Eucalyptol and Para-Hydroxy-Benzoic Acid.—Preparation like the previous compound. Yield, about 7 Gm. of long prisms which lose eucalyptol rapidly on exposure, and melt, with decomposition, at 63–65°. Analysis: 2.29 Gm. dissolved in alcohol required 10.8 ml 0.5 *N* KOH, equivalent to 0.745 Gm. *p*-hydroxy-benzoic acid, or 32.5%. (Calc. for $C_6H_4OH.COOH.C_{10}H_{18}O$, 47.2% acid. Calc. for $C_6H_4OH.COOH.2C_{10}H_{19}O$, 30.9% acid.)

The analysis is not very exact, owing partly to the ready dissociation of the compound, and also to the fact that the acid yields high figures on titration, due to the presence of the hydroxyl group. The conclusion, however, appears justified, that the compound is analogous to those with resorcinol and hydroquinone, which contain two molecules of eucalyptol to one of the phenol.

The preparation of molecular compounds with tri-brom-, tri-chlor-, tri-nitro-phenol; guaiacol, eugenol and isoeugenol; salicylic, meta-hydroxybenzoic, anisic, veratric, ortho-, meta-, para-nitrobenzoic or anthranilic acids; ortho- or para-hydroxy-benzaldehyde was unsuccessful.

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FURTHER OBSERVATIONS UPON THE BROMINE METHOD FOR THE ESTIMATION OF ALKALOIDS.

BY H. B. HAAG.*

Several years ago Weiss and Hatcher (1) described a method for the quantitative estimation of quinine and quinidine, both in pure solutions and in tissue extracts. The adaptability of this test depends upon the fact that these alkaloids promptly decolorize diluted bromine water by uniting chemically with the bromine with resulting disappearance of the yellow color.

This summer, while working in the Department of Pharmacology of Cornell University Medical College, New York City, the thought occurred that this procedure might be extended to include other common alkaloids and related compounds. The technic employed was essentially identical to that previously outlined by Weiss and Hatcher. Diluted bromine water was prepared by diluting a saturated aqueous solution ten times with distilled water. It was concluded from several tests that this diluted bromine solution, when kept in a glass-stoppered bottle, did not rapidly deteriorate and hence the freshly diluted preparation certainly retained, for purposes of this test, its original concentration for at least several hours. The standard solution of the alkaloid was prepared so that each cubic centimeter corresponded to 1.0 mg. of the alkaloidal base, and was made up in 0.5% sulphuric acid. In this connection it should be mentioned that all solutions tested against the bromine water should be acid, as alkalies themselves decolorize the solution. The bromine water was standardized against this known solution as follows: 0.5 cc. of the diluted bromine water, accurately measured, was placed in a test-tube of about 5 cc. capacity, and then the standard was gradually added from a micro-pipette until complete decolorization of the bromine water had taken place, as viewed by reflected light against a white background. This was repeated so that an average value could be obtained from several fairly

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concordant titrations. The solution of unknown concentration was then titrated in a similar manner and the calculations made by dividing the number of cubic centimeters of the standard solution necessary for the decolorization of 0.5 cc. of the diluted bromine water by the corresponding number for the unknown. The resulting figure represented the amount of alkaloid, in mg. in 1 cc. of the unknown solution. By employing such a procedure it was possible to estimate within 5 per cent of the concentration of unknown solutions.

The test is also applicable to tissue extracts upon which quantitative studies as to alkaloidal content are desired. In addition to quinine and quinidine mentioned by Weiss and Hatcher it was found that the following alkaloids, when present in a concentration of about 1–1000, lend themselves well to the test: ethylmorphine, diacetylmorphine, methylmorphine, cinchonidine, pilocarpine, strychnine, procaine, theobromine, caffeine, histamine, brucine, and to a limited extent, epinephrine. The following were found to be without influence upon the color of bromine water, and hence not suitable for the test: atropine, scopolamine, cocaine, betaine, sparteine, hydrastine, ephedrine and morphine. Physostigmine and papaverine first produced a white cloudiness which cleared upon the addition of a slight excess of the solution; whether practical use could be had in the case of these two is questionable. Apomorphine gave rise to a cherry-colored solution which did not decolorize. Nicotine had no decolorizing effect when used in a 1–1000 solution, but was quite effective in a concentration of 1 per cent.

REFERENCE.

(1) Soma Weiss and Robert A. Hatcher, *Proc. Soc. Exptl. Biol. Med.*, 23 (1925), 33–35.

A METHOD OF DETERMINING A SMALL AMOUNT OF STRYCHNINE IN THE PRESENCE OF LARGER AMOUNTS OF QUININE AND CINCHONIDINE.*

BY GUSTAVE A. STICHT.

When the cinchona alkaloids are dissolved in an excess of hydrochloric acid, and these salts evaporated on a water-bath to dryness, until no more excess of acid is present, the so-called *di* salts are formed, and as is known, one-half of their acid radical is acid to methyl red when they are in solution, and both acid radicals are acid to phenolphthalein. Most other alkaloids, as strychnine, under the same treatment, only form salts that are neutral to methyl red, and acid to phenolphthalein. If a *di* acid and a *mono* acid alkaloidal salt are present together, then using methyl red and phenolphthalein indicators, the respective amounts of alkaloids can be estimated.

If the proportion of cinchona alkaloids to strychnine is not very large, and their acid radicals are combined as stated, then titrated as described below, the amounts of acid due to the cinchona alkaloid and strychnine, respectively, can be estimated with a fair degree of accuracy.

But in elixirs and such preparations, the amount of cinchona alkaloids is usually much larger than the strychnine, hence the bulk of the cinchona alkaloids must be separated. This is best done in the case of quinine and cinchonidine as a

* Scientific Section, A. PH. A., Toronto meeting, 1932.