structure/reactivity discontinuity, we have examined leaving group effects and the effects of general acids on an expanded set of sulfilimines with aniline and substituted ethylamine leaving groups. The present data suggest that *concurrent* stepwise and concerted pathways are being observed in the reduction catalyzed by the proton and by general acids, respectively; it gets "curiouser and curiouser".

Experimental Section

Synthesis. *N*-(Substituted phenyl)-*S*,*S*-dimethylsulfilimmonium salts were prepared from trifluoroacetic anhydride, dimethyl sulfoxide, and the corresponding aniline according to the method described by Swern et al.[9] All sulfilimines were isolated as the picrate salts and subsequently converted to the chloride by passing methanolic solutions over Dowex anionic exchange resins.[7] Sulfilimines derived from substituted ethylamines, with the exception of trifluoroethylamine, were prepared from dimethyl sulfide, and *N*-chlorobenzotriazole and the amine[10] and were isolated directly as the chloride salt. The sulfilimine derived from 2,2,2-trifluoroethylamine was prepared with trifluoroacetic anhydride and dimethyl sulfoxide, as described above. All compounds were recrystallized from dichloromethane/ether mixtures at 4 °C and had melting points and spectra consistent with literature values. Elemental analyses were performed on all new compounds, and these were within acceptable error limits on carbon, hydrogen, and nitrogen.[11]

Kinetic Studies. All kinetic runs were performed by following the appearance of I_3^- at 353 nm on a Hitachi 100-60 UV–vis spectrophotometer equipped with an automatic cell changer and a thermostated cell compartment. Temperature was maintained at 25 °C and the ionic strength was maintained at 1.0 with KCl. The pH of each cell was determined at the end of each run with a Corning pH meter equipped with a combined glass electrode. First-order rate constants were obtained from semilogarithmic plots of $A_\infty - A_t$ against time. Such plots were typically linear for over 4 half-lives. Apparent constants for buffer catalysis were obtained from the slopes of plots of k_{obsd} vs. [buffer]; catalytic constants for each buffer were obtained by extrapolating linear replots of apparent catalytic constants vs. fraction of the buffer in the acid form, to 100% buffer acid; no general-base catalysis was evident. For strongly acidic buffers, catalytic constants were obtained from solutions that were >99% buffer base with use of a dilute solution of glycolate buffer to maintain the experimental pH; typically three pH values were examined. Catalytic constants were calculated from the slopes of these plots and the calculated fraction of the buffer in the acidic form at that pH. Although acid catalysis being observed at >99% buffer base sounds odd, it is readily apparent[12,13] that under these conditions the ratio between the apparent catalytic constant (the slope) and the observed rate constant for the proton catalyzed reaction (the intercept) approaches its upper limit. Errors which might arise from uncertainties in the buffer pK_a are essentially balanced out since the same pK_a value is also in the Brønsted correlation.[12]

Solvent deuterium isotope effects were determined by parallel kinetic runs of samples prepared by dilution of a small amount of concentrated DCL solution into cells containing KCl, sulfilimine, iodide, and either H_2O or D_2O. Typically, 5–7 concentrations of DCl were examined in the pH range 0.5–3 and isotope effects were determined from the slopes of linear plots of log (k_{obsd}) vs. [DCl]. The calculated proton activities were confirmed by pH measurements; pD was obtained from the observed pH reading by adding 0.42. Solutions of buffers for the determination of solvent deuterium isotope effects on the general catalyzed reaction were prepared from the potassium salt of the acid in the appropriate solvent, neutralized to the desired fraction of acid with either DCl or HCl. Apparent catalytic constants were determined as described above.

Results

Rate constants for the iodide reduction of *N*-(substituted)-*S*,*S*-dimethylsulfilimines derived from anilines and from primary ethylamine derivatives are strictly first order with respect to iodide and proton concentrations within the pH range 0.5–5.0. Third-order rate constants for the reduction of these compounds (Table I) were calculated from proton activities, as measured by the glass electrode, and from the iodide concentration (typically 0.1 M) corrected for the activity coefficient under these conditions (0.778).[14] For all of the compounds examined, an inverse solvent

Table I. Rate Constants for the Iodide Reduction of *S*,*S*-Dimethyl-*N*-(substituted)sulfilimmonium Salts[a]

substituent	pK_a[b]	$k_{H^+}/M^{-2}\ s^{-1}$[c]	k_{H^+}/k_{D^+}[d]
primary amines			
ethylamine	10.63	1.77	0.26
n-propylamine	10.53	1.51	
2-methoxyethylamine	9.2	1.18	0.30
2-cyanoethylamine	7.7	0.28	0.44
2,2,2-trifluoroethylamine	5.7	0.013	0.48
anilines			
4-methylaniline	5.07	1.13	
aniline	4.63	0.592	0.36
3-nitroaniline	2.45	0.0445	

[a] Reactions in aqueous solution, 25 °C, ionic strength 1.0 with KCl. [b] From: Jencks, W. P.; Regenstein, J. In *Handbook of Biochemistry and Molecular Biology*; Fasman, GD., Ed.; CRC Press, Inc.: Cleveland, OH, 1975; or, Sayer, J. M.; Peskin, M.; Jencks, W. P. *J. Am. Chem. Soc.* **1973**, *95*, 4277–4287. [c] Third-order rate constant for reduction by iodide anion. [d] Observed solvent deuterium isotope effect on the proton-catalyzed reaction.

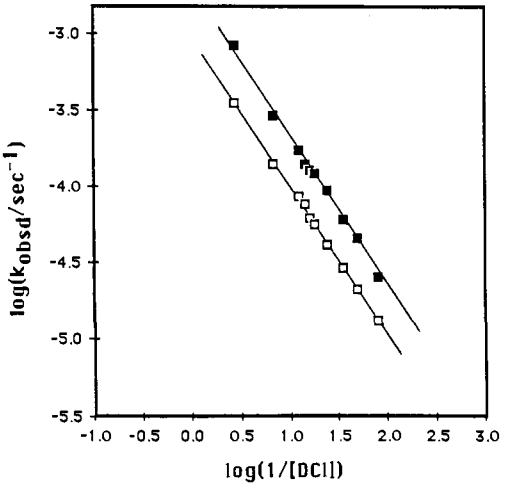

Figure 1. Double logarithmic plot of the rate constants for the reduction of *N*-(2,2,2-trifluoroethyl)-*S*,*S*-dimethylsulfilimine as a function of added acid concentration in H_2O (□) and in D_2O (■). Aqueous solution, 25 °C, $[I^-]$ = 0.1 M, ionic strength 1.0 with KCl.

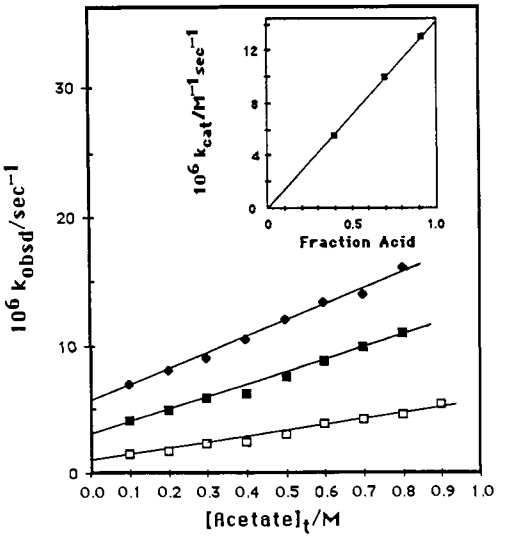

Figure 2. Plot of observed rate constants as a function of acetate buffer concentration for the iodide reduction of *N*-(2-cyanoethyl)-*S*,*S*-dimethylsulfilimine for the following buffer ratios: 40% acid (□), 70% acid (■), and 92% acid (◆). Aqueous solution, 25 °C, $[I^-]$ = 0.1 M, ionic strength 1.0 with KCl.

(9) Sharma, A. K.; Ku, T.; Dawson, A. D.; Swern, D. *J. Org. Chem.* **1975**, *40*, 2758–2764.
(10) Dawson, A. D.; Swern, D. *J. Org. Chem.* **1977**, *42*, 592–597.
(11) Huang, H. C. Thesis, University of Illinois at Chicago, Chicago, IL, 1986. Analytical and spectroscopic data available on request.
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(13) Jensen, J. L.; Jencks, W. P. *J. Am. Chem. Soc.* **1979**, *101*, 1476–1488.

Table II. Catalytic Constants for Buffer Catalysis of the Iodide Reduction of *N*-(Substituted)-*S*,*S*-dimethylsulfilimmonium Salts[a]

	pK_a[b]	$10^5 k_{BH}/M^{-2}\ s^{-1}$[c]		
substituted aniline		*p*-CH_3	H	*m*-NO_2
buffer				
acetic acid	4.60	3.8	2.8	0.84
(k_{BH}/k_{BD}[d])			(1.47)	
glycolic acid	3.82	4.7	8.2	1.38
chloroacetic acid	2.70	55.2	29.8	7.6
(k_{BH}/k_{BD}[d])			(2.32)	
dichloroacetic acid	1.29	618	348	33.2
trifluoroacetic acid	0.23			
			2-cyano	2,2,2-trifluoro
buffer				
acetic acid	4.60		1.40	0.81
(k_{BH}/k_{BD}[d])			(1.36)	
glycolic acid	3.82		3.60	2.03
chloroacetic acid	2.70		12.2	3.82
(k_{BH}/k_{BD}[d])			(2.24)	
dichloroacetic acid	1.29		149	15.9
trifluoroacetic acid	0.23		910	75.0

[a] Reactions in aqueous solution, 25 °C, ionic strength 1.0 with KCl. [b] From: Jencks, W. P.; Regenstein, J. In *Handbook of Biochemistry and Molecular Biology*; Fasman, G. D., Ed.; CRC Press, Inc.: Cleveland, OH, 1975; or, Sayer, J. M.; Peskin, M.; Jencks, W. P. *J. Am. Chem. Soc.* **1973**, *95*, 4277–4287. [c] Second-order rate constant for general-acid-catalyzed reduction by iodide anion. [d] Observed solvent deuterium isotope effect on the general-acid-catalyzed reaction.

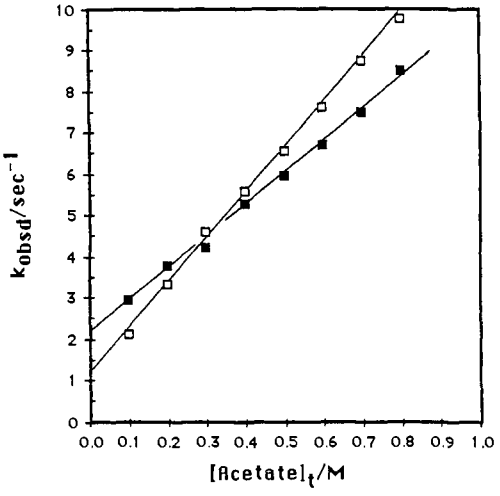

Figure 3. Plot of observed rate constants for the iodide reduction of *N*-phenyl-*S*,*S*-dimethylsulfilimine as a function of the concentration of acetic acid buffer, 50% ionized, in H_2O (□) and in D_2O (■). Aqueous solution, 25 °C, $[I^-]$ = 0.1 M, ionic strength 1.0 with KCl.

deuterium isotope effect was observed for the proton-catalyzed reaction (Table I, Figure 1).

Rate constants for the reduction of sulfilimines derived from anilines and from trifluoroethyl- and cyanoethylamine were dependent upon the concentration of buffer acid (Figure 2). Catalytic constants for the general-acid-catalyzed reaction are collected in Table II. No buffer catalysis was evident for the reduction of the sulfilimines derived from ethyl-, *n*-propyl- or methoxyethylamine. For the sulfilimines derived from aniline and cyanoethylamine, the solvent deuterium isotope effect on the *general-acid*-catalyzed reaction is normal (Figure 3) and is dependent upon the pK_a of the catalyzing acid (Table II). The generalized rate law for the reduction of the compounds investigated is shown below in eq 1. The dissociation constant for the formation of the sulfilimine ylide is K_a; k_H and k_{BH} represent the constants for proton and general catalysis, respectively. For all

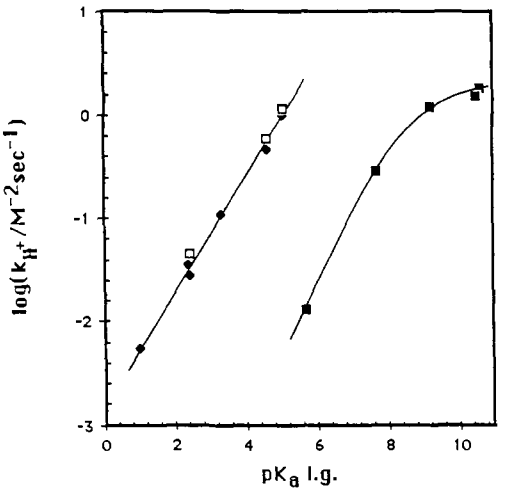

Figure 4. Plot of the logarithm of the third-order rate constant for the iodide reduction of *N*-(substituted)-*S*,*S*-dimethylsulfilimines as a function of leaving group pK_a for the following N substituents: (as ■), ethylamine, *n*-propylamine, 2-methoxyethylamine, 2-cyanoethylamine, 2,2,2-trifluoroethylamine; (as □), 4-methylaniline, aniline, 3-nitroaniline. Data for anilines from ref 7 are also shown (◆) for comparison. Aqueous solution, 25 °C, $[I^-]$ = 0.1 M, ionic strength 1.0 with KCl. The line has a slope of −0.67.

of the compounds investigated, $K_a \ll [H^+]$, making the reaction first order in proton activity.

$$k_{obsd} = \{(k_H[H^+] + k_{BH}[BH])[H^+][I^-]\}/(K_a + [H^+]) \quad (1)$$

Estimated pK_a Values. The acid dissociation constants for protonated (dicationic) sulfilimines and protonated sulfuranes in Scheme I are estimated, as previously described,[7] to be about 16 and 7 pK_a units below the parent amine for the sulfilimine and sulfurane, respectively. As before, these numbers are gross estimates but are probably accurate to within one or two pK_a units. Leaving group effects were estimated as previously described.[7]

Discussion Section

Specific-Acid-Catalyzed Reduction. The effect of changing the solvent from water to deuterium oxide on the third-order rate constant for the specific-acid-catalyzed reaction is to *increase* the rate of the reaction (Figure 1); the isotope effect, k_H/k_D, is therefore inverse (Table I). An inverse isotope effect such as this is generally observed when the reaction in question involves a pre-equilibrium protonation step.[15] The inverse effects that are observed in the present work (0.26–0.48) are similar to the effects of 0.26 and 0.31 which are observed for the ionization of anilinium and semicarbazidium ions, respectively.[16] The increase in the inverse isotope effect that is observed as the amine is changed from ethyl- to trifluoroethylamine (0.26–0.48) could represent the simple effect of amine basicity on the equilibrium isotope effect or it could indicate a genuine transition state movement toward the higher energy cationic intermediate which would be formed from the more acidic amines (Hammond postulate movement).[17] The magnitude of the change (0.22; ΔpK_a = 4.93) is somewhat larger than the change observed for ammonium vs. semicarbazidium ions (0.064; ΔpK_a = 5.61),[16] suggesting that effects *other* than amine basicity are being observed.

The effect of electron-withdrawing substituents on the third-order rate constants for the proton-catalyzed reaction is to decrease the value of the observed rate constant. The data, shown in Figure 4, appear to be somewhat nonlinear with approximate values for β_{lg} of ≈0.1 for the strongly basic amines (ethyl-, propyl-, and methoxyethylamine) and ≈0.7 for cyanoethyl- and trifluoro-

(14) Weast, R. C., Ed. *Handbook of Chemistry and Physics*, 51st ed.; The Chemical Rubber Co.: Cleveland, OH, 1971; p D-123.

(15) Schowen, R. L. *Prog. Phy. Org. Chem.* **1972**, *9*, 275–332.

(16) Laughton, P. M.; Robertson, R. E. In *Solute–Solvent Interactions*; Coetzee, J. F., Ritchie, C. D., Eds.; Marcel Dekker: New York, 1969; Chapter 7.

(17) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334–338. Marcus, R. A. *J. Phys. Chem.* **1968**, *72*, 891–899.

Scheme II

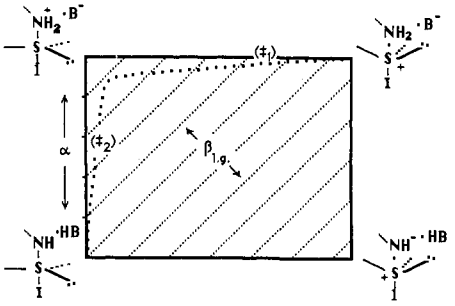

Table III. Brønsted Coefficients for the Iodide Reduction of *N*-(Substituted)-*S*,*S*-dimethylsulfilimmonium Salts[a]

substituent	pK_a[b]	α[c]	β_{lg}[d]
primary amines			
ethylamine	10.63	≈1.0	≈0.1
n-propylamine	10.53		
2-methoxyethylamine	9.2		
2-cyanoethylamine	7.7	0.59	≈0.69
2,2,2-trifluoroethylamine	5.7	0.39	≈0.69
anilines			
4-methylaniline	5.07	0.67	0.58
aniline	4.63	0.63	0.58
3-nitroaniline	2.45	0.5	0.58

[a] Reactions in aqueous solution, 25 °C, ionic strength 1.0 with KCl. [b] From: Jencks, W. P.; Regenstein, J. In *Handbook of Biochemistry and Molecular Biology*; Fasman, G. D., Ed.; CRC Press, Inc.: Cleveland, OH, 1975; or, Sayer, J. M.; Peskin, M.; Jencks, W. P. *J. Am. Chem. Soc.* **1973**, *95*, 4277–4287. [c] Brønsted coefficient for the general-acid-catalyzed reduction by iodide anion. [d] Brønsted coefficient for leaving group effects for the specific-acid-catalyzed reduction by iodide anion.

ethylamines. This nonlinearity could represent a change in the rate-limiting step of the reaction which is occurring or it could be a result of an actual change in the nature of the transition state.

In previous work,[7,8] a mechanism for the iodide reduction of sulfilimines was suggested in which iodide anion reacted with the sulfilimine to form a tetracoordinate sulfurane addition intermediate. This intermediate was suggested[7] to partition by a number of parallel pathways to form products. For strongly basic amines, the mechanism of the reaction was suggested to involve pre-equilibrium protonation followed by rate-limiting expulsion of the leaving group (Scheme I). The observed magnitude of the solvent deuterium isotope effect (k_H/k_D = 0.26–0.48) is consistent with this mechanism[15] and suggests that, for the most basic leaving groups, S–N bond cleavage is almost entirely rate limiting. In Scheme II, the transition state would be placed along the top edge of the More O'Ferrell–Jencks energy surface[1,18] in the region marked $\ddagger_1$. On the basis of previous estimates,[7] the leaving group effect in this region should be about 0.1 and should increase toward the left edge of the diagram. Placing electron-withdrawing substituents on the nitrogen of the cationic sulfurane intermediate should destabilize this intermediate, increase it's energy level relative to the neutral sulfurane and the products, and cause a Hammond-postulate shift in the transition state toward the intermediate, with the observed effect of increasing the Brønsted β_{lg} value,[18] consistent with the data in Table III.

If S–N bond breaking is truly rate limiting for these compounds in the proton-catalyzed reaction, then k_N, the microscopic rate constant for S–N bond breaking, must be less than k_{-H}, the microscopic rate constant for protonation of the solvent, so that k_s, the steady state expression describing proton transfer and S–N cleavage, simplifies to $k_s = K_H k_N$ (eq 2). For strongly basic

$$k_s = k_H k_N/(k_{-H} + k_N) \Rightarrow k_s = K_H k_N \qquad (2)$$

leaving groups such as ethylamine, the pK_a of the sulfurane cation might be expected[7] to be about 3 ± 1. Assuming a rate constant

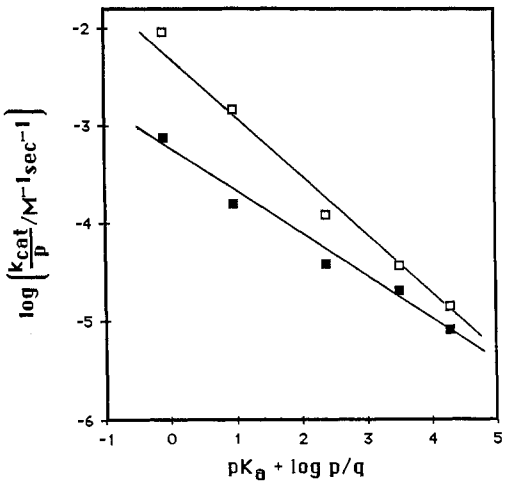

Figure 5. Brønsted plots for the general-acid-catalyzed iodide reduction *N*-(substituted)-*S*,*S*-dimethylsulfilimines for the following N substituents: 2-cyanoethyl (□) and 2,2,2-trifluoroethyl (■). Aqueous solution, 25 °C, [I^-] = 0.1 M, ionic strength 1.0 with KCl. The slopes are 0.59 and 0.39, respectively.

for proton transfer in the thermodynamically favorable direction of about 3×10^{11} s^{-1}, the rate constant k_{-H} should be[19] approximately 10^8 s^{-1}, making $k_N \leq 10^8$ s^{-1}. For the sulfurane derived from trifluoroethylamine, $\Delta pK_a \approx 0$ with respect to the proton[7] and k_{-H} would approach the limiting value of about 10^{11} s^{-1}. However, the Brønsted β_{lg} for the k_N term is likely to be large, and it is possible that the increase in this term will exceed the change in the k_{-H} term as the leaving group is changed from ethyl- to trifluoroethylamine. In order for S–N bond-breaking to remain totally rate limiting, the increase in k_N which occurs on going to the better leaving group must not make this rate constant approach limits imposed by heavy-atom rearrangement or solvation changes.[20] It is possible that k_N is sufficiently large in the acidic ethylamine derivatives so that proton transfer has become at least partially rate limiting and the increase that is observed in the solvent isotope effect reflects some contribution from the k_H term.

The data for the specific-acid-catalyzed reduction reaction are therefore consistent with a stepwise reaction in which proton transfer is essentially complete, and the rate-limiting transition state largely involves S–N bond cleavage. Electron-withdrawing substituents tend to cause a Hammond postulate shift of the transition state toward the sulfurane cation causing an increase in the observed value of β_{lg}. The steady increase in the value of the solvent deuterium isotope effect could result from this transition-state movement or from a partial change in rate-limiting step caused by rate constants for proton transfer approaching the constants for S–N bond-breaking.

General-Acid-Catalyzed Reduction. As the concentration of buffer acid is increased at constant pH, the observed rate constants for the iodide reduction of sulfilimines derived from anilines and from acidic ethylamines increases linearly (Figure 2). The catalytic constants for the buffers examined are collected in Table II, and representative data appear plotted in the Brønsted plots in Figure 5. The slopes of these plots, the Brønsted α values (Table III), decrease as the pK_a of the amine leaving group decreases. Although there is a slight numerical discontinuity, this same basic trend is evident in both the aniline series and in the acidic ethylamine derivatives.

Basic ethylamine derivatives did not show general catalysis. For ethylamine, propylamine, and methoxyethylamine the Brønsted α must be ≈1.0 since no general catalysis was observed at molar concentrations of buffer acid for any of these compounds. It is somewhat surprising that general catalysis is *not* observable for these compounds since the point for proton catalysis falls *below*

(18) Jencks, W. P. *Chem. Rev.* **1985**, *85*, 511–527.

(19) Calculated by using a diffusion controlled rate constant of 5×10^9 M^{-1} s^{-1} and a solvent concentration of 55 M. See: Young, P. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 7318–7323.

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the extrapolated line in plots for the acidic amine leaving groups. Under these conditions, it is not unusual to observe general catalysis, even with large α values.[13]

The solvent deuterium isotope effect for the general-catalyzed reaction is normal and is dependent on the acid strength of the catalyzing acid (Table II). For both the primary amines and the aniline derivatives, increasing the acid strength causes an increase in the observed isotope effect. The magnitudes of the observed effects, 1.36–2.32, are consistent with solvent effects which are observed in general-catalyzed reactions[15] which are generally <4 and may exhibit a maximum,[21,22] depending upon transition-state structure.

As stated above, the data for the specific-acid-catalyzed reduction reaction strongly suggest that a stepwise mechanism is being observed and that, for the proton-catalyzed reaction, S–N bond cleavage is rate limiting. If the general-catalyzed reaction was also following the stepwise mechanism, the transition state would be located along the left edge of the diagram, approximately two-thirds of the way toward the protonated sulfurane intermediate. For a stepwise reaction along this edge, electron-withdrawing groups in the leaving group should *destabilize* the protonated sulfurane intermediate relative to the neutral sulfurane, and a Hammond postulate effect should be observed with a movement to *larger* values of the Brønsted α.[18] The effect that is observed, both for the aniline derivatives and the primary amines, is *opposite* to this prediction; electron-withdrawing groups *decrease* the Brønsted α. Likewise, the observed leaving group effect decreases with decreasing acid strength, following the relationship[18]

$$(\partial\beta_{lg}/\partial pK_a^{HA}) = (\partial\alpha/\partial pK_a^{lg}) \quad (3)$$

Again, a simple Hammond postulate movement of the transition state would generate an increase in the leaving group effect with decreasing acid strength. The numerical evaluation of eq 3 yields a value of $p_{xy} = -0.06$ to -0.1 which is consistent with the value of -0.07 observed by Gravitz and Jencks[23] for the expulsion of alcohols from phtalimidium cations but much smaller than and opposite to the value of $+0.54$ observed for the highly coupled transition state for the thiolate reduction of sulfilimines.[24]

The data for the general-catalyzed reaction are most consistent with a reaction that is truly concerted; that is, proton transfer occurs in a manner that is coupled with S–N bond cleavage. With use of linear free energy parameters as rough guides to located the transition state on the surface of a More O'Ferrell–Jencks reaction surface,[18] the transition state would appear to be in the upper left-hand quadrant of the surface shown in Scheme II ($\ddagger_2$). For a transition state in this quadrant, the major effect of electron-withdrawing substituents in the leaving group is going to be to *destabilize* the protonated sulfurane and *stabilize* the amine anion in the lower right. The effect on the transition state is going to be an anti-Hammond movement *away from* the high energy protonated sulfurane intermediate. The net result in this movement will be a *decrease* in the Brønsted α value, consistent with the data in Table III. An increase in acid strength will *destabilize* the bottom edge of the surface, causing a coupled Hammond and anti-Hammond shift of the transition state. The larger of these forces is likely to be the Hammond effect since the reaction coordinate in this quadrant has a large vertical component resulting in a movement of the transition state toward larger values of β_{lg}. Likewise, a stronger acid will move the transition state closer to the point where proton transfer is 50% and the solvent deuterium isotope effect is expected to be at a maximum, consistent with the observed *increase* in isotope effect with *increasing* acid strength.

Concurrent Mechanisms for the Reduction Reactions. The data for the specific-acid-catalyzed reduction strongly suggest that a stepwise mechanism is being observed. The salient points of these data are the following: (1) The solvent deuterium isotope effect for the proton-catalyzed reaction is inverse, consistent with a pre-equilibrium protonation step. (2) A Hammond postulate effect is observed in both the magnitude of the solvent deuterium isotope effect and in the value for β_{lg}; anti-Hammond effects are predicted for the concerted reaction mechanism.

For the general-acid-catalyzed reduction reaction, the data strongly suggest that the mechanism involves proton transfer which is concerted with S–N bond cleavage. The data supporting this conclusion are the following: (1) the term $p_{xy} = (\partial\beta_{lg}/\partial pK_a^{HA}) = (\partial\alpha/\partial pK_a^{lg})$ is negative; a positive value is predicted for a stepwise reaction; (2) the solvent deuterium isotope effect on the general-catalyzed reaction is normal and increases with increasing acid strength; a decrease is predicted for the stepwise reaction.

The simplest conclusion, based on these data, is that the major mechanism of the reduction reaction changes depending upon the nature of the catalyzing acid. The overriding factor is not acid strength, since trifluoroacetic acid catalyzes the reduction, falls on the Brønsted plots, and shows no structure/reactivity discontinuity with the other acetates. The major difference in the catalysis by proton vs. acetates is charge type; electrostatic repulsion could work against the formation of the same type of encounter complex that could form between the reactants and the neutral acetic acids. The actual proton transfer steps could then be occurring through intermediate water molecules in the case of proton catalysis and *direct* transfer may be occurring in the case of the neutral acetic acids. Support for these differences in proton transfer mechanism may be found in the fact that, while H_3O^+ is known to be highly hydrated in solution, the observed solvent isotope effect for the ionization of acetic acids can be accounted for simply by the fraction factor for H_3O^+ with no contribution from the solvation of the carboxylation anion.[25] Mechanistically, the presence of the high pK_a carboxylate anion in a contact encounter complex with the sulfurane complex may accelerate the k_{-H} step sufficiently so that the lifetime of the intermediate is quite short and the concerted mechanism becomes energetically accessible. In conclusion, the data seem to support an energy surface with parallel pathways for concerted and stepwise mechanisms of proton transfer. The energy differences in the different microscopic mechanisms for proton transfer.

Acknowledgment. This work was supported by a grant from the National Science Foundation (CHE 8511865).

Registry No. D_2, 7782-39-0; D_2O, 7789-20-0; I^-, 20461-54-5; $HOCH_2CO_2H$, 79-14-1; $ClCH_2CO_2H$, 79-11-8; Cl_2CHCO_2H, 79-43-6; CF_3CO_2H, 76-05-1; CH_3CO_2H, 64-19-7; *S,S*-dimethyl-*N*-propylsulfiliminium picrate, 106375-41-1; *S,S*-dimethyl-*N*-(2-methoxyethyl)sulfiliminium picrate, 106358-18-3; *S,S*-dimethyl-*N*-(2-cyanoethyl)sulfiliminium picrate, 106358-20-7; *S,S*-dimethyl-*N*-(2,2,2-trifluoroethyl)-sulfiliminium picrate, 106358-22-9; *S,S*-dimethyl-*N*-(4-methylphenyl)-sulfiliminium picrate, 55871-35-7; *S,S*-dimethyl-*N*-phenylsulfiliminium picrate, 55975-86-5; *S,S*-dimethyl-*N*-(*m*-nitrophenyl)sulfiliminium picrate, 106358-23-0; *S,S*-dimethyl-*N*-ethylsulfiliminium picrate, 60978-59-8.

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