temperature on the entrainment when precipitation is made in the absence of acrolein. The decrease in entrainment with increasing acidity is doubtless the result of a decreased concentration of sulfide (or hydrosulfide) ions on the surface of the precipitate. Opportunity for the formation of hydrogen sulfide would be increased at the higher concentration of hydrogen ions. This would, in turn, reduce the chance for cobalt sulfide to form on the surface of the precipitate. (That cobalt actually is entrained as the sulfide seems probable, since the precipitate is brown in color.)

The effect of increased temperature in reducing the entrainment is more pronounced at the lower acidity, and roughly the same amount of cobalt is carried down in 0.3 molar acid at 95° as in 1 molar acid at 23° (or 95°).

The action of acrolein in flocculating the precipitate of tin(IV) sulfide doubtless can be explained as in certain other cases.[5] The removal of adsorbed sulfide (or hydrosulfide) ions from the surface of the precipitate by the acrolein is again the chief factor in preventing entrainment of the foreign ion.

The fact that the precipitate of tin(IV) sulfide obtained under these conditions is micro crystalline, as shown by the X-ray diffraction patterns, indicates that no aging takes place. This would result from a large decrease in surface, and consequent reduction of the solubility of the precipitate. As no evidence of postprecipitation of cobalt on tin(IV) sulfide thus prepared was found, it may be supposed that the surface remains covered by the acrolein and its addition products, or that it remains completely bare of any adsorbed layer of ions capable of reacting with the cobalt.

Certain practical aspects of this study might be mentioned in connection with the separation of cobalt and tin. If tin is to be separated as the sulfide in the absence of a flocculating agent, the least entrainment will occur at about 95° from 0.3 molar hydrochloric acid, or from 1 molar acid, regardless of the temperature. However, it is suggested that the precipitation be made in the presence of acrolein, preferably at about 60°. The advantages are: (1) speed in flocculation, filtration, and washing of the tin(IV) sulfide; (2) freedom of the precipitate from cobalt. The disadvantages are: (1) contamination of the filtrate with acrolein and its addition products; (2) the necessity for working in good ventilation. The method obviously operates most favorably for the isolation of tin, when cobalt is to be disregarded.

Summary

1. Freshly precipitated tin(IV) sulfide entrains cobaltous ion by a process which follows a log $\mathbf{x/m}$ *vs.* log $\mathbf{c}$ relation. The entrainment is decreased by increase of temperature and(or) acidity of the solution.

2. The entrainment of cobaltous ion by tin(IV) sulfide can be made negligible by precipitation in the presence of acrolein.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POLYTECHNIC INSTITUTE OF BROOKLYN]

Syntheses in the Pyrazine Series. IV. 2-Sulfanilamidopyrazine

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In view of the valuable bacteriostatic properties exhibited by many heterocyclic sulfanilamide derivatives, it was considered worthy to prepare 2-sulfanilamidopyrazine. For this purpose, aminopyrazine prepared by a method of Gabriel and Sonn[1] which has been modified and improved by Hall[2] and Hall and Spoerri[3] was condensed with N-acetylsulfanilyl chloride. In the line of synthesis of aminopyrazine, however, considerable difficulty was met in isolating pure pyrazine-2,3-dicarboxylic acid after alkaline oxidation of quinoxaline with permanganate. For this reason and also because the method of the previous investigators was found to be very long, a shorter, more direct means of isolating the acid was devised.

While the latter work was in progress, the first ionization constant of pyrazine-2,3-dicarboxylic acid was determined from the half-neutral point in electrometric titrations at the hydrogen electrode. The value of the constant is $1.7 \times 10^{-3} \pm 0.4 \times 10^{-3}$. The second carboxylic group was

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(1) Gabriel and Sonn, *Ber.*, **40**, 4850 (1907).

(2) Stanley A. Hall, Thesis, Polytechnic Institute of Brooklyn, June, 1939.

(3) Hall and Spoerri, THIS JOURNAL, **62**, 664 (1940).

found too weak to produce an inflection on the titration curve. However, the constant for the decarboxylation product of the di-acid, pyrazinecarboxylic acid, was measured and found to be $1.2 \pm 0.3 \times 10^{-3}$. Pyrazine-2,5-dicarboxylic acid, which was also available, is too insoluble in water to produce reliable values through electrometric titrations.

2-(N^4-Acetylsulfanilamido)-pyrazine was prepared by condensing aminopyrazine and N-acetylsulfanilyl chloride in dry acetone–pyridine mixture. This was then subjected to acid hydrolysis to produce free 2-sulfanilamidopyrazine.

Properties of 2-Sulfanilamidopyrazine.—2-Sulfanilamidopyrazine is almost insoluble in water, methyl and ethyl alcohols, diethyl ether, dioxane, acetone, ethyl acetate, chloroform, and benzene, cold cyclohexanol and nitrobenzene, while soluble to about 1 p. p. 1000 in hot cyclohexanol and appreciably soluble in boiling nitrobenzene. The compound is extremely soluble in hot or cold pyridine, quinoline, and isoquinoline.

2-Sulfanilamidopyrazine melts at 251–251.5°. It crystallizes in light clusters of tiny needles and is white, odorless, and tasteless.

The compound is soluble in acid and in alkali, presumably forming a hydrochloride and a metal salt. Marshall's test[4] for a free amino group was positive. Thrice recrystallized 2-sulfanilamidopyrazine gave the following analyses: C, 48.22, 48.16; H, 3.93, 4.07; N, 22.52, 22.43. Calcd. for $C_{10}H_{10}O_2N_4S$: C, 47.99; H, 4.03; N, 22.39.

An equivalent weight determination was made by means of an electrometric titration in glacial acetic acid with the chloranil electrode, using perchloric acid as the titrating agent. The entire setup was the same as that first used by Hall and Conant[5] except that the quadrant electrometer of their experiments was replaced in this work by an ordinary potentiometric circuit in conjunction with a Leeds and Northrup thermionic amplifier #7673. The equivalent weight of 2-sulfanilamidopyrazine determined in this way was 249. The calculated value is 250.3.

Experimental

Pyrazine-2,3-dicarboxylic Acid.—A solution of 62.0 g. of quinoxaline (m. p. 30°) in 6 liters of water to which 20 g. of sodium hydroxide had been added was heated to 90° and to this was added over a period of one and one-half to two hours a solution of 440 g. of potassium permanganate in 2700 cc. of water at 75°. After the oxidation was complete, the precipitated manganese dioxide was filtered from the solution and washed thoroughly until test washings no longer produced a red color on addition of a few cc. to a solution of ferrous sulfate.

The filtrates were evaporated to 1 liter over an open flame and then taken to dryness on a steam-bath. The dry residue was immersed in an ice-bath and treated with enough concd. hydrochloric acid to acidify the mass, followed by the addition of 245 cc. (400 g.) of thionyl chloride. After the reaction had subsided, the excess thionyl chloride was driven off at 100°.

The residue was transferred to a Soxhlet extractor and extracted with ethyl acetate. After evaporation of the main portion of solvent, a mixture of pyrazine-2,3-dicarboxylic acid, its dihydrate, and its anhydride was obtained. This was recrystallized from water after decolorizing with charcoal to yield pyrazine-2,3-dicarboxylic acid dihydrate, m. p. 186° dec., which when dried at 110° for four hours changed to the anhydrous compound, m. p. 190° dec.; yield, 50.8 g., 66.8%.

2-(N^4-Acetylsulfanilamido)-pyrazine.—A solution of 0.9 g. of pure aminopyrazine (m. p. 117°) and 2.3 g. of N-acetylsulfanilyl chloride (m. p. 149–150°) in 5 cc. of a 50% solution of carefully dried acetone and pyridine was refluxed for one hour. A solution of 0.4 g. of sodium hydroxide in 1 cc. of water was stirred into the reaction mixture which was then allowed to stand for one hour. The precipitated crude condensation product was filtered off from the intensely red solution, washed with water, and dried over sulfuric acid. The above treatment produced a pink solid (m. p. 240–242°) which was not purified further; yield, 1.2 g., 43%.

2-(N^4-Acetylsulfanilamido)-pyrazine is almost insoluble in water and in acid and is very soluble in alkali. Marshall's test[4] for a free amino group was negative.

2-Sulfanilamidopyrazine.—A mixture of 0.5 g. of 2-(N^4-acetylsulfanilamido)-pyrazine and 3 cc. of 6 *N* HCl was heated on a steam-bath with stirring for about ten minutes until the solid material completely dissolved. The heating was continued for one minute after solution was effected, after which the reaction mixture was poured onto 10 g. of ice, decolorizing charcoal added, and the mixture allowed to stand for one-half hour. When the pale yellow solution obtained after filtering was neutralized with 10% sodium hydroxide to methyl red, white needle clusters of 2-sulfanilamidopyrazine separated out. These were filtered, washed, and dried, then recrystallized from nitrobenzene; yield, 0.25 g., 58%.

Summary

1. A shorter, more direct method for the isolation of pyrazine-2,3-dicarboxylic acid has been described.

2. The ionization constants of pyrazine-2,3-dicarboxylic acid have been determined.

3. Two new compounds, 2-sulfanilamidopyrazine and 2-(N^4-acetylsulfanilamido)-pyrazine, have been synthesized and described.

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[4] E. K. Marshall, *J. Biol. Chem.*, **122**, 263 (1936).

[5] Hall and Conant, THIS JOURNAL, **49**, 3047 (1927).