

CHLOROBUTANOL.*

BY ARTHUR GEORGE FISHBURN AND HERBERT BEN WATSON.

Chlorobutanol (Chlorbutol, Chloretone, Acetone-chloroform) is described in the United States Pharmacopœia (XIth Revision) as trichlorotertiarybutyl alcohol either anhydrous or containing up to about half a mol of water and having m. p. not below 78°; the British Pharmacopœia (1932) also describes the water of crystallization as variable, while the French Pharmacopœia (1937) formulates the compound with $\frac{1}{2}\text{H}_2\text{O}$ and gives m. p. 75–78°. The presence of addition compounds in mixtures of acetone and chloroform has been indicated by freezing point and dielectric polarization data (1), but these are probably quite distinct from chlorobutanol and the molecules have been represented as linked through the hydrogen atom of the chloroform.

In the usual preparation of chlorobutanol (2), (3), rather more than half an equivalent of potassium hydroxide is added (during a period of 48 hours or more) to a mixture of approximately molar quantities of acetone and chloroform. After filtration from the precipitated potassium chloride, a low-boiling fraction containing acetone and chloroform is removed by distillation, and the remaining liquid (A) treated with water. Nowhere does a yield much exceeding 10% of the theoretical seem to have been recorded. The liquid A was first thought to be an isomeride (2); the discovery that the treatment with water was accompanied by a loss of 13% of its weight, and that a similar liquid was obtainable by distillation of solid chlorobutanol with a little acetone, however, led to the conclusion that it was a mixture of chlorobutanol with some acetone (3).

EXPERIMENTAL.

We have treated mixtures containing varying quantities of acetone and chloroform with different substances. In absence of a catalyst no reaction occurred (as found by earlier workers). Nor was any product obtained when the reagents were brought together in presence of a little sulfuric acid, piperidine (3% of wt. of reagents), calcium hydroxide or ammonia (10% by wt.), borax, sodium carbonate or bicarbonate (up to 40% by wt.); neither long standing nor refluxing led to reaction. Solid sodium hydroxide was almost as effective as potassium hydroxide, but concentrated aqueous solutions were not so good.

Equimolecular quantities of reagents in presence of 5% or 10% of potash gave only 10% of the theoretical yield; an excess of acetone gave a much higher conversion of the chloroform, as follows:

Per Cent KOH (Referred to Wt. of $\text{Me}_2\text{CO} + \text{CHCl}_3$).	Mols. Me_2CO Per Mol CHCl_3 .	Per Cent Yield (Calcd. on CHCl_3).
5 (added as solid or sat. alcoholic solution)	2	12–13
5 (ditto)	5	24–26
10 (added as solid)	5	18

When the potash is added in the solid state, there is a *slow* precipitation of potassium chloride (per cent KCl in ppt. from 97.3 to 98.4, compare ref. 3); on addition of a saturated solution of potash in alcohol, however, the precipitation is immediate and the yield is not improved by standing. The rate of reaction in the former case is probably governed by the slow solution of the potash. The addition of solid potash leads, moreover, to the development of a distinct

* From the Pharmaceutical Chemistry Research Laboratory of the Technical College, Cardiff, Wales.

yellow color which is retained to some extent by the product, but alcoholic potash gives a perfectly white product.

The formation of potassium chloride is due to decomposition of chlorobutanol by the alkali. The products of this decomposition are potassium chloride, acetone and carbon monoxide (compare ref. 3) according to the equation $\text{Me}_2\text{C}(\text{OH})\text{CCl}_3 + 3\text{KOH} = 3\text{KCl} + \text{Me}_2\text{CO} + \text{CO} + 2\text{H}_2\text{O}$.

The liquid product A boils over a range of 165-170°, and solidifies fairly rapidly on exposure to air. If a considerable excess of acetone is used, the tendency to solidify is less marked and the loss of weight on addition of water is greater. Thus, in a preparation from 10 mols acetone and 1 mol chloroform this loss was as great as 25% of the weight of the liquid; this liquid, moreover, contained only 41.7% Cl, indicating 73% of trichlorotertiarybutyl alcohol. If acetone and solid chlorobutanol are placed in separate open vessels in the same desiccator, the chlorobutanol liquefies after a few hours but begins to solidify when the desiccator is opened.

In order to gain information regarding the substance which is removed by water from the liquid product A, we added 2:4-dinitrophenylhydrazine hydrochloride to the aqueous solution obtained after filtration of the solid chlorobutanol. This gave a red product which was purified (with but little loss) by three extractions with boiling alcohol. The residue, which was identical with the crystalline product from the third extract, had m. p. 200°, and was quite different from the 2:4-dinitrophenylhydrazone of acetone (yellow, m. p. 128°). This observation led us to prepare a specimen of diacetone alcohol (b. p. 166°, soluble in water) by the method described in *Organic Syntheses* (4), and this gave a 2:4-dinitrophenylhydrazone identical with the red product described above (m. p. 200°).

Solid chlorobutanol, crystallized from aqueous alcohol, melts at 77°. Its chlorine content is 57.1%, and it is therefore a hydrate with $\frac{1}{2}\text{H}_2\text{O}$ (Cl required, 57.1%). The crystals form two layers on melting; the upper aqueous layer distils first on further heating, and finally anhydrous chlorobutanol distils at 166°. Specimens of this compound after 72 hours in a vacuum desiccator in tubes sealed immediately after removal melted at 96.2° (Cl 60% as required). On exposure to air the m. p. fell to 77° after 25 mins., and thereafter remained constant.

SUMMARY AND CONCLUSIONS.

Our results show that the activation of the carbonyl bond which is necessary for the production of chlorobutanol from acetone is brought about only by a very strong base; weaker bases and acids are ineffective. The failure of calcium hydroxide to exert any influence may be due to its insolubility in the reaction mixture. The best results are obtained when an excess of acetone is employed. In view of the decomposition of the product by potash, the yields are never good, and a relatively small quantity of the catalyst is advantageous.

The liquid product obtained from acetone, chloroform and potassium hydroxide contains diacetone alcohol, with which, it may be presumed, chlorobutanol forms some type of constant boiling mixture. This substance is removed by water, and the product is a solid of the formula $\text{Me}_2\text{C}(\text{OH})\text{CCl}_3 \cdot \frac{1}{2}\text{H}_2\text{O}$ (m. p. 77°). The anhydrous compound (m. p. 96.2°) is converted into this hydrate on standing in air for less than half an hour.

We recommend the following procedure for the preparation of chlorobutanol. One hundred grams acetone (5 mols) and 40 Gm. chloroform (1 mol) are mixed, and 7 Gm. potassium hydroxide (5%) dissolved in the minimum quantity of alcohol, are added. The addition occupies fifteen minutes; cooling is usually unnecessary. The precipitated potassium chloride is filtered off and washed with a little acetone. The filtrate is distilled on the water-bath and when no further liquid distils about 200 ml. of water are added. The chlorobutanol is filtered off as a white solid. Yield (calc. on CHCl_3), 25% theoretical. The acetone distilled off is used in a subsequent preparation.

REFERENCES.

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- (2) Willgerodt, *Ber.*, 14, 2451 (1881); Willgerodt and Genieser, *J. prakt. Chem.* [2], 37, 361 (1888).
- (3) Cameron and Holly, *J. Phys. Chem.*, 2, 322 (1898).
- (4) *Organic Syntheses*, Collective Volume 1, page 193.

STUDIES ON THE GLUCOSIDES CONTAINED IN TAXUS BREVIFOLIA.

BY GEORGES MASSON.*

In a study made by I. Jones and E. V. Lynn (1), the authors report that they attempted the isolation and identification of the glucosides contained in *taxus brevifolia* and especially for taxicatine as found by Lefevre (2) in *taxus baccata*. They used the method of extraction by ethyl acetate as indicated by Bourquelot. They obtained a grayish powder which did not present the characteristics of the taxicatine. Other unsuccessful extractions made with alcohol and with water led them to the conclusion that "one cannot say positively that the leaves do not contain a glucoside, but the evidence indicates that they do not."

Since the author was working on experiments with *taxus canadensis*, it occurred to him to make comparative studies of *taxus brevifolia*. These are the experiments related below. We used for identification of glucosides the biochemical method of Bourquelot (3, 4).

Two hundred fifty grams of leaves, gathered in January 1939 in the region of Seattle, Washington, were put in boiling alcohol at 80°, to which had been added calcium carbonate, and maintained at boiling point for twenty minutes. The leaves were ground and the treatment, with new alcohol, repeated twice. After filtration of the liquid, it was evaporated under reduced pressure. We had then 280 cc. of solution on which our experiments were made.

We took out 50 cc. and the rest, to which we added 1 cc. of toluol and 2 Gm. of invertase, was placed in an incubator at 30° C.

After defecation of the above-mentioned 50 cc. with 12 cc. of lead acetate, we made an examination with the polarimeter and calculated the reducing sugars by Bertrand's method.

Polarimetric examination: + 20'

Reducing sugars: 0.908 Gm. per 100 cc. of solution.

After 13 days in the incubator, 50 cc. of the solution to which invertase had been added were examined in the same way. The rest was put in a boiling bath for fifteen minutes to destroy the invertase and after the addition of emulsin was replaced in the incubator.

Examination of the 50 cc. gave the following results:

Polarimetric examination: -1° 56'

Reducing sugars: 2.725 Gm. per 100 cc. of solution.

* Department of Chemistry, Veterinary School of Oka, P. Q., Canada.