

co-workers¹⁰ is appropriate albeit only at the numerical level and not of the methods themselves. The present result is in better agreement with the experimental value than the Monte Carlo result because the dispersion contribution has been included in the calculations.

In this connection it must be emphasized that the present method is temperature independent and, consequently, the above numerical comparison is required in order to provide a justification of its usefulness. In this regard, the energetic and structural agreement obtained in this as well as in previous work⁵⁻⁷ is very encouraging.

(12) See ref 1 for a complete review and references.

Conclusions

A recently developed method has been used in the study of the tautomeric equilibrium of the 4-oxypyridine in solution. The small amount of computer time needed, relative to other theoretical approaches, as well as the excellent agreement with the experimental values indicate that it constitutes an excellent tool for the study of solvation problems in systems of chemical and biochemical interest.

Acknowledgment. One of us (J.A.S.) thanks the Ministerio de Educacion y Ciencia (Spain) for a fellowship which made possible his stay at the University of Alberta.

Registry No. 4-Hydroxypyridine, 626-64-2; 4-pyridone, 108-96-3.

Iodide Reduction of Sulfilimines. Evidence for the Partitioning of Sulfurane Intermediates

Paul R. Young* and Patrick E. McMahon

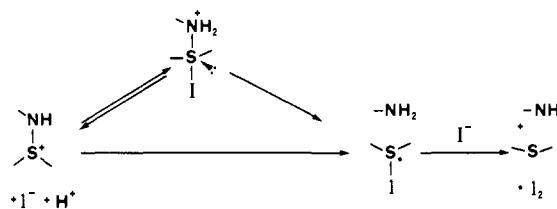
Contribution from the Department of Chemistry, University of Illinois at Chicago, Chicago, Illinois 60680. Received February 1, 1985

Abstract: The iodide reduction of *N*-(substituted phenyl)-*S,S*-dimethylsulfilimmonium salts (aqueous solution, 25 °C, $\mu = 1.0$ with KCl) is first order in proton activity in the pH range 0.5-3.0. The reduction of *N*-phenyl-*S,S*-dimethylsulfilimmonium chloride is also catalyzed by general acids with a Brønsted α of 0.7. Electron-donating groups on the aniline leaving group accelerate the rate of the reduction with a $\beta_{lg} = 0.54$. Rate constants for the reduction of sulfilimines derived from higher pK_a amines are also linear with proton activity. For *N*-benzyl-*S,S*-dimethylsulfilimmonium chloride, no general catalysis is observed. For sulfilimines with unhindered primary amines as leaving group, a small β_{lg} of about -0.1 is observed. For sulfilimines with benzamide and sulfonamide leaving groups the proton-catalyzed reaction contains both first- and second-order terms in proton activity. The rate of the reduction of the sulfilimine ylide is accelerated by electron-withdrawing substituents with $\beta_{lg} = -0.5$. These data are interpreted in terms of a mechanism involving rate-limiting partitioning of a common tetracoordinate sulfurane intermediate. For aniline leaving groups, proton transfer to the neutral sulfurane is suggested to be rate limiting. For higher pK_a leaving groups, the protonated sulfurane is solvent equilibrated and breakdown of this intermediate becomes rate limiting. For sulfilimines with very low pK_a leaving groups, the predominant pathway is suggested to involve uncatalyzed breakdown of the neutral sulfurane intermediate with expulsion of sulfonamide anion. A parallel pathway involving the general catalyzed breakdown of the neutral sulfurane is also suggested to account for the greater than first-order proton dependence.

Introduction

An interesting and fundamental question regarding the mechanism of bimolecular substitution reactions concerns the relationship between the lifetimes of potential intermediates and the observed reaction mechanism.¹⁻³ It has been suggested¹ that, in carbonyl additions, proton transfer must become concerted with nucleophile attack whenever the lifetime of the zwitterionic addition intermediate approaches the vibrationally limited rate constant, kT/\hbar . A similar argument could hold for substitution reactions in general; when the lifetime of the intermediate in an addition-elimination reaction approaches the vibrational limit, the mechanism should become unfavorable and a concerted displacement reaction should be observed. Thus, for an S_N2 reaction occurring at carbon, the instability of the bipyramidal pentavalent intermediate would allow the concerted process to become observable. While this suggestion seems fundamentally sound, it

Scheme I



is very difficult to test since pentavalent carbon complexes cannot be readily generated and their lifetimes experimentally determined. Second-row elements, however, are well known to exist in expanded valence states and to undergo substitution reactions that can be described kinetically as bimolecular displacements.⁴ The iodide reduction of sulfilimines is such an example (Scheme I). The rate-limiting step in these reductions generally occurs before iodosulfonium ion formation, and complete reduction to the sulfide and iodine occurs rapidly.^{5,6} In previous work⁷ have presented

(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, 4691-4692.

(3) Westheimer, F. H. *Chem. Rev.* 1961, 61, 265-273. Buddenbaum, W. E.; Shiner, V. J., Jr. In "Isotope Effects on Enzyme-Catalyzed Reactions"; Cleland, W. W., O'Leary, M. H., Northrop, D. B., Eds.; University Park Press: Baltimore, MD, 1977; p 1-36.

(4) Tillett, J. G. *Chem. Rev.* 1976, 76, 747-772. Gilchrist, T. L.; Moody, C. J. *Ibid.* 1977, 77, 409-435.

(5) Dell'Erba, C.; Guanti, G.; Leandri, G.; Corrallo, G. P. *Int. J. Sulfur Chem.* 1973, 8, 261-265.

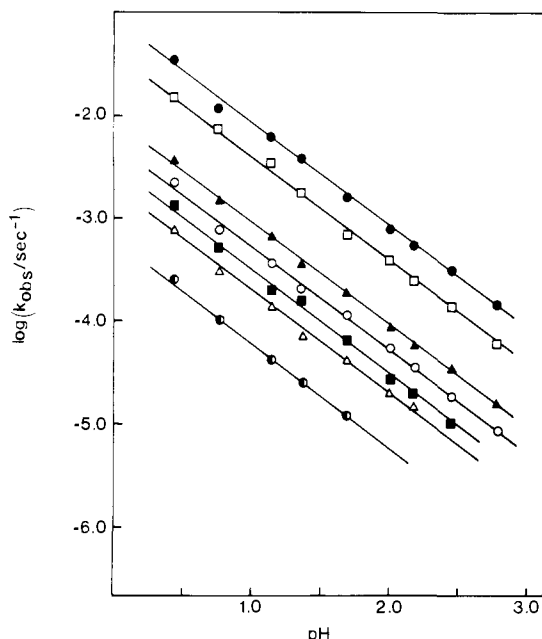


Figure 1. Plot of the observed rate constant for the iodide reduction of *N*-(substituted phenyl)-*S,S*-dimethylsulfilimmonium salts as a function of pH for the following compounds: (●) *p*-NO₂; (▲) *m*-NO₂; (■) *p*-CO₂Et; (○) *m*-CF₃; (▲) *m*-Cl; (□) H; (●) *p*-CH₃. Aqueous solution, 25 °C, [I⁻] = 0.10 M, ionic strength 1.0 with KCl. The lines have slopes of 1.00.

kinetic evidence that the iodide reduction of the sulfilimine "dehydromethionine" proceeds through the formation of an obligatory sulfurane intermediate. Sulfilimine reduction therefore offers a system in which concerted displacement reactions of S_N2 type and stepwise reactions involving bipyramidal intermediates can both occur. In order to approach a more formal understanding of the role of intermediate lifetime in determining the reaction mechanism, we have undertaken a systematic study of the iodide reduction of *N*-substituted *S,S*-dimethylsulfilimines in dilute acidic solution.

Experimental Section

Synthesis. *N*-(Substituted phenyl)-*S,S*-dimethylsulfilimmonium salts were prepared from trifluoroacetic anhydride and dimethyl sulfoxide and the corresponding aniline according to the method described by Swern et al.⁸ All sulfilimines were isolated as the picrate salts and subsequently converted to the chloride by passing methanolic solutions over Dowex anionic exchange resins. *N*-Carboxyphenyl- and *N*-benzenesulfonyl-*S,S*-dimethylsulfilimines were also prepared by the TFA/Me₂SO method and were isolated as the neutral ylide.⁸ Sulfilimines derived from primary amines were prepared from dimethyl sulfide, *N*-chlorosuccinimide, and the amine and were isolated directly as the chloride salt.⁹ All compounds were recrystallized from dichloromethane/ether mixtures at 4 °C and had melting points and NMR spectra consistent with literature data. Elemental analyses were performed on all new solid compounds, and these analyses were within acceptable error limits on carbon, hydrogen, and nitrogen.¹⁰

Kinetic Studies. All kinetic runs were performed by following the appearance of I₃⁻ 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 immediately after each run with a Corning pH meter with a combined glass electrode. For primary amine and aniline leaving groups, observed 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. Kinetic studies involving sulfilimines with amide and

Table I. Rate Constants for the Proton-Catalyzed Iodide Reduction of *N*-Substituted *S,S*-Dimethylsulfilimines^a

amine	pK _a ^b	k/M ⁻² s ⁻¹ c
anilines		
<i>p</i> -nitro	1.0	0.00536
<i>m</i> -nitro	2.45	0.0276
<i>p</i> -carboxyethyl	2.38	0.0358
<i>m</i> -chloro	3.32	0.108
<i>m</i> -trifluoro	3.49	0.0622
unsubstituted	4.63	0.467
<i>p</i> -methyl	5.07	0.995
primary amines		
<i>m</i> -chlorobenzylamine	9.01 ^d	0.877
<i>p</i> -chlorobenzylamine	9.14 ^d	1.17
benzylamine	9.38 ^d	1.29
<i>p</i> -methylbenzylamine	9.54 ^d	1.42
methoxyethylamine	9.72	0.914
phenethylamine	9.83	0.830
propylamine	10.58	0.767
cyclohexylamine	10.64	0.923
<i>tert</i> -butylamine	10.55	0.528
amides ^e		
<i>p</i> -chlorobenzenesulfonamide	-3.65	0.0030, ^f 0.0018 ^f
benzenesulfonamide	-3.45	0.0023, ^f 0.0014 ^f
toluenesulfonamide	-3.30	0.0021, ^f 0.0018 ^f
<i>p</i> -nitrobenzamide	-2.29	0.00030, ^f 0.00013 ^f
benzamide	-1.85	0.00017, ^f 0.00007 ^f

^a In aqueous solution, 25 °C, ionic strength 1.0 with KCl. ^b From ref 12, unless otherwise noted. ^c Third-order rate constant for the proton-catalyzed reduction by iodide anion. ^d From: Blackwell, L. F.; Fischer, A.; Miller, I. J.; Topsom, R. D. Vaughan, J. J. *Chem. Soc.* **1964**, 3588-3591. ^e Values for pK_as are from ref 13. ^f Fourth-order rate constant for proton-catalyzed iodide reduction of the protonated sulfilimine, M⁻³ s⁻¹.

Table II. Catalytic Constants for Buffer Catalysis of the Iodide Reduction of *N*-Phenyl-*S,S*-dimethylsulfilimine^a

buffer	pK _a ^b	k _{BH} /M ⁻² s
glycolic acid	3.83	1.17 × 10 ⁻³
chloroacetic acid	2.70	4.47 × 10 ⁻³
phosphoric acid	2.08	3.41 × 10 ⁻²
dichloroacetic acid	1.29	5.49 × 10 ⁻²
H ₃ O ⁺	-1.74	4.67 × 10 ⁻¹

^a Aqueous solution, 25 °C, ionic strength 1.0 with KCl. ^b From: Young, P. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1978**, *100*, 1228-1235. ^c Catalytic constant for catalysis by the buffer acid.

sulfonamide leaving groups were too slow to follow to completion, and observed rate constants for these compounds were calculated from the initial rate of the first 1% of reaction. The value of 26 400 was used for the extinction coefficient of I₃⁻ at 353 nm.⁶ All cells were purged with nitrogen prior to beginning the kinetic studies in order to minimize oxidation of *2* at low pH values. Constants for buffer catalysis of the iodide reduction of *N*-phenylsulfilimines were obtained from replots of apparent catalytic constant against the fraction of the buffer in the acidic form.

Results

Rate constants for the iodide reduction of *N*-substituted *S,S*-dimethylsulfilimines derived from anilines, benzylamines, and simple primary amines in dilute aqueous acid solution are strictly first order with respect to iodide and proton concentrations within the pH range 0.7-2.0. The pH dependence of the aniline series is shown in Figure 1, and the data for other amines are comparable. 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 0.10 M) corrected for the activity coefficient under these conditions (0.778).¹¹ Sulfilimines with sulfonamide or benzamide leaving groups are also reduced by iodide anion under these conditions. The iodide dependence for these compounds is also 1.00 ± 0.01; the proton dependence, however, is slightly greater than 1 as shown by the deviation from the dashed lined in Figure

(6) Gensch, K.-H.; Higuchi, T. *J. Pharm. Sci.* **1969**, *56*, 177-184.
 (7) Young, P. R.; Hsieh, L.-S. *J. Am. Chem. Soc.* **1978**, *100*, 7121-7122.
 (8) Sharma, A. K.; Ku, T.; Dawson, A. D.; Swern, D. *J. Org. Chem.* **1975**, *40*, 2758-2764 and references cited therein.
 (9) Dawson, A. D.; Swern, D. *J. Org. Chem.* **1977**, *42*, 592-597.
 (10) McMahon, P. E. Ph.D. Thesis, University of Illinois at Chicago, Chicago, IL, 1982. Analytical and spectroscopic data available on request.

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

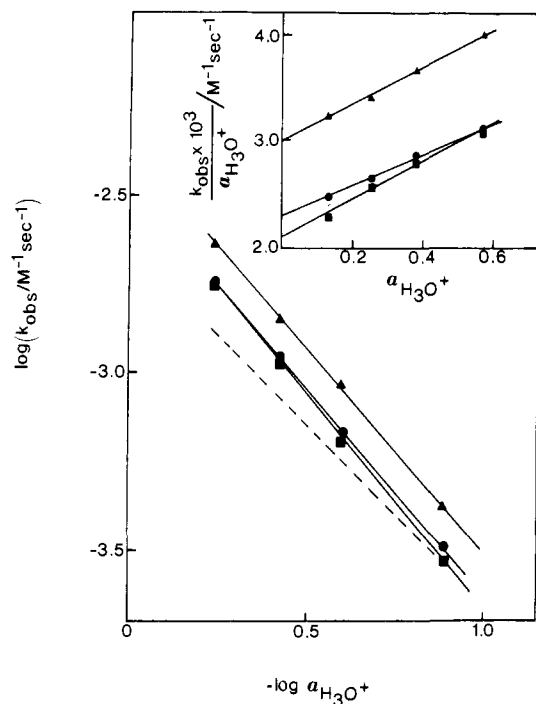


Figure 2. Plot of the observed second-order rate constant for the iodide reduction of *N*-(substituted benzenesulfonyl)-*S,S*-dimethylsulfilimmonium salts as a function of proton activity for the following compounds: (●) H; (▲) *p*-Cl; (■) *p*-CH₃. Aqueous solution, 25 °C, ionic strength 1.0 with KCl. The dashed line has a slope of 1.0. Inset: Second-order plot of ($k_{\text{obsd}}/\text{proton activity}$) vs. proton activity for the three compounds given above. The slopes and intercepts of these plots give the fourth- and third-order rate constants for the reduction reaction.

2. The presence of the additional proton term is most clearly shown by the "second-order" plot (inset, Figure 2) in which (k_{obsd} proton activity) is plotted against proton activity. The slopes and y intercepts of these second-order plots, divided by iodide activity, give the fourth- and third-order rate constants given in Table I.

Rate constants for the reduction of *N*-phenyl-*S,S*-dimethylsulfilimine were found to be independent of ionic strength changes within the range $\mu = 0.4$ –1.0. The rate constants were, however, dependent upon the concentration of buffer acid (Figure 3). Catalytic constants for the general acid catalyzed reaction are collected in Table II. No buffer catalysis was evident for the reduction of the *N*-benzyl-*S,S*-dimethylsulfilimmonium compound (Figure 3, Δ). The general rate law for all 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 compounds investigated, with the exception of the amide leaving groups, $K_a \gg [H^+]$, making the reaction cleanly first order in proton activity.

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

Estimated pK_a Values. The acid dissociation constants for protonated (dicationic) sulfilimines and protonated sulfuranes in Scheme I are estimated by the following procedure. The effect of a cation immediately adjacent to an ammonium ion is estimated to be approximately -10 pK_a units, based on the pK_a shift observed between ammonium and hydrazine cations (9.24 to -0.88).¹² The further effects of π overlap and the increased nuclear charge of a sulfur atom, relative to a nitrogen, can be estimated by the pK_a shift of -6.1 units observed between trimethylamine *N*-oxide (pK_a 4.6)¹² and dimethyl sulfoxide (pK_a -1.54).¹³ The acid dissociation constant for a dicationic sulfilimine is therefore estimated to be

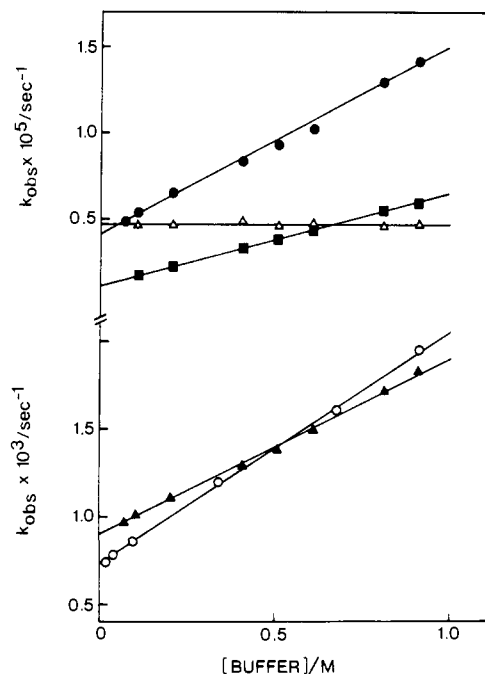


Figure 3. Plots of observed rate constants for the iodide reduction of *N*-phenyl-*S,S*-dimethylsulfilimmonium chloride as a function of buffer concentration for the following buffers: (●) chloroacetate; (■) glycolate; (○) phosphate; (▲) dichloroacetate. Rate constants for the reduction of *N*-benzyl-*S,S*-dimethylsulfilimmonium chloride as a function of glycolate buffer are also shown (Δ). Aqueous solution, 25 °C, $[I^-] = 0.10$ M, ionic strength 1.0 with KCl, all data collected at constant buffer ratio in the pH range 2–6.

about 16 pK_a units below the pK_a of the corresponding amine. The actual shift may be as much as 20 pK_a units if the reported pK_a of hydrazine is incorrect and more closely approximates the pK_a of *N*-aminopyridinium ion (-7.2).¹²

The pK_a of the nitrogen in a tetracoordinate sulfurane can be estimated to be lower than that of the amine by at least 4.6 pK_a units, based on the shift observed between ammonia and methoxyamine (pK_a 4.60).¹² The inductive effect of the sulfur, relative to oxygen, is difficult to gauge, but is probably about -3 ± 1 , based on the break in the Brøsted plot for general base catalysis of the iodine oxidation of methionine,⁷ which is suggested to represent rate-limiting proton transfer to a tetracoordinate sulfurane. The acid dissociation constant for a cationic sulfurane is therefore estimated to be about 7 ± 1 pK_a units below the corresponding amine.

Discussion Section

Leaving Group Effects. The effect of electron-withdrawing substituents on the third-order rate constants for the proton-catalyzed iodide reduction of *N*-phenyl-*S,S*-dimethylsulfilimmonium cations is to reduce the rate of the reaction (Figure 1, Table I). A plot of these rate constants against the pK_a of the corresponding aniline is fairly linear with a slope $\beta_{lg} = 0.54$ (Figure 4, ●). The data are slightly better correlated by a Hammett treatment using the substituent constant $[\sigma^n + (\rho^r/\rho)(\sigma^- - \sigma^n)]$, as described by Yukawa and Tsuno¹⁴ and modified by Young and Jencks.¹⁵ The slope of the Hammett plot is -1.7 with $\rho^r = -1.2$. By either criteria, the "effective charge" on the nitrogen atom in the rate-limiting step has increased about half a unit relative to that of the nitrogen atom in the sulfilimine ground state.

For strongly basic unhindered primary amines there appears to be very little effect of amine pK_a on the third-order rate constants for iodide reduction (Table I). These data are plotted in Figure 4 (■) and a line of slope = -0.1 has been drawn through

(12) Jencks, W. P.; Regenstein, J. In "Handbook of Biochemistry and Molecular Biology"; Fasman, G. D., Ed.; CRC Press, Inc.: Cleveland, OH, 1975. Sayer, J. M.; Peskin, M.; Jencks, W. P. *J. Am. Chem. Soc.* 1973, 95, 4277–4287.

(13) Arnett, E. M.; Scorrano, G. *Adv. Phys. Org. Chem.* 1976, 13, 84–153.

(14) Yukawa, Y.; Tsuno, Y. *Bull. Chem. Soc. Jpn.* 1959, 32, 965–971, 971–981. Yukawa, Y.; Tsuno, Y.; Sawada, M. *Ibid.* 1966, 39, 2274–2286.

(15) Young, P. R.; Jencks, W. P. *J. Am. Chem. Soc.* 1979, 101, 3288–3294.

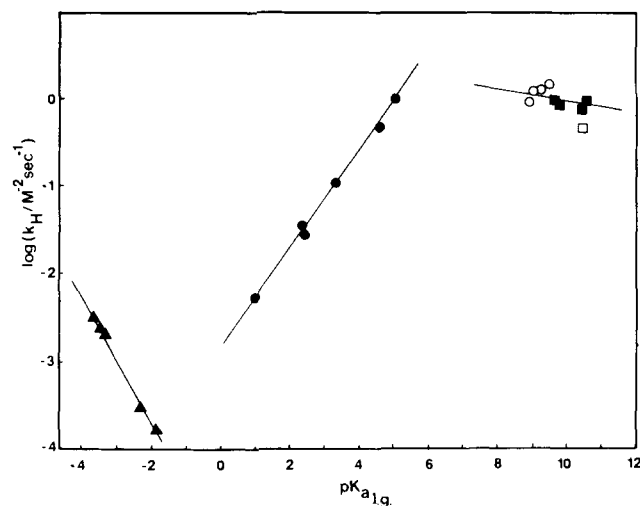


Figure 4. Plot of observed third-order rate constants for the iodide reduction of *N*-substituted *S,S*-dimethylsulfilimmonium salts as a function of the pK_a of the corresponding substituted amine or amide. The classes of compounds include the following: (●), *p*-NO₂, *m*-NO₂, *p*-COOEt, *m*-CF₃, *m*-Cl, -H, and *p*-CH₃ anilines; (▲), *p*-Cl, -H, and *p*-CH₃ sulfonamides, $p < \text{hyd}$ benzamide; (■) phenethyl-, methoxyethyl-, propyl-, and cyclohexylamine; (○), *m*-Cl, *p*-Cl, -H, and *p*-CH₃ benzylamine. The following slopes have been drawn: amides, -0.5 ; anilines, -0.54 ; ethylamine derivatives, -0.1 .

the points for the four simple primary amines (methoxyethylamine, phenylethylamine, propylamine, and cyclohexylamine). This line can be extended through the benzylamine series, where electron-donating substituents seem to slightly enhance the rate of the reduction reaction. The data, however, are not linear against σ^n , suggesting that other, more subtle effects may be involved. In general, the leaving group effect for higher pK_a amines appear to be significantly smaller than that observed for the aniline series. Although the observed rate constants for the basic amines are approximately equal to the largest rate constant for the aniline series, it is doubtful that the data are actually described by a single nonlinear correlation since solvation and steric effects would be expected to be significantly different for the aniline and primary amines series. The observation of a significant change in leaving group effects between the two series, however, strongly suggests that the two regions represent different rate-limiting steps.

In sharp contrast to the substituent effect observed for anilines, electron-withdrawing substituents *accelerate* the rate of reduction of sulfilimines derived from sulfonamides and benzamides with an approximate values of β_{lg} of -0.5 (Figure 4, ▲). This is consistent with the positive ρ value (0.33) reported by Dell'Erba and co-workers for the iodide reduction of these compounds in aqueous perchloric acid. Unlike the sulfilimines derived from anilines and more basic amines, sulfonylsulfilimines are strong acids with pK_a s of approximately -2 to -3 .¹⁶ Under the conditions of the reduction experiments, therefore, these compounds exist almost entirely as the zwitterionic ylide. The pK_a s of these compounds for N-protonation show a large dependence on the pK_a of the corresponding sulfonamide, giving a β_H of about 0.92.¹⁶ Since the observed β for the proton-catalyzed reduction reaction is the sum of the β values for protonation of the ylide and for the approach to the transition state ($\beta_{obsd} = \beta_H + \beta_k$), the actual leaving group effect, β_k , is about -1.4 , suggesting a mechanism with a large amount of charge accumulation on the nitrogen leaving group. The fourth-order rate constants for the pathway dependent on $[H^+]^2$ most likely represents a proton-catalyzed decomposition of the protonated sulfilimine. The data for the fourth-order reaction are subject to much experimental error, making it difficult to determine the leaving group effect. It is probably negative (≈ -0.5), however, based on the decrease in the fourth-order term on going from sulfonamides to benzamides.

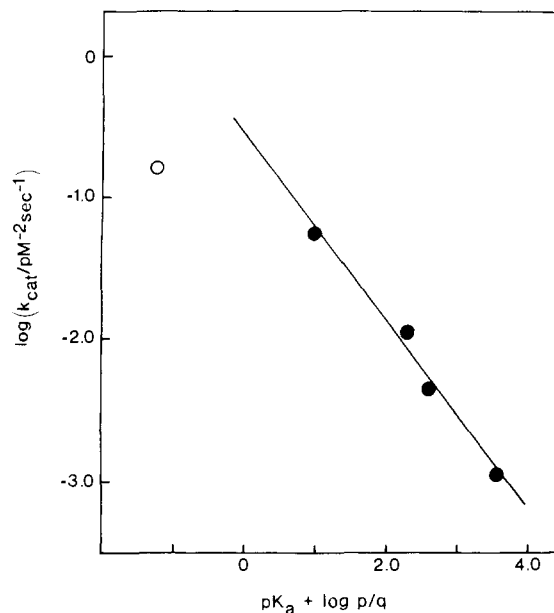


Figure 5. Brønsted plot for the general acid catalyzed iodide reduction of *N*-phenyl-*S,S*-dimethylsulfilimmonium chloride for the following general acids: chloroacetate, glycolate, acetate, and phosphate. A line of slope 0.7 has been drawn through the four general acids; the point for proton catalysis is given as the open symbol.

The very large change in β_{lg} that is observed as the leaving group is changed from anilines to amides (a total change in β of ≈ -1.9 ; the $[H^+]^2$ term for amides is considered here) is far too abrupt to have arisen from simple Hammond or anti-Hammond movement of a transition state in response to perturbations in the ground-state energies of the reaction intermediates. The experimentally observed pK_a values for benzamides and sulfonamides lie in the range of -2 to -4 , for the compounds examined. These, however, are equilibrium constants for protonation on the amide oxygen, not for N-protonation.¹⁷ The pK_a for N-protonation would be considerably lower than these values and can be estimated by the method of Fersht¹⁷ to be between -9 and -13 for the compounds examined. If the change in β resulted from systematic changes in transition-state structure, a curvature should be observed over the aniline series with $\partial\beta_{lg}/\partial pK_{lg} \approx 0.12$.¹⁸ This curvature would be sufficient to change the β for anilines from 0.5 to about 0 as the substituents is changed from *p*-methyl to *m*-nitro, which is clearly not observed.

General Acid Catalysis. As the concentration of buffer acid is increased at constant pH, the observed rate constants for the iodide reduction of *N*-phenyl-*S,S*-dimethylsulfilimmonium ion increase regularly (Figure 3). The catalytic constants for the buffers examined are plotted in the Brønsted plot in Figure 5. A good line can be drawn through the data for neutral and anionic acids with a slope of $\alpha = 0.7$. The point for proton catalysis falls below the extrapolated line by about a factor of 10. This could represent genuine curvature in the Brønsted plot, indicative of a stepwise "trapping" of "preassociation" mechanism,¹⁹ or could simply be an electrostatic effect related to unfavorable association between the cationic acid and the cationic sulfilimine ground state. The observation of an α of about 0.7 requires a mechanism with the rate-limiting proton transfer. Kresge,²⁰ however, has shown that proton transfer involving nitrogen bases is sometimes slow relative to proton transfers between oxygen acids resulting in anomalous Eigen curves for stepwise (trapping) mechanisms which have extended regions of rate-limiting proton transfer and Brønsted slopes of between 0.5 and 0.7. The present data require proton transfer in the rate-limiting transition state but say little regarding the coupling of heavy-atom movements to this proton transfer.

(17) Fersht, A. J. *J. Am. Chem. Soc.* **1971**, *93*, 3504-3515.

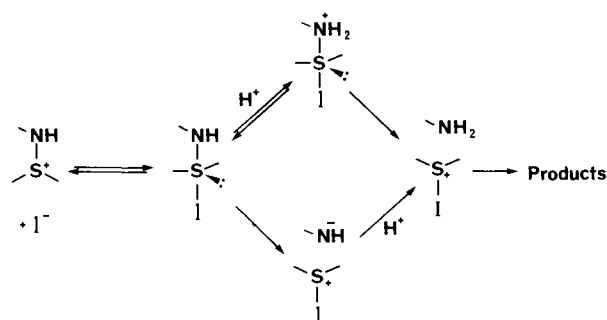
(18) Jencks, D. A.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 7948-7960.

(19) Jencks, W. P. *Acc. Chem. Res.* **1976**, *9*, 425-432.

(20) Kresge, A. J. *Pure Appl. Chem.* **1981**, *53*, 189-200.

(16) Kapovits, I.; Ruff, F.; Kucsman, A. *Tetrahedron* **1972**, *28*, 4413-4417.

Scheme II



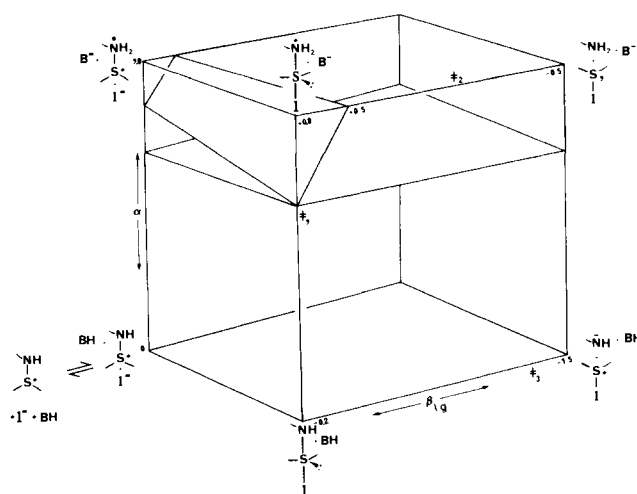
The value of the Brønsted α that is observed (0.7) is probably too large to represent catalysis by "hydrogen bonding" with little actual proton transfer.

For the sulfilimine prepared from benzylamine, no general catalysis is observed with glycolic acid up to 1 M concentration (figure 3, Δ). Assuming that the proton point would also show a negative deviation in the Brønsted plot for this compound as it does in Figure 5 and in other cases,²¹ the limit of the Brønsted α for the benzyl compound is very close to one.¹⁹ This is consistent with a transition state in which complete and equilibrium proton transfer has occurred.

Predicted Leaving Group Effects. The interpretation of the observed changes in β_{lg} in terms of the rate-limiting step of the reaction requires an accurate prediction of the changes in "effective charges" for the intermediates in Scheme I, relative to the sulfilimine ground state. The sulfur–nitrogen bond in sulfilimines is probably best described as a single bond, based on the observation that both the sulfur and the nitrogen appear to be tetrahedral in the crystal.²² The effective charge on the nitrogen is therefore expected to be less than +1 and greater than an amine in free solution. In previous work,²³ structure–reactivity data have suggested that the effective charge on the ester oxygen in an *O*-acyl sulfoxide is approximately +0.5. The change to nitrogen (which can better accommodate the positive charge) will increase this slightly to about +0.7 in the ground state and +0.3 for the partial charge in the (highly polarizable) sulfilimine–iodide encounter pair (Scheme I). Protonating the sulfilimine to give the dicationic intermediate would be expected to increase the positive charge by one unit which gives an effective charge (EC) of +1.3 and a β_{lg} of +0.6. Addition of iodide anion to the sulfur to form the sulfuranone will decrease the charge felt by the nitrogen making it approximately comparable to free amine, giving a β_{lg} of about -0.2 (EC = +0.5) for this intermediate. Protonating the sulfuranone would increase the positive charge by one unit, giving a β_{lg} of +0.8 (EC = +1.5), and stepwise cleavage to give amine anion would represent a significant increase in negative charge, giving a β_{lg} of about -1.5 for the anion (EC = -0.8). This latter value is consistent with the Brønsted β value of +1.5 previously reported²³ for carboxylate anions reacting with an iodosulfonium ion to give *O*-acyl sulfoxides. Although all of these values represent some conjecture, they are probably accurate to within 0.2 units.

Mechanisms for the Reduction Reactions. The simplest mechanism for the attack of iodide anion on a sulfilimine to yield an iodosulfonium ion and the free amine (or its conjugate base) is a direct S_N2 displacement. For relatively high *pK_a* amines the nitrogen anion would be an unacceptably poor leaving group, and protonation on this nitrogen will occur either as a pre-equilibrium step or in a reaction concerted with amine leaving. For sulfilimines with substituted anilines as leaving groups, general acid catalysis is observed, and for the unsubstituted compound a Brønsted α of 0.7 is observed. Since the rate of this reaction is a simple linear function of iodide concentration, the general acid, the sulfilimine, and iodide must combine in the rate-limiting transition state. Two distinct preassociation type¹⁹ mechanisms can be written to

Scheme III



describe this reaction. The first involves concerted general catalysis of the formation or breakdown of a tetracoordinate sulfurane intermediate (Scheme II, top pathway). The driving force for this mechanism of catalysis is clearly seen since the concerted proton transfer would avoid the formation of the dicationic sulfilimine in the attack step and avoid the buildup of anionic charge on the leaving group during sulfurane breakdown. The suggestion of a sulfurane intermediate in this reaction finds precedence in the observation of a similar intermediate in the iodide reduction of the cyclic sulfilimine, dehydromethionine,⁷ and the suggested roles of sulfuranes in the iodide reduction of *O*-acyl sulfoxides.^{23–26}

A second mechanism, representing general acid catalysis of an S_N2 reaction, involves proton transfer to the amine concerted with iodide attack and cleavage of the S–N bond (Scheme II, bottom pathway). While general catalysis of intramolecular displacement reactions has been reported,^{27,28} the Brønsted coefficients for this catalysis are generally small (0.2 to 0.36) and have been attributed to hydrogen bonding effects.²⁸ The entropic requirements for extensive proton transfer to the leaving group concerted with both S–N cleavage and S–I bond formation would be expected to be large, although it would be improper to dismiss the mechanism simply because of lack of precedence.

It can be effectively argued that the leaving group data shown in Figure 4 require at least two mechanisms for the reduction reaction, simply from the fact that the leaving group dependence for the basic amines is significantly less than that observed for the anilines suggests that the mechanism of these reductions proceeds through the formation of at least one stable intermediate and that the change in β_{lg} represents a simple change in the rate-limiting step. The further fact that the Brønsted α increases from 0.7 to 1.0 as the leaving group is changed from aniline to benzylamine strongly suggests that these intermediates differ with respect to their proton-transfer equilibria. Thus, the data effectively rule out the catalyzed S_N2 reaction for the anilines and primary amines, although the new mechanism which energies for amide leaving groups could possibly represent the S_N2 reaction. Stronger arguments supporting stepwise mechanisms for all leaving group classes can be made based on analysis of multi-dimensional reaction surfaces, as follows:

In order to represent the general catalyzed reduction of sulfilimines on a reaction surface, coordinates must be available to show distances along the S–I axis and the S–N axis and motion of the proton from the general acid to the sulfilimine nitrogen. Concerted motion along all of these axes would represent a general catalyzed S_N2 reaction. Obviously, motion along three axes cannot

(24) Young, P. R.; Hsieh, L.-S. *J. Org. Chem.* **1982**, *47*, 1419–1423.

(25) Young, P. R.; Till, M. *J. Org. Chem.* **1982**, *47*, 1416–1419.

(26) Doi, J. T.; Musker, W. K.; deLeeuw, D. L.; Hirschon, A. S. *J. Org. Chem.* **1981**, *46*, 1239–1243.

(27) Knipe, J. O.; Vasquez, P. J.; Coward, J. K. *J. Am. Chem. Soc.* **1982**, *104*, 3202–3209 and references cited therein.

(28) Thibblin, A.; Jencks, W. P. *J. Am. Chem. Soc.* **1979**, *101*, 4963–4973.

(21) Young, P. R.; Huang, H. C., in preparation.

(22) Glass, R. S.; Duchek, J. R. *J. Am. Chem. Soc.* **1976**, *98*, 965–969.

(23) Young, P. R.; Hsieh, L.-S. *J. Am. Chem. Soc.* **1982**, *104*, 1612–1616.

be shown in a standard More O'Ferrall²⁹-Jencks¹⁹ diagram. Such motion is readily shown, however, on the "reaction cube" in Scheme III. In this diagram, proton transfers are shown by vertical movement and the observed Brønsted α of 0.7 (for aniline leaving groups) is described by the horizontal plane. Movement along the S-I axis (β_{nuc}) is shown by vertical planes along the horizontal axes and S-N movement (β_{lg}) is shown by movement along the axes extending into and out of the page. The planes describing a given β_{lg} can be constructed by connecting those points on each axis which correspond to that β value. In Scheme III, the plane of $\beta_{\text{lg}} = 0.5$ is shown intersecting the cube at an angle. For a given reaction where a complete set of reaction parameters are available, the transition state will be located at the intersection of the planes for β_{nuc} , β_{lg} , and α . For aniline leaving groups, a β_{lg} of +0.5 is observed along with a Brønsted α of 0.7. In the diagram in Scheme III, these parameters appear together at only one section of the surface, marked as \mp_1 . In this section of the diagram, the kinetic process involves formation of the neutral sulfurane followed by rate-limiting proton transfer from the general acid to give the cationic sulfurane intermediate. Expulsion of good amine leaving groups, such as the anilines, would then proceed rapidly. The pK_a of the sulfurane nitrogen is estimated to be about -3, making the proton transfer from carboxylates highly unfavorable. In order for proton transfer to be entirely rate limiting, the rate constant for cleavage of the heavy atom bond (the S-N bond) would have to exceed the rate constant for internal proton return in the favorable direction. While this is normally thought not to be the case,²⁰ the slow proton transfer from nitrogen acids observed by Kresge²⁰ and the instability of sulfurane intermediates may combine to give the observed partitioning.

It is also possible that some degree of motion along the S-N bond is coupled with the transfer of the proton to the leaving group. In an N-protonated sulfurane, the S-N bond length should be a simple function of the electronegativity of the ammonium group. In a stepwise transfer to a stable intermediate, proton transfer can occur separately from heavy-atom reorganization steps. With a very unstable intermediate, however, the lifetime of the initial product from proton transfer may be so short that heavy-atom rearrangement becomes rate limiting. When this happens, there should be an energetic advantage to a mechanism in which proton transfer and heavy-atom movement are coupled. In the case of the anilines, if these coupled movements are occurring, the reaction coordinate in the origin of the transition state must have a large vertical component to be consistent with the observed Brønsted coefficients. One would predict a decrease in the Brønsted α as the leaving group becomes better due to an anti-Hammond slide of the reaction coordinate toward the stepwise anionic intermediate.

General acid catalysis is not observed for benzylamine leaving groups. This requires a mechanism in which proton transfer is essentially complete and α is 1.0. The β_{lg} for higher pK_a amines, in general, is significantly less than that observed for the anilines. The fact that the leaving group effect is less, coupled with the fact that general acid catalysis is no longer observed, strongly suggests that the rate-limiting step has changed as the pK_a of the sulfilimine nitrogen is increased. The data are most readily explained by simply allowing the rate constant for S-N cleavage to decrease steadily with poor leaving groups. The pK_a of the

sulfurane derived from the benzylamine is about +2, making it reasonable to suggest that this intermediate has become solvent equilibrated in dilute acid solution. For sulfilimines prepared from basic amines, the kinetic mechanism then involves equilibrium formation of the protonated sulfurane with rate-limiting cleavage of the S-N bond. The intersection of $\alpha = 1.0$ and $\beta_{\text{lg}} > 0.4$ occurs on the top surface of the cube in Scheme III in the region marked as \mp_2 .

For sulfilimines with amide and sulfonamide leaving groups, β_{lg} is -1.4, corrected for the protonation of the ylide and both uncatalyzed and proton-catalyzed pathways are evident for the reduction of the cationic sulfilimine. The major pathway must represent expulsion of amide anion from the neutral sulfurane. The observed value of β places the transition state for this reaction on the lower edge of the right-hand face of the cube in Scheme III with approximately 90% S-N bond cleavage (\mp_3).

It is also possible that the rate-limiting step involves proton transfer to the amine anion (vertical movement along the back edge of the cube), allowing a common pathway for both the solvent- and proton-catalyzed pathways. The pK_a of *p*-toluenesulfonamide is reported to be 10.24.³⁰ Proton transfer from the solvent (water) to this intermediate can be estimated³¹ to occur with a rate constant of about 10^6 s^{-1} . Proton transfer from a strong acid such as the solvated proton would be expected to be diffusion controlled so that in the presence of one molar acid, protonation of the anion would occur predominantly (by a factor of 10^3 - 10^4) through a "trapping"¹⁹ mechanism involving H_3O^+ . The ratio between the third- and fourth-order rate constants in Table I are, however, less than one, strongly suggesting that the proton and the solvent are *not* catalyzing the same reaction. The simplest explanation, therefore, is that the neutral sulfurane partitions through two parallel mechanisms, one involving direct expulsion of the amine anion and the second involving a proton-catalyzed breakdown of the neutral sulfurane. Preliminary data, showing general catalysis of the reduction of the sulfilimine derived from *p*-chlorobenzenesulfonamide ($\alpha = 0.5$),²¹ are consistent with this suggestion and will be described separately. This reaction, then, represents a clear example of a concurrent concerted and stepwise partitioning of a common reaction intermediate.

Acknowledgment. This work was supported by a grant from the National Science Foundation, CHE 80-00054.

Registry No. *p*-NO₂C₆H₄N=SMe₂·HCl, 52259-96-8; *m*-NO₂C₆H₄N=SMe₂·HCl, 97763-72-9; HO₂C(CH₂)₂-*p*-C₆H₄N=SMe₂·HCl, 97731-97-0; *m*-ClC₆H₄N=SMe₂·HCl, 52259-92-4; *m*-CF₃C₆H₄N=SMe₂·HCl, 97731-98-1; PhN=SMe₂·HCl, 35357-64-3; *p*-MeC₆H₄N=SMe₂·HCl, 60978-80-5; *m*-ClC₆H₄CH₂N=SMe₂·HCl, 97731-99-2; *p*-ClC₆H₄CH₂N=SMe₂·HCl, 97732-00-8; PhCH₂N=SMe₂·HCl, 35357-68-7; *p*-MeC₆H₄CH₂N=SMe₂·HCl, 97732-01-9; MeO(CH₂)₂N=SMe₂·HCl, 97732-02-0; Ph(CH₂)₂N=SMe₂·HCl, 97749-33-2; CH₃(CH₂)₂N=SMe₂·HCl, 97732-03-1; *c*-HexN=SMe₂·HCl, 60978-63-4; *t*-BuN=SMe₂·HCl, 60978-62-3; *p*-ClC₆H₄SO₂N=SMe₂·HCl, 97732-04-2; PhSO₂N=SMe₂·HCl, 97732-05-3; *p*-MeC₆H₄SO₂N=SMe₂·HCl, 97732-06-4; *p*-NO₂C₆H₄C(O)N=SMe₂·HCl, 97732-07-5; PhC(O)N=SMe₂·HCl, 24978-57-2; I₂, 20461-54-5.

(30) Exner, O.; Janak, P. *Collect. Chem. Commun.* **1975**, *40*, 2510-2523.

(31) Calculated by using a rate constant for proton transfer in the favorable direction of $5 \times 10^9 \text{ s}^{-1}$, patterned after the value of $5 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ previously used for the diffusion constant. See: Young, P. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 7318-7323.

(29) More O'Ferrall, R. A. *J. Chem. Soc. B* **1970**, 274-277.