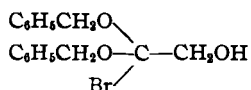
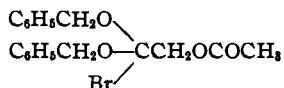


Fraction 195-200°.—Both yields were bulked and carefully refractionated, collecting the portion distilling between 194-196°. This fraction contained 21.1 p. c. and 22.4 p. c. bromine. The theoretical for



is 23.6 p. c. bromine.

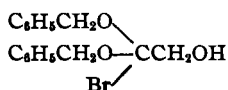
This oil was acetylated, forming a very penetrating liquid acetate which, when analyzed for bromine, was found to contain 19.9 p. c. in contrast to the theoretical for



which is 21.1 p. c. bromine.

Fraction 215-218°.—The bulked oil from both experiments was carefully refractionated, collecting the distillate between 216-218°.

This fraction contained 21.5 p. c. and 22.3 p. c. bromine, respectively, corresponding also to the configuration



This compound was also acetylated, yielding an equally sharp, somewhat lachrymating liquid acetate. Its bromine content was not determined.

Fraction 230-240°.—This was redistilled, but again came over between 230-240°, and judging from the low bromine contents (8 to 12.5 p. c.) is very probably a mixture of several substances, hence was not investigated any further.

Fraction 270-280°.—This oil distilled over very sharply between 285-286°. It contained no bromine and refused to acetylate. Dibenzyl boils at 284° C.

The pharmacological investigation of the derivatives of avertin described thus far will be reported elsewhere.

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QUININE HYDROBROMIDE WITH CHLOROFORM AND BROMOFORM OF CRYSTALLIZATION.

BY W. SCHNELLBACH AND JOSEPH ROSIN.

During our work on the solubilities of the U. S. P. chemicals, the solubility of quinine hydrobromide in chloroform was to be checked. The U. S. P. states that one Gm. quinine hydrobromide dissolves in 0.6 cc. of chloroform. Quinine hydrobromide contains 1 mol of water, or 4.26%. The material we used substantially contained this amount of water. When it was treated with the proportion of chloroform given in the U. S. P. a turbid solution resulted. This turbidity was attributable to the water in the quinine hydrobromide. Upon allowing the turbid

solution to stand at 25° C. for two days, well-formed, clear crystals separated. The quinine hydrobromide used consisted of small scale-like crystals. The crystals that separated from the chloroform solution were of a different type—stout and about $\frac{1}{4}$ " in size. It did not seem likely that the original quinine hydrobromide with its water of crystallization would have thus crystallized out, and the idea suggested itself that the salt had crystallized out with solvent of crystallization. A qualitative examination of the composition of the crystals, after removing adherent solvent, confirmed the surmise—they contain chloroform of crystallization.

To study the composition of the crystals, and with especial reference to the amount of chloroform of crystallization, experiments were made with a view to eliminate any other solvents that may interfere, such as the water present in the quinine hydrobromide and alcohol contained in U. S. P. chloroform. For this purpose two procedures were followed:

No. 1.—The quinine hydrobromide containing water of crystallization was treated with chloroform and warmed to aid the solution of the salt. To remove the water derived from the quinine salt and the alcohol from the chloroform, anhydrous calcium chloride was added to the solution and kept at about 60° for an hour or so, under a reflux condenser. It was then filtered, while still warm, and allowed to crystallize. The crystals were separated from the mother liquor by filtering with suction, and to remove adhering mother liquor they were washed a couple times by agitating with carbon tetrachloride and decanting. It was found that the product does not appreciably dissolve in carbon tetrachloride, and, consequently, its composition was not affected to a noticeable degree by washing it with this solvent. The crystals were then dried between filter paper and exposed to the air until they began to show a slight efflorescence. The product was then transferred into tightly stoppered bottles, or sealed in tubes.

No. 2.—The quinine hydrobromide was dehydrated by drying at 120° C. The chloroform was dealcoholized by shaking it with about one-fifth of its volume of concentrated sulphuric acid, washed with water to remove acid, and the water removed by allowing to stand with anhydrous calcium chloride with frequent agitation. The chloroform thus obtained was found to show a slight reaction for free chlorine after 24 hours, so it was freshly prepared when needed. The dehydrated quinine hydrobromide was dissolved in the chloroform at a slightly elevated temperature, filtered, if necessary, while warm, crystallized, washed with carbon tetrachloride and dried as described in procedure No. 1.

With either of these procedures we obtained the product in the form of relatively large, clear, colorless, or nearly colorless crystals, or in the form of white, or nearly white crystalline powder. The large crystals were most readily obtained by using a larger proportion of chloroform and allowing to crystallize by spontaneous cooling and evaporation. The crystalline powder was readily obtained by using about an equal weight of chloroform for dissolving the quinine hydrobromide and cooling the solution during the crystallization with running water, while stirring.

The product loses its chloroform of crystallization, or at least a part of it, quite readily on exposure to the air. Therefore, when obtained in the form of crystalline powder, greater efflorescence would be expected than with large crystals. Our object in preparing the powder form was to obviate, as much as possible, occlusion of solvent in the crystals.

The amount of chloroform of crystallization was determined from the loss by drying to constant weight under vacuum in a steam-jacketed tube. The following results were obtained:

Large crystals.	41.8 and 42.3%
Crystalline powder, sample No. 1.	37.0%
Crystalline powder, sample No. 2.	37.9%

A sample of the crystalline powder, kept in a cork-stoppered bottle for nearly one year, lost 34.4% of its weight on drying in a similar manner.

The quantity of chloroform thus found in the product corresponds to 2.5 mols. The theoretical percentage for 2.5 mols is 42.4%. The difference between the percentage of chloroform found and the theoretical is most probably due to efflorescence, the crystalline powder, as would be expected, having effloresced more than the large crystals.

The proportion of acid, calculated as HBr, was also determined in a sample of the large crystals. For this determination the salt was dissolved in diluted alcohol and titrated with *N*/10 sodium hydroxide and thymolphthalein indicator.

Theory, for product with 2.5 mols CHCl_3 , is 11.50% HBr. Found, 11.47, 11.65 and 11.44%; average 11.52% HBr.

The successful preparation of quinine hydrobromide with chloroform of crystallization led us to attempt to prepare quinine hydrobromide with bromoform of crystallization. A rough trial was made by dissolving anhydrous quinine hydrobromide in hot bromoform and allowing to crystallize. An impure crystalline mass was obtained which, after removing from mother liquor and washing to remove the solvent, proved to contain bromoform of crystallization.

The preparation of quinine hydrobromide with bromoform of crystallization in a pure state proved somewhat difficult, because of the ease with which bromoform undergoes decomposition. The best quality of bromoform available in commerce contains about 4% alcohol added as a stabilizer. The presence of the alcohol might interfere with the preparation of a product with bromoform of crystallization, either by increasing the solubility of the quinine hydrobromide, thereby suppressing crystallization, or by crystallizing with it. It was, therefore, necessary to use absolute bromoform. Such bromoform, however, is unstable, decomposes readily, some of the decomposition products, which may include free bromine, acting on the quinine and causing the solution to become dark and discolor the resulting product. After several attempts we finally succeeded in obtaining a tolerably pure crystalline product.

The best commercial bromoform available was dealcoholized by washing with water and drying over calcium chloride. Anhydrous quinine hydrobromide was dissolved in an excess of the bromoform, filtered, if necessary, and allowed to stand in the dark at room temperature. A dark syrupy mass resulted from which, upon long standing, a crystalline conglomerate separated. The crystalline mass was separated from the mother liquor, broken up into small fragments, washed with small quantities of cold absolute bromoform, until the washings ran colorless, or nearly so, and dried between filter paper and finally exposed to air for a short time. Attempts to carry out this preparation with the aid of vacuum did not improve the appearance or quality of the product.

The determination of the bromoform of crystallization by loss in weight on drying was unsuccessful. A sample kept under vacuum for 18 hours at 20° lost about 24%. When it was dried at 80° for 3 hours the total loss amounted to about 40%, which was not appreciably increased by longer drying at this temperature. Further drying at successive higher temperatures progressively raised the loss. At 120° C. the loss was nearly 70%, but the residue appeared much decomposed. We, therefore, had recourse to the determination of the total bromine. This determination was made by the method of Bacon.¹

The analysis of two samples gave the following results:

0.4013 Gm. substance required 31.58 cc. 0.1 *N* AgNO₃ equivalent to 62.9% bromine

0.4710 Gm. substance yielded 0.7240 Gm. AgBr equivalent to 65.5% bromine

The bromine found in the preparation approximates two mols of bromoform. The theoretical bromine for quinine hydrobromide with two mols of bromoform is 61.4%.

Attempts to titrate the hydrobromic acid, as was done in the case of the crystals containing chloroform of crystallization, failed. The acid found was higher than the theoretical amount corresponding to two mols of bromoform. The reason for this we ascribe to the decomposition of bromoform when in contact with alkali during the titration.

We expect to continue our investigation for an improved method for the preparation of the bromoform compound, and to study the physical and chemical properties of the new compounds.

SUMMARY.

Two crystalline compounds of quinine hydrobromide with trihalogenmethane of crystallization have been prepared and their composition established. One contains two and one-half mols of chloroform and the other two mols of bromoform of crystallization. Their chemical and physical properties will be reported at a later date.

MICROSCOPIC IDENTIFICATION OF EPHEDRINE WITH NITROUS ACID.

BY FREDERICK GRILL.*

It has been suggested that a more efficient means be developed of identifying ephedrine microscopically. Ephedrine appears to crystallize slowly with the usual alkaloidal reagents and sometimes the crystals are not characteristic. Tsiang and Brown (1) have obtained well-defined crystals from solutions of ephedrine using gold chloride, platinic chloride and Kraut's reagent. However, it would seem that the crystals appear rather slowly at times with the reagents mentioned.

The purpose of this paper is to present another means of identifying ephedrine by the formation of characteristic crystals, using nitrous acid.

The structural formula of ephedrine shows it to be a secondary amine of the aromatic series (2).

¹ *J. Am. Chem. Soc.*, 31 (1909), 50.

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