	%
Carbon	31.35
Hydrogen	4.09
Chlorine	10.29
Nitrogen	8.13
Oxygen	27.85
Sulfur	9.30
Phosphorus	8.99
	100.00
Methoxyl	9.00

PREPARATION

The following procedures are suggested because they are readily conducted and do not require elaborate equipment. Vanillin is chlorinated by sodium hypochlorite to form 5-chlorovanillin. The aldehyde group is reduced by sodium borohydride and the resulting alcohol is condensed in one step with thiourea and phosphoric acid.

5-CHLOROVANILLIN

A method for the chlorination of vanillin by aqueous sodium hypochlorite has been developed by Hopkins and Chisholm (*2*).

Mix 60.8 grams of vanillin and a solution of 16 grams of sodium hydroxide in 500 ml. of water. Stir until the vanillin has been dissolved. Establish a temperature of about 20° C. and maintain it during addition of 28.4 grams of chlorine available in the form of sodium hypochlorite dissolved in 1200 ml. of water. Stir at intervals. When a negative test is obtained with starch-iodide paper, acidify with a mixture of equal volumes of concentrated hydrochloric acid and water. Separate the precipitate of crystalline plates and wash it with water until free from acid. The minimum yield is 75%. Some resin is formed during the reaction. Purify by crystallization from a mixture of boiling acetone and water and afterward, with the addition of adsorbent carbon, from a mixture of boiling ethyl alcohol and water. Dry the product and recrystallize it from benzene.

The capillary melting point of a preparation made by this procedure was 165° C. This value agrees with that obtained by Hann (*1*), who prepared this compound by passing chlorine into a solution of vanillin in glacial acetic acid in the presence of fused sodium acetate.

5-CHLOROVANILLYL ALCOHOL

Mix 45 grams of 5-chlorovanillin with a solution of 45 grams of sodium hydroxide in 1 liter of distilled water. Stir until the vanillin is in solution and heat to 80° C. Add 3 grams of sodium borohydride in several successive portions. Stir occasionally, allow to cool to room temperature, and filter to remove resinous material. Acidify the filtrate with about 55 ml. of 85% phosphoric acid, and dilute with 2 volumes of water. Separate the crystalline needles and wash them with water until free from acid. The yield is about 90%. Crystallize from hot water with the addition of adsorbent carbon. Afterward crystallize twice from benzene to remove residual resin.

The capillary melting point of a product prepared by the procedure was 118.5° C.

5-CHLORO-4-HYDROXY-3-METHOXYBENZYLISOTHIOUREA PHOSPHATE

Heat the following mixture to the boiling point under a reflux condenser.

5-Chlorovanillyl alcohol, g.	47
Thiourea, g.	21
Phosphoric acid, 85%, ml.	17
Ethyl alcohol, 99.5%, ml.	400

After about 6 hours a portion of the phosphate separates. Allow the contents of the container to cool to room temperature and separate the crystalline material by filtration. Reflux the filtrate as before and again remove the product which separates. When the filtrate is again heated, a third portion will appear after the mixture is allowed to cool. The minimum yield is approximately 60% of the theoretical value. If the reaction products are not removed as described, the mixture may bump violently.

Table I. Microanalytical Determination of Chlorine, Phosphorus, and Sulfur in Standard Compound

(Analyses by Rolf Paulson and Lorna Tregoning)

Samples[a]	Chlorine, %	Phosphorus, %	Sulfur, %
1	10.28	9.14	9.38
	10.40	9.06	9.39
2	10.30	9.00	9.33
3	10.31	9.09	9.39
	10.37	9.09	9.34
4	10.18	8.95	9.43
	10.14	8.98	9.36
5	10.10	8.92	9.40
	10.27		
Theoretical values	10.29	8.99	9.30

[a] 1, 2, 4, and 5. Separate preparations.

3. From same preparation as sample 2, but after storage in laboratory for about 9 months.

To purify the product, transfer it to a beaker and cover it with a mixture of 9 volumes of acetone and 1 volume of water. This amount of solvent does not completely dissolve the crystals but is sufficient to effect purification by digestion. Heat at 50° for 1 hour, allow to cool to room temperature, and filter. Remove the phosphate, place it in a beaker, cover it with water, and heat to 50° for 1 hour as before. Then add at least 6 volumes of a mixture of equal volumes of acetone and ethyl alcohol to precipitate the phosphate. Separate by filtration through a sintered-glass funnel. Repeat the treatment with water, followed by precipitation. Dry the final product in vacuo at 105° and grind to a powder in an agate mortar.

The phosphate melts with decomposition at about 175°. When the dried salt is exposed to a humid atmosphere it absorbs moisture. In 24 hours a sample of about 5 grams in a layer about 1 cm. deep gained 0.06% in weight in an atmosphere of 50% relative humidity. Under similar conditions, in an atmosphere of 80% relative humidity, the gain in weight was 0.45%. It is therefore necessary to dry the phosphate to constant weight, preferably at 105° in vacuo, before it is used as a standard.

Table I indicates the consistency in composition that may be expected by using these methods of preparation and purification.

LITERATURE CITED

(1) Hann, R. M., *J. Am. Chem. Soc.* **47,** 2000 (1925).
(2) Hopkins, C. Y., Chisholm, M. J., *Can. J. Research* **24B,** 208 (1946).
(3) Ogg, C. L., Willets, C. O., IND. ENG. CHEM., ANAL. ED. **18,** 334 (1946).

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Quality Control of Pharmaceuticals. Applications of Quantitative Paper Chromatography in Conjunction with Instrumental Methods—Correction

In the paper on "Quality Control of Pharmaceuticals. Applications of Quantitative Paper Chromatography in Conjunction with Instrumental Methods" [ANAL. CHEM. **49,** 1649 (1957)] three errors occurred.

Page 1650, column 1, 3rd paragraph, 8th line, μ should be deleted.

Page 1651, Figure 2, "pH 5/2" should read "pH 5.2."

Page 1651, column 2, third line below Figure 2 should read "retaining the *fourth* as a blank."

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