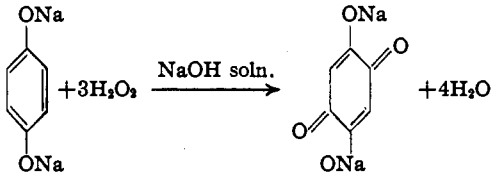
m-hydroxybenzoic acid, *p*-hydroxybenzoic acid, phenol, catechol, resorcinol and hydroquinone.

It has now been found that good yields of 2,5-dihydroxyquinone can be obtained by rapidly oxidizing hydroquinone in concentrated sodium hydroxide solution with 30% hydrogen peroxide. The reaction appears to be represented by the equation:



The red-orange crystalline disodium salt, which precipitated from the sodium hydroxide solution during the reaction, liberates 2,5-dihydroxyquinone upon treatment with acid.

Two factors which greatly influenced the yields of 2,5-dihydroxyquinone were the reaction temperature and the concentration of the sodium hydroxide solution. The reaction, which was exothermic, proceeded extremely slowly below 25°, but in the temperature range of 40 to 60° the oxidation could be completed in about two hours to give 59 to 62% yields of the desired product. At temperatures of 85 to 95° the reaction was vigorous, resulting in a 35% yield of 2,5-dihydroxyquinone.[5]

From a series of reactions carried out at 40–50° it was found that the yield of 2,5-dihydroxyquinone was directly proportional to the concentration of the sodium hydroxide. Thus in 50 and 65% sodium hydroxide solution the yields were 70 and 80%, respectively. When the sodium hydroxide concentration was 20%, only 14% of the 2,5-dihydroxyquinone was obtained while none was obtained with a 15% sodium hydroxide concentration.[6]

The ability of sodium hydroxide to depress the solubility of the disodium salt of 2,5-dihydroxyquinone probably accounts for the increased yields of 2,5-dihydroxyquinone in highly concentrated sodium hydroxide solutions since the disodium salt is almost completely precipitated and thus removed from the action of the hydrogen peroxide. In 15% sodium hydroxide solution the disodium salt appears to be sufficiently soluble that the hydrogen peroxide completely oxidizes it to other products.

In preliminary experiments, solutions of phenol, salicylic acid, resorcinol, catechol, and quinone in 36% sodium hydroxide solution were treated with hydrogen peroxide. After one week, a small yield of the disodium salt of 2,5-dihydroxyquinone was obtained from phenol and salicylic acid. Resorcinol reacted very slowly at room temperature, but no recognizable products were isolated. On the other hand, both catechol and quinone reacted vigorously at or below room temperature giving dark brown solutions which were not further investigated.

(5) In these reactions 0.30 mole of hydroquinone in 330 cc. of 36% sodium hydroxide solution was treated with 120 cc. (1.05 moles) of 27% hydrogen peroxide.

(6) The ratio of reactants was 1.0 mole of 27% hydrogen peroxide, 0.3 mole of hydroquinone and 4.2 moles of sodium hydroxide. The initial concentration of sodium hydroxide was varied by varying the quantity of water used.

Experimental

A specific example is given which will illustrate the general procedure.

A 500-cc. three-necked flask was provided with a dropping funnel, a thermometer and a heavy glass stirrer. In the flask was placed 200 g. of 50% sodium hydroxide solution (2.5 mole) and 27.5 g. (0.25 mole) of hydroquinone. This mixture was well stirred while 100-cc. of 27% hydrogen peroxide (0.88 mole) was added dropwise from the dropping funnel. As soon as the temperature of the reaction reached 45°, the flask was surrounded with an ice-bath and the rate of addition of the hydrogen peroxide was adjusted so that the temperature was maintained between 45 and 50°. About thirty minutes was required for the addition. Stirring was continued for one and one-half hours. The ice-bath was removed, but the temperature was watched closely and kept below 50° by occasional cooling. The reaction mixture now consisted of a thick paste of the red-orange sodium salt of 2,5-dihydroxyquinone. It was worked up in either of the two following ways:

(1) An equal volume of 95% alcohol was added to the mixture, and, after stirring well, the sodium salt was collected on an asbestos mat in a large Büchner funnel. The solid was washed on the filter with two 100-cc. portions of 95% alcohol and then dissolved in the smallest possible volume (1 to 2 liters) of water at 70°. The resulting cherry-red solution was filtered and acidified with concentrated hydrochloric acid to precipitate the yellow crystalline 2,5-dihydroxyquinone which was collected after the mixture had been cooled to room temperature.

(2) The entire reaction mixture was stirred into 500 g. of cracked ice and acidified with a mixture of 225 cc. of 36% hydrochloric acid and 300 g. of ice. The resulting yellow precipitate of 2,5-dihydroxyquinone was collected and washed by suspension in 200 cc. of ice water.

The yield of pure 2,5-dihydroxyquinone (m. p. 212–14° dec.) dried in vacuum over calcium chloride, was 23 to 25 g. (66 to 70%).

THE LILLY RESEARCH LABORATORIES
ELI LILLY AND COMPANY
INDIANAPOLIS INDIANA
RECEIVED JANUARY 29, 1945

A Nomogram for Acetate Buffers[1]

BY WILLIAM C. BOYD

In the preparation and study of proteins, particularly plasma proteins,[2] acetate buffers of known *p*H and ionic strength have proved of the greatest usefulness. The preparation of such buffers is possible from the use of the charts of Green,[3] which were in turn based on data obtained by Cohn, Heyroth and Menkin.[4] It has been found, however, that there is another form in which it is more convenient to use this information.

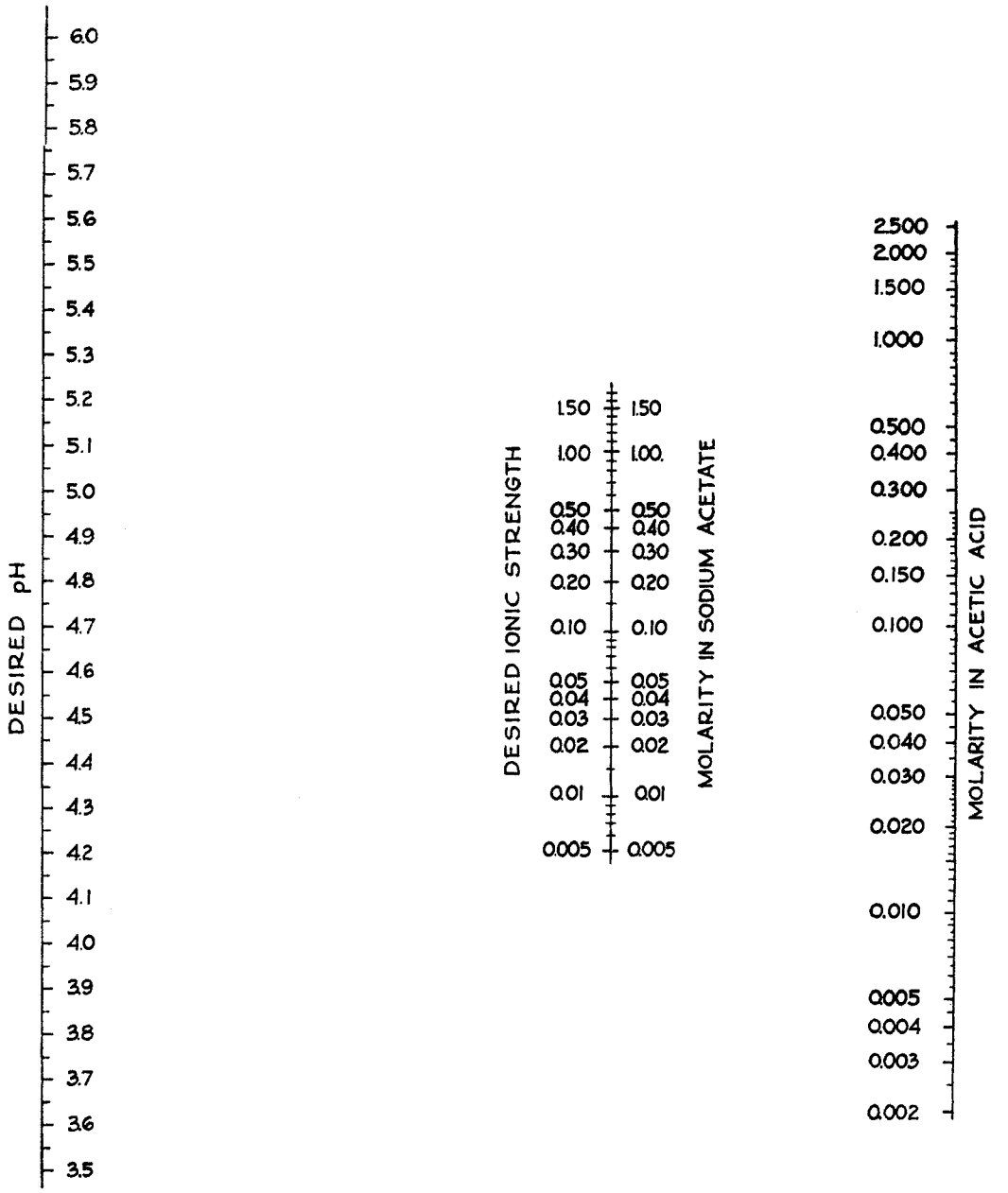
(1) This work was carried out under contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

(2) E. J. Cohn, *et al.*, *J. Clin. Invest.*, **23**, No. 4 (1944).

(3) A. A. Green, THIS JOURNAL, **55**, 2331 (1933).

(4) E. J. Cohn, F. F. Heyroth and M. F. Menkin, *ibid.*, **50**, 696 (1928).

TABLE I
NOMOGRAM FOR ACETATE BUFFERS



This new form is represented by the attached nomographic or alignment chart, which enables buffer mixtures to be made up of sodium acetate and acetic acid varying in ionic strength from 0.005 to 1.50 and of *p*H varying from 3.5 to 6.0. The buffer capacity at these extremes of *p*H is of course much less (about $^1/_{16}$) than that of mixtures at a *p*H corresponding to the *pK* value of acetic acid (about 4.7).

To use the nomogram, it is only necessary to use a stretched thread or ruler, or preferably a ruled black line on some transparent substance such as celluloid, and connect any two of the variables which it is desired to control. These will generally be *p*H and ionic strength. From the intersection with the right-hand scale the molarity of acetic acid which the mixture must contain is easily read off and the required molarity in sodium acetate is read from the middle scale. Molarity of salt is in this case the same as the ionic strength, to a high degree of accuracy.

Nomograms are discussed in the classical book by D'Ocagne,[5] which, however, may prove too mathematical and not practical enough for the

(5) M. D'Ocagne, "Traité de Nomographie," Gauthier-Villars, Paris, 1899.

average reader. Methods of construction of nomograms are discussed in L. J. Henderson's book on blood[6] and in an admirable little book in French by Frechet and Rouillet[7] and in other books, such as those by Swett,[8] Davis[9] and Allcock and Jones.[10]

(6) L. J. Henderson, "Blood, a study in general physiology," Yale University Press, New Haven, Conn., 1928.
(7) M. Frechet, and H. Rouillet. "Nomographie," Armand Colin, Paris, 1928.
(8) G. W. Swett, "Construction of Alignment Charts," John Wiley and Sons, Inc., New York, N. Y., 1928.
(9) D. S. Davis, "Empirical Equations and Nomography," McGraw-Hill Book Company, Inc., New York, N. Y., 1943.
(10) H. J. Allcock, and J. R. Jones, "The Nomogram," 2nd ed., Pitman, N. Y., 1932.

DEPARTMENT OF PHYSICAL CHEMISTRY
HARVARD MEDICAL SCHOOL
BOSTON, MASS. RECEIVED APRIL 3, 1945

Condensation of Vinyl Acetate with Ethyl β-Aminocrotonate

BY JOHN A. KING

Although the instability of aliphatic aldimines is well known,[1] it was hoped that by slow generation of the aldehyde *in situ*, under mild condensing conditions, it might be possible to prepare ethyl β-ethylideneaminocrotonate which then, in the reaction mixture or subsequently, could be cyclized to 2-methyl-4-pyridone. The slow generation of acetaldehyde under condensing conditions was accomplished by the use of vinyl acetate in an aqueous alkaline medium but neither the intermediate ethylideneaminocrotonate nor the pyridone was obtained. Instead there was formed dihydrocollidine dicarboxylic ester, probably via a Hantzsch synthesis[2] from the aldehyde, the amino ester and acetoacetic ester produced by hydrolysis of some of the amino ester.

Although Collie[3] prepared this ester from ethyl β-aminocrotonate and acetaldehyde, he used warm sulfuric acid as the condensing agent and noted that the reactants did not condense if the acid catalyst were omitted.

(1) After this work was done the elegant synthesis of aldimines by Campbell, Sommers and Campbell, THIS JOURNAL, 66, 82 (1944), was published.
(2) Hantzsch, *Ann.*, 215, 8 (1882).
(3) Collie, *ibid.*, 226, 314 (1884).

Experimental

A mixture of ethyl β-aminocrotonate (12.9 g., 0.10 mole), vinyl acetate (17.2 g., 0.20 mole), potassium carbonate (27.6 g., 0.20 mole) and water (100 cc.) was allowed to stand for three weeks at room temperature in a stoppered flask, by which time all the water-insoluble reactants had disappeared and a semi-solid precipitate had formed. This semi-solid material (12.3 g., 92% yield, crude) was recrystallized four times from aqueous ethanol to give a nicely crystalline solid, m. p. 130°. When this was mixed with a sample of dihydrocollidine dicarboxylic ester, m. p. 129–130°, prepared from acetaldehyde ammonia and ethyl acetoacetate by the procedure of Hantzsch,[2] the mixture melted at 129–130°.

RESEARCH LABORATORIES
WINTHROP CHEMICAL COMPANY, INC.
RENSSELAER, NEW YORK RECEIVED MARCH 26, 1945

The Reduction of Ethyl Oxindole-3-glyoxalate under Clemmensen Conditions

BY WARD C. SUMPTER, MARION MILLER AND LAURA NELL HENDRICK

In 1923 Gränacher and Mahal[1] prepared a compound which they designated as oxindoleacetic acid (I) from β-rhodanal oxindole (II) by reduction and subsequent hydrolysis of the reduction product.

(I) (II)

Subsequently Aeschlimann[2] found that Gränacher's "oxindole-acetic acid" was in reality 2-keto-1,2,3,4-tetrahydroquinoline-4-carboxylic acid (III) a fact later recognized by Gränacher and Kouniniotis[3] and confirmed by Hill, Schultz and Lindwall.[4] Aeschlimann found that compound III could be prepared quite readily by the reduction of 2-quinolone-4-carboxylic acid (IV) which in turn was prepared by condensing isatin with malonic acid[2,5] or by the action of alkali on acetylisatin.[2,6]

(III) (IV)

In 1941 Horner[7] prepared ethyl oxindole-3-glyoxalate (V) by condensing ethyl oxalate and

(1) Gränacher and Mahal, *Helv. Chim. Acta*, 6, 467 (1923).
(2) Aeschlimann, *J. Chem. Soc.*, 2902 (1926).
(3) Gränacher and Kouniniotis, *Helv. Chim. Acta*, 11, 1241 (1928).
(4) Hill, Schultz and Lindwall, THIS JOURNAL, 52, 769 (1930).
(5) Borsche and Jacobs, *Ber.*, 47, 354 (1914).
(6) Camps, *Arch. Pharm.*, 237, 687 (1889).
(7) Horner, *Ann.*, 548, 117 (1941).