Evidently the chemical proof of structure[2] of our isopropylthiophene (based on the oxime and *p*-nitrophenylhydrazone of 2-isopropyl-5-acetylthiophene[3]) accounted for only the major component (*ca.* 75%) of the mixture.

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

Koppers Multiple Fellowship on Tar Synthetics
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Pittsburgh, Penna.
Received January 13, 1949

The Apparent Ionization Constants of Acethydrazide and Glycylhydrazide

By Carl R. Lindegren[1] and Carl Niemann

In considering the reactions of glycylhydrazide with nitrous acid[2] the apparent ionization constants of acethydrazide and glycylhydrazide have been determined at 24 ± 1° and 25 ± 2°, 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

$$[CH_3CONHNH_3]^+ \rightleftarrows CH_3CONHNH_2 + [H]^+$$

The titration data for glycylhydrazide, obtained as described below, were evaluated by the method of Britten[3] 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 glycine[4] it is not unreasonable to assume that $pK_{A_1} = 2.38$ for the reaction

$$[H_3NCH_2CONHNH_3]^{++} \rightleftarrows [H_3NCH_2CONHNH_2]^+ + [H]^+$$

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

$$[H_3NCH_2CONHNH_2]^+ \rightleftarrows H_2NCH_2CONHNH_2 + [H]^+$$

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 acethydrazide 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 $[CH_3CH_2CH_2NH_3]^+ - [NH_3CH_2CH_2CH_2NH_3]^{++}$ ($\Delta pK = 10.6 - (8.6 + 0.3) = 1.7$) if 0.3 is added to the observed pK'_{A_1} of the latter species to correct for a statistical factor of two.[5]

Experimental

Reagents.—Acethydrazide, prepared from redistilled ethyl acetate and 85% hydrazine[6] 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 acethydrazide 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 *p*H meter equipped with a Beckman type E glass electrode. In every case the *p*H meter was calibrated against a standard buffer solution before a titration.

Results.—With acethydrazide five determinations using solutions 0.20 formal in sodium chloride gave a value for pK'_A 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 $pK'_{A_2} = 7.69$.

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[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.

[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
California Institute of Technology
Pasadena 4, Calif.
Received November 26, 1948

The Preparation of 2-Nitro-3,4-xylenol

By George P. Mueller and Walter S. Pelton[1]

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 phenolsulfonic 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

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

Experimental

2-Nitro-3,4-xylenol.—Purified 3,4-xylenol, 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 nitroxylenols. Sodium chloride added to the clear filtrate salted out 2-nitro-3,4-xylenol-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-xylenol, 2-nitro-3,4-xylenol, 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 xylenol 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-xylenol		Crude precipitated nitroxylenols, g.
	Grams	%	
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 nitroxylenols, 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-xylenol, m. p. 122.5–124.0°. The low-melting material was not identical with 2-nitro-3,4-xylenol 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-dinitroxylenols 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; N, 12.61. Found: C, 50.41, 50.35; H, 3.15, 3.25; N, 12.38, 12.14.

2-Amino-3,4-xylenol.—Reduction of 2 g. of the nitrophenol with 10 g. of sodium hydrosulfite, 5 g. of sodium bicarbonate and 33 ml. of water[5] 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 catalyst[6] 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-xylenol in accordance with the previously published procedure[3] 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-xylenol.—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.

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RECEIVED NOVEMBER 8, 1948

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

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

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

[6] Hartung, THIS JOURNAL, **50**, 3370 (1928).

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

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,