Table I
Kinetic Data for Hydrolysis of Phenylacetohydroxamic Acid in Aqueous Sulfolane

Wt % sulfolane	Mole fraction of sulfolane	[Water], M	[HCl], N	Temp, °C	$10^5 k$,[a] sec^{-1}
0	0	55.51	0.240	50.5	4.12
32.58	0.0675	39.98	0.240	50.5	4.58
52.50	0.142	29.55	0.240	50.5	5.63
70.20	0.261	19.33	0.240	50.5	8.13
95.80	0.774	2.90	0.240	50.5	23.2
0	0	55.51	0.0479	70.3	4.45
34.92	0.0744	38.46	0.0479	70.3	5.03
49.09	0.126	31.56	0.0479	70.3	5.83
67.89	0.241	20.80	0.0479	70.3	8.02
88.57	0.537	7.785	0.0479	70.3	19.8

[a] Average pseudo-first-order rate constant.

constants. A least-squares multiple regression analysis of the data at 70.3° in Table I yields a value of 0.82 for n, the order with respect to water. The coefficient of multiple regression for eq 5 is 1.000 to three significant figures. Figure 1 shows a graph of this data for log $k/[H_2O]$ *vs.* mole fraction sulfolane where n is taken to be 1. An excellent linear relationship results. This represents a range of 0–88.6 wt % sulfolane (0–0.54 mol fraction sulfolane). A graph of log $k/[H_2O]$ *vs.* mole fraction sulfolane for the data at 50.5° (0–95.8 wt %, 0–0.77 mol fraction sulfolane) is linear but not as exact as Figure 1.

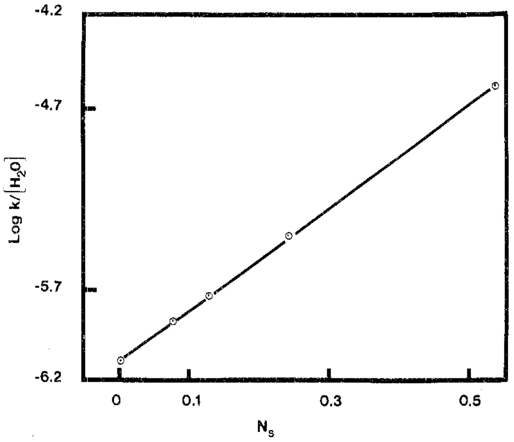

Figure 1. Log $k/[H_2O]$ as a function of mole fraction of sulfolane for hydrolysis of phenylacetohydroxamic acid in aqueous sulfolane mixtures 0.0479 N with respect to HCl at 70.3°.

Equation 4 is a linear free-energy relationship. Koppel and Palm[9] have discussed in detail linear free-energy relationships in solvent effects. A linear relationship between log k and the mole fraction of one component of a binary solvent system is predicted under certain conditions, namely, that the nonspecific and specific solvent–solute interactions of each solvent component are invariable (including the absence of shifts in solvation equilibria) throughout the range of solvent composition involved. Koppel and Palm[9] consider two types of nonspecific solvent effects, dielectric effects and polarizability interactions. Since a linear relationship between log $k/[H_2O]$ and the reciprocal of the dielectric constant does not exist for this system (see above) and since the reciprocal of the dielectric constant is not linear in mole fraction sulfolane, dielectric effects can be discounted in the system reported herein.

It is noteworthy that linear relationships between log k and mole fraction sulfolane are not evident in the alkaline hydrolysis of dimethylacetylacetone[10] or in the alkaline hydrolysis of benzoate esters[11] in aqueous sulfolane.

Experimental Section

Phenylacetohydroxamic acid has been described previously.[5] Sulfolane was distilled at low pressure from sodium hydroxide pellets, $n^{30}\mathrm{D}$ 1.4816 (lit.[12] 1.4820). All solutions were prepared with double-distilled water with concentrations referred to ambient temperature. The kinetic measurements were made and the rate constants were calculated as described before.[5] Initial concentration of phenylacetohydroxamic acid for rate measurements at 50.5° was 0.0120 M and for those at 70.3° was 0.00600 M. Average deviation from the mean for average rate constants in Table I is less than 1.5%.

Registry No.—Phenylacetohydroxamic acid, 5330-97-2.

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Proximity Effects. Correlation of Ortho-Substituted Benzohydroxamic Acid Reactivities[1]

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The role of ortho substituents in chemical reactivity is complicated by several factors which may contribute to the reactivity effect of these substituents.[2,3] Empirical correlation schemes are useful for systematizing the data and for comparison of effects in related systems which will lead to further understanding of reactivity parameters and reaction mechanisms. The Pavelich–Taft equation (eq 1)

$$\log k/k_0 = \rho^*\sigma^* + \delta E_s \qquad (1)$$

is based upon reactions of esters and was developed for analysis of systems in which steric effects are expected to be present.[2,3]

Table I
Hydrolysis Rates of 2-Substituted Benzohydroxamic Acids in 0.605 *M* Hydrochloric Acid at 90.0°

Registry no.	2 Substituent	$10^5 k$[a]	$-\log k$	$-\log k$ (calcd)[b]
31791-97-6	Methoxy	21.5	3.668	3.669
50357-86-3	Ethoxy	16.4	3.785	3.772
17512-73-1	Methyl	2.53	4.597	4.611
17512-69-5	Chloro	1.82	4.740	4.796
50357-88-5	Bromo	1.00	5.000	4.941

[a] Average pseudo-first-order rate constant, $\sec^{-1}$. [b] Calculated from eq 4.

In eq 1, σ^* is the polar contribution and E_s the steric contribution of the substituent to relative reactivity. ρ^* and δ are proportionality constants which indicate the susceptibility of the reaction system to the substituent effects measured by the σ^* and E_s parameters, respectively. Equation 1 has been successfully applied to various aliphatic and ortho-substituted benzene systems (with ρ^* *or* δ equal to zero in some instances) and has been the subject of a recent review.[2]

The acid-catalyzed hydrolyses of aliphatic amides[4] and ortho-substituted benzamides[5] are well correlated by the E_s parameter alone; *i.e.*, polar effects are zero or nearly so in these systems. Reactivities in the acid-catalyzed hydrolysis of a series of aliphatic hydroxamic acids were recently determined and are not correlated by E_s alone.[6] Equation 1 provides a fair correlation between these reactivities and σ^* and E_s with ρ^* and δ of comparable magnitude but of opposite sign. Consequently, polar effects are not zero in the acidic hydrolysis of aliphatic hydroxamic acids[6] in contrast to the amide hydrolyses.

Equation 1 should be applicable to the hydrolysis of acyl compounds following the bimolecular mechanism[2,3] which is the accepted mechanism for the hydrolysis of amides[7] and hydroxamic[6,8,9] acids (eq 2 and 3) at moderate acidity.

$$\mathrm{RCONHOH} + \mathrm{H}^+ \rightleftharpoons \mathrm{R\overset{+}{C}(OH)NHOH} \qquad (2)$$

$$\mathrm{R\overset{+}{C}(OH)NHOH} + \mathrm{H_2O} \longrightarrow \mathrm{RCO_2H} + \mathrm{H_2\overset{+}{N}OH} \qquad (3)$$

This paper reports a study of the acid-catalyzed hydrolysis of a series of ortho-substituted benzohydroxamic acids at moderate acidity. The results are in Table I. Included are log k values calculated from eq 4 where k is a pseudo-first-order rate constant directly proportional to the catalytic acid concentration under these conditions.[6,8,9]

$$\log k = -0.868\sigma_o^* + 0.759E_s - 4.611 \qquad (4)$$

The parameters of eq 4 were calculated by the method of least squares.[10] The ortho methyl group is the reference substituent with the ortho polar substituent constant, σ_o^*, scale[3] adjusted accordingly (range -0.22 to $+0.38$). E_s values (range 0–0.99) for ortho substituents[3] with methyl as the reference substituent are applied in eq 4. The correlation coefficient[10] is 0.998. The F test[10] for statistical significance indicates that the correlation by eq 4 is significant at the 1% level, a very satisfactory result. Figure 1 illustrates the correlation graphically.

The correlation by eq 4 extends the range of usefulness of eq 1 as well as indicating that eq 1 is applicable to hydroxamic acid reactivities and that the substituent effects studied in this system are adequately represented by the σ_o^* and E_s parameters. Since $\rho^*\sigma_o^*$ and δE_s measure the contribution of polar and steric effects, respectively, these quantities may be used to compare polar and steric effects of the substituents *relative* to methyl. Examination of these quantities reveals that the polar effect is greater than the steric effect for chloro and bromo while the reverse is true for the methoxy and ethoxy substituents *relative* to methyl. This result is in contrast to the acid-catalyzed hydrolysis of amides,[4,5] in which only steric effects as measured by E_s are significant.

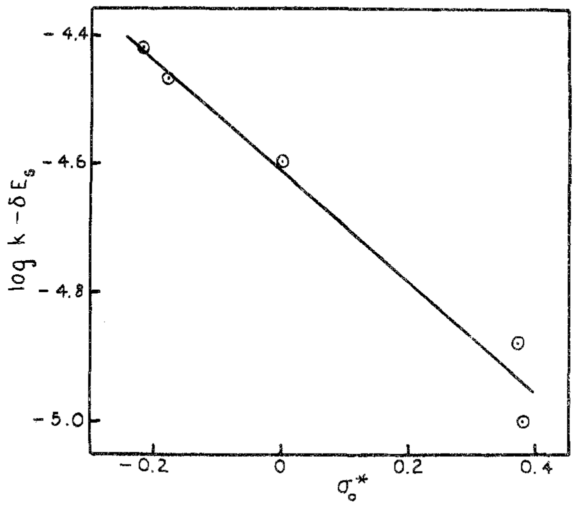

Figure 1. Experimental log k corrected for steric effects, δE_s, plotted as a function of σ_o^*. The line is the least-squares line (eq 4).

The rate constants in Table I are overall rate constants, *i.e.*, a composite for steps 2 and 3; consequently, ρ^* and δ are for the overall process. Since $\rho^* < 0$ in eq 4, electron-donating groups accelerate the rate compared to that of the reference compound, 2-methylbenzohydroxamic acid. This is consistent with the greater electronegativity of hydroxyl compared to hydrogen in changing from amides to hydroxamic acids, provided that the polar effect on the protonation step (eq 2) is greater than the polar effect for nucleophilic attack by water on the protonated intermediate (eq 3). The positive value of δ means that the rate is decelerated as E_s becomes smaller; smaller E_s values presumably correspond to increasing effective steric bulk,[2,3] although a resonance contribution is probably present.[2] In any event, the substituent effects in the present system parallel those in the system which defines σ_o^* and E_s. Analogous results with respect to polar and steric effects were observed in the acid-catalyzed hydrolysis of aliphatic hydroxamic acids.[6]

Experimental Section

All hydroxamic acids exhibited positive ferric chloride tests. All analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

2-Chloro- and 2-methylbenzohydroxamic acids were prepared from the corresponding substituted benzoyl chlorides according to the method of Jones and Hurd.[11] 2-Chlorobenzohydroxamic acid, crystallized from toluene, had mp 159.5–160.1 (lit.[12] mp 158–159°). 2-Methylbenzohydroxamic acid, crystallized from ethyl acetate, had mp 130.5–131°. *Anal.* Calcd for $C_8H_9NO_2$: C, 63.56; H, 6.00; N, 9.27. Found: C, 63.82; H, 6.14; N, 9.18.

2-Bromo-, 2-methoxy-, and 2-ethoxybenzohydroxamic acids were prepared from the correspondingly substituted methyl benzoates by adaptations of the "Organic Syntheses" procedure[13] and crystallized from 3:7 (v/v) ethanol-water. 2-Bromobenzohydroxamic acid had mp 177.5–178.5° (lit.[12] mp 178–180°). 2-Methoxybenzohydroxamic acid had mp 124–126°. *Anal.* Calcd for $C_8H_9NO_3$: C, 57.48; H, 5.43; N, 8.38. Found: C, 57.65; H, 5.28; N, 8.44. 2-Ethoxybenzohydroxamic acid had mp 124–125.5°. *Anal.* Calcd for $C_9H_{11}NO_3$: C, 59.65; H, 6.13; N, 7.73. Found: C, 59.76; H, 6.29; N, 7.66.

The 0.605 *M* hydrochloric acid was prepared from double-distilled water and standardized by titration. The kinetic measurements were made by the spectrophotometric method reported previously[8] employing a Beckman DU spectrophotometer set at 520 nm. Pseudo-first-order rate constants were obtained from the slope of the appropriate graph[8] with the numerical values computed by least squares.

The rate constants in Table I are the average of three to four runs for each compound. Average deviation from the mean is less than 4.5%. Temperature control was ±0.05°. Initial concentration of hydroxamic acids in the kinetics runs was 0.012 *M*.

Acknowledgment. The authors wish to thank J. R. McDowell for the preparation of two hydroxamic acids.

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Skipped Diynes. IV. Diacetylenic Ketone Reactions[1]

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Ketones with geminal triple bonds (**1**) are vulnerable to attack at several sites. As is the case with the more common monoethynyl ketones, additions of nucleophiles,[2-10] electrophiles,[11,12] dienes,[2] and dipolarophiles[13] to **1** have been observed. These were particularly interesting to us when both ethynyl groups became involved in conversions to families such as cyclopentenones, thiolenones, (5-triazolyl)isoxazoles, (pyrazolyl)pyrazoles, etc.[2,7] To expand this still relatively unfamiliar area, we investigated the chemistry of **1** with emphasis on **1a**.

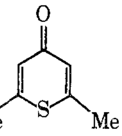
$$(RC{\equiv}C)_2C{=}O$$

1a, $R = CH_3$

b, $R = C_6H_5$

Those reactions of **1a** which proceed as expected will simply be mentioned, while those with new features will be described.[2,3,6] Thus, with primary or secondary amines, **1a** yields isolable monoadducts which may be cyclized to pyridones; with hydrazines and **1a**, the monoadduct may not always be isolable but the cyclization can usually be made to take place; with thiols, **1a** yields symmetrical diadducts; with tetracyclone, **1a** forms a Diels-Alder monoadduct.

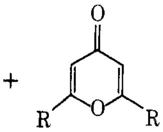
The reaction of diethynyl ketones with thiourea and substituted thioureas occurs readily but often unpredictably. Penta-1,4-diyn-3-one is reported to react with *N,N'*-diphenylthiourea to give an adduct of unspecified structure.[5] Compound **1b** reacted with both thiourea and *N,N'*-diphenylthiourea to give the same dihydrothiophene derivative,[2] but **1a** reacted with thiourea to give 2,6-dimethyl-4*H*-thiopyran-4-one as the only isolable product (eq 1).

$\mathbf{1a} + (H_2N)_2C{=}S \longrightarrow$  (1)

Our reaction conditions are quite different from the formally similar addition of hydrogen sulfide to **1b,** which proceeds in a bomb at 180° to give an analogous thiopyranone.[11]

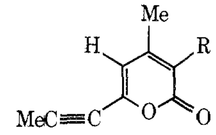
While not defined in every detail, the course of the additions of alcohols or water to **1** has been clarified. With **1b** Russian workers have recently shown that a monoalkoxy adduct of **1** as well as the products of eq 2 may be formed.[4] In the presence of acid the γ-pyrone is generally the major product.[12]

$1 + R'OH \longrightarrow$

$[RC(OR'){=}CH]_2C{=}O\ +$  $+\ (RCOCH_2)_2C{=}O$ (2)

When **1a** was treated with sodium ethoxide in ethanol, the only isolable product was 2,6-diethoxyhepta-2,5-dien-4-one, but with sodium methoxide in methanol, a 3:2 mixture of 2,6-dimethyl-4-pyrone and 2,6-dimethoxyhepta-2,5-dien-4-one was produced. The pyrone presumably arises from the slow acid-catalyzed hydrolysis of the bis(enol) ether to 2,4,6-heptanetrione, which then spontaneously condenses under the reaction conditions to give the pyrone. Indeed, **1a** yields 2,6-dimethyl-4-pyrone upon treatment with aqueous acid.[12]

Additions of Grignard reagents to the carbonyl group are possible, but additions of other carbon nucleophiles to **1** have varying success.[2,9] In the case of **1a** these additions are usually foiled by its sensitivity to the strongly basic conditions usually employed in such reactions. This problem was circumvented by employing inverse addition of the anions of diethyl malonate and ethyl cyanoacetate in solution to a cold solution of **1a.**

$\mathbf{1a} + \overset{+}{Na}\overset{-}{R}CHCO_2Et \longrightarrow$  (3)

$R = CO_2Et,\ CN$

The mode of attack and the resulting products are typical of monoethynyl ketones.[2] Under similar reaction conditions, **1b** reacts with carbon nucleophiles to give exclusively cyclopentenones.[2]

Experimental Section

For general details see ref 1, 2, and 14. **1a** had mp 80-81° (lit.[6a] mp 78-80°); ir (CCl_4) 2260, 2230, 1630 cm^{-1}; nmr (CCl_4) δ 2.05 (s, 6 H). **1b** had mp 65° (lit.[2] mp 64-66°); ir (CCl_4) 2240, 2180, 1605 cm^{-1}.

3-Propynyl-5-methylpyrazole. To a solution of **1a** (0.5 g) in 10 ml of methanol at 0°, hydrazine hydrate (1 ml) was added dropwise. Work-up followed by chromatography (twice) on silica gel with ether-chloroform (2:1, v/v) gave a yellow solid: mp 93.5-94.5°; ir ($CHCl_3$) 3490 (NH), 2230 (C≡C), 1580, 1465, 1410 cm^{-1}; nmr ($CDCl_3$) δ 2.0 (s, 3 H), 2.4 (s, 3 H), 6.0 (s, 1 H), 12.1 (broad, 1 H).

Anal. Calcd for $C_7H_8N_2$: C, 69.97; H, 6.76. Found: C, 69.86; H, 6.75.

2,4-Dinitrophenylhydrazone of 1a, as orange needles from ethyl acetate, had mp 201-203°; ir (KBr) 3220 (NH), 2220 (C≡C), 1618 cm^{-1} (C=N); nmr ($CDCl_3$) δ 2.1 (s, 3 H), 2.3 (s, 3 H), 8.6 (m, 3 H), 12.0 (broad, 1 H).

Anal. Calcd for $C_{13}H_{10}N_4O_4$: C, 54.54; H, 3.57. Found: C, 54.55; H, 3.05.

1-(2,4-Dinitrophenyl)-3-propynyl-5-methylpyrazole. A solu-