can be readily determined from the equations given above. In Equation 1, it is seen that the barometric pressure does not appear, but a change in 3° in temperature causes a variation of approximately 1 per cent of the value of ΔR. This effect is vanishingly small in the case of purer samples of nitrous oxide and in the case of a 5 per cent nitrogen impurity where the drum reading for the Zeiss instruments is approximately 70, the variation is considerably less than the limit of reproducibility of the drum reading. Two calibrations carried out at different selected temperatures should therefore cover the range of normal seasonal temperature variations.

Equation 3 can be solved for any desired temperature and pressure. The variations in ΔR with temperature are the same as in the case of Equation 1. A variation of 8 mm. in the barometric pressure causes a variation of approximately 1 per cent of the value of ΔR.

The total volume of the interferometer system should be restricted as far as practicable in favor of the efficiency and rapidity with which it can be swept out. The inner walls of all rubber tubing connections should be freed of dust and the exits of the calcium chloride tubes should be well plugged with cotton to filter out all calcium chloride dust.

The actual reading of the interferometer is doubtless a matter of individual variation. We have found, however, that in making readings, eyestrain is greatly reduced if the reading is made as accurately as possible within ten or fifteen seconds. After the eye is rested a few seconds, the final reading is made. Prolonged staring into the instrument is to be avoided. In making several determinations on the same gas sample it is desirable to rotate the drum 10 or 20 divisions in either direction from the previous reading before making a subsequent reading.

The zero reading of the interferometer should be checked from time to time especially when any unusual temperature changes have occurred. Any gas or gas mixture can be used for this purpose, the requirements being that both cells of the interferometer contain the same gas at the same temperature and pressure.

SUMMARY

1. A method for the assay of nitrous oxide based on the use of the gas interferometer has been described.

2. A simple method for the calibration of the interferometer has also been indicated.

3. The interferometric method of assay yields results accurate to within 0.2 per cent and therefore compares favorably with other proposed methods in this respect. The method is unusually rapid.

Determination of Free Phenols in Methyl Salicylate

*By R. W. Towne, R. M. Hitchens and M. S. McCauley**

INTRODUCTION

On numerous occasions during the last several years need has arisen for an accurate, sensitive method for determining traces of phenolic impurities in methyl salicylate. The Dodge (1) method, used extensively, is limited in value since it is sensitive to only 0.02 per cent phenol and since it does not preclude errors caused by volatilization of some salicylic acid along with the phenols. Because of these faults this method is unsatisfactory in cases where it is desired to know the exact phenol content.

EXPERIMENTAL

Principle of Proposed Method.—Since methyl salicylate is itself a phenol, the determination of traces of phenol in this product resolves itself into the separation of two phenols. Fortunately, methyl salicylate is a much weaker acid than phenol itself, although both are extremely weak acids. It should be possible to effect a concentration of the phenol present by extracting the ester with a dilute solution of sodium hydroxide, thus removing all of the phenol together with a little of the methyl salicylate. The reactions:

$$C_6H_5OH + NaOH \rightleftarrows C_6H_5ONa + H_2O$$

$$C_6H_4OHCOOCH_3 + NaOH \rightleftarrows C_6H_4.ONa.COOCH_3 + H_2O$$

The small amount of methyl salicylate extracted may be converted into sodium salicylate and methanol by saponification:

$$C_6H_4.ONa.COOCH_3 + H_2O \rightarrow C_6H_4.OH.COONa + CH_3OH$$

The excess alkali may be removed by acidification to a p_H value of 9, at which point the phenol will be present largely as such with a small amount of the sodium salt, the salicylate as sodium salicylate and the methanol as such. If the solution is buffered at this p_H value the phenol may be distilled quantitatively and thus separated completely from the salicylate. The phenol in the distillate may be determined by the customary volumetric conversion to tribromphenol.

Details of Proposed Method.—Solutions and Reagents:

(1) Sodium hydroxide solution, 1 Gm. per 100 cc. water.

* Analytical Laboratory, Monsanto Chemical Co., St. Louis, Mo.

(2) Sodium hydroxide solution, 20 Gm. per 100 cc. water.

(3) Hydrochloric acid, concentrated.

(4) Sodium borate, 2 Gm. $Na_2B_4O_7.10H_2O$ per 100 cc. water.

(5) 0.1*N* bromide-bromate solution, standardized against potassium iodate through sodium thiosulfate, 0.1*N*.

(6) 0.1*N* sodium thiosulfate solution, standardized against potassium iodate.

(7) Potassium iodide, AR.

(8) Thymol blue, 0.1 Gm. per 100 cc. made as the one-half monosodium salt in aqueous solution.

(9) Benzene of good quality. If quality is in question wash thoroughly with 1 per cent sodium hydroxide solution before use.

Procedure.—Weigh 25 Gm. of methyl salicylate a 125-cc. pear-shaped separatory funnel. Add 45 cc. benzene. Add 20 cc. of sodium hydroxide solution, 1 Gm. per 100 cc. water. Agitate thoroughly for a few seconds. Allow to separate. Drain off the aqueous layer through a cotton plug in a small, short-stem funnel into a 250-cc. beaker. Make two more extractions with 20-cc. portions of the sodium hydroxide solution. To the combined extracts add 5 cc. of a solution of sodium hydroxide, 20 Gm. per 100 cc. of water. Heat on the steam-bath for 30 minutes. Cool in an ice-bath to 20° C.

Add a few drops of thymol blue indicator. Add a slight excess of hydrochloric acid with constant stirring, keeping the solution in the ice-bath to prevent volatilization of phenol. Redissolve any precipitated salicylic acid with a drop or so of the 1 per cent sodium hydroxide solution, adjusting the acidity so that the solution has a greenish color.

Transfer to a 250-cc. round-bottom flask fitted with a S.T. 19/38 ground glass joint (Fig. 1). Rinse the beaker with 40 cc. of sodium borate solution, 2 Gm. per 100 cc. and add to the flask. Connect the flask to a short spray column filled with small glass helices and fitted with a reservoir at the top of the column. Distil into a 250-cc. glass-stoppered flask. When the volume of the solution being distilled has been reduced to 30 cc. add 20 cc. of water and redistil to a 30-cc. volume.

To the distillate add 10.00 cc. of 0.1*N* bromide-bromate solution. This is sufficient to take care of 0.05 per cent phenol. If the phenol content is in excess of 0.05 per cent, proportionately more bromide-bromate must be added. If more than 20 cc. is required, repeat the analysis with a sample sufficiently small to bring the titration below 20 cc. Add 4 cc. concentrated hydrochloric acid. Let stand five minutes at not over 25° C. Add 1 Gm. potassium iodide. Rinse the stopper carefully. Titrate with 0.1*N* sodium thiosulfate solution to a soluble starch end-point.

$$\text{Per cent Phenol} = \frac{(\text{cc. } 0.1N \text{ bromate} - \text{cc. } 0.1 \text{ thio}) \times 100 \times 0.001567}{\text{weight of sample}}$$

Notes: The possibility of decomposition of sodium salicylate to phenol and sodium carbonate during the analysis was studied by distilling a solution of borax and sodium salicylate. The complete absence of phenolic bodies in the distillate is evidence that decomposition does not take place. That methyl alcohol does not interfere was proved by running a blank with a large excess of methanol.

Verification of the Proposed Method.—Phenol-free methyl salicylate for the preparation of knowns was made by washing methyl salicylate repeatedly with 1 per cent sodium hydroxide solution. A total of six such washings was made even though the third washing was found to be phenol-free.

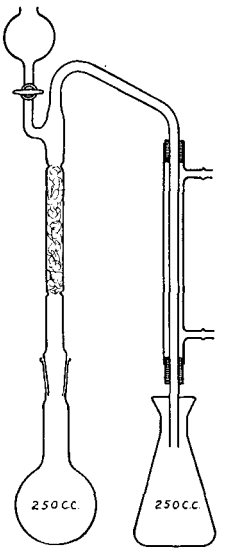

Fig. 1—Phenol distillation apparatus.

The efficiency of the alkali extraction during analysis was determined by adding a known amount of phenol to the phenol-free material and then determining the phenol content of each extract. It was found, with 0.0138 per cent phenol added, that about 90 per cent was removed by the first extraction and the remainder by the second. None whatever could be detected in the third. When the three extracts were combined for distillation 0.0139 per cent phenol was recovered.

Similar knowns were made by adding various amounts of phenol to the phenol-free product and were analyzed by the suggested procedure. The results are given in Table I.

Table I.—Determination of Phenol in Known Mixtures of Phenol and Methyl Salicylate

Test No.	Per Cent Phenol Added	Per Cent Phenol Found	Error, Per Cent Phenol
1	0.0037	0.0040	+0.0003
2	0.0073	0.0075	+0.0002
3	0.0138	0.0139	+0.0001
4	0.0220	0.0218	−0.0002
5	0.0220	0.0216	−0.0004
6	0.0440	0.0439	−0.0001

CONCLUSION

The method described for the determination of traces of phenolic impurities in methyl salicylate is both rapid and accurate. It permits the detection of as little as 0.001 per cent free phenolic bodies and is reproducible to ±0.0003 per cent. This is a decided improvement over the customary method which is sensitive only to 0.02 per cent phenol.

REFERENCE

(1) Dodge, F. D., *Drug Markets*, 22 (1928), 609.

A Method for the Determination of Calomel in Tablets

By R. A. Bosee and L. A. Perlenfein†*

The well-known reaction which occurs when calomel is heated in the dry state with sodium carbonate or bicarbonate may be used to assay mercurous chloride in tablets. The method is especially useful for those tablets in which the presence of other ingredients renders the iodine method inapplicable, and makes filtration of the entire tablet mass difficult.

$$Hg_2Cl_2 + 2NaHCO_3 \rightarrow 2Hg\uparrow + 2NaCl + CO_2\uparrow + H_2O\uparrow$$

The method was first used in our laboratories for the assay of calomel and soda tablets.

EXPERIMENTAL

Assay for Calomel.—Weigh not less than 20 of the tablets, reduce them to a fine powder without an appreciable loss, transfer an aliquot portion equivalent to about 0.5 Gm. of mild mercurous chloride to a nickel crucible and ignite. Leach the carbonized mass with boiling water, add 30 cc. of tenth-normal silver nitrate, 5 cc. of nitric acid and filter. To the filtrate add ferric ammonium sulfate T.S. and titrate the excess of silver nitrate with tenth-normal ammonium thiocyanate.

Each cc. of tenth-normal silver nitrate is equivalent to 0.02361 Gm. of mild mercurous chloride, HgCl.

Assay for Sodium Bicarbonate.—It is also possible to obtain a figure for both sodium bicarbonate and calomel on the same sample. After igniting and leaching with boiling water, the filtrate can be first titrated with normal sulfuric acid in the presence of methyl orange, and then a chloride titration run.

The number of cc. of normal sulfuric acid multiplied by 0.08401 represents the amount of sodium bicarbonate not entering into the reaction with the calomel. The figure obtained for calomel multiplied by 0.356 represents the quantity of sodium bicarbonate entering into reacton. The sum of these two results gives the entire amount of sodium bicarbonate present in the sample.

If the method is to be used for assaying calomel in tablets not containing soda, carbonate or bicarbonate may be added and either titration used. If the alkalimetrical titration is used, a definitely measured quantity of reagent must be added. If the chloride titration is used, an excess of the reagent is all that is necessary. In either case, however, care must be exercised that the calomel does not volatilize before it has a chance to react with the carbonate. Best results were obtained by adding a few drops of water and mixing into a smooth, thick paste. In the case of the calomel and soda tablets the thorough mixing of the ingredients and the compression of the tablets make the addition of moisture before igniting unnecessary.

Procedures similar to both of those given have been used before for the determination of calomel in aqueous media. M. Kohn (1), (2), (3) showed that mercuric halides could be decomposed in alkaline solution and the halogens subsequently determined by the method of Volhard. D. Köszegi (4) pointed out that calomel could be determined by treating with a known quantity of normal NaOH, filtering and titrating the remaining NaOH with normal acid. However, for the usual calomel tablets, heating in the dry state with carbonate furnishes a quick and accurate method of eliminating troublesome fillers and at the same time volatilizes the metallic mercury formed during the reaction.

Results.—The following are examples of the results obtained by following these procedures:

Results of Assay of Calomel Tablets

Weight of Sample, Gm.	Gm. Calomel Calculated[a]	Found	Error, %
1.5056	0.4926	0.4925	0.02
1.5022	0.4914	0.4880	0.72
1.5040	0.4920	0.4904	0.32
Weight of Sample, Gm.	**Gm. Sodium Bicarbonate Calculated[a]**	**Found**	**Error, %**
1.5056	1.0017	0.9940	0.77
1.5022	0.9997	0.9966	0.31
1.5040	1.0009	0.9996	0.13

[a] Calculated amounts are based on assay of each separate ingredient by U. S. P. method.

REFERENCES

(1) Kohn, M., *Zeit. anorg. Chemie*, 59 (1908), 108–110.

(2) Kohn, *Ibid.*, 59 (1908), 271.

(3) Kohn, M., and Ostersetzer, A., *Ibid.*, 80 (1913), 218–220.

(4) Köszegi, D., *Pharm. Zeit.*, 76 (1931), 524.

* Director of Laboratories, Endo Products, Inc., New York, N. Y.

† Analytical Chemist, Endo Products, Inc., New York, N. Y.