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Organic Reagents used in Inorganic Analysis. I. Acid Dissociation Constants of Hydroxamic Acids and *N*-Arylhydroxamic Acids

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A number of derivatives of hydroxamic acids and *N*-arylhydroxamic acids have been prepared and their acid dissociation constants have been determined in aqueous solutions. The variation of pK has been discussed.

Analytical applications of hydroxamic acids and of *N*-arylhydroxamic acids have been extensive. In 1950 Shome[1] suggested that *N*-benzoyl-*N*-phenylhydroxylamine was useful for gravimetric estimations and separations of many metals. Since then numerous papers have been published[2-4] on gravimetric and spectrophotometric determination of metals with the use of this and other reagents of this group. In spite of volumes of analytical work on these reagents reports of physico-chemical studies on these are rather limited. Such investigations of several substituted phenylhydroxylamines have been described by Ryan and others[5,6] to study the effect of change in the nature of the acyl group on their usefulness as analytical reagents. However, they have not determined the dissociation constants of the reagents and have not studied the change in their donor property with change in the nature of the acyl group as well as their behaviour towards various metals. The dissociation constant of benzohydroxamic acid has recently been determined by Alimarin and others,[7] potentiometrically as well as spectrophotometrically.

The present study has been conducted to make-

1) S. C. Shome, *Analyst*, **75**, 27 (1950).
2) I. P. Alimarin, F. P. Sudakov and B. G. Golovkin, *Russ. Chem. Revs.*, (A translation of *Uspekhi Khimii*), **31**, 466 (1962).
3) W. W. Brandt *Record. of Chem. Progr.*, **21**, 159 (1960).
4) A. M. Macdonald, *Ind. Chemist*, **36**, 512 (1960).
5) C. D. Ludwick and D. E. Ryan, *Can. J. Chem.*, **32**, 949 (1954).
6) C. A. Armour and D. E. Ryan, *ibid.*, **35**, 1454 (1957).
7) I. P. Alimarin, N. P. Borzenkova and R. I. Shmatko, *J. Anal. Chem. U.S.S.R.* (A translation of *Zhur. Anal. Khimii)*, **18**, 342 (1963).

a comprehensive physico-chemical investigation of these reagents. Twenty such reagents shown in Table 1 have been prepared and their acid dissociation constants have been determined.

Experimental

Chemicals. Phenylhydroxylamine, tolylhydroxylamines and several of the acid chlorides and the esters used for the syntheses of these reagents were prepared and purified by the methods reported in the literature.[8,9]

Preparations of Substituted Hydroxamic Acid. The derivatives of hydroxamic acid prepared in this study are listed in Table 1. The compounds I to XV were prepared from respective hydroxylamines and the desired acid chloride as described by Shome for the preparation of benzoyl-phenylhydroxylamine while in the case of compound VII benzene was used as solvent instead of water.

The compounds XVI to XX were synthesized from free hydroxylamine and esters as described in the literature.[10,11] Melting point and nitrogen analysis of the compounds were taken as the criterion of purity.

Determination of Dissociation Constants. The determinations of acid dissociation constants were carried out by the method of potentiometric titration. Solutions of reagents were prepared in double distilled water to which the requisite amount of sodium perchlorate was added to maintain an ionic strength of 0.1 with respect to $NaClO_4$. The solutions were then titrated with about 0.1 N NaOH (standardised). Titrations were carried out in a titration cell which was kept in an electrically regulated thermostat at 30 ± 0.5°C. Stirring was effected with a magnetic stirrer. The pH was measured with a Cambridge Bench type pH meter which was calibrated with aqueous buffers (pH 4 and 9) before and after titration. Corrections for hydrogen ion concentration and change in volume of solution during the titration were applied. The pH meter readings were converted to the concentration by using the following formula

$$-\log f_{H^+} = \frac{0.509\sqrt{I}}{1+2.2\sqrt{I}}$$

and was checked by our own experiment.

The reagents XIX and XX are dibasic acids and the reagents XVIII is a monohydrochloride. Except these three compounds others are obviously monobasic (HR).

For the monobasic acids titrations were performed on both sides of the mid-point, so that Henderson's equation can be applied as reviewed by Meites *et al.*[12]

For dibasic acids complete titrations were performed and $\bar{n}$ values were evaluated using the following relation. pK^s were determined from the plot of $\bar{n}$ (pH) (Figs. 1 and 2).

$$\bar{n} = 2 - C_b/T_R + [OH^-]/T_R - [H^+]/T_R \qquad (1)$$

For $(pK_2 - pK_1) \leq 2$, the pK values thus obtained were treated as preliminary values. Final values were obtained by the method of Irving and Rossotti[13] using the following equation

$$\frac{2-\bar{n}}{\bar{n}-1}\cdot 10^{-pH} = \frac{\bar{n}}{\bar{n}-1}\cdot 10^{pH}K_1K_2 + K_1 \qquad (2)$$

Results are shown in Table 1.

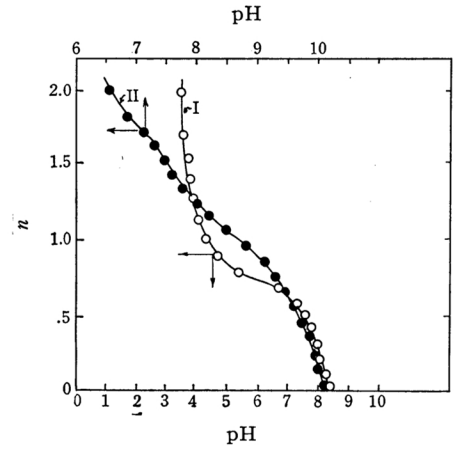

Fig. 1. Plot of $\bar{n}$ *vs.* (pH).
Curve I. Nicotinohydroxamic acid hydrochloride
Curve II. Salicylhydroxamic acid

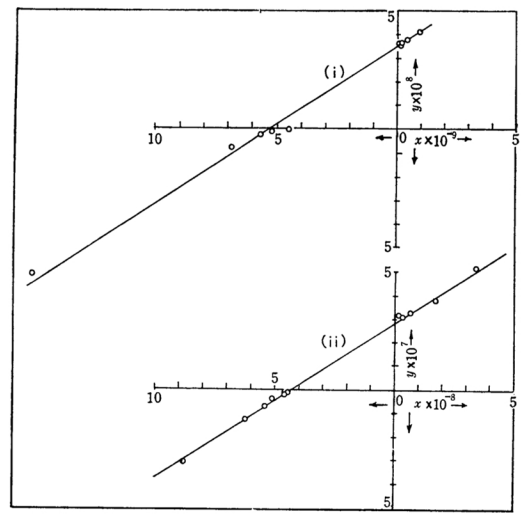

Fig. 2. Plot of Eq. (2) (page 2281) where
$X = \frac{\bar{n}}{\bar{n}-1}\cdot 10^{pH}$ and $Y = \frac{2-\bar{n}}{\bar{n}-1}\cdot 10^{-pH}$.
Curve I. Salicylhydroxamic acid
Curve II. Oxalodihydroxamic acid.

8) a) H. Gilman and A. H. Blatt, "Organic Syntheses," Coll. Vol. 1, p. 445 (1947); b) R. Willstatter, *Ber.*, **41**, 1908 (1937); c) E. Bamberger and M. M. Rising, *Ann.*, **316**, 273 (1901).
9) F. B. Laforge, *J. Am. Chem. Soc.*, **50**, 2479 (1928).
10) a) A. H. Blatt, "Organic Syntheses," Coll. Vol. 2, p. 67 (1948); b) A. S. Bhaduri and P. Ray, *Z. anal. Chem.*, **154**, 103 (1957); c) S. K. Dhar and A. K. Das Gupta, *J. Sci. Ind. Res.*, **11B**, 520 (1952).
11) T. S. Gardner, E. Wenis and F. A. Smith, *J. Am. Chem. Soc.*, **73**, 5455 (1951).
12) L. Meites and J. A. Goldman, *Anal. Chim. Acta*, **30**, 28 (1964).
13) H. Irving and H. S. Rossotti, *J. Chem. Soc.*, **1953**, 3399.

TABLE 1. DISSOCIATION CONSTANTS OF HYDROXAMIC ACIDS AND *N*-ARYLHYDROXAMIC ACIDS

General formula $R_1-\underset{\underset{O}{\|}}{C}-\underset{\underset{OH}{|}}{N}-R_2$

Temperature = 30±0.5°C Ionic strength = 0.1 maintained with $NaClO_4$

S. No.	Reagent	R_1	R_2	Mp, °C[a]	%Nitrogen[b] found	T_R[c] $\times 10^{-3}$	pK[d]
I	*N*-Benzoyl-*N*-phenylhydroxylamine (BHPA)	C_6H_5	C_6H_5	121 (121)	6.52 (6.57)	1.218	8.14 (8.15±0.01)[14]
II	*N*-*o*-toluyl-*N*-phenylhydroxylamine	*o*-$(CH_3)C_6H_4$	C_6H_5	98	6.07 (6.16)	1.573	8.08
III	*N*-*p*-toluyl-*N*-phenylhydroxylamine	*p*-$(CH_3)C_6H_4$	C_6H_5	116	6.22 (6.16)	0.851	8.31
IV	*N*-*p*-methoxybenzoyl-*N*-phenylhydroxylamine	*p*-$(OCH_3)C_6H_5$	C_6H_5	118	5.68 (5.76)	1.019	8.15
V	*N*-*o*-chlorobenzoyl-*N*-phenylhydroxylamine	*o*-(Cl)C_6H_4	C_6H_5	106	5.64 (5.66)	1.232	7.60
VI	*N*-*m*-Nitrobenzoyl-*N*-phenylhydroxylamine	*m*-$(NO_2)C_6H_4$	C_6H_5	115	10.79 (10.85)	1.168	7.67
VII	*N*-Acetyl-*N*-phenylhydroxylamine	CH_3	C_6H_5	67 (67.5)	8.96 (9.27)	0.999	8.10
VIII	*N*-Phenylacetyl-*N*-phenylhydroxylamine	$C_6H_5CH_2$	C_6H_5	87	6.14 (6.16)	1.086	8.43
IX	*N*-Cinnamoyl-*N*-phenylhydroxylamine	$C_6H_5CH=CH$	C_6H_5	162 (162)	5.82 (5.86)	0.831	8.64
X	*N*-Furoyl-*N*-phenylhydroxylamine	C_4H_3O	C_6H_5	134 (134)	6.81 (6.90)	1.368	7.69
XI	*N*-Phenylacetyl-*N*-*o*-tolylhydroxylamine	$C_6H_5CH_2$	*o*-$(CH_3)C_6H_4$	103	5.79 (5.81)	1.053	8.46
XII	*N*-Furoyl-*N*-*o*-tolylhydroxylamine	C_4H_3O	*o*-$(CH_3)C_6H_4$	97— 98	6.52 (6.45)	1.374	7.77
XIII	*N*-Benzoyl-*N*-*o*-tolylhydroxylamine	C_6H_5	*o*-$(CH_3)C_6H_4$	104 (104)	6.25 (6.16)	1.385	8.18
XIV	*N*-*p*-methoxybenzoyl-*N*-*o*-tolylhydroxylamine	*p*-$(OCH_3)C_6H_4$	*o*-$(CH_3)C_6H_4$	114	5.50 (5.45)	1.052	8.44
XV	*N*-Benzoyl-*N*-*p*-tolylhydroxylamine	C_6H_5	*p*-$(CH_3)C_6H_4$	111	6.10 (6.16)	1.303	8.27
XVI	Benzohydroxamic acid	C_6H_5	H	127—128 (128)	10.17 (10.22)	1.055	8.43 (8.07)[7] (8.75)[15]
XVII	*p*-Methoxybenzohydroxamic acid	*p*-$(OCH_3)C_6H_4$	H	163 (163)	8.30 (8.38)	1.338	8.91 (9.00)[16]
XVIII	Nicotinohydroxamic acid hydrochloride	C_5H_4N	H	186 (186)	15.90 (16.10)	1.5020	pK_1 3.75[e] pK_2 7.60[e]
XIX	Salicylhydroxamic acid	*o*-$(OH)C_6H_4$	H	168 (168—169)	8.93 (9.15)	1.1530	pK_1 7.46[e] pK_2 9.72[e]
XX	Oxalodihydroxamic acid			164 (165)	22.94 (23.33)	2.333	pK_1 6.55[e] pK_2 8.63[e]

a) Figures in the parentheses are the reported melting points.
b) Figures in the parentheses are the calculated percentages.
c) T_R = Total analytical concentration of the reagent at the start of titration
d) pK = $-\log K$; $K = \dfrac{[H][L]}{[HL]}$
e) pK values are obtained from curves (Figs. 1 and 2).

Discussion

The reagents under study can be classified into the following groups:

(i) compounds with substitutions in the benzoyl group in benzoyl-phenylhydroxylamine (Compounds I—VI);

(ii) compounds with substitutions in the phenyl group with or without any substituent in the

14) D. Dyrssen, *Acta Chem. Scand.*, **10**, 353 (1956).
15) A. L. Green, G. L. Sainsbury, B. Saville and M. Stansfield, *J. Chem. Soc.*, **1958**, 1583.
16) B. E. Hackley, Jr., R. Palpinger and T. W. Jauregg, *J. Am. Chem. Soc.*, **77**, 3651 (1955).

benzoyl group (Compounds XIII—XV);

(iii) other compounds where acyl group is other than benzoyl group, substituted or unsubstituted (compounds VII to XII); and (iv) hydroxamic acids (XVI—XX).

For group (i) compounds the following order of pK values are observed, o-Cl(V) < m-nitro(VI) < o-toluyl(II) < BPHA(I) < p-methoxy(IV) < p-toluyl (III). Effects of substitutions may now be summarised as o-Cl (V) (pK 7.60), o-toluyl (II) (pK 8.06) BPHA (I) (pK 8.14). Substitution in the p-position has little effect, as p-methoxy (IV) (pK 8.15) and BPHA (I) (pK 8.14). These observations also correspond with those obtained by Hammett[17] for substitutions in the benzoic acid. Similar effects were observed with N-substituted acetoacetamides.[18]

The following order of pK values are obtained for o-tolyl compounds of group (ii). BPHA(I) < o-tolyl (XIII) < p-methoxybenzoyl-o-tolyl (XIV). This is also in the order given by Hammett (*loc. cit*). N-benzoyl-N-p-tolyl compound (XV) shows a greater pK than N-benzoyl-N-o-tolyl compound (XIII) in spite of similar electronic effects because of increased distance of the substituent in the p-compound.[19]

For group (iii) compounds following order of pK values are obtained. Furoyl (X) < furoyl-o-tolyl (XII) < acetyl (VII) < BPHA (I) < phenylacetyl (VIII) < phenylacetyl-o-tolyl (XI) < cinnamoyl(IX). It is evident that o-methyl substitution in the phenyl ring has increased the pK (*cf.* the pairs of compounds X and XII and VIII and XI). When the compounds VII and VIII are considered, it is seen that replacement of one hydrogen of the acetyl group by phenyl group has lowered the acidity. This is only possible if the phenyl group is not in the same plane with the –C=O group which will reduce the electron attracting capacity of the phenyl group.

In case of the hydroxamic acids pK of XVI and XVII increases over that of I and IV respectively. This may be expected due to the absence of the phenyl group. However, the difference between the latter set seems to be too large. The present pK value of XVI is higher than that reported by Alimarin[7] at an ionic strength I=0.25. Earlier pK values of XIX are in dioxane-water (75 : 25) medium. pK_2 of this compound can be attributed to the dissociation of the phenolic group. The pK_2 value of 9.72 being comparable to 9.9 of phenol.

Lastly, for similar substitutions on either of the phenyl ring it is found that the substitution in the acyl group has shown a lower pK for ortho substitution (II and III) and the reverse order for the para substitution (XIII and XV) though the difference is very small in the latter case.

The effect of ionic strength has been studied with several of the reagents and it is found that with the exception of acetyl phenylhydroxylamine, pK values are functions of ionic strength (Fig. 3).

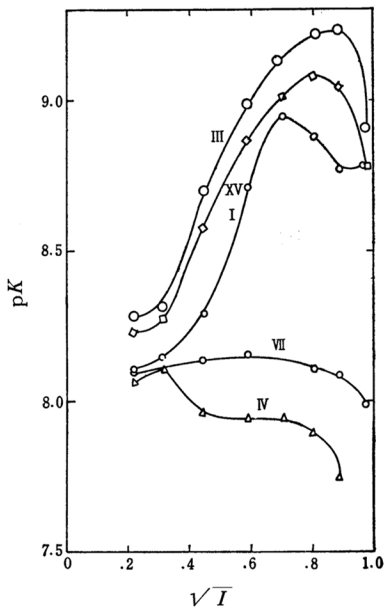

Fig. 3. Plot of p$K(I)$ where I=ionic strength. Figures on the curves refer to the serial number of ligands in Table 1.

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18) H. J. Harries, *J. Inorg. Nucl. Chem.*, **25**, 519 (1963).
19) A. Albert and E. P. Serjeant, "Ionization Constants of Acids and Bases," John Wiley & Sons Inc., New York (1962), p. 123.