

to dryness. The residual clear amber glass was dissolved in 95 per cent. alcohol, the solution concentrated and benzene added. The acetyl derivative separated in a fine yellowish powder, and was washed thoroughly with benzene and dried. Yield, 0.35 gram.

Calculated for $C_{13}H_{18}O_4N_3$: N, 23.10.

Found: N, 23.16.

The pure substance melts at 125° (corr.). It is easily soluble in water, alcohol or chloroform, but does not crystallize well from these solvents, evaporation of the solvent leaving finally a clear glass. On long boiling with benzene, small transparent plates were obtained, carrying benzene of crystallization.

Attempts to eliminate water from this compound and condense the side chains to a cycle proved unsuccessful.

NEW YORK, N. Y.

PREPARATION OF CHOLINE AND SOME OF ITS SALTS.

By R. R. RENSHAW.

Received November 22, 1909.

In connection with some work on the bactericidal properties of lecithins the author had occasion to prepare some of the salts of choline. In looking through the literature it was found that the choline used in recent investigations was prepared and isolated by methods which it was thought might be simplified.

Wurtz in 1867¹ prepared choline by heating trimethylamine with an excess of ethylene chlorohydrin, and later (1868) he and also Griess and Harrow² (1885) obtained it by the action of a concentrated solution of trimethylamine on ethylene oxide. The products were purified by means of the gold salt.

Later investigators have used different procedures or new methods. In 1889 Bode³ made choline by the prolonged action of dilute nitric acid on bromomethyltrimethylamine bromide which he had made from ethylene bromide by Hofmann's method. No yield was given. Gulewitsch in 1898⁴ in an extended article on choline described its preparation in quantity by a modification of Wurtz's method. Redistilled anhydrous ethylene chlorohydrin in large excess was heated with a 15-20 per cent. solution of trimethylamine in absolute alcohol for 24 hours in a water bath. The choline from the resulting slightly acid solution was separated partly as the mercuric, and partly as the platinic chloride double salts. Yield, 61 per cent. Krüger and Bergell in 1903⁵ got choline by the action of

¹ *Compt. rend.*, 65, 1015; *Ann. Spl.*, 6, 116.

² *Ber.*, 18, 707 (1885).

³ *Ann.*, 267, 268.

⁴ *Z. physiol. Chem.*, 24, 509.

⁵ *Ber.*, 36, 2901.

water on bromocholine bromide at 160° for 4 hours. No yield given. A large number of investigators have prepared choline from egg lecithin. For the most part these later methods are either tedious or give poor yields or both.

The author has found that a practically quantitative yield (97.3 per cent.) of choline chloride can be obtained by the following method. Fourteen grams of freshly distilled anhydrous ethylene chlorohydrin were placed in a bomb tube cooled to -12 to -20° (saturated salt solution and snow). Trimethylamine, generated by dropping a concentrated solution of its hydrochloride (18 grams) on solid sodium hydroxide, was passed through a U-tube containing solid potassium hydroxide and then through a freezing bath into the ethylene chlorohydrin contained in the bomb tube. If the amine hydrochloride was added slowly, practically complete condensation ensued. After all the hydrochloride had been added the generating flask was warmed gently and air passed through slowly. The tube was then sealed and heated two hours at 80 – 90° when the contents had completely crystallized. On opening the tube after a further two hours' heating there was a little pressure due to a slight excess of trimethylamine. The contents, composed of perfectly white, well-formed crystals, were washed a number of times with dry ether, and allowed to stand for some time in a vacuum desiccator. The product so obtained, while sufficiently pure for most purposes, still contained too high a percentage of chlorine—probably due to a slight amount of ethylene chlorohydrin held mechanically in or on the crystals. A pure product was obtained by dissolving in absolute alcohol and adding ether gradually until complete precipitation was obtained. The fine white needle crystals were filtered, washed with ether, and dried in a vacuum.

Choline Acetate was prepared by neutralizing an aqueous solution of the base (obtained by the action of moist silver oxide on choline chloride) with acetic acid. Very long evaporation under high vacuum at 50° and cooling caused the product to crystallize to a fan-shaped mass of needle crystals. These were extremely hygroscopic, and practically insoluble in carbon disulphide, benzene, petroleum ether, acetone and ethyl ether; very soluble in alcohol and water. Choline acetate is very easily hydrolyzed.

Choline Sulphate, $(\text{HOCH}_2\text{CH}_2\text{N}(\text{CH}_3)_3)_2(\text{SO}_4)$, prepared by the action of silver sulphate on choline chloride, separates from a very concentrated aqueous solution in short needles. The salt was purified by evaporating to dryness under high vacuum at 50 – 100° (almost no decomposition occurred), dissolving in alcohol, filtering, adding petroleum ether and refrigerating. Perfectly white well-formed needle crystals separated out. These were practically insoluble in carbon disulphide, ether, ben-

zene and petroleum ether; easily soluble in alcohol and water. The sulphate is fairly hygroscopic.

Calculated for $(\text{HOCH}_2\text{CH}_2\text{N}(\text{CH}_3)_3)_2\text{SO}_4$: S, 10.52 per cent.

Found: S, 10.63, 10.77 per cent.

Choline Dihydrogen Phosphate, $\text{HOCH}_2\text{CH}_2\text{N}(\text{CH}_3)_3\text{H}_2\text{PO}_4$.—On agitating a concentrated solution of choline chloride with silver phosphate and filtering from the excess of silver phosphate and silver chloride, a very basic solution was obtained, indicating that the tricholine phosphate was largely hydrolyzed. A dilute solution of phosphoric acid was added to permanent acidity. The ratio of phosphate ions to the choline was then practically 1 : 1. The solution was evaporated under high vacuum at 80–90° to a horny mass. The product was purified by extracting with boiling absolute alcohol in which the phosphate is slightly soluble. By this means beautiful, long white, fairly hygroscopic needle crystals were obtained, which were practicably insoluble in benzene, carbon disulphide, petroleum ether, acetone and ethyl ether; slightly soluble in alcohol; very soluble in water. After washing in ether and drying in a vacuum desiccator the product was analyzed.

Calculated for $\text{HOCH}_2\text{CH}_2\text{N}(\text{CH}_3)_3\text{H}_2\text{PO}_4$: P, 15.42 per cent.

Found: P, 15.48 per cent.

The chemistry of the choline derivatives is being further investigated by the author.

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BACTERICIDAL PROPERTIES OF LECITHINS AND CHOLINE SALTS.

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Received November 22, 1909.

There is some disagreement in the literature concerning the bactericidal properties of lecithins. The existence of cobra lecithides, the speculation regarding a possible relation between lecithin and the amboceptors,¹ and, among others, the fact that such a product as fresh milk, containing certain amounts of lecithins, has some germicidal constituent, gives interest to the problem in question. In view of this the authors have attempted to determine what influence, if any, lecithins might have upon the growth of some of the more common organisms. Along with this, since it is possible that the presence of a decomposition product, *i. e.*, choline, might have been responsible for the disagreement, a few of its salts were prepared and their bactericidal properties determined.

The procedure was as follows: Pure cultures of the different organisms were grown at room temperature for about twelve hours in an ordinary broth medium. One loopful of this was transferred to a flask con-

¹ Kyes, *Z. physiol. Chem.*, 41, 273.