

Evidently the chemical proof of structure² of our isopropylthiophene (based on the oxime and *p*-nitrophenylhydrazone of 2-isopropyl-5-acetylthiophene³) accounted for only the major component (ca. 75%) of the mixture.

(3) Scheibler and Schmidt, *Ber.*, **54**, 139 (1921).

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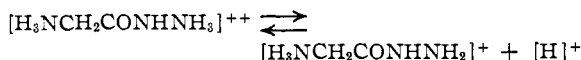
The Apparent Ionization Constants of Acetylhydrazide and Glycylhydrazide

BY CARL R. LINDEGREN¹ AND CARL NIEMANN

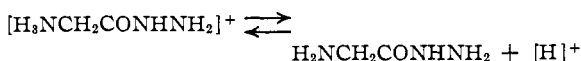
In considering the reactions of glycylhydrazide with nitrous acid² the apparent ionization constants of acetylhydrazide and glycylhydrazide have been determined at $24 \pm 1^\circ$ and $25 \pm 2^\circ$, respectively. With the former compound potentiometric titration of approximately 0.1 formal solutions, which were also 0.05, 0.10 or 0.20 formal in sodium chloride, with standard hydrochloric acid indicated that pK'_A was independent of the ionic strength over the range studied and had a value of 3.24 for the reaction



The titration data for glycylhydrazide, obtained as described below, were evaluated by the method of Britten³ because preliminary calculations indicated that the two constants were not sufficiently separated to permit evaluation on the basis of assumed non-interaction. pK'_{A_1} was found to have a value of 2.38 and pK'_{A_2} a value of 7.69. From these data and those available for other derivatives of glycine⁴ it is not unreasonable to assume that $pK_{A_1} = 2.38$ for the reaction



and $pK'_{A_2} = 7.69$ for the reaction



since the ionization constants of all the simpler α -amino acid esters and amides are in the neighborhood of $pK'_A = 7.7$.⁴ The greater acidity of the hydrazinium group in the doubly protonated glycylhydrazide relative to the singly protonated acetylhydrazide appears to be a logical consequence of the presence of the positively charged ammonium group in the former compound though the difference ($\Delta pK = 0.86$) is only approximately one-half of that obtaining in the case of $[\text{CH}_3\text{CH}_2\text{CH}_2\text{NH}_3]^+ - [\text{NH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_3]^{++}$ ($\Delta pK = 10.6 - (8.6 + 0.3) = 1.7$) if 0.3 is added to the

(1) Present address: Department of Chemistry, University of California at Los Angeles.

(2) T. Curtius and L. Levy, *J. prakt. Chem.*, **70**, 89 (1904).

(3) H. T. S. Britten, "Hydrogen Ions," 3rd edition, Vol. I, Van Nostrand, New York, N. Y., 1943, pp. 197-200.

(4) E. J. Cohn and J. T. Edsall, "Proteins, Amino Acids and Peptides," Reinhold Publ. Corp., New York, N. Y., 1943.

observed pK'_{A_1} of the latter species to correct for a statistical factor of two.⁵

Experimental

Reagents.—Acetylhydrazide, prepared from redistilled ethyl acetate and 85% hydrazine⁶ was recrystallized twice from an ether-chloroform mixture and dried over potassium hydroxide. Glycylhydrazide was prepared essentially as described by Curtius and Levy,² the product recrystallized as described above and dried over phosphorus pentoxide.

Procedure.—Solutions were prepared which were approximately 0.10 formal in acetylhydrazide or 0.05 formal in glycylhydrazide and 0.05, 0.10 or 0.20 formal in sodium chloride. Five-ml. aliquots of these solutions were titrated with standard 0.10 normal hydrochloric acid using a Beckman Model G pH meter equipped with a Beckman type E glass electrode. In every case the pH meter was calibrated against a standard buffer solution before a titration.

Results.—With acetylhydrazide five determinations using solutions 0.20 formal in sodium chloride gave a value for pK'_{A_1} for the first half of the titration curve of 3.21 ± 0.10 ; five determinations using solutions 0.10 formal in sodium chloride a value of 3.25 ± 0.10 ; and three determinations with solutions 0.05 formal in sodium chloride a value 3.23 ± 0.05 . The average of all determinations was 3.24. With glycylhydrazide the following values were obtained for pK'_{A_1} and pK'_{A_2} in the order named: with 0.2 formal sodium chloride 2.38 and 7.68, 2.36 and 7.68; with 0.1 formal sodium chloride 2.42 and 7.68, 2.40 and 7.73; and with 0.05 formal sodium chloride 2.36 and 7.69; 2.38 and 7.67. The average of all of the above was $pK'_{A_1} = 2.38$ and $pK'_{A_2} = 7.69$.

(5) The authors are indebted to Dr. J. T. Edsall for bringing this relation to their attention.

(6) T. Curtius and T. S. Hoffman, *J. prakt. Chem.*, **53**, 513 (1896).

CONTRIBUTION No. 1256

GATES AND CRELLIN LABORATORIES OF CHEMISTRY
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The Preparation of 2-Nitro-3,4-xylenol

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A need for 2-nitro-3,4-xylenol, for which no preparation has been described, prompted its synthesis in this Laboratory. The method selected was the sulfonation of 3,4-xylenol in the 6-position and nitration in the 2-position, followed by desulfonation. The well-known exchange of nitro- for sulfo-group during nitration of phenol-sulfonic acids occurred here, and some 2,6-dinitro-3,4-xylenol was always formed. However, by varying the temperature and the amounts of nitric and sulfuric acids used, conditions were found which permitted yields of 40% to be obtained.

It was observed that the 2,6-dinitro-3,4-xylenol, m.p. 125-126°² separating during nitration carried 2-nitro-3,4-xylenol with it to form a molecular compound, m.p. 67-68°. The presence of 2-nitro-3,4-xylenol here indicates that the reaction conditions bring about nitration and some desulfonation without introducing a second

(1) This note was taken from the thesis submitted by Walter S. Pelton to the Committee on Graduate Study of the University of Tennessee in partial fulfillment of the requirements for the M.S. degree.

(2) Datta and Varma, *THIS JOURNAL*, **41**, 2039 (1919).

nitro-group, and represents a certain loss of the desired product.

Proof of the structure was obtained by reduction to 2-amino-3,4-xyleneol, m.p. 138–139°. The previously reported value for this aminophenol, prepared by reducing 6-hydroxy-2,3-dimethylazobenzene, was 126°. Repetition of this earlier work gave a compound, m.p. 138–139°, identical with that obtained from the nitrophenol.

Experimental

2-Nitro-3,4-xyleneol.—Purified 3,4-xyleneol, 122 g. (1.0 mole) was dissolved in 122 ml. of concentrated sulfuric acid and the solution warmed on the steam-bath until reaction was under way and the temperature had risen to 60–70°. Heating was then discontinued and the mixture stirred until crystallization occurred, and to the cooled mixture 600 ml. of water and 240 ml. of concentrated sulfuric acid were added. Nitration was accomplished by adding 70 ml. of nitric acid, sp. gr. 1.42 (1.1 moles), diluted with 100 ml. of water, dropwise, with stirring at 0–5° and allowing the temperature to remain thus for an hour after addition was complete. The mixture was poured into 1200 ml. of ice-water and filtered from the precipitated nitroxyleneols. Sodium chloride added to the clear filtrate salted out 2-nitro-3,4-xyleneol-6-sulfonic acid as a thick, orange precipitate. The latter was collected, the filtrate saturated with salt and a second crop of sulfonic acid collected after cooling for several hours. The crude nitrosulfonic acid was steam distilled at 130–140° from an initial volume of 1050 ml. of 70% sulfuric acid. After the initial distillate, mainly 3,4-xyleneol, 2-nitro-3,4-xyleneol, crystallizing in the condenser as an orange solid, was collected. After separating and drying this, it was recrystallized once from petroleum ether (b. p. 60–90°) yielding 68 g. (41%) of a slightly impure product, m. p. 67–70°. After recrystallizing six times from the same solvent it melted at 71.5–72.0°.

Anal. Calcd. for $C_8H_9O_3N$: C, 57.48; H, 5.43; N, 8.38. Found: C, 57.46, 57.58; H, 5.21, 5.25; N, 8.51, 8.61.

Nitration in glacial acetic acid and at lower and higher temperatures proved less satisfactory. Also, the amount of nitric acid proved to be critical. For example, 0.25-mole quantities of the xyleneol in corresponding amounts of water and sulfuric acid were sulfonated and then nitrated at 0–5° with 40-ml. quantities of nitric acid in varying concentrations:

Moles of HNO_3 in 50 ml. of solution	Yield of crystallized 2-nitro-3,4-xyleneol Grams	Crude precipitated nitroxyleneols, %	Crude precipitated nitroxyleneols, g.
0.22	10.6	25	2.6
.28	16.7	40	4.0
.34	13.9	33	7.1
.40	6.0	14	9.0

The crude nitroxyleneols, precipitating on dilution of the nitrated mixture, when dried and treated with petroleum ether separated into a soluble portion, crystallizing on cooling, m. p. 67–68°, and an insoluble fraction which was recrystallized from alcohol. The latter was 2,6-dinitro-3,4-xyleneol, m. p. 122.5–124.0°. The low-melting material was not identical with 2-nitro-3,4-xyleneol and could be made to yield the 2,6-dinitro-compound on crystallization from alcohol. An equimolecular mixture of the 2-nitro- and 2,6-dinitroxyleneols melted at 67–68° and did not depress the m. p. of the above material.

2,4-Dinitrophenyl 2-Nitro-3,4-Xylyl Ether.—This derivative was prepared by the procedure of Bost and Nicholson,⁴ and recrystallized three times from ethyl alcohol; m. p. 157.0–157.5°.

Anal. Calcd. for $C_{14}H_{11}O_7N_3$: C, 50.45; H, 3.33;

(3) Hinkel, Ayling and Bevan, *J. Chem. Soc.*, 2529 (1928).

(4) Bost and Nicholson, *ibid.*, 57, 2368 (1935).

N, 12.61. Found: C, 50.41, 50.35; H, 3.15, 3.25; N, 12.38, 12.14.

2-Amino-3,4-xyleneol.—Reduction of 2 g. of the nitrophenol with 10 g. of sodium hydrosulfite, 5 g. of sodium bicarbonate and 33 ml. of water⁵ gave a solid which darkened readily. This was decolorized in alcoholic solution, the solvent removed *in vacuo* and the buff-colored residue recrystallized from benzene. The m. p. was 138–139°.

Catalytic reduction in absolute alcohol at 50 p. s. i. over palladium-on-charcoal catalyst⁶ gave the identical compound in 98% yield.

Anal. Calcd. for $C_8H_{11}ON$: C, 70.05; H, 8.06; N, 10.21. Found: C, 70.15, 70.12; H, 7.82, 7.89; N, 10.10, 10.16.

6-Hydroxy-2,3-dimethylazobenzene was prepared and purified as described by King.⁷ It was reduced to 2-amino-3,4-xyleneol in accordance with the previously published procedure⁸ and the product purified. The m. p. and mixed m. p.'s with samples prepared by the above methods were all 138–139°.

2-Acetamino-3,4-xyleneol.—The aminophenol, 0.5 g., was treated with 2 ml. of acetic anhydride, the resulting solid dissolved in 10% potassium hydroxide and the desired derivative precipitated with dilute acid; yield 0.35 g., m. p. 159–160° after four recrystallizations from benzene.

Anal. Calcd. for $C_{10}H_{13}O_2N$: C, 67.02; H, 7.31; N, 7.81. Found: C, 67.05, 66.94; H, 7.11, 7.09; N, 7.77.

(5) Hodgson and Beard, *J. Chem. Soc.*, 127, 498 (1925).

(6) Hartung, *This Journal*, 50, 3370 (1928).

(7) King, *J. Chem. Soc.*, 1157 (1939).

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A Simple Device for Regulating Pressure or Vacuum

By J. HOWARD MUELLER

In certain experimental procedures it is often necessary to apply moderate air pressure to a piece of apparatus over a considerable period of time. The increasing use of chromatographic columns for various purposes is a case in point. A simple device which may readily be constructed at little expense has proved extraordinarily useful for this purpose and possibly merits brief description. A compressed air supply is essential to its use, but this is almost universally available.

The principle employed is to form a valve between a stainless steel ball and a narrow "seat" turned in the end of a hole drilled through a lucite or metal rod. By applying more or less pressure on top of the ball, a slow stream of air passing upward through the hole is impeded, and variable pressures are obtained in a closed system of which this valve forms the outlet. The drawing illustrates the manner in which this may be accomplished. The stem of the regulator passes through a stopper inserted into a small filter flask, which is connected to the system. A very slow stream of air is admitted by slight opening of an ordinary valve on the supply line, and the pressure is set where desired by regulating the tension on the spring by means of the knurled headed screw. The air escapes through a small vent drilled in the wall of the cylinder just above the ball. In this way,