sample of N-β-chloroethyl-N′-nitroguanidine.[10] It was further characterized by refluxing 300 mg. of the material for three minutes in a solution of *n*-pentyl alcohol. This gave 240 mg. (80%) of 1-nitro-2-amino-2-imidazolinium hydrochloride (m.p. 189° dec.). This product did not depress the melting point of an authentic specimen of 1-nitro-2-amino-2-imidazolinium hydrochloride.[10] The infrared spectra of these two samples were also identical. Finally the picrate of 1-nitro-2-amino-2-imidazoline (m.p. 190–191°) was prepared in the usual manner for comparison with a known sample of 1-nitro-2-amino-2-imidazolinium picrate (m.p. 189°).[10] These samples on admixture gave no depression in melting point.

The filtrate from the second crop of N-β-chloroethyl-N′-nitroguanidine was allowed to evaporate spontaneously to dryness. A sample of the residue was examined by infrared spectroscopy. The spectrum showed the absence of 1-nitro-2-amino-2-imidazolinium salts and/or urea derivatives. The spectrum was similar to that obtained for pure N-β-chloroethyl-N′-nitroguanidine.

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[10] A. F. McKay and J. E. Milks, THIS JOURNAL, **72**, 1616 (1950).

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An Investigation of Some Hydroxamic Acids

BY WARREN M. WISE AND WARREN W. BRANDT

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For the purposes of another investigation it became necessary to synthesize various aliphatic and aromatic hydroxamic acids. In order to obtain conveniently a number of these compounds, a general method for preparing and purifying them was sought. Several procedures recorded in the literature were tried; however, they were found to be somewhat unsatisfactory. The method proposed by Hoffman[1] involving the preparation of the cupric salts of the hydroxamic acids and the subsequent decomposition of the salts in absolute alcohol with hydrogen sulfide was found to be quite time consuming, and the desired products could not always be isolated. The method of Blatt[2] was found to be satisfactory only for the preparation of benzohydroxamic acid. The alkali metal salts of the other hydroxamic acids tried can be prepared by this procedure; however, they are so soluble in methyl alcohol that obtaining the pure acid is difficult. Since the free acids are usually very soluble in water and insoluble in most of the common organic solvents, after hydrolysis it is extremely difficult to isolate them.

It was found that in methyl alcohol an acid charged cation-exchange resin can be employed to convert the potassium salts of hydroxamic acids to the corresponding acids and remove any unreacted basic constituents from the reaction mixture. After removing the excess solvent under vacuum, only the desired hydroxamic acids remain. This procedure has been utilized as a satisfactory general method for isolating hydroxamic acids.

After the desired hydroxamic acids were purified by successive recrystallizations, the ionization constant of each was determined by measurement of the *p*H of a solution containing known amounts of the free acid and its sodium salt. Since the values obtained did not agree with those reported in the literature,[3,4] the electrical conductance method was also used to evaluate the K_a of benzohydroxamic acid.

Experimental

(A General Method for Preparing Hydroxamic Acids). **Procedure.**—The method of Blatt[2] was used to prepare a methyl alcohol solution of the potassium salt of the desired hydroxamic acid. If small amounts of the potassium salt of the hydroxamic acid crystallized out upon standing, the solid was crushed finely before the following procedure was carried out.

One pound of Amberlite IRC-50 resin was charged with 1000 ml. of 1 *N* hydrochloric acid and washed three times with 300-ml. portions of methyl alcohol. The reaction mixture was mixed with the charged resin and allowed to stand for one-half hour. During this time the slurry was stirred intermittently and the apparent *p*H was checked. If the solution was not acidic, more charged resin was added to remove the basic constituents.

The resin was filtered with suction and washed. The combined filtrate and washings were reduced to dryness or a thick sirup under vacuum at room temperature. The residue was recrystallized from the smallest possible quantity of ethyl acetate. Small amounts of insoluble material were removed by filtration. If necessary, precipitation was aided by reducing the volume or by the addition of petroleum ether. The latter procedure had to be used to purify *n*-butyrohydroxamic acid. The crystals were filtered, washed twice with small amounts of cold ether, and dried in a vacuum desiccator. The product was recrystallized from ethyl acetate until a melting point range of 1° was obtained.

Determination of the Ionization Constants of Some Hydroxamic Acids. Apparatus and Reagents: Leeds and Northrup *p*H meter, Wheatstone bridge circuit,[5] Potassium chloride (J. T. Baker), Sodium hydroxide (J. T. Baker).

Buffer Method.—A known amount of the hydroxamic acid was dissolved in water and enough standardized sodium hydroxide was added to neutralize approximately one-half of the acid. (If the acid was insoluble in water, sufficient sodium hydroxide was added to neutralize almost all of the acid.) In some cases potassium chloride was added to regulate the ionic strength. The solution was diluted to volume at 20° with carbon dioxide-free distilled water, and the *p*H was measured.

Conductance Method.—A Wheatstone bridge type circuit[5] was used, and the resistances of all solutions were measured at 25.0°. A Washburn conductance cell was calibrated with 1.000×10^{-3} *M* potassium chloride. Potassium benzohydroxamate was prepared,[2] purified by recrystallizing twice from distilled water, and dried in a vacuum desiccator. Solutions varying in concentrations from 1.000×10^{-4} to 1.000×10^{-1} *M* were prepared from the salt and conductance water, and the resistances of these solutions were measured. Benzohydroxamic acid was purified by recrystallizing twice from ethyl acetate and drying in a vacuum desiccator. From benzohydroxamic acid and conductance water two solutions were prepared, 1.000×10^{-2} and 1.000×10^{-3} *M*; and their resistances were determined.

Discussion of Results

By employing a carboxylic acid cation-exchange resin a satisfactory general method for isolating hydroxamic acids was developed. Since the conditions of the reaction are mild, very small amounts of the desired compounds undergo decomposition. Aceto-, adipo-, benzo-, *n*-butyro-, *p*-chlorobenzo-, *p*-methoxybenzo-, phenylaceto-, propiono- and salicylohydroxamic acids were isolated and purified by the procedure given. The compounds were analyzed for C, H and N; and the values agreed with the theoretical ones. The melting points of

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[1] C. Hoffman, *Ber.*, **22**, 2854 (1889).

[2] A. H. Blatt, "Organic Syntheses," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 67.

[3] E. Oliveri-Mandala, *Gazz. chim. ital.*, **40I**, 102 (1910).

[4] E. Oliveri-Mandala, *ibid.*, **46I**, 298 (1916).

[5] H. Hunt, "Experiments in Physical Chemistry," Edwards Brothers, Ann Arbor, Michigan, 1945, pp. 87–89.

all except one[6] agreed with the values recorded in the literature. A melting point of 42–43° was found for *n*-butyrohydroxamic acid.

In general hydroxamic acids are such weak acids in water that when they are titrated with sodium hydroxide potentiometric titration curves with satisfactory inflection points cannot be obtained. Therefore, the ionization constant of each hydroxamic acid given in Table I was determined by employing the following procedure. After the *p*H of a solution of the free acid and its sodium salt was measured, the K_a was found by solving the usual ionization constant expression, where $[A^-]$ the conjugate base of the hydroxamic acid was obtained from

$$[\mathrm{Na}^+] + [\mathrm{H}^+] = [\mathrm{OH}^-] + [\mathrm{A}^-]$$

TABLE I

THE IONIZATION CONSTANTS OF SOME HYDROXAMIC ACIDS

In these experiments no diverse salt was used to adjust the ionic strengths of the solutions to a given value.

Hydroxamic acid	At Equilibrium Molarity of $(A^- + HA) \times 10^2$	Molarity of $Na^+ \times 10^3$	*p*H of soln.[a]	$K_a \times 10^9$
Aceto	1.00	4.98	9.39	0.40
Benzo	1.00	4.98	8.88	1.3
n-Butyro	1.00	4.98	9.47	0.33
p-Chlorobenzo	0.500	2.47	8.58	2.6
p-Methoxybenzo	0.500	2.47	8.99	1.0
α-Naphtho[b]	0.100	1.00	9.40	2×10^1
Phenylaceto	1.00	4.98	9.18	0.65
Propiono	1.00	4.98	9.45	0.35
Salicylo	0.500	2.13	7.25	42

[a] Average value of two runs. [b] The sodium salt was used, for the free acid is very insoluble in water.

The effects of ionic strength and concentration of the buffer mixture on the ionization constant of benzohydroxamic acid were investigated. The results showed that the effects of these two variables are very small. As the ionic strength is varied from 0.5 to 1.00, the K_a changes from 1.3×10^{-9} to 2.1×10^{-9}. If the ionic strength is held constant, the K_a varies from 1.6×10^{-9} to 3.0×10^{-9} as the volume is increased from 100 to 1000 ml.

The values given for the ionization constants of the hydroxamic acids listed in Table I do not agree with those reported in the literature.[3,4] In each case the literature value is about 100 times larger than the one that was obtained by the previously mentioned procedure. Since the values given in the literature were calculated from electrical conductance data, the K_a of the benzohydroxamic acid was evaluated by this method.

The equivalent conductances of the solute (Table II) were plotted against the square roots of the corresponding ionic strengths; and upon extrapolating the latter to zero, the equivalent conductance of potassium benzohydroxamate at infinite dilution was found to be 82. The equivalent conductance of the free benzohydroxamic acid was then calculated to be 358 by applying Kohlrausch's law.

The equivalent conductances of 1.000×10^{-3} and 1.000×10^{-2} *M* benzohydroxamic acid solutions were found by employing the previously mentioned procedure. The ionization constant was calculated at the two concentrations, and the values are given in Table III.

TABLE II

CONDUCTANCE DATA FOR POTASSIUM BENZOHYDROXAMATE AT VARIOUS CONCENTRATIONS

Potassium benzohydroxamate, *M*	Specific conductance of soln.	Specific conductance of solute	Equiv. conductance of solute
1.000×10^{-1}	4.78×10^{-3}	4.78×10^{-3}	47.8
1.000×10^{-2}	5.52×10^{-4}	5.50×10^{-4}	55.0
1.000×10^{-3}	5.94×10^{-5}	5.78×10^{-5}	57.8
1.000×10^{-4}	8.58×10^{-6}	7.00×10^{-6}	70.0

TABLE III

CONDUCTANCE DATA FOR CALCULATING THE IONIZATION CONSTANT OF BENZOHYDROXAMIC ACID

Benzohydroxamic acid, *M*	1.000×10^{-3}	1.000×10^{-2}
Specific conductance of soln.	3.64×10^{-6}	1.00×10^{-5}
Specific conductance of solute	2.06×10^{-6}	8.4×10^{-6}
Equiv. conductance of solute	2.06	0.84
Degree of ionization	0.0058	0.0023
K_a = ionization constant	3.4×10^{-8}	5.3×10^{-8}

Upon comparing the data in Tables I and III, it can be seen that the two methods which were used for determining the ionization constant of benzohydroxamic acid give different results. Several reasons for this discrepancy may be postulated. In order to determine the equivalent conductance of the potassium salt at infinite dilution a fairly long extrapolation is required. In solution it is questionable whether large organic ions adhere to Kohlrausch's law. If the sample of benzohydroxamic acid contained a fraction of 1% of a highly ionizable impurity or if a small amount of carbon dioxide were present in the solution, serious errors would have been introduced. For these reasons the authors consider that in the case of a hydroxamic acid, data obtained from the measurement of the *p*H of a buffer solution yield a more correct value for the ionization constant than conductance data.

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[6] L. Francesconi and A. Bastianini, *Gazz. chim. ital.*, **34I**, 432 (1904).

The Effect of Anion Exchange Resins on Reducing Sugars

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In a recent joint communication from this Laboratory and the Textile Research Institute, Princeton, N. J.,[1] the interconversion and degradation of sugars on anion exchange resins were described. Subsequent work has revealed facts which necessitate the correction and amplification of this report.

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[1] E. Pacsu and L. Rebenfeld, THIS JOURNAL, **75**, 4370 (1953).