

with hydrogen sulfide. The silver precipitated as silver sulfide but the acetyl choline chloride readily dissolved. In order to separate the silver sulfide more easily, activated charcoal which previously had been washed with absolute alcohol was added. The mixture was shaken for a few minutes and then filtered. Acetyl choline chloride was reprecipitated from the filtrate by the addition of dry ether; m. p. 151°; yield, 65%. It was very soluble in water and alcohol, but insoluble in ether. It was extremely hygroscopic.

Anal. Subs., 0.2344: AgCl, 0.1867. Calcd. for $C_7H_{16}O_2NCl$; Cl, 19.53. Found: Cl, 19.70.

Chloroplatinate.—The calculated amount of a concentrated solution of chloroplatinic acid in absolute alcohol was added to 0.1 g. of acetyl choline chloride in absolute alcohol. An orange-colored precipitate soon formed. It was recrystallized from hot water and then washed with water and alcohol; m. p. 227° with decomposition.

Anal. Subs., 0.1296: Pt, 0.0362. Calcd. for $C_{14}H_{34}O_4N_2PtCl_6$; Pt, 27.81. Found: Pt, 27.93.

Chloro-aurate.—To 0.46 g. of acetyl choline chloride dissolved in water was added the calculated amount of a concentrated solution of auric chloride in water. An orange-colored solid at once precipitated. It was recrystallized from hot water; m. p. 168–169°.

Anal. Subs., 0.2212: Au, 0.0894. Calcd. for $C_7H_{16}O_2NAuCl_4$; Au, 40.55. Found: Au, 40.42.

Summary

1. Dimethylamino-ethyl acetate has been prepared by adding alkali to the product formed by the interaction of acetyl chloride and dimethylamino-ethyl alcohol.

2. Acetyl choline iodide was formed when dimethylamino-ethyl acetate was treated with methyl iodide. From the iodide the corresponding chloride, chloroplatinate and chloro-aurate were made.

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PAPAVERINE: AN ATTEMPTED RÜGHEIMER SYNTHESIS

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A simple general synthesis of the papaverine type of alkaloid is for many reasons of great importance, particularly so as it would offer a possible means of synthesizing the tetrahydroberberine type of alkaloid.¹ The two methods² for synthesizing papaverine which have been worked out are probably only of scientific interest on account of the inaccessibility of the starting materials. An ideal starting point for the synthesis of isoquinoline alkaloids would be a benzoïn or a benzil. Such a synthesis was attempted by Fritsch,³ who condensed desoxyveratrin with amino-acetal and at-

¹ Späth and Kruta, *Monatsh.*, **50**, 341 (1928).

² Pictet and Gams, *Ber.*, **42**, 2943 (1909); Buck, Haworth and Perkin, *J. Chem. Soc.*, **125**, 2176 (1924).

³ Fritsch, *Ann.*, **329**, 37 (1903).

Experimental

Veratril.—Veratric aldehyde, prepared by the method of Buck and Perkin¹⁰ was converted into veratril substantially as described by Vanzetti.¹¹

Desoxyveratroin. First Method.¹²—Twenty grams of veratril, 200 cc. of alcohol, 40 g. of granulated tin and 5 cc. of saturated copper sulfate solution were heated on the water-bath for four hours, during which time 200 cc. of concentrated hydrochloric acid containing 15 cc. of copper sulfate solution was gradually added. The mixture was filtered, diluted with an equal volume of water and allowed to stand. The product which separated was filtered off and recrystallized from alcohol. It forms colorless needles melting at 107°.

Anal. Calcd. for $C_{18}H_{20}O_8$: C, 68.36; H, 6.33. Found: C, 68.31; H, 6.29.

Second Method.¹³—Seven grams of homoveratric acid (prepared by the method of Haworth and co-workers)¹⁴ was dissolved in 20 cc. of chloroform and 5.0 g. of thionyl chloride added. The mixture was refluxed for forty minutes on the water-bath, the chloroform then distilled off and 30 cc. of carbon disulfide and 11 g. of veratrole (prepared from guaiacol and methyl sulfate) added; 12 g. of anhydrous aluminum chloride was introduced in portions through the condenser and the whole refluxed for two hours, allowed to stand for a further two hours and then treated with water. The carbon disulfide layer was separated and water added, after which steam was passed through to remove the solvent and excess veratrole. After purification from dilute alcohol, the product melted at 107° and was identical with the desoxyveratroin prepared by the first method. It corresponded exactly with the description given by Fritsch.³

Desoxypiperoin.—Fifty grams of piperoin (prepared after the method of Perkin),¹⁵ 40 g. of granulated tin and 200 cc. of alcohol were heated on a steam-bath under a reflux condenser, 73 cc. of concentrated hydrochloric acid containing a little copper sulfate was added and the whole refluxed for three hours. A further 50 cc. of alcohol and 20 cc. of acid with a little copper sulfate were then added and the heating continued for one and one-half hours. On cooling, the product crystallized out. A further amount separated on diluting the liquor; yield, 23 g. Desoxypiperoin forms small white needles melting at 114° when crystallized from alcohol, in which it is sparingly soluble.

Anal. Calcd. for $C_{18}H_{21}O_8$: C, 67.61; H, 4.24. Found: C, 67.48; H, 4.40.

Desoxyveratroin Oxime.—Fifty grams of desoxyveratroin and 12.5 g. of hydroxylamine hydrochloride were heated with 125 cc. of pyridine on a boiling water-bath for five hours. The solution was then diluted with water to 500 cc. and allowed to stand. The oil which separated became crystalline on standing; yield, 38 g. The oxime forms fine white needles melting at 128° when crystallized from alcohol.

Anal. Calcd. for $C_{18}H_{21}O_8N$: C, 65.27; H, 6.34; N, 4.2. Found: C, 65.03; H, 6.26; N, 4.5.

Desoxypiperoin Oxime.—Twenty grams of desoxypiperoin was heated on a water-bath for two hours with 50 cc. of pyridine and 5 g. of hydroxylamine hydrochloride. On adding water to incipient precipitation and allowing the mixture to stand, the oxime crystallized out; yield, 19 g. Desoxypiperoin oxime crystallizes from alcohol, in which it is sparingly soluble, in colorless needles melting at 158°.

¹⁰ Buck and Perkin, *J. Chem. Soc.*, **125**, 1678 (1924).

¹¹ Vanzetti, *Gazz. chim. ital.*, **57**, 162 (1927).

¹² Cf. Zinin, *Ann.*, **119**, 177 (1861); Wachter, *Ber.*, **25**, 1727 (1892).

¹³ Cf. Cain, Simonsen and Smith, *J. Chem. Soc.*, **103**, 1035 (1913).

¹⁴ Haworth and co-workers, *ibid.*, **125**, 1686 (1924).

¹⁵ Perkin, *ibid.*, **59**, 150 (1891).

Anal. Calcd. for $C_{16}H_{18}O_6N$: C, 64.21; H, 4.35; N, 4.7. Found: C, 64.40; H, 4.51; N, 4.7.

Tetramethoxystilbylamine.¹⁶—Twenty grams of desoxyveratroin oxime dissolved in 200 cc. of alcohol was treated while hot with 800 g. of 3.5% sodium amalgam, and 100 cc. of glacial acetic acid added in portions during one hour, the mixture being kept hot and water being added as required to keep the sodium acetate formed in solution. When cool, the mixture was diluted to 400 cc. with water and allowed to stand overnight to permit the separation of unchanged oxime. After removing the mercury and filtering, a slight excess of ammonia was added. The resulting precipitate was filtered off and recrystallized; yield, 15 g. Tetramethoxystilbylamine forms glistening plates melting at 107° when crystallized from water, in which it is sparingly soluble. It is soluble in cold alcohol and benzene, sparingly soluble in ether and insoluble in petrol ether. The hydrochloride forms white crystals melting at 195°. The hydrobromide is pale yellow and melts at 241°.

Anal. Calcd. for $C_{18}H_{23}O_4N$: C, 68.14; H, 7.25; N, 4.4. Found: C, 68.06; H, 7.48; N, 4.5.

Acetyl Derivative.—Acetylation by means of acetic anhydride gave the acetyl compound, which crystallized from alcohol in a felted mass of colorless needles melting at 160–162°.

Anal. Calcd. for $C_{20}H_{25}O_5N$: N, 3.9. Found: N, 4.0.

Dimethylenedioxytilbylamine.—This compound was prepared in the same manner as the foregoing tetramethoxy compound, the same quantities being used; yield, 17 g. It is best purified by recrystallizing the hydrochloride from alcohol and then suspending the salt in hot water and adding an excess of ammonia. The base is readily soluble in cold alcohol and benzene and sparingly soluble in ether and petrol ether. Recrystallized from water, in which it is sparingly soluble, it forms long shining needles melting at 111°. The hydrochloride forms colorless needles melting at 245°.

Anal. Calcd. for $C_{16}H_{15}O_4N$: C, 67.38; H, 5.26; N, 4.9. Found: C, 67.79; H, 5.44; N, 5.2.

Acetyl Derivative.—The acetyl derivative prepared by acetylation of the base with acetic anhydride crystallizes from dilute acetic acid in small clusters of tiny colorless needles melting at 141°.

Anal. Calcd. for $C_{18}H_{17}O_5N$: N, 4.3. Found: N, 4.1.

Tetramethoxystilbylamino-acetal.—Three grams (1 mole) of tetramethoxystilbylamine and 1.0 g. (0.5 mole) of bromo-acetal were heated slowly in an oil-bath until the temperature reached 150° (forty-five minutes). After cooling, the mixture was sludged with ether and filtered. The precipitate of tetramethoxystilbylamine hydrobromide was filtered off with suction and washed with ether. The filtrate and washings were united and the ether was evaporated. The product, like practically all compounds of this class, formed a reddish oil which could not be crystallized and which gave no crystalline derivatives. In the presence of reagents it gave back the original amine by fission with rather unusual ease. The material obtained was used directly for subsequent experiments.

Dimethylenedioxytilbylamino-acetal.—This was prepared in the same manner as the foregoing tetramethoxy compound except that the heating was carried out at 125°. It also forms a reddish oil, uncrystallizable and giving no crystalline derivatives.

Action of Cyclizing Agents on Tetramethoxystilbylamino-acetal.—The method of

¹⁶ Cf. Goldschmidt and Polonowska, *Ber.*, 20, 492 (1887); Strandmark, *Svensk Kem. Tid.*, 18, 3 (1906).

investigation was to take 1.5 g. of tetramethoxystilbylamino-acetal and 2.0 g. of arsenic pentoxide, together with 20 cc. of sulfuric acid, and to heat the mixture on the water-bath for thirty minutes. The reaction mixture was poured into water and neutralized. Nothing but black amorphous material which could not be purified and from which no derivatives were obtainable was ever found. The starting material was evidently completely destroyed. Acid of 30, 50, 65 and 75% strength was tried in the hot as well as 65 and 75% acid in the cold. Dimethylenedioxystilbylamino-acetal was completely destroyed by 75% sulfuric acid and arsenic pentoxide in the cold.

It is, therefore, evident that the stilbylamino-acetals are unstable under the rather drastic treatment required to produce a Rügheimer cyclization and that further work along these lines would be profitless.

Summary

Tetramethoxystilbylamino-acetal and dimethylenedioxystilbylamino-acetal were prepared from veratric aldehyde and piperonal, respectively, in an attempt to synthesize papaverine and the corresponding dimethylenedioxybenzylisoquinoline. The stilbylamino-acetals were found to be unstable to the usual cyclizing agents, thus precluding the synthesis of papaverine and its homologs by this method.

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STUDIES ON POLYMERIZATION AND RING FORMATION. III. GLYCOL ESTERS OF CARBONIC ACID

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The glycol esters of dibasic acids described in a previous paper¹ are all highly polymeric. This was expected from the generalization² that bi-functional reactions which, if intramolecular, could lead only to larger-than-6 rings proceed intermolecularly. It seemed desirable to examine an homologous series of similar compounds in which the length of the structural unit might be as short as 5 or 6 atoms, since in these cases reaction should be intramolecular and the products monomeric, and in the longer chains of the same series reaction should be intermolecular and the products polymeric.

Such a series is found in the glycol esters of carbonic acid. The first member of this series, ethylene carbonate, $\text{O}=\text{C} \begin{array}{l} \diagup \text{O}-\text{CH}_2 \\ \diagdown \text{O}-\text{CH}_2 \end{array}$, has long been known.³ It is a crystalline solid which boils at 238° and it is definitely

¹ Carothers and Arvin, *THIS JOURNAL*, **51**, 2560 (1929).

² Carothers, *ibid.*, **51**, 2548 (1929).

³ Nemirowski, *J. prakt. Chem.*, [2] **28**, 439 (1883); *Chem. Zentr.*, 23 (1884).