

in a sealed tube at 100° C. without a solvent. The method is inconvenient and usually incomplete due to caking of the phthalimide and the amine hydrobromide.

It has also been prepared by condensing diethylamino ethyl chloride with potassium phthalimide, followed by acid hydrolysis.

RESEARCH DEPARTMENT OF THE CHEMICAL AND PHARMACEUTICAL LABORATORIES,  
E. R. SQUIBB AND SONS, BROOKLYN, N. Y.

## STEROL GLUCOSIDES.

BY OLE GISVOLD.

Whereas a survey of the literature reveals the fact that phytosterols, for the most part, occur as such, it also shows that several sterol glucosides have been reported, the so-called phytosterolins (1). If the amounts of sterols present in plants are small, those of the phytosterolins reported are even smaller. Hence the sugars obtained upon hydrolysis have not been identified completely.

Under these circumstances it naturally seemed desirable to synthesize sterol glucosides with glucose and other sugars. Thus the glucose glucosides of sitosterol and cholesterol were prepared by Salway (2) in 1913, and that of ergosterol by Mac Corquodale (3) in 1930. Having worth-while amounts of several phytosterols on hand, the synthesis of as many of their glucosides as time and material permitted was undertaken.

The method of preparation employed was essentially that used by Power and Salway in 1913 in the preparation of the sitosterol and cholesterol glucosides and again by Mac Corquodale in 1930 in the preparation of ergosterol glucoside.

The procedure is essentially as follows, with some modification of deacetylation.

Two Gm. of dry sterol, 3 Gm. of pure, freshly crystallized tetracetyl bromoglucose were dissolved in 100 cc. of dry ether and 3 Gm. of dry freshly precipitated silver oxide were added. The mixture was shaken continuously for 8 hours, centrifuged, filtered and the ether distilled off. The residue thus obtained was recrystallized once from 95% alcohol. The partially purified product was dissolved in warm absolute alcohol and deacetylated with a solution of freshly prepared sodium ethoxide. The insoluble precipitate thus obtained was filtered off and washed twice with small quantities of hot alcohol. The crude product thus obtained was recrystallized from a hot saturated solution using a mixture of 95% alcohol and pyridine as a solvent. The glucoside crystallized very well and a pure product was thus obtained.

*Preparation of Aceto-Brom Glucose* (4).—The procedure employed was that described by Levene and Raymond, and excellent yields were obtained.

Dry HBr was passed into acetic anhydride until the latter contained 40 Gm. of the gas per 100 Gm. of the finished reagent. For each 50 Gm. of pure anhydrous powdered glucose, 250 cc. of the reagent were used. The glucose was divided into 10-Gm. portions, each kept in a stoppered test-tube. The reagent was cooled to 10° and the glucose added under constant shaking. The temperature was not allowed to exceed 30°. The first portion of glucose dissolved quite slowly but the later portions more rapidly. Before additional portions were added the solution was cooled to 10°. After all the glucose had been added, the solution was cooled to 0° and dry HBr was passed into it until the total content was 60 Gm. per 100 Gm. of acetic anhydride. The solution should be only a light straw color. It was permitted to stand for one hour and then concentrated to half its original volume. Thirty cc. of toluene were added and the distillation continued until the residue became a thick syrup. Three additional portions of toluene were added and removed by distillation. All reagents were removed as completely

as possible. The thick syrup thus obtained was taken up in ether, shaken with charcoal and the mixture filtered. To this warm solution, petroleum ether was added until the cloudiness obtained just threatened to remain. The solution was allowed to cool when the product crystallized readily. If the product fails to crystallize, a few seed crystals will readily induce crystallization.

*Preparation of Dry HBr.*—10–15 Gm. of naphthalene were dissolved in a small quantity of xylene (or high boiling kerosene) and the solution placed in a 500-cc. Florence flask. The flask was connected by means of a bent glass tube with a Woolff bottle which contained 48% HBr solution with a little red phosphorus in suspension. This, in turn, was connected with a U tube containing red phosphorus distributed by means of glass wool. The gas was led through a CaCl<sub>2</sub> tower and then through two U tubes of P<sub>2</sub>O<sub>5</sub> in glass wool. The bromine was added to the naphthalene by means of a separatory funnel at a slow rate.

*Preparation of Dry Ether.*—The ether was shaken first with a saturated solution of KCl. It was then allowed to stand over CaCl<sub>2</sub> for several days and filtered. P<sub>2</sub>O<sub>5</sub> was added in excess. The decanted ether was finally dried with sodium and potassium alloy prepared in the following manner: Xylene was heated to 80°–90° in an evaporating dish and the previously cleaned sodium and potassium were placed into it and pressed together with a stiff spatula until a liquid alloy was obtained. The ether thus dried was distilled and kept in 100-cc. bottles previously dried in an oven at 110°.

*Preparation of the Silver Oxide.*—The silver oxide first used was prepared by precipitating equimolecular portions of silver nitrate and sodium hydroxide. However, no condensation could be effected even though it was freshly prepared. If, however, the silver oxide was prepared in the following manner (5), condensation could be effected.

A 10% solution of silver nitrate was heated to 86° and added rapidly, with rapid stirring, to a hot 2.3% solution of sodamide. The precipitate was washed 5 times by decantation with hot water, then by decantation with 5 parts of absolute alcohol, and filtered by means of suction. It was washed once with absolute alcohol, dried in the air and then dried over P<sub>2</sub>O<sub>5</sub> in a vacuum and used within 48 hours.

In order to become acquainted with the technique in effecting condensation, cholesterol and ergosterol were experimented with. As was mentioned before in the preparation of the silver oxide, several attempts were made before effecting condensation. The elaborate procedure needed to run one experiment required some time. However, the technique once mastered, no further difficulty was encountered although the yields were not high.

*Ergosterol Glucoside.*—The ergosterol used in this synthesis was obtained from oil of ergot. The glucoside was obtained in fine white needles m. p. 314.5°. The melting point recorded by Mac Corquodale was 315°.

*Stigmasterol Glucoside.*—The stigmasterol used was obtained from Echinacea. It had a melting point of 170°. Very fine needles of the glucoside were obtained which melted at 299°.

*Phytosterol Glucoside.*—The phytosterol used in this synthesis was obtained from milfoil and melted at 134°. The synthesized glucoside was obtained in fine white needles which melted at 293°.

*Chloesterol Glucoside.*—The chloesterol used in this experiment was obtained from gall stones and had a melting point of 146°. The glucoside was obtained in the form of fine white needles which melted between 280° and 284°. The melting point recorded by Salway (2) was 270–285°.

#### REFERENCES.

- (1) F. B. Power and A. Salway, *J. Chem. Soc.*, 103 (1913), 399.
- (2) A. Salway, *Ibid.*, 103 (1913), 1022.

- (3) Mac Corquodale, *J. Chem. Soc.*, 52 (1930), 2512.
- (4) P. A. Levene and A. L. Raymond, *J. Biol. Chem.*, 90 (1931), 247.
- (5) Helferich and Klein, *Annalen*, 450 (1926), 219.

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## THE GRAVIMETRIC AND VOLUMETRIC DETERMINATION OF BRUCINE AND STRYCHNINE AS DICHROMATE.\*

BY I. M. KOLTHOFF AND J. J. LINGANE.

Brucine and strychnine salts give crystalline precipitates with alkali dichromates and chromates. No use for quantitative purposes has been made of these precipitation reactions. In the following, the properties of the alkaloid dichromates are described and a procedure is developed by which brucine and strychnine can be determined quantitatively as dichromates. These are much less soluble than the corresponding chromates, the latter not being suitable for quantitative purposes.

*Materials Used.*—*Brucine* hydrochloride and *strychnine* sulphate solutions of known concentration<sup>1</sup> were used.

*Brucine Dichromate.*—This salt was prepared by precipitation of brucine hydrochloride with a slight excess of potassium dichromate solution. The precipitate was washed thoroughly with water; it consisted of very fine crystals. (Portion I.) Part was recrystallized from hot water in order to obtain larger crystals. (Portion II.) Both portions were dried in the air.

*Strychnine Dichromate.*—Two portions were prepared in a way similar to that described above.

*Potassium Dichromate.*—A C.P. product was thrice recrystallized from water and dried at 200°. Standard solutions were prepared by dissolving weighed samples in a known volume of water.

*Ferrous Ammonium Sulphate.*—C.P. Solutions were prepared in 0.5 to 1*N* sulphuric acid and standardized against dichromate.

### SENSITIVITY OF PRECIPITATION OF BRUCINE AND STRYCHNINE AS DICHROMATE.

One cc. of 1*N* potassium dichromate was added to 10 cc. of the alkaloid solution. A 0.004 molar brucine hydrochloride solution gave a crystalline precipitate after 1 minute of standing, 0.002 molar after 5 minutes, 0.001 molar after 15 minutes and 0.0005 molar solution a slight precipitate after 2 hours.

The sensitivity of the strychnine precipitation was the same but the precipitate was formed more quickly. Thus a 0.0005 molar strychnine solution gave a slight precipitate after 10 minutes of standing. According to the above about 2 mg. of brucine or strychnine can be detected in 10 cc. of solution by the dichromate test.

### COMPOSITION OF THE PRECIPITATES.

*Water Content.*—The samples were kept over deliquescent sodium bromide until constant weight was attained. They were then placed in vacuum desiccators

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\* Scientific Section, A. P. H. A., Madison meeting, 1933.

<sup>1</sup> See THIS JOURNAL, April 1934, page 302.