Preparation and Properties of *N*-Arylhydroxamic Acids†

Rama Pande and S. G. Tandon*

Department of Chemistry, Ravishankar University, Raipur-492 002, India

The preparation and properties of eight new *N*-arylhydroxamic acids are reported.

The preparation and properties of a number of *N*-arylhydroxamic acids of the general formula,

$$\begin{matrix} R_1-N-OH \\ | \\ R_2-C=O \end{matrix}$$

were reported from this laboratory (*1*-*11*).

In the present communication the preparation and properties of eight new *N*-arylhydroxamic acids, of which six are derived from *N*-(*p*-chlorophenyl)hydroxylamine and two from *N*-*m*-tolylhydroxylamine, are described. Earlier attempts in the preparation of some of these compounds had not succeeded (*1*, *6*). On acylation of the *N*-arylhydroxylamine with acid chloride, oily products were obtained which could not be transformed into crystalline compounds. It is a common experience that hydroxylamine derivatives have a tendency to form oily products which by use of proper crystallizing solvents change into crystalline compounds. The formation of oils can as well be avoided by proper choice and control of experimental variables. In the present study both these approaches have been utilized and met with success. The general procedure reported earlier (*2*) for the preparation of *N*-arylhydroxamic acids was adopted with modifications. Use of a mixture of diethyl ether and petroleum ether (boiling range 40–60 °C) as reaction medium instead of diethyl ether alone, reaction at lower temperature but for longer period, efficient neutralization of liberated hydrochloric acid, inert atmosphere (CO_2), and use of highly purified hydroxylamine generally helped in the formation of crystalline product. These hydroxamic acids are generally sparingly soluble in petroleum ether and freely soluble in diethyl ether and hence addition of petroleum ether to the reaction mixture generally led to the formation of crystalline products. Still, in two preparations formation of oily products could not be avoided and oils were converted with difficulty into crystalline compounds by slow cooling of their dilute solutions in 95% ethanol to low temperatures (–30 °C). Solid product, thus obtained, did not change in oil unless heated for long periods in solvents.

Experimental Section

Materials and Apparatus. UV spectra of the hydroxamic acids were recorded on a Carl-Zeiss, Jena SPECORD recording spectrophotometer using 10-mm matched silica cells. Fixed wavelength measurements for the calculation of molar absorptivities were made with an Electronic Corporation of India, Model GS 865, spectrophotometer. Molar absorptivity is expressed in units of L mol^{-1} cm^{-1}. Specially purified solvents (*12*) were used for spectroscopic work. The spectroscopic grade ethyl alcohol was prepared by twice distilling 95% ethyl alcohol over silver nitrate and potassium hydroxide. B.D.H. AnalaR dioxane was refluxed successively over solid potassium hydroxide and sodium metal and distilled twice before use. A graduated apparatus of standard calibration was used for measurements. All melting points were measured using a calibrated thermometer by the capillary method and are uncorrected.

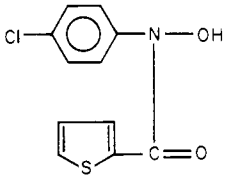
IR spectra were recorded on Perkin-Elmer Model 221 or Model 177 spectrophotometers as KBr pellets.

Preparation. *N*-(*p*-Chlorophenyl)hydroxylamine, mp 86 °C, and *N*-*m*-tolylhydroxylamine, mp 68 °C (*6*), were freshly prepared and scrupulously purified.

All of the acid chlorides were prepared by the action of excess thionyl chloride on the corresponding carboxylic acids (13) and vacuum distillation. The boiling points and yields of these acid chlorides were in agreement with literature values (*13*). Precautions were exercised in the distillation of *o*-nitrobenzoyl chloride (*13*) which is an explosive. Conversion of *o*- and *p*-bromobenzoic acids to the respective acid chlorides required longer period of reflux and treatment with 80–100% excess thionyl chloride.

A typical preparation of *N*-arylhydroxamic acid is described below.

***N*-(*p*-Chlorophenyl)-2-thenohydroxamic Acid (CPTHA).** In



a two-necked round-bottom flask fitted with a dropping funnel and a thermometer, 4.3 g (0.03 mol) of freshly crystallized *N*-(*p*-chlorophenyl)hydroxylamine in 20 mL of diethyl ether, 10–15 mL of petroleum ether (boiling range 40–60 °C), and a slurry of 8.4 g (0.1 mol) of sodium bicarbonate in 5 mL of water were cooled to 0 °C and vigorously stirred with a magnetic stirrer in an atmosphere of CO_2. A solution of 4.4 g (0.03 mol) of freshly distilled 2-thienyl chloride in 20 mL of diethyl ether was added dropwise over a period of 1 h. After the addition was completed, stirring of the mixture at 0 °C or below was continued for 0.5 h. Some of the product precipitated which was separated and reserved. The mixed ethereal solution was evaporated under vacuum to get more product. This residue was combined with precipitated product and triturated in a glass mortar for 15 minutes with a saturated solution of sodium bicarbonate in water to remove the acid and other impurities. The solid was filtered off, washed with cold water, and air-dried, mp 140 °C. The yield of once crystallized product was 6.1 g (80%). On crystallization from a mixture of benzene and petroleum ether (boiling range 60–80 °C), the melting point was raised to 143 °C. One more crystallization gave a product in the form of fine needles, with unchanged melting point, which on drying over P_2O_5 was found suitable for analytical work.

Following this procedure all of the hydroxamic acids could be prepared except those derived from *m*-tolylhydroxylamine which produced sticky brown oils. Dissolution of oil in a minimum volume of benzene and dilution with the maximum possible volume of petroleum ether (boiling range 60–80 °C) and gradual cooling up to –20 °C gave a brown solid after 7 days. Charcoal treatment of this product in cold benzene gave a colorless solution which on addition of petroleum ether and deep freezing gave a crystalline product.

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Table I. Properties of Hydroxamic Acids[a]

compd no	hydroxamic acid	formula	mol wt	mp, °C	yield, %	λ_{max}, nm	$10^{-3}\epsilon$, L mol^{-1} cm^{-1}	ν(O-H), cm^{-1}	ν(C=O), cm^{-1}
1	*N*-(*p*-chlorophenyl)-*o*-bromobenzo-	$C_{13}H_9NO_2ClBr$	326.58	151	89	264	13.0	3100	1625
2	*N*-(*p*-chlorophenyl)-*p*-bromobenzo-	$C_{13}H_9NO_2ClBr$	326.58	162	76	275	12.5	3180	1600
						238	13.0		
3	*N*-(*p*-chlorophenyl)-*o*-nitrobenzo-	$C_{13}H_9N_2O_4Cl$	292.68	165	67	259	19.0	3150	1638
4	*N*-(*m*-tolyl)-1-naphtho-	$C_{18}H_{15}NO_2$	277.32	126	53	284	9.5	3060	1622
						225	50.0		
5	*N*-(*p*-chlorophenyl)-1-naphtho-	$C_{17}H_{12}NO_2Cl$	297.74	171	82	282	12.5	3100	1618
						222	43.0		
6	*N*-(*m*-tolyl)-2-theno-	$C_{11}H_9NOS$	230.26	80	76	290	11.0	3100	1602
						255	9.5		
7	*N*-(*p*-chlorophenyl)-2-theno-	$C_{11}H_8NO_2ClS$	253.70	143	80	295	17.0	3190	1580
						254	11.5		
8	*N*-(*p*-chlorophenyl)-*p*-chlorophenoxyaceto-	$C_{14}H_{11}NO_3Cl_2$	312.15	163	50	260	18.5	3170	1658
						228	14.0		

[a] Elemental analyses for C, H, N, and Cl etc. were in agreement with theoretical values. IR spectra were determined as KBr pellets while UV spectra were determined in 95% ethanol. Yields are reported in terms of once crystallized product.

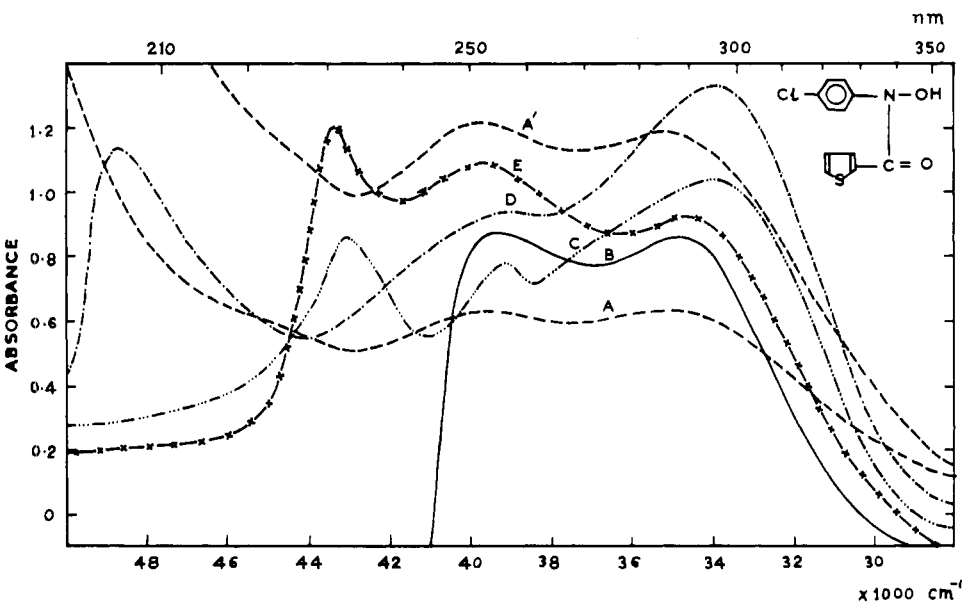

Figure 1. Effect of solvents on UV absorption spectra: A and A', water; B, chloroform; C, dioxane; D, ethanol, 95%; E, cyclohexane.

Discussion

All the hydroxamic acids are white crystalline compounds except *N*-(*p*-chlorophenyl)-*o*-nitrobenzohydroxamic acid which is light yellow. These are stable to normal storage. Their solutions in water, chloroform, and ethanol are stable for several weeks when stored in amber bottles at room temperature. The solutions of hydroxamic acids in sodium carbonate or hydroxide are very unstable and gradually acquire light blue, deep green, and brown color and finally give a greenish brown precipitate. Solutions in mineral acids are also unstable. Hydroxamic acids derived from 2-thenoic acid are more stable than PBHA in both solid state and solutions. These are sparingly soluble in water but display enhanced solubility in mineral acid solutions. Hydroxamic acids are protonated in acidic solutions and the protonated species being hydrophilic in nature is presumably responsible for enhanced solubility in solutions of increasing acid concentration. However, protonation alone cannot account for the increased solubility quantitatively and, therefore, other factors such as salting-in effect of acid may also be responsible for the enhanced solubility.

All of the hydroxamic acids are soluble in common organic solvents and gave the characteristic colorations with ferric chloride in weakly acidic media. Aqueous ammonium metavanadate in more than 2 M hydrochloric acid, when added to these acid solutions, in water-immiscible solvents gave characteristic violet extracts.

The ultraviolet spectra were obtained primarily for characterizing the newly prepared compounds. The applicability of Beer's law for each hydroxamic acid at the absorption band was confirmed for calculating the molar absorptivities. The data are presented in Table I. The influence of solvents on the ultraviolet spectra of *N*-(*p*-chlorophenyl)-2-thenohydroxamic acid (CPTHA) is shown in Figure 1. The bands are sharp in nonpolar solvents. In ethanol too the bands are fairly well defined but in water the bands become broader or are obliterated. With increasing polarity of solvents the solvent–solute interactions become pronounced and are responsible for differences in spectra.

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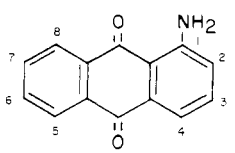
Synthesis and Fluorescence Properties of Halogenated Aminoanthraquinones

Jules Weinstein,† Richard C. Clapp,* Masato Nakashima, and John A. Sousa

U.S. Army Natick Research and Development Command, Natick, Massachusetts 01760

Derivatives of 1-aminoanthraquinone containing the heavy atoms bromine and iodine have been prepared, and their relative fluorescence intensities in three solvents have been determined. The results demonstrate that the fluorescence of 1-aminoanthraquinone can be significantly reduced by appropriate substitution.

In an attempt to identify groups that would reduce or control the level of fluorescence in aminoanthraquinones, we have prepared a number of derivatives of 1-aminoanthraquinone (**1**)



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containing the heavy atoms bromine and iodine. Although various bromo derivatives of 1- and 2-aminoanthraquinone have been described and are important intermediates in the synthesis of anthraquinone dyes (*1*), to our knowledge no iodo derivatives of an aminoanthraquinone have been reported. Application of the Sandmeyer reaction to the preparation of the 4-chloro and 4-bromo derivatives of 1-aminoanthraquinone has been reported (*2*), and we have employed this reaction for the preparation of 1-amino-4-iodoanthraquinone. 1-Amino-4-(benzoylamino)-anthraquinone, prepared from 1,4-diaminoanthraquinone by monobenzoylation, was converted to 1-(benzoylamino)-4-iodoanthraquinone through the diazonium salt. Removal of the benzoyl group by hydrolysis yielded 1-amino-4-iodoanthraquinone. 1-Amino-5-iodoanthraquinone was prepared from 1,5-diaminoanthraquinone by the same sequence of reactions.

Attempts to prepare 1-amino-2-iodoanthraquinone from 2-amino-1-(benzoylamino)anthraquinone in a similar manner were unsuccessful since the starting material underwent cyclization to an imidazole under the reaction conditions required for the Sandmeyer reaction. Although 1-amino-2-bromoanthraquinone is readily obtained by bromination of 1-aminoanthraquinone, attempts to iodinate 1-aminoanthraquinone under a variety of conditions were not successful.

The fluorescence spectra of the iodo derivatives were measured, and the intensities of the fluorescence bands at the peaks relative to the fluorescence intensity of 1-aminoanthraquinone were determined. Since light emission intensity was found to be strongly influenced by environment, measurements were carried out in three solvents: benzene (nonpolar), acetonitrile (polar), and ethanol (polar and hydrogen bonding). The data, normalized to the same scale, are given in Table I, together with data obtained for some bromo derivatives of 1-aminoanthraquinone. The results demonstrate that the fluorescence intensity of 1-aminoanthraquinone can be significantly reduced by the introduction of bromine or iodine. The combination of a halogen atom and an acetyl or benzoyl substituent on the amino group is particularly effective in reducing the intensity.

Experimental Section

Melting points were obtained in capillary tubes in a Mel-Temp apparatus and are corrected. The fluorescence spectra were determined in a Perkin-Elmer MPF-3 spectrofluorometer equipped with a correction attachment and the infrared spectra in Perkin-Elmer spectrometers, Models 267 and 521. Merck-Darmstadt silica gel, 0.05–0.2 mm, 70–325 mesh ASTM, was used for column chromatography. TLC was carried out on plates of silica gel GF with benzene as eluent for the iodo derivatives. Elemental analyses were performed by Midwest Microlab, Indianapolis, Ind., and were in agreement with theoretical values and have been submitted for review.

1-Amino-4-iodoanthraquinone. 1-Amino-4-(benzoylamino)anthraquinone was prepared by treatment of 1,4-diaminoanthraquinone with a slight excess of benzoyl chloride in nitrobenzene and pyridine at 140 °C (*3*).

To 6 mL of concentrated sulfuric acid at 20 °C was added 1.71 g (5.0 mmol) of 1-amino-4-(benzoylamino)anthraquinone with stirring over 25–30 min. Sodium nitrite (375 mg, 5.4 mmol) was then added over 20–25 min, and stirring at 20 °C was continued for 2 h. The reaction mixture was added in portions to 200 g of ice and 100 mL of water, and after 10–15 min of stirring the mixture, the brown precipitate of diazonium salt was filtered off and washed once with ice water. To a vigorously stirred mixture of the brown precipitate and 950 mL of water was added 3.4 g (20 mmol) of potassium iodide. After the resulting mixture had been stirred at room temperature for 1.5 h and on the steam bath for 1 h, cooling and filtration afforded 1.83 g (81% crude yield) of 1-(benzoylamino)-4-iodoanthraquinone, melting from 175 to 190 °C.

A 500-mg portion of the 1.83 g and 3 mL of concentrated sulfuric acid were heated on the steam bath for 25 min. The cooled mixture was poured onto ice, and filtration gave 387 mg of a dark red solid. A 250-mg portion of this product was chromatographed in benzene solution on a silica gel column with benzene as eluent. An orange-red band was collected from the

† Deceased May 7, 1976.