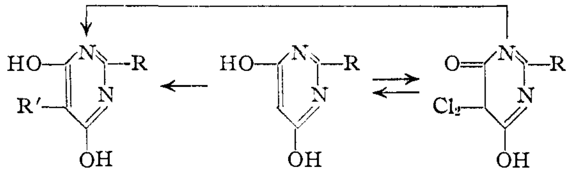
sample of the monochloro derivative, 2-amino-4,6-dihydroxy-5-chloropyrimidine (V), was obtained.



V R = NH_2 R′ = Cl I R = NH_2 III R = NH_2
VI R = NH_2 R′ = I II R = OH IV R = OH

Johnson[5] has described the use of a mixture of 30% hydrogen peroxide and concentrated hydrochloric acid to convert 2-amino-4-hydroxypyrimidine to 2-amino-4,6-dihydroxy-5,5-dichlorodihydropyrimidine. By applying this procedure to 2-amino-4,6-dihydroxypyrimidine (I) the desired product was obtained. Unlike the monochloro derivative or the starting material this compound was rather unstable. In hot water it dissolved and decomposed rapidly with the production of carbon dioxide.[6] Therefore in order to demonstrate that the pyrimidine ring was still intact the compound was reduced by two methods. Reduction with hydriodic acid and glacial acetic acid gave 2-amino-4,6-dihydroxy-5-iodopyrimidine (VI) while stannous chloride and hydrochloric acid gave 2-amino-4,6-dihydroxypyrimidine (I).

Experimental[7]

2-Amino-4,6-dihydroxy-5-chloropyrimidine (V).—2-Amino-4,6-dihydroxypyrimidine (2.5 g.) was suspended in a solution of 10 cc. of concentrated hydrochloric acid and 15 cc. of water; 1.6 g. of potassium chlorate was added slowly while keeping the temperature at 25–35°. After thirty minutes the product was filtered off, washed with water and dried; yield 1.0 g. This was nearly pure but to obtain an analytical sample it was dissolved in dilute ammonium hydroxide, filtered, and precipitated by adding acetic acid. This was repeated and a white crystalline product was obtained.

Anal. Calcd. for $C_4H_4N_3O_2Cl$: C, 29.74; H, 2.50; N, 26.01; Cl, 21.95. Found: C, 29.36; H, 2.52; N, 25.70; Cl, 22.38.

2-Amino-4-hydroxy-6-keto-5,5-dichlorodihydropyrimidine (III).—2-Amino-4,6-dihydroxypyrimidine (10.0 g.) was suspended in 70 cc. of cold 30% hydrogen peroxide (Superoxol) and 70 cc. of concentrated hydrochloric acid was added. While stirring or shaking the solid slowly dissolved and the solution became warm. This was allowed to react for ten to twenty minutes while keeping the temperature between 40° and 60° by cooling. During this time a crystalline precipitate appeared. (It was necessary to control the temperature of the reaction since if the solution became too hot the reaction became violent and the product decomposed. Even when the temperature was controlled during the initial reaction period if the mixture was allowed to stand at room temperature overnight the product would redissolve and decompose.) The reaction mixture was then well cooled, filtered and the precipitate washed with water, ethanol and ether and dried; yield 6.5 to 8.0 g. (42–52%). The product did not require purification.

Anal. Calcd. for $C_4H_3N_3O_2Cl_2$: C, 24.51; H, 1.54; N, 21.44; Cl, 36.18. Found: C, 24.50; H, 1.65; N, 21.63; Cl, 35.81.

This compound is insoluble in cold water and in most organic solvents but is somewhat soluble in pyridine. It is insoluble in all concentrations of cold hydrochloric acid. It dissolves in hot water or hot dilute acid solutions and immediately decomposes giving off carbon dioxide. A sample of the compound was recrystallized by dissolving it in cold ammonium hydroxide and then acidifying the cold solution with acetic acid. The product crystallized as platelets. Analytical data on this material were the same as before recrystallization.

Reduction of 2-Amino-4-hydroxy-6-keto-5,5-dichlorodihydropyrimidine (III). A. Hydriodic Acid in Glacial Acetic Acid.—2-Amino-4-hydroxy-6-keto-5,5-dichlorodihydropyrimidine (0.5 g.) was suspended in 5 cc. of glacial acetic acid; 5 cc. of hydriodic acid (sp. gr. 1.7) was added and the resulting solution was heated on the steam-bath for thirty minutes. It was then diluted to 50 cc. with water and enough sodium hydroxide added to neutralize the hydriodic acid present. The resulting precipitate was filtered off, redissolved in dilute sodium hydroxide, filtered and precipitated again by the addition of acetic acid; yield 0.4 g. (62%) of a white powder insoluble in water. This material gave a good qualitative test for iodine.

Anal. Calcd. for $C_4H_4N_3O_2I$: C, 19.00; H, 1.59; N, 16.61. Found: C, 19.37; H, 2.02; N, 16.74.

B. Stannous Chloride in Hydrochloric Acid.—To a suspension of 1.0 g. of 2-amino-4-hydroxy-6-keto-5,5-dichlorodihydropyrimidine in 10 cc. of water were added 4 g. of stannous chloride dihydrate and 15 cc. of concentrated hydrochloric acid. This was warmed to 70° for fifteen minutes, cooled, neutralized, and then made distinctly alkaline with ammonium hydroxide. This was centrifuged and filtered to remove the stannous hydroxide. The filtrate was neutralized with acetic acid and a white crystalline product appeared; yield 0.3 g. (47%). This contained no halogen and had physical properties resembling 2-amino-4,6-dihydroxypyrimidine. To further purify it, it was dissolved in dilute ammonium hydroxide, filtered, and crystallized by adding acetic acid.

Anal. Calcd. for $C_4H_5N_3O_2$: C, 37.80; H, 3.97; N, 33.06. Found: C, 37.67; H, 4.35; N, 33.19.

All of these products are characteristic of this type of pyrimidine compound in that they have no melting point but decompose slowly at high temperatures. Also they are all insoluble or only slightly soluble in water and most organic solvents.

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[5] Johnson, THIS JOURNAL, **65**, 1218 (1943).

[6] Although 5,5-dichlorobarbituric acid (IV) can be recrystallized from water, Blitz and Hamburger[8] have shown that it decomposes slowly in boiling water.

[7] The microanalyses were carried out by Mr. Louis Brancone and staff of this Laboratory.

The Reaction of 2-Amino-2-methyl-1-propanol with Sulfuric Acid[1]

BY ROBERT E. BUCKLES AND GENE V. MOCK

The synthesis[2] of 2,2-dimethylethyleneimine by the dehydration of 2-amino-2-methyl-1-propanol would be expected to be analogous to Wenker's[3] synthesis of ethyleneimine. In the latter case the first step of the reaction has been shown to be the esterification of monoethanolamine by sulfuric

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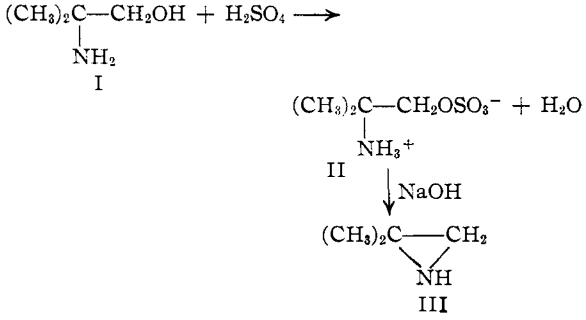
[1] Part of a thesis presented by Gene V. Mock to the Graduate College of the State University of Iowa.

[2] (a) Cairns, THIS JOURNAL, **63**, 871 (1941); (b) Karabinos and Serijan, *ibid.*, **67**, 1856 (1945); (c) Campbell, Sommers and Campbell, "Org. Syntheses," **27**, 12 (1947).

[3] Wenker, *ibid.*, **57**, 2328 (1935).

acid to give aminoethylsulfuric acid.[4] A similar procedure is used as the first step in the synthesis of 2,2-dimethylethyleneimine, but no published report of the actual identification of the reaction product has been made.

It has now been found that 2-amino-2-methyl-1-propanol (I) is esterified directly by sulfuric acid to give the expected 2-amino-2-methyl-1-propylsulfuric acid (II).



$$(CH_3)_2C(NH_2)—CH_2OH + H_2SO_4 \longrightarrow (CH_3)_2C(NH_3^+)—CH_2OSO_3^- + H_2O$$

The mixture of the amine I, water and sulfuric acid was distilled slowly to remove the water according to the method of Cairns.[2a] The solid product obtained was identical with that formed during a more rapid distillation of the water similar to that described by Leighton, Perkins and Renquist[5] for the synthesis of β-aminoethylsulfuric acid. Both products yielded 2,2-dimethylethyleneimine (III) when treated with alkali.

The pure salt II was found to give no precipitate with barium chloride. This behavior parallels that of β-aminoethylsulfuric acid.[4] It was possible, however, to hydrolyze completely either β-aminoethylsulfuric acid or II in hot dilute hydrochloric acid containing barium chloride. This hydrolysis in the case of II yielded the hydrochloride of the amine I.

The possibility that the imine III might be an intermediate in the formation of the salt II was investigated. When 2,2-dimethylethyleneimine III reacted with sulfuric acid under conditions similar to those used in the preparation of II, a dark viscous product was obtained. None of the salt II could be isolated from the product, and no imine III was generated from it by alkali. It is clear from these results that the imine is not an intermediate in the preparation of II. The salt II, is formed directly from I, and III is produced by an intramolecular alkylation of II in the presence of alkali.

Experimental

2-Amino-2-methyl-1-propylsulfuric Acid (II).—A hundred grams (1.12 moles) of 2-amino-2-methyl-1-propanol (I) in 200 ml. of water was heated with 110 g. (1.06 moles) of sulfuric acid in 200 ml. of water until most of the water was distilled from the mixture. The temperature of the heating bath was then slowly raised to 175°, while the rest of the original water and that formed from the reaction was removed under the reduced pressure obtained with an aspirator. A modified method[5] was also carried out. Only about a quarter of the original amount of water was used. The solution of I was mixed with the slightly diluted sulfuric acid with cooling. The water was removed by distillation at reduced pressure over a free flame. In either case the light brown solid product was softened with 500 ml. of 95% alcohol, filtered and washed with absolute alcohol. Recrystallization from 50% alcohol yielded a white crystalline material which gave only a slight milkiness with aqueous barium chloride. The yield of purified product from the first procedure was 113 g. (63%); m. p. 253–255° (dec.).

Anal. Calcd. for $C_4H_{11}O_4NS$: C, 28.4; H, 6.56; N, 8.29. Found: C, 28.5; H, 6.48; N, 8.35.

Hydrolysis.—Two grams of II was dissolved in 25 ml. of water and 10 ml. of concentrated hydrochloric acid and 10 ml. of a saturated solution of barium chloride were added. The solution was heated overnight on a steam-bath. The barium sulfate was removed by filtration, and the filtrate was evaporated to dryness. The residue was recrystallized from absolute alcohol. The product had a m. p. 200–201° as compared with an authentic sample of 2-amino-2-methyl-1-propanol hydrochloride, m. p. 199–201°. There was no lowering of the m. p. on mixing the two. The recorded m. p. for the hydrochloride is 203–206°.[6]

Determination of Sulfur by Hydrolysis.—From 0.2 to 0.4 g. of the sulfuric ester was weighed and dissolved in 10% barium chloride solution so that there was 100% excess of barium chloride. Ten milliliters of 6 *N* hydrochloric acid was added and the solution was heated twenty hours on the steam-bath. The barium sulfate was determined gravimetrically. This analytical procedure was applied to the determination of sulfur in both II and β-aminoethylsulfuric acid.

Anal. Calcd. for $C_4H_{11}O_4NS$: S, 19.0. Found: S, 19.4, 19.8. Calcd. for $C_2H_7O_4NS$: S, 22.7. Found: S, 22.7.

Reaction of 2,2-Dimethylethyleneimine (III) with Sulfuric Acid.—A mixture of 57 g. (0.80 mole) of 2,2-dimethylethyleneimine[2] in 100 ml. of water and 79 g. (0.78 mole) of 96% sulfuric acid in 100 ml. of water was distilled with a water pump until the residue was a very viscous, black material. Treatment of some of this residue with alcohol gave no appreciable amount of crystalline product. Distillation of the residue from 40% sodium hydroxide (*ca.* 300% excess) gave some volatile material but little which distilled below 120°. 2,2-Dimethylethyleneimine boils at 70–72°.

Addendum.—It has been brought to our attention by one of the referees that J. V. Karabinos[7] has isolated 2-amino-2-methyl-1-propylsulfuric acid and β-aminoethylsulfuric acid from the reactions of the amino alcohols with sulfuric acid. Analysis of the esters for amino nitrogen by the Van Slyke method checked with the theoretical values.

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[4] Rollins and Calderwood, THIS JOURNAL, **60**, 2312, 2751 (1938).

[5] Leighton, Perkins and Renquist, *ibid.*, **69**, 1540 (1947).

(6) Jones, *J. Assoc. Official Agr. Chem.*, **27**, 467 (1944).

(7) Karabinos, "Dissertation," Ohio State University, 1946, p. 74b.

The Friedel–Crafts Reaction on Highly Methoxylated Compounds

BY H. R. FRANK[1] AND D. S. TARBELL

The following observations give some information about the behavior of derivatives of anisole

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(1) Abbott Laboratories Fellow, 1946–1947.