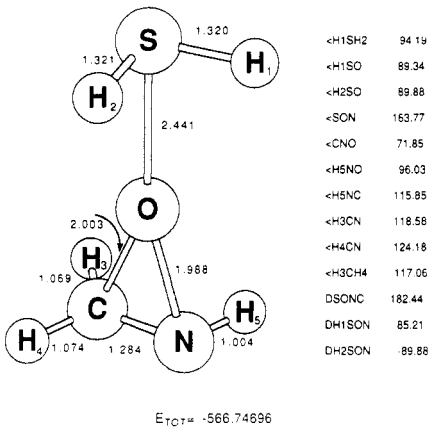

Figure 8. Transition structure for oxygen transfer from oxaziridine to hydrogen sulfide (HF/4-31G(d).

for epoxidation of ethylene. In all cases, the magnitude of the barrier is largely due to geometric distortions of the oxaziridine attending the bond breaking step or displacement of the imine from the oxaziridine. This is dramatically demonstrated by the relatively small difference in activation barriers with no apparent trend reflecting the nucleophilicity of the oxidant (Tables I and II). Very little enthalpic contribution from S–O bond formation was in evidence. The close-shell repulsion between the lone pairs on oxygen and sulfur serves as a driving force to elevate the developing HOMO (Ψ_B) in energy, to transfer electron density to the virtual orbital of the oxaziridine fragment, and to lower the overall activation barrier through the net stabilization of the attending three molecular orbital four-electron interaction. The salient point to be gained from these studies is that there are no stereoelectronic factors that favor a planar or spiro transition state orientation for the oxidation of sulfides to sulfoxides or for the epoxidation of alkenes by *N*-sulfonyloxaziridines. Rather the transition state orientation is steric in origin, dictated by the substituents attached to the oxaziridine carbon and nitrogens. Experimentally this has been observed for the asymmetric oxidation of enolates to optically active α-hydroxy carbonyl compounds using (+)-(camphorylsulfonyl)oxaziridine where both orientations are necessary to explain the structure reactivity trends.[2d]

Registry No. $H_2C{=}NH$, 2053-29-4; H_2S, 7783-06-4; H_2SO, 25540-60-7; HSO_2H, 81824-08-0; oxaziridine, 6827-26-5; ethylene oxide, 75-21-8; ethene, 74-85-1.

Acidities of Carboxamides, Hydroxamic Acids, Carbohydrazides, Benzenesulfonamides, and Benzenesulfonohydrazides in DMSO Solution

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A comparison of acidities of six series of analogous oxygen, nitrogen, and carbon acids in dimethyl sulfoxide (DMSO) solution and the gas phase has shown that the element effect usually causes nitrogen acids to be more acidic than their carbon acid counterparts by an average of 17 ± 5 kcal/mol, and oxygen acids to be more acidic than their nitrogen counterparts by a like amount. A much smaller difference was observed between the NH acidities of carboxamides and the CH acidities of ketones (1–2 kcal/mol in DMSO and 7–8 kcal/mol in the gas phase). Equilibrium acidities in DMSO for a number of substituted benzamides, acetamides, *N*-phenylacetamides, acetohydroxamic acids, benzohydroxamic acids, carbohydrazides, and benzenesulfonamides are reported. Aceto- and benzohydroxamic acids were found to be 9.8 and 10.1 pK_{HA} units more acidic in DMSO, respectively, than acetamide and benzamide. In each instance the effect of N-alkylation decreased the acidity more than did O-alkylation, which indicates that the parents are NH, rather than OH, acids in DMSO. Conclusive supporting evidence for the NH acid assignment was provided by the observation that the *N*-alkylhydroxamic acids exhibited strong homo-H-bonding, whereas the parent acids and their *O*-alkyl derivatives did not. Oxidation potentials of hydroxamate anions in DMSO are close to those of *O*-alkylhydroxamate ions, confirming that their conjugate acids are NH acids, but in MeOH they are close to those of *N*-alkylhydroxamate ions showing that their conjugate acids can act as OH acids in hydroxylic solvents. The *N*-alkyl- and *O*-alkylhydroxamic acids exhibited much stronger chelating power toward K^+, Na^+, and Li^+ ions than did the parent acids.

It has been recognized for many years that oxygen acids are more acidic than nitrogen acids and that nitrogen acids are more acidic than analogous carbon acids, but quantitative data have been lacking. Recent gas-phase measurements[1] have shown, however, that oxygen acids, such as phenol or water, are more acidic than their nitrogen acid counterparts, aniline and ammonia, by 12 or more kcal/mol and that these nitrogen acids are, in turn, more acidic than their carbon acid counterparts, toluene and methane, by similar amounts. Measurements in dimethyl sulfoxide (DMSO) solution of acidities of phenol, water, and aniline, together with estimates of acidities for ammonia, toluene, and methane, suggest that like differences also prevail in solution. In fact, they appear to be exaggerated therein.[2] Carboxamides exhibit anomalous behavior, relative to

(1) See the gas-phase acidity scale of Prof. J. E. Bartmess (available by request in care of the Department of Chemistry, University of Tennessee, Knoxville, TN 37996-1600).

(2) (a) Taft, R. W.; Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 463–469. (b) Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456–463.

0022-3263/90/1955-3330$02.50/0

Table I. Acidities of Oxygen, Nitrogen, and Carbon Acids in the Gas Phase and in Dimethyl Sulfoxide Solution

acid	$(\Delta G°)^a$	acid	$(\Delta G°)^a$	$(\Delta\Delta G°)_I{}^d$	acid	$(\Delta G°)^a$	$(\Delta\Delta G°)_{II}{}^e$
H_2O(g)	384[a]	NH_3(g)	396[a]	12	CH_4(g)	408[a]	12
H_2O	43	NH_3	(56)[c]	13	CH_4	(77)[c]	21
PhOH(g)	342[a]	$PhNH_2$(g)	359[a]	17	$PhCH_3$(g)	373[a]	14
PhOH	25	$PhNH_2$	42	17	$PhCH_3$	(59)[c]	17
CH_3SO_3H	2	$CH_3SO_2NH_2$	24	22	$(CH_3)_2SO_2$	43	19
HOCN	(2)[b]	H_2NCN	23	21	CH_3CN	43	20
CH_3CO_2H	17	CH_3CONH_2	35	18	$(CH_3)_2C{=}O$	36	1
$PhCO_2H$	15	$PhCONH_2$	32	17	$PhCOCH_3$	34	2
CH_3CO_2H(g)	341[a]	CH_3CONH_2(g)	355[a]	14	$(CH_3)_2C{=}O$(g)	362[a]	7
$PhCO_2H$(g)	331[a]	$PhCONH_2$(g)	347[a]	16	$PhCOCH_3$(g)	355[a]	8

[a] Gas-phase acidities are $\Delta G°$ values in kilocalories/mole taken from a list compiled by J. E. Bartmess.[1] DMSO acidities are in kcal/mol (1.37 pK_a) taken, unless otherwise noted, from Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456–463. [b] Estimated. [c] Extrapolated [Bordwell, F. G.; Algrim, D. J. *J. Am. Chem. Soc.* **1988**, *110*, 2965–2967]. [d] $(\Delta\Delta G°)_I = \Delta G°(NH) - \Delta G°(OH)$ (not statistically corrected). [e] $(\Delta\Delta G°)_{II} = \Delta G°(CH) - \Delta G°(NH)$ (not statistically corrected).

other types of nitrogen acids in this respect, however, being only slightly more acidic than their carbon acid analogues, the ketones.

Carboxamides, like ketones, are too weakly acidic to dissociate to any appreciable extent in aqueous solution. Substitution of one of the hydrogen atoms on nitrogen by a hydroxyl or amino group gives rise, however, to acids that are strong enough to be measured in aqueous solution. For example, benzohydroxamic acid ($C_6H_5CONHOH$) has pK_{HA} = 8.8 in aqueous solution.[3] Substitution at the acidic site in analogous ketones by OH or NH_2 produces much smaller effects.

There is a long-standing controversy as to whether hydroxamic acids are NH or OH acids. Extensive IR and UV spectroscopic and acidity measurements by Exner and his associaties in dioxane and aqueous alcohol solvents indicate that they are NH acids,[4] and this conclusion has been supported by a ^{17}O NMR study of benzohydroxamate ion in MeOH.[4e] The assignment of the NH acid structure was further supported by the observation that in 80% (by weight) methyl cellosolve (50 mol % aqueous 2-methoxyethanol) the *N*-alkylbenzohydroxamic acids were *weaker* than *O*-alkylbenzohydroxamic acids by more than one order of magnitude.[4c] Exner's analysis indicated that less than 10% of the $C_6H_5CONHO^-$ ion was present in the solution. (It was pointed out, however, that ortho- or para-electron-releasing groups in benzohydroxamic acids could conceivably weaken the NH acidic site sufficiently to lead to a measurable amount of $GC_6H_4CONHO^-$ ion on dissociation.) On the other hand, in aqueous solution UV data for meta- and para-substituted benzohydroxamate ions have been interpreted as indicating that the negative charge is on oxygen,[5a] and measurements of pK_a values for *N*-methylaceto- and -benzohydroxamic acids have shown that they are slightly *stronger* acids than their parents,[5b,c] and this is true also for *N*-phenylbenzohydroxamic acid.[3] These observations led to the conclusion that in aqueous solution $RCONHO^-$ ions were at least as prevalent as $RCON(OH)^-$ ions.[5] More recently, Crumbliss and his students have shown that data for aceto- and benzohydroxamic acids fit a correlation of ΔH_a vs ΔS_a for 14 *N*-methyl and *N*-arylhydroxamic acids in aqueous 2 M $NaNO_3$ solution, and conclude that in this medium they are acting as OH, rather than NH acids.[6] It would appear, then, that hydroxamic acids may be NH acids in dioxane, 50 mol % 2-methoxyethanol, and MeOH, but OH acids in water. One of our objectives was to determine whether hydroxamic acids are NH or OH acids in DMSO solution.

Comparisons of the effects of certain structural changes on the acidities of carboxamides and sulfonamides also have some intriguing aspects. Carboxamides are about 10^5 times less acidic in aqueous solution than are the corresponding sulfonamides, but *N*-hydroxybenzamide (benzohydroxamic acid) is slightly *more* acidic than *N*-hydroxybenzenesulfonamide, and *N*-aminobenzamide (benzohydrazide) is nearly as acidic as *N*-aminobenzenesulfonamide.[7] Whereas the leveling effect of water allows only limited comparisons of this type to be made in aqueous solution, it is possible to make general quantitative comparisons of acidities of carboxamides, sulfonamides, and their *N*-hydroxy and *N*-amino derivatives in DMSO solution. Acidity measurements in this medium have now been carried out on these and related compounds in order to explore further these unusual aspects.

Results and Discussion

Relative Acidities of Oxygen, Nitrogen, and Carbon Acids in the Gas Phase and in DMSO. Examination of the results of acidity measurements on a variety of oxygen, nitrogen, and carbon acids summarized in Table I shows that the effects of changing the element to which the acidic proton is attached are, for the most part, remarkably constant. The average for the $(\Delta G°)_I$ effects between NH and OH acids is 17 ± 5 kcal/mol, and the average of $(\Delta G°)_{II}$ effects between CH and NH acids is the same, if we exclude the final four values in the last column. These comparisons suggest that the intrinsic (gas phase) increases in acidity caused by the differences in electronegativity of the atom to which the proton is attached (the element effects) usually amount to about 12–14 kcal/mol and that they are enhanced in DMSO by 5 or more kcal/mol by a solvation effect, presumably due to enhanced solvation of the anion.

The $(\Delta G°)_{II}$ values between ketones and carboxamides given in the final four values in the last column in Table I are smaller than the average by 15–16 kcal/mol in DMSO and by 9–10 kcal/mol in the gas phase. It is evident, therefore, that about half of these smaller effects is due to solvation and about half is intrinsic. Since $(\Delta G°)_I$ appears to be normal between carboxylic acids and carbox-

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(4) (a) Exner, O.; Kakáč, B. *Collect. Czech. Chem. Commun.* **1963**, *28*, 1656–1663. (b) Exner, O.; Holubek, J. *Ibid.* **1965**, *30*, 940–951. (c) Exner, O.; Simon, W. *Ibid.* **1965**, *30*, 4078–4093. (d) Bauer, L.; Exner, O. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 376–384. (e) Lipczynńska-Kochany, E.; Iwamura, H. *J. Org. Chem.* **1982**, *47*, 5277–5282.

(5) (a) Plapinger, R. E. *J. Org. Chem.* **1959**, *24*, 802–805. (b) Gerstein, J.; Jencks, W. P. *J. Am. Chem. Soc.* **1964**, *86*, 4655–4663. (c) Steinberg, G. M.; Swidler, R. *J. Org. Chem.* **1965**, *30*, 2362–2365.

(6) (a) Monzyk, B.; Crumbliss, A. L. *J. Org. Chem.* **1980**, *45*, 4670–4675. (b) Brink, C. P.; Crumbliss, A. L. *J. Org. Chem.* **1982**, *47*, 1171–1176. (c) Brink, C. P.; Fish, L. L.; Crumbliss, A. L. *J. Org. Chem.* **1985**, *50*, 2277–2281.

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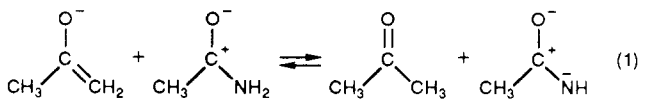
Table II. Equilibrium Acidities in DMSO for Aceto- and Benzohydroxamic Acids and Their *N*- and *O*-Alkyl Derivatives

acid	in.	pK_{in}	pK_{HA}	log K_{hb}[k]
CH_3CONH_2			25.5[j]	
$CH_3CONHOH$	9-PhSFlH[a]	15.4	16.03 ± 0.02	
	9-TNFlH[b]	17.0	15.99 ± 0.01	
$CH_3CONHOMe$	2-$PhSO_2$FlH[c]	18.1	17.10 ± 0.02	
	2-*i*-PrSFlH[d]	16.9	16.90 ± 0.02	
$CH_3CON(Me)$-OH	2NPANH[e]	20.66	19.60 ± 0.06	4.3
CH_3COCH_3			26.5	
CH_3COCH_2OMe	*t*-BuFlH	24.35	24.57 ± 0.04	
	$Ph_2C{=}NCH_2Ph$	24.3	24.50 ± 0.04	
$PhCONH_2$			23.5[j]	
PhCONHOH	HZFP2[f]	14.15	13.65 ± 0.01	
PhCONHO-CH_2Ph	HZFP2[f]	14.15	14.43 ± 0.01	
PhCON(Me)OH	CNAH[g]	18.9	18.2 ± 0.04	4.4
	9-*o*-TolFlH[h]	18.8	18.8 ± 0.08	4.2
	DB-*t*-BuFlH[i]	19.4	18.5 ± 0.07	4.3
$PhCON(CH_2$ Ph)OH	CNAH[g]	18.9	18.0 ± 0.02	4.0
$PhCOCH_3$			24.7	
$PhCOCH_2OMe$			22.85	

[a] 9-(Phenylthio)fluorene. [b] 9-(N^1-1,2,4-triazolyl)fluorene. [c] 9-(Phenylsulfonyl)fluorene. [d] 2-(Isopropylthio)fluorene. [e] 2-Naphthylacetonitrile. [f] 9-Fluorenone (4-chlorophenyl)hydrazone. [g] 4-Chloro-2-nitroaniline. [h] 9-(*o*-Tolyl)fluorene. [i] 2,7-Dibromo-9-*tert*-butylfluorene. [j] Bordwell, F. G.; Algrim, D. *J. Org. Chem.* **1976**, *41*, 2507–2508. [k] K_{hb} is the homo-hydrogen-bonding constant (L/mol) for the association AHA^- [Olmstead, W. N.; Margolin, Z.; Bordwell, F. G. *J. Org. Chem.* **1980**, *45*, 3296–3299].

amides, the small values for $(\Delta G°)_{II}$ indicate that either the carboxylic and carboxamide acidities are both unusually low or the ketone acidities are unusually high. A traditional interpretation would be that the latter is true because the enolate ion, but not the neutral ketone, can be stabilized by resonance whereas *both* the neutral carboxamide and its conjugate base can be stabilized by resonance. Recently, however, calculations by Wiberg and Laidig discount the importance of resonance in carboxamides and indicate that electrostatic effects cause the adjacent polarized carbonyl group to transfer negative charge *to* nitrogen, rather than *away from* nitrogen.[8a] Similar calculations indicate that electrostatic effects caused by lone pair–lone pair repulsions in enolate ions derived from esters introduce a destabilizing effect that is primarily responsible for the lower acidities of esters than ketones.[8b,c] By the same reasoning, lone pair-lone repulsions between the carbonyl oxygen atom and those on the negatively charged nitrogen atom of the carboxamide conjugate base can be pictured as destabilizing the anion thereby lowering the carboxamide acidity to a point where it is only slightly greater than that of an analogous ketone (eq 1). The 6 kcal/mol smaller difference in



(1)

$-\Delta$ = 0.72 kcal/mol

acidities between carboxamides and ketones in DMSO than in the gas phase suggests that solvation is stabilizing the $CH_2{=}C(CH_3)O^-$ ion to a greater extent than it is stabilizing the CH_3CONH^- ion.

(8) (a) Wiberg, K. B.; Laidig, K. E. *J. Am. Chem. Soc.* **1987**, *109*, 5935–5943. (b) Wang, X.; Houk, K. N. *J. Am. Chem. Soc.* **1988**, *110*, 1870–1872. (c) Wiberg, K. B.; Laidig, K. E. *J. Am. Chem. Soc.* **1988**, *110*, 1872–1874.

The Acidities of Hydroxamic Acids and Their *N*- and *O*-Alkyl Derivatives and a Test for Homo-H-bonding. The results of equilibrium acidity measurements in DMSO of aceto- and benzohydroxamic acids and their *N*- and *O*-alkyl derivatives are summarized in Table II.

We see from Table II that acetohydroxamic acid is a stronger acid in DMSO than acetamide by 9.8 pK_{HA} units (statistically corrected) and that a similar difference (10.8 units) is observed for benzohydroxamic acid compared to benzamide. These effects are similar to, but larger than, that estimated by Exner in aqueous solution, where acetohydroxamic acid is estimated to be 5 or 6 pK_{HA} units more acidic than acetamide.[4c,d] The effects on acidity of N- and O-alkylation of aceto- and benzohydroxamic acids in DMSO are also similar to those observed by Exner in 50 mol % aqueous 2-methoxyethanol. In the latter medium, O-methylation decreases the acidity of acetohydroxamic acid by 1.0 pK_{HA} unit, whereas N-methylation decreases it by 2.6 units. The discrepancy is larger in DMSO, where O-benzylation decreases the acidity of benzohydroxamic acid by only 0.78 unit, whereas N-benzylation decreases it by 4.3 pK_{HA} units. Also, N-methylation causes about a 4.8 pK_{HA} unit decrease in acidity in DMSO. These differences indicate that acetohydroxamic and benzohydroxamic acid are acting as nitrogen acids in DMSO solution. Conclusive evidence on this score was obtained during the pK_{HA} measurements by the observation of strong homo-hydrogen bonding for *N*-alkylhydroxamic acids, but not for the parent or for *O*-alkylhydroxamic acids. It has been demonstrated that oxygen acids such as carboxylic acids, phenols, and alcohols form strong homo-hydrogen-bonding complexes when partially neutralized by bases in polar non-hydrogen-bond-donor solvents such as DMSO or NMP (*N*-methyl-2-pyrrolidone).[9] For example, the homo-H-bonding constant for phenol (eq 2) in DMSO is 2.3×10^3.[9c] Nitrogen

$$PhO^- + HOPh \rightleftharpoons PhO^-\cdots H{-}OPh \qquad (2)$$

$$K_{hb} = 2.3 \times 10^3 \text{ L/mol at } 25\ °C$$

acids, such as anilines, fail to show any indication of homo-H-bonding at low concentrations in DMSO.[10] The acidity measurements in DMSO show that neither aceto- nor benzohydroxamic acids, nor their *O*-alkyl derivatives, exhibit homo-H-bonding with their conjugate bases, whereas their *N*-alkyl derivatives show evidence of strong homo-H-bonding ($\log K_{hb} \simeq 4$). Since homo-H-bonding has been shown to be characteristic of oxygen acids and not nitrogen acids,[10] there can be no doubt but what hydroxamic acids behave as nitrogen acids in DMSO solution, and that *N*-alkylhydroxamic acids behave as oxygen acids.

The 3.6 and 4.5 pK_{HA} unit higher acidities in DMSO of the nitrogen acids $CH_3CONHOH$ and PhCONHOH than the oxygen acids $CH_3CON(Me)OH$ and PhCON(Me)OH may appear, at first sight, to be contrary to the usual order of acidities of NH and OH acids (Table I). The difference is that the NH and OH acids in Table I are analogous, whereas these acids are not. In the latter the proton is one atom further removed from the carbonyl group.

Remote Substituent Effects in Benzamides and Benzohydroxamic Acids. Exner found that the Hammett ρ values for benzoic acids, benzohydroxamic acids,

(9) (a) Kolthoff, I. M.; Chantooni, M. K., Jr.; Bhownik, S. *J. Am. Chem. Soc.* **1968**, *90*, 23–28. (b) Bordwell, F. G.; Branca, J. C.; Hughes, D. L.; Olmstead, W. N. *J. Org. Chem.* **1980**, *45*, 3305–3313. (c) Bordwell, F. G.; McCallum, R. J.; Olmstead, W. N. *J. Org. Chem.* **1984**, *49*, 1424–1427.

(10) Bordwell, F. G.; Algrim, D. J. *J. Am. Chem. Soc.* **1988**, *110*, 2965–2968.

Table III. Equilibrium Acidities in DMSO for 3- and 4-Substituted Benzamides and Benzohydroxamic Acids

acid	pK_{HA}[a]	acid	pK_{HA}[a]
$C_6H_5CONH_2$	23.35	$C_6H_5CONHOH$	13.65
$4\text{-}ClC_6H_4CONH_2$	22.6	$4\text{-}ClC_6H_4CONHOH$	13.0
$3\text{-}FC_6H_4CONH_2$	22.4	$3\text{-}ClC_6H_4CONHOH$	12.7
$3\text{-}ClC_6H_4CONH_2$	22.3	$3\text{-}F_3CC_6H_4CONHOH$	12.4
$3,5\text{-}(F_3C)_2C_6H_3CONH_2$	20.4		

[a] Average values from 3-point titrations against two indicators; standard deviations within a run were generally ±0.04, or less. Agreement for runs with different indicators was generally <0.1 pK_{HA} unit.

and *O*-benzylbenzohydroxamic acids were about the same in 50 mol % aqueous 2-methoxyethanol, whereas the ρ for *N*-methylbenzohydroxamic acids was about 50% smaller.[4c] These observations are consistent with the negative charge in the anions derived from the first three substrates all being concentrated on an atom two atoms removed from the benzene ring, i.e., $ArCON(OH)^-$, whereas that in the $ArCON(Me)O^-$ ions is on an atom three atoms removed. This is additional evidence showing that hydroxamic acids are NH acids in this medium, and similar results were obtained in DMSO.

Acidities in DMSO for a few 3- and 4-substituted benzamides and benzohydroxamic acids are summarized in Table III. The Hammett ρ values derived from these limited data are 2.8 and 2.7 for benzamides and benzohydroxamic acids, respectively, which agree well with the ρ value of 2.6 reported for benzoic acids in DMSO.[11] These results are consistent with the negative charge in the anion being two atoms removed from the benzene ring in benzohydroxamate ions in each instance, i.e., it is on nitrogen rather than on oxygen.

Oxidation Potentials and Chelation of Hydroxamate Ions with Alkali Metal Cations. The oxidation potentials, $E_{ox}(A^-)$, of aceto- and benzohydroxamate ions and some of their *N*-alkyl and *O*-alkyl derivatives are given in Table IV.

Examination of Table IV shows that in DMSO acetohydroxamate ion has an oxidation potential within experimental error of its *O*-methyl derivative (an N^- anion). This result demonstrates that an N^- ion is formed in each instance on neutralization with base and provides additional evidence that acetohydroxamic acid is an NH acid in DMSO. *N*-Methylhydroxamate ion (an O^- anion) has an oxidation potential 0.348 V more negative than that of its *O*-methyl isomer, an N^- anion. The more facile oxidation of this O^- ion by about 8 kcal/mol is consistent with other data, indicating that oxanions are much easier to oxidize than nitranions of the same basicity. For example, phenoxide ions have been found to be more readily oxidized in DMSO by about 10 kcal/mol compared to anilide ions of comparable basicity.[12] Similar results were obtained with benzohydroxamic acid and its *O*-benzyl and *N*-benzyl derivatives (Table IV).

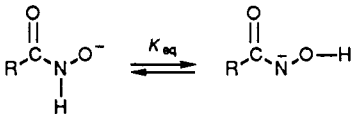
A change in the solvent from DMSO to MeOH caused the oxidation potentials of acetohydroxamate ion and its *O*-methyl and *N*-methyl derivatives to shift to sharply higher positive potentials due to increases in ion solvation. The shift for the *N*-methylhydroxamate ion was larger than for its *O*-methyl isomer. The extent of these shifts provides a rough measure of the relative increases in solvation energies for the $CH_3CON(Me)O^-$ and $CH_3CON(OMe)^-$ ions in changing from a non-H-bond-donor solvent (DMSO) to a H-bond donor solvent (MeOH), i.e., 14 kcal/mol for O^- and 10.5 kcal/mol for N^-.[13] The shift in oxidation potential is only 0.272 V (6.3 kcal/mol) for the acetohydroxamate ion, evidently because the shift is accompanied by a change from an N^- ion in DMSO to an O^- ion, at least in part, in MeOH. This change is apparent from a comparison of the oxidation potentials of the three ions in MeOH. Whereas in DMSO the acetohydroxamate and *O*-methylacetohydroxamate ions have closely similar oxidation potentials (both N^- ions), in MeOH the acetohydroxamate and *N*-methylacetohydroxamate ions have closely similar oxidation potentials (both O^- ions). The results with benzohydroxamate ions and their *N*-benzyl and *O*-benzyl derivatives (Table IV) are confirmatory.

Table IV. Oxidation Potentials of Hydroxamate Ions in DMSO and MeOH: Chelating Effects of Alkali Metal Cations

	DMSO solvent		methanol solvent	
acid	$E_{ox}(A^-)$[a]	$\Delta E_{ox}(A^-)$[b] (M^+)	$E_{ox}(A^-)$[c]	$\Delta E_{ox}(A^-)$-Li^+
$CH_3CONHOH$	0.620 (95)	no shift (Li^+)	0.859 (125)	0.060
$CH_3CON(Me)OH$	0.255 (120)	0.220 (Li^+)	0.823 (95)	0.046
$CH_3CONHOMe$	0.608 (50)	0.283 (Li^+)	1.043 (95)	0.050
PhCONHOH	0.703 (75)	no shift	0.838 (120)	0.040
$PhCON(CH_2Ph)$-OH	0.239	0.392 (Li^+)	0.722	0.052
	0.257	0.411 (Li^+)		
	0.242	0.054 (Na^+)		
	0.255	no shift (K^+)		
$PhCONH(OCH_2Ph)$	0.713	0.198 (Li^+)	1.001	0.012
	0.722	0.198 (Li^+)		
	0.700	0.052 (Na^+)		
	0.723	no shift (K^+)		

[a] Oxidation potentials measured in DMSO by cyclic voltammetry versus a Ag/AgI electrode using the ferrocene couple as a standard (0.874 V).[15] Numbers in parentheses are peak widths. The CV's are all irreversible, but the irreversible peaks of amides of this type correlate linearly with reversible peaks, as is demonstrated in the accompanying paper. [b] Shifts to more positive potentials observed by adding 20–50 mg (30–100 equiv) of alkali metal salts prior to recording the CV. [c] Oxidation peaks obtained using the same electrochemical setup, but in MeOH solvent.

In solution, we can expect a tautomeric equilibrium between O^- and N^- anions to exist, which can be represented by eq 3 (ignoring hydrogen bonding).



(3)

In DMSO, K_{eq} is of the order of 10^4, and the effective concentration of the O^- ion at the electrode is evidently too small to allow observation of its peak by CV. In water or methanol, PhCON(Me)OH is a slightly stronger acid than PhCONH(OMe) or PhCONHOH,[4e,5c] and K_{eq} is apparently about unity. In MeOH, only the CV of the O^- anion was observable. When a methanol solution of

(11) Ritchie, D. D.; Uschold, R. E. *J. Am. Chem. Soc.* **1968**, *90*, 2821–2804.
(12) Cheng, J.-P. Ph.D. Dissertation, Northwestern University, 1987.
(13) Somewhat smaller effects have been estimated for the free energies of transfer of AcO^- and N_3^- ions from MeOH to DMSO (–6.5 and –3.5 kcal/mol, respectively).[14]
(14) Parker, A. J. *Chem. Rev.* **1969**, *69*, 1–32, Table V.

$PhCONHOCH_2Ph$ was treated with 0.4 equiv of sodium methoxide, the CV peak at 1.01 V characteristic of the N^- anion was obtained. On addition of 1 equiv of $PhCON(CH_2Ph)OH$ a scan revealed only a broad peak at 0.84 V. (That for the $PhCON(CH_2Ph)O^-$ alone is at 0.722 V.) Repetition of the scan after addition of an excess of $PhCONHOCH_2Ph$ caused a 60 mV shift to a more positive potential. Apparently the presence of the N^- ion perturbs the peak for the O^- ion, but no peak for the N^- ion itself is observable. We conclude that equilibrium (4) for which K_{eq} is near unity in MeOH,[4e] shifts to the left as the supply of O^- ion at the electrode is depleted.

$$PhCONHOCH_2Ph + PhCON(CH_2Ph)O^- \rightleftarrows PhCON(OCH_2Ph)^- + PhCON(OH)CH_2Ph \quad (4)$$

In DMSO, where K_{eq} for eq 4 is about 10^5 (Table II), the peak for the O^- ion was completely suppressed in a similar experiment by addition of $PhCONHOCH_2Ph$.

These experiments support the conclusions drawn in earlier work[5,6] that in aqueous or methanol solutions the conjugate bases of hydroxamic acids are predominantly oxanions, but in non-hydrogen-bond-donor solvents they are predominantly nitranions.

Chelation of Hydroxamate Ions with Alkali Metal Cations. In a recent paper we have found that when $Li^+ClO_4^-$ was used in place of $Et_4N^+BF_4^-$ as an electrolyte in CV measurements, the oxidation potential of the acetylacetonate ion in DMSO solution was shifted to a more positive potential by 0.520 V because of chelation with the Li^+ cation.[15] We have now found that almost as large a shift (0.429 V) can be obtained by adding one-third this amount of $Li^+ClO_4^-$ to the DMSO solution of the acetylacetonate ion. This provides a simple semiquantitative method of testing for chelation. Application of this test shows that the $PhCON(CH_2Ph)O^-$ ion chelates with Li^+ in DMSO about as strongly as does the acetylacetonate ion (~400 mV shift; Table IV). Chelation of the $CH_3CON(Me)O^-$, $CH_3CONOMe^-$, and $PhCON(OCH_2Ph)^-$ ions with Li^+, is weaker (200–280 mV-shifts). The parent hydroxamate ions $CH_3CON(OH)^-$ and $PhCON(OH)^-$ give no evidence of chelating with Li^+, however, perhaps because their oxygen ligands are engaged in intramolecular hydrogen bonding. Weak chelation with the parent hydroxamate ions as well as their *N*-alkyl and *O*-alkyl derivatives occurs also with Li^+ in MeOH.

The determinations of K_{as} constants for $PhCON(OH)^-$, $PhCON(OCH_2Ph)^-$, and $PhCON(CH_2Ph)O^-$ were carried out for chelation with K^+ and Na^+ ions by measuring the apparent change in pK_{HA} on addition of K^+I^- to DMSO solutions of K^+A^- in equilibrium with K^+In^-, and on addition of Na^+I^- to solutions of Na^+A^- in equilibrium with Na^+In^-, as previously described.[16] The parent benzohydroxamate ion, $PhCON(OH)^-$, exhibited no appreciable chelating effect with either K^+ or Na^+ ($\log K_{as} \leq 1$). On the other hand, $PhCON(OCH_2Ph)^-$ ion gave $\log K_{as} = 2.1 \pm 0.2$ with K^+ ion and 2.7 ± 0.05 with Na^+ ion (average of 2 runs). The $PhCON(CH_2Ph)O^-$ ion chelated more strongly, as expected (Table IV), but the measurements were complicated by homo-hydrogen bonding. By keeping the $[HA]/[A^-]$ ratio in the range of 1 to 1.5, $\log K_{as}$ with K^+ was found to be about 2; with Na^+ it was 3.2 ± 0.1. Chelation with Li^+ was strong enough to allow K_{as} to be measured by adding $Li^+ClO_4^-$ to a solution of $PhCON(CH_2Ph)O^-K^+$; $\log K_{as} = 4.6 \pm 0.1$, a value close to that obtained earlier with acetylacetonate ion, $K_{as} = 4.77$.[16]

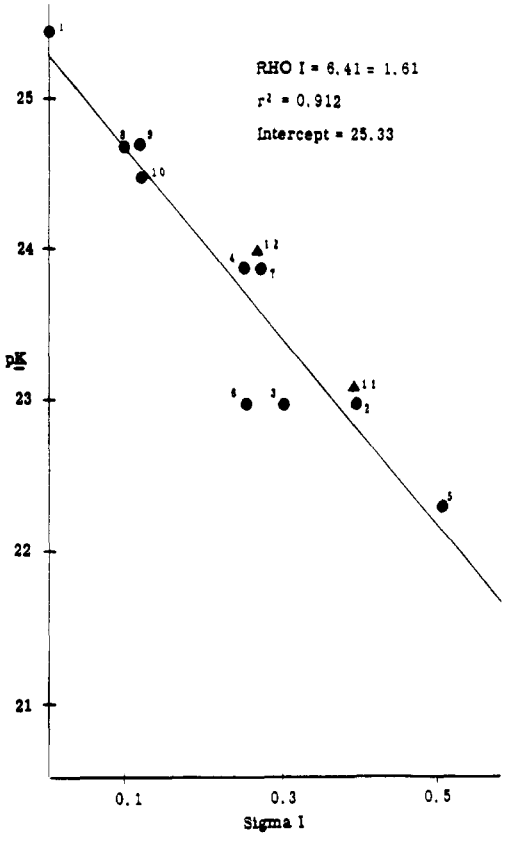


Figure 1. Carboxamide acidities (GCH_2CONH_2) in Me_2SO vs σ_I (Table V). ▲ = Acids were not included in the correlations.

What Makes Hydroxamic Acids Strong? In aqueous solution acetohydroxamic acid is a stronger acid than acetamide by about 6 pK_{HA} units.[17] Exner attributed this increase to an enhanced contribution of resonance delocalization in the hydroxamate ion, relative to the acetamide ion, together with the polar (field/inductive or *F*) effect of the hydroxyl group. He estimated that the *F* effect accounted for about 70% of the increase.[4c]

In DMSO, acetohydroxamic acid is 9.8 pK_{HA} units more acidic than acetamide (statistically corrected for the number of acidic protons) and *O*-methylacetohydroxamic acid is 8.7 pK_{HA} units more acidic than acetamide. The larger ΔpK_{HA}'s in DMSO result from the absence of the leveling effect of the H-bond-donor effects of the hydroxylic solvent. For benzohydroxamic acid and its *O*-benzyl derivative, the ΔpK_{HA} values are 10.1 and 9.4 units, respectively.

A rough estimate of the size of the *F* effect was obtained from measurements of the acidities in DMSO of 13 α-substituted acetamides, GCH_2CONH_2 and 6 α-substituted *N*-phenylacetamides $GCH_2CONHPh$ (Table V).

A Taft plot of σ_I vs pK_{HA} for these substituted amides is shown in Figure 1. The regression analysis indicates a poor correlation ($R^2 = 0.912$), but the points for G = MeO (no. 7) fits reasonably well with the other points on the plot. On the other hand, the point for $HOCH_2CONH^-$ (no. 6) falls about 1 unit below the line, indicating the presence of appreciable stabilization of the $HOCH_2CONH^-$ ion by intramolecular hydrogen bonding (**5**). The acidities of $MeOCH_2CONH_2$ and $MeOCH_2CONHPh$ are each greater than those of their parents by 1.6 units (Table V).

(15) Bordwell, F. G.; Harrelson, J. A., Jr.; Satish, A. V. *J. Org. Chem.* **1989**, *54*, 3101–3105.

(16) Olmstead, W. N.; Bordwell, F. G. *J. Org. Chem.* **1980**, *45*, 3299–3305.

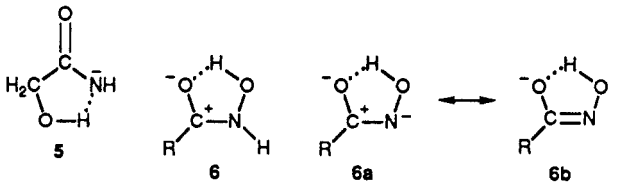
(17) Branch, G. E. K.; Clayton, J. O. *J. Am. Chem. Soc.* **1928**, *50*, 1680–1686 report $K_a = 8.3 \times 10^{-16}$ for acetamide in aqueous solution.

Table V. Equilibrium Acidity Constants and σ_I Values for α-Substituted Acetamides (GCH_2CONH_2) and $GCH_2CONHPh$ in Me_2SO Solution

compd	G	pK_{HA}[a]	pK_{HA}[b]	σ_I[c]
1	H	25.5	21.45	(0.0)
2	PhO	23.0	18.9	0.39
3	PhS	23.0	19.0	0.30
4	EtS	23.9		0.25
5	F	22.3	18.25	0.50
6	HO	23.0		0.25
7	CH_3O	23.9	19.9	0.27[d]
8	Ph	24.7	20.6	0.10
9	NH_2	24.7		0.12[d]
10	1-$C_{10}H_7$	24.5		0.12
11	PhSe	23.1		0.27[e]
12	*t*-BuS	24.0		0.25[e]
13	Me_3N^+	15.3		0.93[e]

[a] For GCH_2CONH_2. [b] For $GCH_2CONHPh$. [c] Charton, M. *J. Org. Chem.* **1964**, *29*, 1222. The symbol σ_F (for field/inductive) is now preferred (Taft, R. W.; Topsom, R. D. *Prog. Phys. Org. Chem.* **1987**, *16*, 1–83). [d] Dayal, S.; Ehrenson, S.; Taft, R. *J. Am. Chem. Soc.* **1972**, *94*, 9113. [e] Estimated.

The fact that the MeO group in these molecules is two atoms further removed from the acidic N–H bond than the MeO group in $CH_3CONHOMe$ suggests that the *F* effect in the latter on acidity could indeed be large, in agreement with Exner's analysis.[4c] These are poor models for hydroxamic acids, however, since the substituents are attached to carbon, rather than to nitrogen. Furthermore, it is likely that the hydroxamic acids will adopt the syn intramolecularly hydrogen bonded structure **6** since there



5 **6** **6a** **6b**

is evidence to indicate that hydroxamic acids exist in cis conformations in solution, as well as the solid state.[18] In **6** the C–O and N–O dipoles are additive, which may provide a sizable electrostatic acidifying effect for reasons similar to those that strengthen Meldrum's acid.[8b,c] Also, in the conjugate base of **6** delocalization of the negative charge, as in contributor **6b**, may serve to stabilize the anion by decreasing lone pair–lone pair interactions in the N–O bond.

Acidities of Ketones, Sulfones, Carboxamides, and Sulfonamides in DMSO. Dimethyl sulfone is estimated to be about 34 kcal/mol more acidic in DMSO than CH_4, whereas the analogous ketone, CH_3COCH_3, is about 41 kcal/mol more acidic (Table I). These acidity increases are believed to be caused by stabilization of the negative charge in the $CH_3SO_2CH_2^-$ and $CH_3COCH_2^-$ ions by field/inductive (*F*) and resonance (*R*) effects.[19] The σ_F parameter for CH_3SO_2 (0.59) is much larger than that for CH_3CO (0.28), but the larger σ_R parameter for CH_3CO (0.17) vs CH_3SO_2 (0.12)[19] evidently controls the acidity order. For the corresponding nitrogen acids the reverse is true. The structural change from NH_3 to $CH_3SO_2NH_2$ is accompanied by a 32 kcal/mol increase in acidity, whereas that from NH_3 to CH_3CONH_2 is accompanied by only a 21 kcal/mol increase (Table I). The difference in effect of the carbonyl group in the carbon and nitrogen acids is presumably due to the relative unimportance of resonance involving the carbonyl group in carboxamides.[8a]

(18) Smith, W. L.; Raymond, K. N. *J. Am. Chem. Soc.* **1980**, *102*, 1252–1255.
(19) Taft, R. W.; Topsom, R. D. *Prog. Phys. Org. Chem.* **1987**, *16*, 1–83.

Table VI. Equilibrium Acidities in DMSO of Benzohydrazides, Benzenesulfonamides, and Related Compounds

acid	pK_{HA}[a]	acid	pK_{HA}[a]
CH_3CONH_2	25.5	4-$NC_5H_4CONHNH_2$	16.8[b]
$CH_3CONHNH_2$	21.8[b]	$C_6H_5NH_2$	30.7
$C_6H_5CONH_2$	23.35	$C_6H_5NHNHC_6H_5$	26.2
$C_6H_5CONHNH_2$	18.9	$C_6H_5SO_2NH_2$	16.1
$C_6H_5CONHNMe_2$	19.7	$C_6H_5SO_2NHOH$	~15.4[d]
3-$NC_5H_4CONH_2$	22.0[c]	$C_6H_5SO_2NHNH_2$	16.8[e]
3-$NC_5H_4CONHNH_2$	17.5[b]	$C_6H_5SO_2NHNMe_2$	15.8
4-$NC_5H_4CONH_2$	21.55[c]		

[a] Average values from 3-point titrations against two indicators; standard deviations within a run are generally ±0.05, or less. Agreement for runs with different indicators was generally <0.1 pK_{HA} unit. [b] Measured by M. E. Stark. [c] Measured by M. Van Der Puy. [d] One-point titration. [e] Measured by W. D. Tumas.

The effect of substituting an OH group at the acidic site of carboxamides and sulfonamides is also markedly different. Whereas the structural change from $PhCONH_2$ to PhCONHOH causes a 10.1 pK_{HA} increase in acidity the increase from $PhSO_2NH_2$ to $PhSO_2NHOH$ is only about 0.5 pK_{HA} unit (Table VI), and in aqueous solution it is only 1.1 pK_{HA} unit.[7] These data point to a substantial difference in the structural characteristics of hydroxamic acids and their sulfonamide analogues. The sulfur atom in $PhSO_2NHOH$ is tetrahedral and the characteristics of the S=O bond are quite different than that of C=O. There is no reason to believe that an intramolecular H-bonding structure analogous to **6** need be considered. Also, the π-accepting ability of the sulfonyl group is much less than that of a carbonyl group, which suggests that the negative charge in the $PhSO_2N(OH)^-$ ion will be localized on nitrogen. Lone pair–lone pair repulsions between the electron pairs on oxygen and nitrogen in this anion are destabilizing and are evidently large enough to nearly balance the acid-strengthening *F* effect of the *N*-OH group.

Acidities of Carbohydrazides and Benzenesulfonohydrazides in DMSO. The relative effects on acidities of substituting an NH_2 group at the acidic site of carboxamides and sulfonamides are similar to those for substituting an OH group (Table VI). We see by examining Table VI that the structural change from CH_3CONH_2 to $CH_3CONHNH_2$ leads to about a 4 pK_{HA} unit increase in acidity in DMSO, and that the hydrazides of benzoic, 3-pyridinecarboxylic and 4-pyridinecarboxylic acids are also 4–5 pK_{HA} units stronger acids than the corresponding amides. (The larger acid-strengthening effect of the 4-aza than the 3-aza ring atom in these amides and hydrazides is not surprising since aza effects are generally larger from the 4-position in a pyridine ring than from the 3-position. For example, the pK_{HA} values of 4-aminopyridine, 3-aminopyridine, and aniline in DMSO are 26.5, 28.5, and 30.6, respectively.[2b]) A structure analogous to **6** is inappropriate for carbohydrazides because there is no precedent for weakly acidic N–H bonds to serve as H-bond donors. The appreciable increases in acidity observed must then be ascribed to the *F* effects of the α-NH_2 group in the $PhCON(NH_2)^-$ anion aided perhaps by delocalization of the negative charge in order to relieve lone pair-lone repulsions. The 1 pK_{HA} unit *decrease* in acidity observed on substitution of an *N*-NH_2 group into $PhSO_2NH_2$ may be due to the localized nature of the charge in the $PhSO_2N(NH_2)^-$ anion, which enhances lone pair–lone pair repulsions between nitrogen atoms and overshadows the acid-strengthening *F* effect of the *N*-NH_2 group. Note also that an *N*-Me_2N group in the sulfonamide is 1 pK_{HA} unit acid strengtheing, relative to an *N*-NH_2 group (polarization

effect?) whereas the reverse is true in the carboxamide (steric effect?).

Summary and Conclusions

The small difference in acidities of carboxamides and analogous ketones (1–2 kcal/mol in DMSO and 7–8 kcal/mol in the gas phase), relative to other nitrogen and carbon acids (17 ± 5 kcal/mol) has been rationalized in terms of destabilization of carboxamide conjugate bases by lone pair–lone pair repulsions, together with some resonance stabilization of the carboxamide.

The observation that N-alkylation decreases acidities of hydroxamic acids in DMSO by about 4.5 pK_{HA} units, compared to about 1 unit for O-alkylation, together with the observation of strong homo-hydrogen bonding in *N*-alkylhydroxamic acids and its absence in the parents in DMSO, has provided conclusive evidence that hydroxamic acids are NH, rather than OH acids in this medium. This finding was confirmed by oxidation potential data on hydroxamate ions in DMSO. But in MeOH the $E_{ox}(A^-)$ values of hydroxamate ions were close to those of their *N*-alkyl derivatives, showing that hydroxamic acids can act as OH acids in this medium. With regard to the question as to whether hydroxamic acids are NH or OH acids, it would appear that, as often happens with long-standing controversies, both sides have some truth on their side, i.e., in non-hydrogen-bonding-donor solvents, such as DMSO, DMF, CH_3CN, etc., hydroxamic acids act as NH acids, but in hydroxylic solvents they can act primarily as OH acids.

The powerful acidifying effects of *N*-OH groups in hydroxamic acids and *N*-NH_2 groups in carboxhydrazides is attributed to stabilization of the anion by the *F* (field/inductive) effects of these substituents together with intramolecular hydrogen bonding in the anion aided by delocalization of the negative charge in the anion in order to relieve lone pair–lone pair repulsions. In $C_6H_5SO_2N(OH)^-$ and $C_6H_5SO_2N(NR_2)^-$ ions delocalization is diminished by the relatively poor conjugative ability of the sulfonyl group, and the *F* acidifying effects of *N*-OH and *N*-NR_2 groups are largely or completely counteracted by acid-weakening lone pair–lone pair repulsive effects in the anions.

Experimental Section

Materials. The amides were either commercially available, or were prepared by methods described in the literature. Acetohydrazide, benzohydrazide, nicotinic and isonicotinic acid hydrazides, benzenesulfonohydrazide, *N*-hydroxybenzenesulfonamide, acetohydroxamic acid, and benzohydroxamic acid were obtained from Aldrich Chemical Co. and purified by crystallization.

3-(Trifluoromethyl)benzohydroxamic acid was prepared by the method of Hynes and Hack.[20] Repeated crystallization from water and from toluene afforded colorless crystals, mp 133–134 °C (lit.[20] mp 134–135 °C).

4-Chlorobenzohydroxamic acid was prepared by the general procedure of Jones and Hurd.[21] Crystallization ($EtOH/H_2O$) gave material of mp 185–186 °C dec (lit.[4c] mp 177 °C).

3-Chlorobenzohydroxamic acid was prepared by the general procedure of Stolberg.[22] Crystallization (toluene) gave material of mp 168–170 °C (lit.[4c] mp 167 °C).

***N*-Methylbenzohydroxamic acid** was prepared by the general procedure of Ulrich and Sayigh.[23] The oil obtained was vacuum distilled twice: NMR (CD_3COCD_3) δ 7.0–8.0 (5 H m), 3.3 (3 H s). HPLC showed only one peak (μ-CN column), 1.5 mL/min flow rate, 20% *i*-PrOH/hexane eluent).

***N,N*-Dimethylbenzenesulfonohydrazide** was prepared by the method of Lemal:[24] mp 94–95 °C (Lit.[24] mp 95–96 °C).

***O*-Benzylbenzohydroxamic acid** was prepared according to the method of Exner and Simon:[4c] mp 103–104 °C (lit.[4c] mp 105 °C).

***N,N*-Dimethylbenzohydrazide.** Benzoyl chloride (2.8 g, 0.02 mol) dissolved in 10 mL of dry THF was added with stirring over a 5-min period to 2.4 g (0.04 mol) of 1,1-dimethylhydrazine dissolved in THF. After 3 h at room temperature the solution was filtered, and the filtrate was evaporated in vacuo. The crude hydrazide was crystallized twice from hexane–EtOAc to give a colorless solid, mp 107–108 °C (lit.[25] mp 106–107 °C).

***N*-Benzylbenzohydroxamic acid** was prepared according to the procedure of Johnson.[26]

Electrochemical Studies. The hydroxamate anions were generated by adding 0.3–0.4 equiv of a DMSO solution of CH_3SOCH_2K to a 3 mM solution of the neutral compound. After the addition of each aliquot the cyclic voltammograms (CVs) were recorded under the conditions previously described.[15]

Ion Pair Association Constants. Ion pair association constants were determined spectrophotometrically by the method previously described.[16] For $PhCON(CH_2Ph)OH$, the concentrations of the acid and its conjugate base were equalized in order to minimize effects from homo-hydrogen bonding. An attempt to measure K_{as} by adding Na^+I^- to a solution containing equal concentrations of $PhCON(CH_2Ph)OH$ and $PhCON(CH_2Ph)O^-K^+$ was unsuccessful, apparently because the Na^+ ion was unable to displace K^+ ion completely from the chelate. (In the successful determination the Na^+I^- solution was added to a solution containing $PhCON(CH_2Ph)O^-Na^+$.) Chelation with Li^+ was strong enough, however, to allow K_{as} to be determined by adding a $Li^+ClO_4^-$ solution to the potassium salt solution. The final concentration of M^+ in the cell for these titrations was of the order of 4–8 mM. Calculations were made using a least-square program.[16]

Acknowledgment. We are grateful to the National Science Foundation for support of this research. We thank the Gaylord Chemical Corp., Slidell, LA 70459-1209, for a gift of DMSO.

Registry No. HOCN, 420-05-3; $CH_3CONHOH$, 546-88-3; $CH_3CONHOMe$, 5806-90-6; $CH_3CONHOMe$, 5806-90-6; $CH_3CON(Me)OH$, 13115-24-7; CH_3COCH_3, 67-64-1; CH_3COCH_2OMe, 5878-19-3; $PhCONHOH$, 495-18-1; $PhCONHOCH_2Ph$, 3532-25-0; $PhCON(Me)OH$, 2446-50-6; $PhCON(CH_2Ph)OH$, 7339-99-3; $PhCOCH_3$, 98-86-2; $PhCOCH_2OMe$, 4079-52-1; $C_6H_5CONH_2$, 55-21-0; 4-$ClC_6H_4CONH_2$, 619-56-7; 3-$FC_6H_4CONH_2$, 455-37-8; 3-$ClC_6H_4CONH_2$, 618-48-4; 3,5-$(F_3C)_2C_6H_3CONH_2$, 22227-26-5; 4-$ClC_6H_4CONHOH$, 1613-88-3; 3-$ClC_6H_4CONHOH$, 4070-53-5; 3-$F_3CC_6H_4CONHOH$, 40069-06-5; CH_3CON^-OH, 2208-22-2; $CH_3CON(Me)O^-$, 26177-07-1; CH_3CON^-OMe, 126191-19-3; $PhCON^-OH$, 53875-19-7; $PhCON(CH_2Ph)O^-$, 58921-18-9; $PhCON^-(OCH_2Ph)$, 126191-20-6; Li, 7439-93-2; Na, 7440-23-5; K, 7440-09-7; CH_3CONH_2, 60-35-5; $CH_3CONHPh$, 103-84-4; $PhOCH_2CONH_2$, 621-88-5; $PhOCH_2CONHPh$, 18705-01-6; $PhSCH_2CONH_2$, 22446-20-4; $PhSCH_2CONHPh$, 4686-01-5; $EtSCH_2CONH_2$, 60247-87-2; FCH_2CONH_2, 640-19-7; $FCH_2CONHPh$, 330-68-7; $HOCH_2CONH_2$, 598-42-5; $CH_3OCH_2CONH_2$, 16332-06-2; $CH_3OCH_2CONHPh$, 126191-21-7; $PhCH_2CONH_2$, 103-81-1; $PhCH_2CONHPh$, 621-06-7; $NH_2CH_2CONH_2$, 598-41-4; 1-$C_{10}H_7CH_2CONH_2$, 86-86-2; $PhSeCH_2CONH_2$, 63801-97-8; *t*-$BuSCH_2CONH_2$, 126191-22-8; $Me_3NCH_2CONH_2$, 16676-71-4; $CH_3CONHNH_2$, 1068-57-1; $C_6H_5CONHNH_2$, 613-94-5; $C_6H_5CONHNMe_2$, 1128-86-5; 3-$NC_5H_4CONH_2$, 98-92-0; 3-$NC_5H_4CONHNH_2$, 553-53-7; 4-$NC_5H_4CONH_2$, 1453-82-3; 4-$NC_5H_4CONHNH_2$, 54-85-3; $C_6H_5NH_2$, 62-53-3; $C_6H_5NHNHC_6H_5$, 122-66-7; $C_6H_5SO_2NH_2$, 98-10-2; $C_6H_5SO_2NHOH$, 599-71-3; $C_6H_5SO_2NHNH_2$, 80-17-1; $C_6H_5SO_2NHNMe_2$, 90197-50-5.

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