under the same conditions, allowed to warm to room temperature, and stirred for 2 h. Workup of the reaction mixture as described for the preparation of **2** from **18** gave a 95% yield (25 mg) of **21**. Recrystallization from chloroform gave pure **21**: mp 298–300 °C; NMR ($CDCl_3$) δ 14.38 (s, 1 H), 12.96 (s, 1 H), 8.64 (d, 1 H), 7.82 (dd, 1 H), 7.77 (m, 1 H), 7.60 (t, 1 H), 7.22 (dd, 1 H), 6.84 (d, 1 H), 4.00 (s, 3 H), 2.55 (s, 3 H); IR (KCl) 1610, 1570 cm^{-1}; exact mass calcd for $C_{20}H_{14}O_5$ 334.0839, found 334.0827.

1,6,10-Trihydroxy-8-methylnaphthacene-5,12-dione (4). To a cooled solution of **20** (60 mg, 0.183 mmol) in methylene chloride (10 mL) at −78 °C was added a solution of boron tribromide (4.7 g, 18.3 mmol) in methylene chloride (1 mL) dropwise under nitrogen. The green colored mixture was stirred for 1 h under the same conditions, allowed to warm to room temperature, and stirred overnight. Workup of the reaction mixture as described for the preparation of **2** from **18** gave a 51% yield (30 mg) of **4**. Recrystallization from methanol–acetone gave pure **4**; exact mass calcd for $C_{19}H_{12}O_5$ 320.0685, found 320.0695.

1,6-Diacetoxy-10-methoxy-8-methylnaphthacene-5,12-dione (22). A solution of **21** (20 mg, 0.06 mmol) and acetic anhydride (1 mL) in pyridine (1 mL) was allowed to stand at room temperature for 12 h and concentrated in vacuo to give a solid, which was purified by column chromatography (benzene–ether 10:1) to give a 92% yield (23 mg) of **22** as yellow crystals. Recrystallization from chloroform–benzene gave pure **22**; exact mass calcd for $C_{24}H_{18}O_7$ 418.1050, found 418.1050.

1,6,10-Triacetoxy-8-methylnaphthacene-5,12-dione (23). A solution of **4** (14 mg, 0.044 mmol) and acetic anhydride (1 mL) in pyridine (1 mL) was allowed to stand at room temperature for 12 h. Workup as described above gave a 50% yield (10 mg) of **23** as yellow crystals. Recrystallization from chloroform–methanol gave pure **23**; exact mass calcd for $C_{25}H_{18}O_8$ 446.1008, found 446.1002.

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Registry No. **2**, 56257-15-9; **3**, 96227-30-4; **4**, 96227-31-5; **9**, 93953-40-3; **10**, 96227-32-6; **11**, 69833-09-6; **12**, 585-81-9; **13**, 62089-34-3; **13** acid chloride, 96227-40-6; **14**, 96227-33-7; **15**, 96227-34-8; **16**, 96227-35-9; **17**, 70351-73-4; **18**, 96227-36-0; **19**, 56257-19-3; **20**, 96227-37-1; **21**, 96227-38-2; **22**, 96227-39-3; **23**, 96245-24-8; 2-amino-2-methyl-1-propanol, 124-68-5; *N*-(2,2-dimethyl-3-hydroxypropyl)benzamide, 96227-41-7.

Temperature-Dependent Acid Dissociation Constants (K_a, ΔH_a, ΔS_a) for some *C*-Aryl Hydroxamic Acids: The Influence of C and N Substituents on Hydroxamate Anion Solvation in Aqueous Solution

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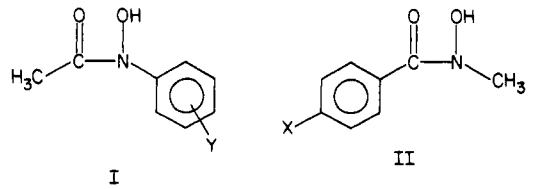
The acid dissociation constants (K_a) of a series of substituted *N*-methylbenzohydroxamic acids, 4-$XC_6H_4C(O)N(OH)CH_3$ (X = H, CH_3O, CH_3, NO_2) and 4-methoxybenzohydroxamic acid, 4-$CH_3OC_6H_4C(O)N(OH)H$, have been determined in aqueous solution (I = 2.0) over a range of temperatures. The pK_a values at 25 °C are as follows: 4-$XC_6H_4C(O)N(OH)CH_3$, X = H (8.28), X = CH_3O (8.67), X = CH_3 (8.50), X = NO_2 (7.94); 4-$CH_3OC_6H_4C(O)N(OH)H$, (8.76). The substituted *N*-methylbenzohydroxamic acids exhibit a trend in pK_a values that is consistent with the Hammett σ substituent parameters but with a ρ value of 0.6. ΔH_a and ΔS_a values fall in a narrow range (ΔH_a = 1.1–2.2 kcal/mol; ΔS_a = −31 to −36 cal/(K mol)) and represent minimum values for these parameters when compared with other C- and N-substituted hydroxamic acids. These results suggest that the C and N substituents influence the water solvation of the hydroxamate moiety −[C(=O)N(O⁻)−] and that the *N*-methylhydroxamate anions are the most highly solvated.

Hydroxamic acids are weak proton donors[1] which have numerous applications in such diverse fields as extractive metallurgy, corrosion inhibition, nuclear fuel processing, pharmaceuticals, fungicides, and analytical reagents. We are interested in structure–reactivity relationships as they apply to hydroxamic acid acidity[2,3] and iron(III) chelation[4–6] in aqueous solution. Of importance is the relative influence of the functional group on the carbon and nitrogen ends of the hydroxamic acid moiety, and the relative contributions of inductive and resonance effects.

In a previous report,[3] we investigated the temperature-dependent acidity of a series of substituted *N*-phenylacetohydroxamic acids (I). In this report, temperature-dependent acid dissociation constants have been determined in aqueous solution for a series of substituted



(1) For general reviews of the organic chemistry of hydroxamic acids, see: (a) Kehl, H., Ed. "Chemistry and Biology of Hydroxamic Acids"; Karger: New York, 1982. (b) Agrawal, Y. K. *Rev. Anal. Chem.* **1980**, *5*, 3. (c) Bauer, L.; Exner, O. *Angew. Chem.* **1974**, *13*, 376. (d) Sandler, S. R.; Karo, W. "Organic Functional Group Preparations"; Academic Press: New York, 1972; Chapter 12. (e) Mojumdar, A. K. *Int. Ser. Monogr. Anal. Chem.* **1972**, *50*, (f) Smith, P. A. S. "The Chemistry of Open-Chain Organic Nitrogen Compounds"; W. A. Benjamin: New York, 1966; Vol. 2, Chapter 8. (g) Brandt, W. W. *Rec. Chem. Prog.* **1960**, *21*, 159. (h) Mathis, F. *Bull. Soc. Chim. Fr.* **1953**, *20*, D9. (i) Yale, H. L. *Chem. Rev.* **1943**, *33*, 209.

(2) Monzyk, B.; Crumbliss, A. L. *J. Org. Chem.* **1980**, *45*, 4670.

(3) Brink, C. P.; Crumbliss, A. L. *J. Org. Chem.* **1982**, *47*, 1171.

(4) Monzyk, B.; Crumbliss, A. L. *J. Am. Chem. Soc.* **1979**, *101*, 6203.

(5) Brink, C. P.; Crumbliss, A. L. *Inorg. Chem.* **1984**, *23*, 4708.

(6) Fish, L. L.; Crumbliss, A. L. *Inorg. Chem.*, in press.

0022-3263/85/1950-2277$01.50/0

N-methylbenzohydroxamic acids (II), 4-$XC_6H_4C(O)N(OH)CH_3$ (X = H, CH_3O, CH_3, NO_2), and 4-methoxybenzohydroxamic acid, 4-$CH_3OC_6H_4(O)N(OH)H$. This investigation allows us to (1) look at a wide range of electronic effects ($\Delta\sigma \sim 1.1$) on the carbonyl side of the hydroxamate moiety, (2) directly compare electron-donating and -withdrawing phenyl substituents on the C vs. N end of the hydroxamate moiety in order to determine their relative influence on hydroxamic acid acidity, (3) expand our earlier analysis of the influence of substituents and solvation effects on the enthalpy and entropy changes associated with hydroxamic acid dissociation, and (4) compare two sets of geometric isomers to confirm that solvation effects are due to solvation of the hydroxamate moiety and not to localized solvation about the substituent group attached to the N or C atoms of the hydroxamate anion. Dissociation constants have been reported for some of the hydroxamic acids reported here,[7-10] although at different conditions and usually at a single temperature. Data for a homologous series of hydroxamic acids over a range of temperatures have not been collected at the same conditions, and therefore an extensive comparison of pK_a, ΔH_a, and ΔS_a values for a wide range of C- and N-substituted hydroxamic acids could not be made. This report, together with our two previous reports[2,3] represents an investigation of the acid dissociation reaction in aqueous solution of a series of 17 C- and N-substituted hydroxamic acids.

Experimental Section

Materials and Methods. Aqueous solutions were prepared by using water distilled once from acidic $K_2Cr_2O_7$ and then slowly from basic $KMnO_4$ in an all-glass apparatus with Teflon sleeves and stopcocks. Sodium nitrate (Fisher and Mallinckrodt, ACS certified) was recrystallized from twice-distilled water prior to use. The following starting materials for synthesizing the hydroxamic acids were used without further purification: *N*-methylhydroxylamine hydrochloride (Aldrich), 4-anisoyl chloride (Aldrich), 4-toluoyl chloride (Aldrich), 4-nitrobenzoyl chloride (Aldrich), and hydroxylamine hydrochloride (Aldrich). The pK_a data were collected in aqueous solution at $I = 2.0$ ($NaNO_3$) over a range of temperatures.[11] Titration methods, data manipulation, and instrumentation have been described previously.[2,3]

Syntheses. The synthesis and purification of the hydroxamic acids were similar to that described in the literature.[3,13] A critical feature is product workup, particularly separation of the hydroxamic acid from the rearranged material $R_1C(O)ON(H)R_2$, which in some cases is the thermodynamically controlled product.[14] Due to the strong iron(III) chelating ability of the hydroxamic acids, an intense absorption band at pH 1 in the presence of a slight molar excess of hydroxamic acid over iron(III) at λ_{max} 500–540 nm ($\epsilon \sim 1200$–1700 cm^{-1} M^{-1}) is diagnostic of mono(hydroxamato)iron(III) complex $Fe(R_1C(O)N(O)R_2)(H_2O)_4^{2+}$ formation.[5] The presence of the rearranged product will lower the observed molar absorptivity (since it does not complex with iron) but will not influence the elemental analysis. Included in this report is a redetermination of our previously reported[2] K_a, ΔH_a, and ΔS_a values for $C_6H_5C(O)N(OH)CH_3$, which is necessitated by our observation that without proper precautions in the product workup, the rearranged product $C_6H_5C(O)ON(H)CH_3$ may be present in significant amount. The synthesis and workup for this particular compound is presented here as an example as the purification of this oily liquid requires more care than the other hydroxamic acids investigated.

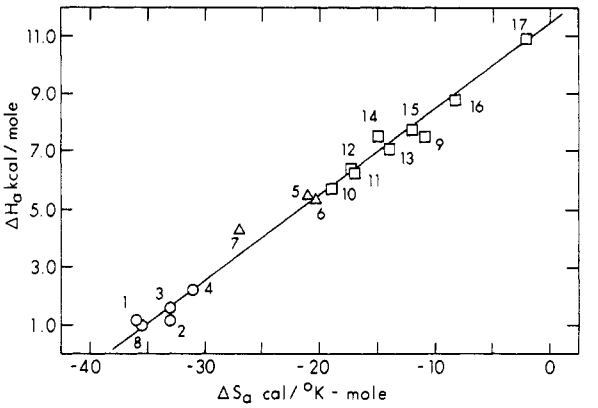


Figure 1. Plot of ΔH_a as a function of ΔS_a for hydroxamic acid dissociation in aqueous solution ($I = 2.0$).[20] (○) Hydroxamic acids with a *N*-methyl group, $RC(O)N(OH)CH_3$ (△) hydroxamic acids with a N–H group, RC(O)N(OH)H; (□) hydroxamic acids with a *N*-aryl group, $RC(O)N(OH)C_6H_4Y$. Compounds 1–5 are from this work, 6–9 are from ref 2, and 10–17 are from ref 3. **1**, 4-$CH_3OC_6H_4C(O)N(OH)CH_3$; **2**, 4-$NO_2C_6H4C(O)N(OH)CH_3$; **3**, 4-$CH_3C_6H_4C(O)N(OH)CH_3$; **4**, $C_6H_5C(O)N(OH)CH_3$; **5**, 4-$CH_3OC_6H_4C(O)N(OH)H$; **6**, $C_6H_5C(O)N(OH)H$; **7**, $CH_3C(O)N(OH)H$; **8**, $CH_3C(O)N(OH)CH_3$; **9**, $C_6H_5C(O)N(OH)C_6H_5$; **10**, $CH_3C(O)N(OH)$-4-C_6H_4I; **11**, $CH_3C(O)N(OH)$-4-C_6H_4Cl; **12**, $CH_3C(O)N(OH)$-3-C_6H_4I; **13**, $CH_3C(O)N(OH)$-4-C_6H_4CN; **14**, $CH_3C(O)N(OH)$-4-$C_6H_4CH_3$; **15**, $CH_3C(O)N(OH)$-4-$C_6H_4C(O)CH_3$; **16**, $CH_3C(O)N(OH)$-3-C_6H_4CN; **17**, $CH_3C(O)N(OH)C_6H_5$.

Benzoyl chloride in benzene was added slowly to a benzene solution of an equimolar amount of *N*-methylhydroxylamine hydrochloride in the presence of a 4-fold molar excess of K_2CO_3 at 0 °C. The stirred solution was slowly warmed to ambient temperature and the solvent removed under reduced pressure, with care being taken to prevent the mixture from being heated above 50 °C. A large volume of water was added to the reaction mixture, the pH adjusted to 6, and the solution extracted with ether by using a continuous extraction apparatus. The ether phase was concentrated in vacuo and the resulting oil dissolved in chloroform and put on a silica gel column where it was eluted by gradually increasing the ether concentration. The rearrangement product, benzoic acid, and unreacted hydroxylamine were eluted before the product, which can be removed from the column with ether or acetone. The product, an oil, was characterized by NMR (a single *N*-methyl peak at δ 3.3) and purity established by complexation with iron(III) and elemental analysis. All of the hydroxamic acids reported here were characterized in a similar manner and were found to exhibit an *N*-methyl ^1H NMR singlet in the range δ 3.2–3.3.

Melting points and elemental analyses are as follows (theoretical values in parentheses). 4-$CH_3OC_6H_4C(O)N(OH)CH_3$: 109–112 °C; %C, 59.40 (59.67); %H, 6.22 (6.08); %N, 7.71 (7.73). 4-$NO_2C_6H_4C(O)N(OH)CH_3$: 176–178 °C; %C, 48.91 (48.48); %H, 4.10 (4.04); %N, 14.20 (14.14). 4-$CH_3C_6H_4C(O)N(OH)CH_3$: 117–120 °C; %C, 65.42 (65.45); %H, 6.73 (6.67); %N, 8.41 (8.48). $C_6H_5C(O)N(OH)CH_3$; %C, 63.29 (63.56); %H, 5.88 (6.00); %N, 8.55 (9.27). 4-$CH_3OC_6H_4C(O)N(OH)H$: 160–161 °C, %C, 57.52 (57.49), %H, 5.16 (5.39), %N, 8.46 (8.38).

Results and Discussion

Acid dissociation constants (K_a) for reaction 1

$$4\text{-}XC_6H_4C(O)N(OH)R \overset{H_2O}{\rightleftharpoons} [4\text{-}XC_6H_4C(O)N(O)R]^- + H^+_{aq} \quad (1)$$

(7) Dessolin, M.; Laloi-Diard, M. *Bull. Soc. Chim. Fr.* **1971**, 2946.
(8) Agrawal, Y. K.; Shukla, J. P. *Aust. J. Chem.* **1973**, *26*, 913.
(9) Dutt, N. K.; Seshadri, T. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2280.
(10) Steinberg, G. M.; Swidler, R. *J. Org. Chem.* **1965**, *30*, 2362.
(11) The K_a values were determined as mixed constants with molar concentrations of protonated and deprotonated acids and H^+ activity determined from the pH meter. Although the concentration changes with temperature due to changes in solution density, the ΔH_a and ΔS_a values reported here do not change significantly when a correction[12] is made for this effect.
(12) Hepler, L. G. *Thermochim. Acta* **1981**, *50*, 69.
(13) Priyadarshini, U.; Tandon, S. G. *J. Chem. Eng. Data* **1967**, *12*, 143.
(14) Ankers, W. B.; Bigley, D. B.; Hudson, R. F.; Thurman, J. C. *Tetrahedron Lett.* **1969** *52*, 4539.

$R = CH_3$, H; X = H, NO_2, CH_3O, CH_3

in aqueous solution (I = 2.0, $NaNO_3$) obtained over a range of temperatures, and the corresponding ΔH_a and ΔS_a values, are listed in Table I for a series of four related substituted *N*-methylbenzohydroxamic acids and 4-$CH_3OC_6H_4C(O)N(OH)H$. These results indicate that hydroxamic acids are weak organic acids and that pK_a variations are small.

Several reports have been made of pK_a values correlated with Hammett σ parameters for substituted benzohydroxamic acid.[7,8,15] The observed ρ values are ca 1. When pK_a values for the substituted *N*-methylbenzohydroxamic acids listed in Table I are plotted as a function of the Hammett σ parameters,[16] the ρ value is 0.6 (±0.1; correlation coefficient = 0.9147) for a σ range from -0.27 to 0.78. This is consistent with results obtained in ethanol/water for a slightly different series of *N*-methylbenzohydroxamic acids.[7] We previously reported[3] a much smaller ρ value (0.1) for a series of substituted *N*-phenylacetohydroxamic acids over a σ range from -0.31 to 0.88. However, the relative magnitude of these ρ values does not necessarily mean that the substituents on the C side of the hydroxamate moiety have the greater effect on the thermodynamic parameters (ΔH_a and ΔS_a) which contribute to the pK_a values. An analysis of these thermodynamic parameters for both the C- and N-substituted hydroxamic acid series allows for a more detailed interpretation of the substituent effect on hydroxamic acid acidity.

Thermodynamic data for the series of *N*-methylbenzohydroxamic acids with a substituent σ range of 1.1 (Table I) indicate that the ΔH_a values are very small and essentially invariant and that the variation in ΔS_a is only 5 cal/(K mol). These changes in ΔH_a and ΔS_a are approximately the same as those found for the substituted benzoic acids, the standard reaction series for the Hammett σ parameters: for a σ range of 0.83, variations in ΔS_a are 3 cal/(K mol) and ΔH_a is essentially invariant ($0 < \Delta H <$ 0.80 kcal/mol).[17-19] In contrast to the substituted *N*-methylbenzohydroxamic acid series reported here, the thermodynamic data for the substituted *N*-phenylacetohydroxamic acid series[3] show a considerable difference from the standard substituted benzoic acid series. For example, the variation in ΔS_a over a Hammett σ range of 0.83 is 17 cal/(K mol), and ΔH_a values are reasonably large positive numbers and show significant variations with substituent.[13] Furthermore, the ρ value for the substituted *N*-phenylacetohydroxamic acids is only one-tenth that for the substituted benzoic acids.

The small variations in ΔS_a and ΔH_a for the substituted *N*-methylbenzohydroxamic acids relative to the substituted *N*-phenylacetohydroxamic acids[3] are best illustrated in Figure 1 where ΔH_a is plotted against ΔS_a.[20] Also included in the plot are the data for other similar hydroxamic acids studied in this laboratory.[2] The data points appear to fall in groups according to the substituent on the N atom of the hydroxamate moiety. As a result of their small range and minimum values of ΔH_a and ΔS_a, the data points for the substituted *N*-methylbenzohydroxamic acids are clustered together at the lower left segment of the plot, along with another *N*-methyl compound, $CH_3C(O)N(OH)CH_3$. Conversely, all of the hydroxamic acids with a substituted phenyl ring on the N atom fell in the upper right range of the plot as a results of maximum relative values of ΔH_a and ΔS_a. $CH_3OC_6H_4C(O)N(OH)H$, along with the other two N-proton hydroxamic acids investigated previously in our laboratory,[2] falls in an intermediate range.

The influence that the substituent has on the entropy changes associated with acid dissociation can be understood in terms of solvent–solute interactions.[3,18,25] In this discussion, it is assumed that differences in solvation among the undissociated acids are unimportant when compared to differences in solvation of the anions. This is consistent with the charged anions being much more highly solvated than the neutral undissociated acids. Furthermore, any small variation in solvation of the R_1 and R_2 substituents in the undissociated form would tend to be cancelled by equivalent solvation effects of the substituents in the dissociated form. Therefore differences in ΔH_a and ΔS_a among the hydroxamic acids are ascribed to differences in the solvation of the anions (relative to the undissociated acids) caused by the electronic influence of the substituents.[26] As the anion becomes less effective in orienting the solvent (water) molecules, ΔS_a becomes more positive. Conversly, as the anion becomes more effective in orienting the solvent (water) molecules, entropy changes for the acid dissociation reaction become more negative. The corresponding changes in ΔH_a are expected to be in the opposite direction to that for ΔS_a. For the *N*-methylbenzohydroxamic acids reported on here, the entropy changes are the most negative relative to the entire series of hydroxamic acids studied in this laboratory.[2,3] This suggests that the substituted *N*-methylbenzohydroxamate anions are the most effective of this series in ordering the solvent molecules; that is, they are more highly solvated. This could be due to either the C-substituted phenyl group or to the *N*-methyl group, or both.

As discussed previously,[3] we propose that delocalization of the N atom lone pair of electrons is fundamental in causing variations in solvent ordering about the hydroxamate anion. When the substituted phenyl ring (C_6H_4Y) is on the N atom, the substituent, Y, can influence the delocalization of the N lone pair of electrons. However, when the substituted phenyl ring (C_6H_4X) is on the C atom, the substituent X cannot directly influence the delocalization of the N atom lone pair of electrons. Therefore, for the *N*-methylbenzohydroxamic acids in Table I, ΔH_a and ΔS_a values are dominated by the CH_3

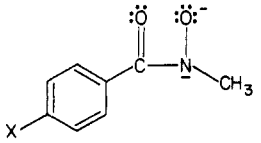
(15) Agrawal, Y. K. *Russ. Chem. Rev.* (*Engl. Transl.*) **1979**, *48*, 948.
(16) Jaffe, H. H. *Chem. Rev.* **1953**, *53*, 191.
(17) Hambly, A. N. *Rev. Pure Appl. Chem.* **1965**, *15*, 87.
(18) Larson, W. M.; Heple, L. G. In "Solute Solvent Interactions"; Coetzee, J. F., Ritchie, C. C., Eds.; Marcel Dekker: New York, 1969; Chapter 1.
(19) Matsui, T.; Ko, H. C.; Hepler, L. *Can. J. Chem.* **1974**, *52*, 2906.
(20) The linear correlation between ΔH_a and ΔS_a shown in Figure 1 does not conform to the strict statistical criteria established by Krug[21] and Exner[22] for a true isokinetic relationship. However, we have applied the error analysis described by Petersen et al.[23] and Wiberg[24] to these data which shows that the ΔH_a and ΔS_a ranges observed are statistically significant and the linear correlation valid. Consequently, the range and number of data points for the correlation are sufficiently large for us to suggest that a compensating effect is operating for reaction 1. For further details, see footnotes 18 and 21 of ref 3.
(21) Krug, R. R. *Ind. Eng. Chem. Fundam.* **1980**, *19*, 50.
(22) Exner, O. *Collect. Czech. Chem. Commun.* **1972**, *37*, 1425; **1975**, *40*, 2762; *Prog. Phys. Org. Chem.* **1973**, *10*, 411.
(23) Petersen, R. C.; Markgraf, J. H.; Ross, S. D. *J. Am. Chem. Soc.* **1961**, *83*, 3819.
(24) Wiberg, K. B. "Physical Organic Chemistry"; Wiley: New York, 1964; pp 376–379.
(25) Edward, J. T. *J. Chem. Educ.* **1982**, *59*, 354 and references therein.
(26) This assumption is supported by the large differences in ΔH_a and ΔS_a observed between $CH_3C(O)N(OH)C_6H_5$ and $CH_3C(O)N(OH)$-4-$C_6H_4CH_3$ in Table II. Little difference would be expected in the solvation of the undissociated acids in these similar compounds, indicating that the ΔH_a, ΔS_a differences arise from the solvation of the anion.

Table I. Hydroxamic Acid Dissociation Constants, K_a, and Computed ΔH_a, ΔS_a and pK_a Values in Aqueous Solution (I = 2.0)

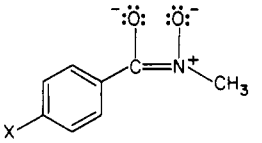
hydroxamic acid	T, °C	$10^9 K_a$[a]	pK_a[b] (25 °C)	ΔH_a,[c] kcal/mol	ΔS_a,[c] cal/(K mol)
4-$CH_3OC_6H_4C(O)N(OH)CH_3$	19.5	2.12 (0.22)	8.67 (0.01)	1.2 (0.1)	−36 (1)
	25.0	2.22 (0.14)			
	30.7	2.28 (0.22)			
	35.2	2.32 (0.28)			
	39.8	2.44 (0.12)			
4-$CH_3C_6H_4C(O)N(OH)CH_3$	20.4	3.16 (0.28)	8.50 (0.01)	1.6 (0.2)	−33 (1)
	25.0	3.18 (0.41)			
	30.2	3.41 (0.50)			
	35.2	3.66 (0.75)			
	40.1	3.70 (0.28)			
$C_6H_5C(O)N(OH)CH_3$[d]	15.5	4.73 (0.01)	8.28 (0.01)	2.2 (0.2)	−31 (1)
	19.5	4.78 (0.03)			
	20.0	4.73 (0.01)			
	25.0	5.28 (0.02)			
	30.0	5.56 (0.02)			
4-$NO_2C_6H_4C(O)N(OH)CH_3$	19.8	11.51 (0.02)	7.94 (0.01)	1.1 (1.5)	−33 (1)
	25.0	12.12 (0.11)			
	30.5	12.39 (0.17)			
	35.7	12.41 (0.32)			
	39.8	13.14 (0.04)			
4-$CH_3OC_6H_4C(O)N(OH)H$	20.0	1.50 (0.03)	8.76 (0.01)	5.7 (0.3)	−21 (1)
	25.0	1.73 (0.01)			
	30.0	2.05 (0.01)			
	35.0	2.31 (0.07)			
	40.1	2.82 (0.04)			

[a] Each K_a value represents an average of 2 or 3 independent determinations. The number in parentheses represents the standard deviation of the average of the independent determinations. The errors associated with ΔH_a and ΔS_a are consistent with those obtained from E. J. King's method of propagation of errors.[29] [b] The number in parentheses represents the reproducibility of each 25 °C pK_a determination. [c] Computed from linear least-squares analysis of replicate K_a determinations at each temperature. Number in parentheses represents the standard deviation obtained from the linear least-squares analysis. [d] Represents a redetermination of results previously reported in ref 2.

group on the N atom, resulting in a narrow range for these parameters even with a wide σ parameter range for the substituent on the C-phenyl ring. Resonance forms III



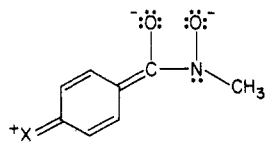
III



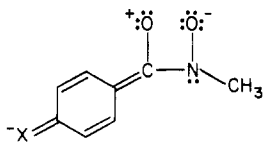
IV

and IV illustrate the possible electron delocalization for the substituted *N*-methylbenzohydroxamate anions when the methyl group on the N atom plays the dominant role. These resonance forms suggest that there is relatively little electron delocalization with respect to the phenyl ring. The increased net molecular dipole for the substituted *N*-methylbenzohydroxamate anion as a result of a contribution from resonance form IV result in a greater interaction with the solvent molecules and hence the more negative entropy changes and smaller ΔH_a values.

Although it is possible to write two other resonance forms, V and VI, to describe possible electron delocaliza-



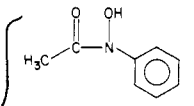
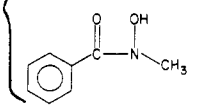
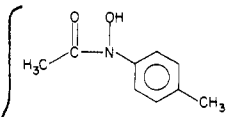
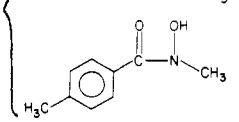
V



VI

tion within the substituted *N*-methylbenzohydroxamate anion, we propose that N atom lone pair delocalization (IV) predominates over resonance delocalization incorporating the phenyl ring (V or VI). This tentative conclusion is based on the following experimental observations: (1) The *N*-methylhydroxamic acids reported here all have roughly

Table II. Comparison of ΔH_a, ΔS_a, and pK_a for Isomeric Pairs of Hydroxamic Acids

hydroxamic acid	ΔH_a, kcal/mol	ΔS_a, cal/(K mol)	pK_a (25 °C)	ref
	10.9	−2	8.42	*a*
	2.2	−31	8.28	this work
	7.6	−15	8.81	*a*
	1.6	−33	8.50	this work

[a] Reference 3.

equivalent ΔH_a and ΔS_a values regardless of the phenyl substituent, which, on the basis of arguments in the preceeding paragraph, indicate similar anion solvent interactions. (2) The substituted *N*-methylbenzohydroxamic acids reported here have ΔH_a and ΔS_a values similar to N-methylacetohydroxamic acid, $CH_3C(O)N(OH)CH_3$, where electron delocalization according to V and VI is not possible. (3) Comparison of ΔH_a and ΔS_a values for 4-$CH_3OC_6H_4C(O)N(OH)CH_3$ with those for 4-$CH_3OC_6H_4C(O)N(OH)H$ (Table I) indicates the former compound to have smaller values for these parameters. (4) Comparison of ΔH_a and ΔS_a values for 4-$NO_2C_6H_4(O)N(OH)CH_3$ (Table I) with those calculated from data reported in the literature[27] for 4-$NO_2C_6H_4C(O)N(OH)H$ (ΔH_a = 6.4

kcal/mol; ΔS_a = −16 cal/(K mol)) also shows that the *N*-methyl compound has smaller values for these parameters. According to arguments presented in the preceeding paragraph, points 3 and 4 suggest stronger anion–solvent interaction for the *N*-methyl compounds.

There is strong evidence that the observed variations in ΔH_a and ΔS_a are due to water solvent interactions with the −[C(=O)N(O⁻)−] moiety rather than with the substituents on the C and/or N atoms. This is nicely illustrated by the comparison of the two pairs of geometric isomers shown in Table II. Significant differences in ΔH_a and ΔS_a values are found for both pairs of isomers, despite the identical substituents for each isomeric pair. Making the reasonable assumption that solvation of these substituents should be the same regardless of attachment to C or N, these isomer comparisons strongly support our arguments concerning solvent interactions specifically with the hydroxamate moiety, which is influenced by the substituents on the C and/or N atom.[28]

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

(27) Reference 7 contains pK_a data obtained at various temperatures in an ethanol/water solvent mixture for a series of hydroxamic acids; the authors did not use these data to calculate ΔS or ΔH values. The 25 °C pK_a values are in excellent agreement with 25 °C pK_a values determined in 100% water in ref 8 for the same hydroxamic acids. We therefore have used the temperature-dependent data of ref 7 to calculate ΔH_a and ΔS_a for 4-$NO_2C_6H_4C(O)N(OH)H$. These values were used in our analysis without further correction for differing conditions, and, therefore, some caution should be exercised in the comparative analysis. However, the ΔH_a and ΔS_a values calculated for 4-$NO_2C_6H_4C(O)N(OH)H$ fall on the linear ΔH_a–ΔS_a correlation shown in Figure 1 for the 17 hydroxamic acids investigated in our laboratory and which were investigated by a common technique and set of experimental conditions.

(28) Although the steric environments about the carbon and nitrogen differ in these isomers, we propose that any contribution to the differences in ΔH_a and ΔS_a of these isomer pairs by steric effects in the undissociated acids is negligible compared to the electronic influence of the substituents on the solvation of the anion. This is supported by the large changes in ΔH_a and ΔS_a ($\Delta\Delta H_a \approx 6$ kcal/mol and $\Delta\Delta S_a \approx 17$ cal/(K mol)) among the substituted *N*-phenylacetohydroxamic acids (compounds 9–17 in Figure 1) which would show no steric differences at the C and N atoms. Furthermore, if the bulk of the substituent on the N would alter hydrogen bonding about the N enough to effect the solvation of the anion, one would expect a reasonable progression to exist between ΔH_a and ΔS_a and the bulk of the substituent. This is not found to be the case for $CH_3C(O)N(OH)H$, $CH_3C(O)N(OH)CH_3$, and $CH_3C(O)N(OH)C_6H_5$,[2,3] where R_2 is varied from H to CH_3 to C_6H_5. This is consistent, then, with our argument that the variations in ΔH_a and ΔS_a are produced by the electronic effects of the substituents and not steric effects.

(29) King, E. J. In "The International Encyclopedia of Physical Chemistry and Chemical Physics"; Topic 15, Guggenheim, E. A., Mayer, J. E.; Tompkins, F. C., Eds.; The MacMillan Co.: New York, 1965; Vol. 4, Topic 15, p 194.

Structural Effects in Phosphates. 1. Comparison of 4-Nitrophenyl 1-Naphthyl and 4-Nitrophenyl Quinolin-8-yl Phosphates

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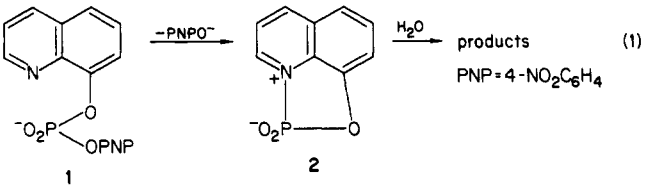
Crystal and molecular structures of quinolin-8-yl bis(*p*-nitrophenyl) (**4**), quinolin-8-yl *p*-nitrophenyl (**4a**), and 1-naphthyl bis(*p*-nitrophenyl) phosphates (**5**) have been determined and compared. In **4** the donor–acceptor nitrogen–phosphorus interactions change the geometry of the molecule from tetrahedral to quasi-tbp, so the structure can be considered as an "early stage" of the intramolecular displacement of the PNPO group. In **4a** this interaction is replaced by intramolecular N··H··O hydrogen bonding. The intramolecular nonbonded potential energies of **4** and **5** were calculated, and the minimum-energy conformations obtained were compared with those determined by X-ray diffraction. The results of calculations confirm the observed differences in the intramolecular interactions operating in **4** and **5**. The mass spectra of **4** and **5** reveal a dramatic difference between these two phosphates with respect to the fragmentation involving the expulsion of the *p*-nitrophenoxy radical and the formation of the corresponding phosphorylium ion by the nitrogen atom. Rate measurements for the base-catalyzed hydrolysis of the P–OPNP linkage show that **4** is not significantly more reactive than **5** and provide no evidence for the intramolecular nucleophilic catalysis in the hydrolysis of **4**.

Intramolecular nucleophilic catalysis in the displacement at the phosphoryl substrates attracts considerable attention.[1] Loran and Williams demonstrated[2] that the hydrolysis of 4-nitrophenyl quinolin-8-yl phosphate (**1**) involves expulsion of 4-nitrophenoxide via intramolecular nucleophilic attack to give a cyclic intermediate (**2**). This results in ca. a 350-fold rate increase for the hydrolysis of **1** relative to the reactivity of 4-nitrophenyl phenyl phosphate.



1 2 (1)

As a continuation of our investigation of structural correlations in organophosphorus chemistry,[3] we were interested to see whether the nitrogen–phosphorus interac-

(1) Lazarus, R. A.; Benkovic, P. A.; Benkovic, S. J. *J. Chem. Soc. Perkin Trans. 2*, **1980**, 373 and references cited therein.
(2) Loran, J. S.; Williams, A. *J. Chem. Soc. Perkin Trans. 2*, **1977**, 64.
(3) Archer, S. J.; Modro, T. A.; Nassimbeni, L. R. *Phosphorus Sulfur* **1981**, *11*, 101.

0022-3263/85/1950-2281$01.50/0