

SCIENTIFIC SECTION

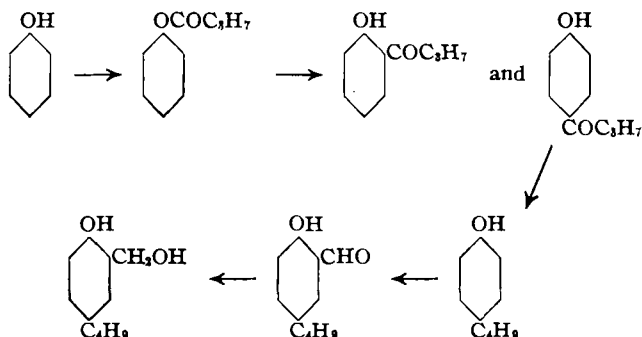
BOARD OF REVIEW OF PAPERS.—*Chairman*, F. E. Bibbins; Glenn L. Jenkins, John C. Krantz, Jr., Heber W. Youngken, L. W. Rowe, L. W. Rising, C. O. Lee, E. V. Lynn, W. G. Crockett, Frederick V. Lofgren.

THE PREPARATION OF *p*-BUTYL SALIGENIN.*¹

BY ROBB V. RICE² AND WILTON C. HARDEN.

The preparation of this compound was undertaken in order to compare some of its physical and pharmacological properties with other substituted saligenins which have been prepared and studied. A comparison of these properties will be reported elsewhere.

The compounds prepared leading to the final formation of *p*-butyl saligenin are shown according to the following scheme:



The synthesis of *p*-butyl phenol necessary for the preparation of *p*-butyl saligenin was tried by three different methods. (a) The method of Fries was used for the rearrangement of phenyl-acyl esters to acyl phenols with the aid of aluminum chloride and subsequent reduction according to Sandulesco and Girard (1) with amalgamated zinc and hydrochloric acid. This procedure involved the formation of phenyl butyrate and its rearrangement to produce both *o*-butyryl phenol and *p*-butyryl phenol. The *p*-butyryl phenol was then reduced to give *p*-butyl phenol. (b) The method of Read and Mullin (2) was attempted according to which butyl benzene is nitrated, reduced to *o*- and *p*-amino-butyl benzenes, then the amino group replaced by a hydroxyl group by diazotization of the sulphate of the amine and slow elevation of the temperature. This method was discarded due to the fact that yields of butyl benzene obtained by the methods of Read and Foster (3), Radziszewski (4) and Balbino (5) were so low that further experimentation seemed impractical. (c) The method of Smith (6) was tried in which *n*-butylphenyl ether was rearranged by means of aluminum chloride and which gave approximately the same yields as method (a). Method (a) was preferred, however, since the mixture of *o*- and *p*-butyryl phenols obtained by rearrangement was easier to separate completely than a mixture of *o*- and *p*-butyl phenols.

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¹ From the laboratories of Glenn L. Jenkins, Department of Pharmaceutical Chemistry, University of Maryland, School of Pharmacy.

² Dunning Fellow, University of Maryland, School of Pharmacy.

5-butyl-salicylaldehyde was made from *p*-butyl phenol by means of the Reimer-Tiemann reaction (7) for the production of aldehydes and this compound was reduced to *p*-butyl saligenin by the Adams platinum oxide catalyst reduction method (8).

EXPERIMENTAL.

Butyl Phenol.—295 Gm. of thionyl chloride was added slowly with shaking to 220 Gm. of butyric acid. A reflux condenser was then attached to the flask and the contents heated on a water-bath until gas evolution ceased; 235 Gm. of phenol was next added in small portions with shaking and the flask was again connected to the condenser and heated on an oil-bath at 130° for three hours or until no more hydrogen chloride was evolved. The resulting liquid was placed in a beaker surrounded with ice and allowed to cool, then 334 Gm. of anhydrous aluminum chloride slowly stirred in. This resulted in an amber-colored viscous mixture which quickly thinned and produced large amounts of hydrogen chloride on warming. Heating was continued at 130° until no more gas was given off, leaving an almost solid red-brown mass which was poured onto a flat plate while hot. On cooling a brittle solid resulted which was powdered and dropped into cold dilute hydrochloric acid with stirring. The dark viscous liquid which separated was diluted with benzene, separated from the acid and dried with anhydrous sodium sulphate. After distilling off the benzene, vacuum distillation of the remaining oil gave three main fractions: (a) a low-boiling fraction of undetermined composition; (b) a fraction distilling at 100–110° at 8-mm. pressure (*o*-butyryl phenol); (c) a fraction distilling at 165–180° at 8 mm. which solidifies immediately on cooling (*p*-butyryl phenol). An average of 100 Gm. each of Fractions *b* and *c* was obtained in several trials of this method. The *p*-butyryl phenol was purified by recrystallizing from ligroin containing 5 per cent benzene until the melting point was constant at 91° (9).

To reduce this substance 50 Gm. was placed in a three-necked flask provided with a mechanical stirrer and reflux condenser, the flask containing 250 Gm. of amalgamated zinc and 250 cc. of concentrated hydrochloric acid. The contents were boiled and stirred very vigorously over a period of twenty hours, more acid being added from time to time. The *p*-butyl phenol produced was diluted with benzene, dried with anhydrous sodium sulphate and distilled in vacuum. It distils at 119° at 10-mm. pressure. A yield of 70–76 per cent was obtained by this reduction. The product melts at 22° and boils at 248°, which is in agreement with data reported by other workers (1). It produces a phenyl urethane melting at 113°. Analysis: Nitrogen found—5.20 per cent; calculated—5.20 per cent.

5-Butyl-Salicylaldehyde.—In a three-necked flask provided with a mechanical stirrer, reflux condenser and thermometer 120 Gm. of chloroform was added to a mixture of 50 Gm. of *p*-butyl phenol and 160 Gm. of sodium hydroxide in 160 cc. of water over a period of three hours. The reaction was carried out at 65–70° by heating in a water-bath. The addition of enough water during the reaction to aid in better stirring did not affect the yield of product. It was necessary to stop the addition of chloroform frequently to prevent the mixture from frothing over. Stirring and heating were continued for an hour after all chloroform had been added. The mixture was then subjected to steam distillation to remove excess chloroform and finally acidified carefully with dilute sulphuric acid and again subjected to steam distillation until no more aldehyde was obtained. The average yield was 10 Gm.

The resulting aldehyde which distilled as a pale yellow, thick liquid was purified by making the sodium sulphite addition product which can be recrystallized from alcohol.

Reduction of 5-Butyl-salicylaldehyde.—About 300 cc. of alcohol and 0.2 Gm. of Adams platinum oxide catalyst were added to 10 Gm. of aldehyde. The container was then attached to a mechanical shaker and placed under a pressure of ten pounds of hydrogen. Shaking was continued until no further reduction took place. Yields of from 80–90 per cent were obtained by this method.

After reduction the alcoholic solution was made faintly alkaline to litmus with ammonia to prevent polymerization and the alcohol evaporated on a water-bath. The *p*-butyl saligenin thus obtained may be recrystallized from carbon tetrachloride. It crystallizes as white plate-like crystals, soapy to the touch. M. p. 81°. The compound is practically insoluble in water but readily soluble in alcohol, carbon tetrachloride, benzene, chloroform and acetone.

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SUMMARY.

p-Butyl saligenin has been prepared from *p*-butyl phenol by the formation of 5-butyl salicylaldehyde and its subsequent reduction with hydrogen.

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BISMUTH-SODIUM-POTASSIUM TARTRATE SOLUTIONS.*

BY A. H. CLARK.¹

Considerable interest has been taken during recent years in the so-called complex bismuth tartrates. The soluble salts have been used extensively in the treatment of syphilis in place of arsenic compounds, and solutions have been used for local applications. This communication deals with the preparation of a neutral solution containing bismuth in combination with tartrate and glycerin.

After many experiments or trials it has been established that such solutions are readily obtained by the procedure outlined:

Bismuth hydroxide is first prepared as free as possible from bismuth salts by dissolving bismuth subnitrate or subcarbonate in water and nitric acid. This solution is then precipitated with ammonia water and washed by decantation and collected by aid of a Büchner filter and moisture removed as completely as possible by suction.

The moist precipitate is then added to glycerin and a solution of Rochelle salt. To this mixture is then added sodium or potassium hydroxide until solution takes place.

To the strongly alkaline solution thus obtained is added tartaric acid until the mixture is neutral to litmus paper.

By this procedure a solution is obtained that is neutral or faintly acid to litmus or phenolphthalein and shows slight alkalinity to methyl orange. It will also contain a small amount of nitrate. Just what is the state of combination between the tartrate, bismuth and glycerin it is impossible to state as the writer has prepared a large number of solutions in which the proportions of the three vary widely. It is possible to vary the proportions of bismuth, glycerin, alkali and tartrate within wide limits. Indeed it is possible to prepare solutions from bismuth hydroxide, glycerin and alkali alone but such solutions are strongly alkaline in reaction. By starting with a stated amount of bismuth salt yielding a known per cent of Bi_2O_3 upon ignition, a solution containing a desired per cent of Bi_2O_3 may be

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¹ University of Illinois, College of Pharmacy, Chicago.