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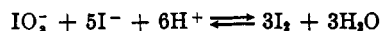
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Carius Iodometric Microdetermination of Iodine in Organic Compounds

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A method is described for the determination of iodine in 5- to 10-mg. samples of organic compounds containing not more than 4 mg. of iodine. Certain samples in aqueous solution also can be analyzed by the method. The method combines the well known and highly respected Carius digestion with a simple modification of the widely used Winkler iodometric titration. Adequate provision is made for elimination of nitrite interference. The method is characterized by simple techniques, specificity, a favorable volumetric factor, an excellent end point, and short working time per sample.

THE classical Carius method is seldom used for the determination of iodine in organic compounds because of the unfavorable gravimetric factor, the interference caused by other halogens, and the impurity of the silver iodide precipitate (7, 18). The silver normally present in the Carius digest interferes with the measurement of the iodine by the excellent iodometric method proposed by Winkler (20), modified by Burgarszky and Horvath (2), Leipert (8), and many others, wherein the iodine originally present in the sample is oxidized and the iodate thus formed is allowed to react with excess iodide to form free iodine according to the reaction



Most analysts, therefore, have adopted the method of either burning the sample in a stream of oxygen in a quartz tube (11, p. 172; 12, p. 94; 17) or decomposing it with sodium peroxide in the all-metal bomb (4) in order to destroy the organic matter and convert the iodine to a form susceptible to iodometric measurement. Such methods are often unsatisfactory because of long working time, incomplete removal of the iodine from ash, reaction of possible constituents of the sample with quartz combustion tubes, and inability to decompose samples that are in aqueous solution. Because the Carius digestion has none of these disadvantages, a method permitting its use with subsequent iodometric measurement of the iodine would have an advantage.

Doering (3) proposed a macromethod for the determination of iodine in organic compounds, in which the sample was heated in a sealed glass tube with mercuric nitrate instead of silver nitrate, as in the Carius method. Mercury, like silver, serves to render the iodine nonvolatile and has the added advantage that it does not interfere in any way with the oxidation of the iodine and its

measurement by the Winkler iodometric method. Neither the method of Doering nor the micromodification proposed by Weygand and Werner (19) appears to be well known in this country.

Chlorine used by Doering in the Winkler method to oxidize the iodide to iodate also oxidizes nitrites and/or other interfering materials in the Carius digest which are capable of liberating iodine from acidified iodide solutions. The use of chlorine as oxidant in the iodometric method for iodine has two serious disadvantages: Bromide, if present, may interfere with the determination of iodine (5, 8, 9, 16), and it is comparatively difficult to remove excess chlorine quantitatively without loss of iodate (6, 9). Incomplete removal of the chlorine leads to high results.

Bromine is far superior to chlorine as the oxidant for this method, because interference from other halogens is not encountered, bromine is more stable than the sodium hypochlorite solutions usually used (8) and is free from blank (2), and the excess bromine can be easily and quickly removed at room temperature without loss of iodate. For these reasons bromine has almost completely supplanted chlorine as oxidant for the iodometric determination of iodine. Bromine, however, cannot be substituted for chlorine in the Doering method, because it is not capable of completely oxidizing the nitrite formed during the Carius digestion (5, 8, 9).

This paper presents a micromethod for the determination of iodine in organic compounds which combines the Carius digestion and the iodometric determination of iodine. Bromine is used as the oxidant and alkaline sulfite-sulfamic acid reagent is employed to remove nitrites. The Carius digestion is applicable to nearly all types of compounds and the reagents are few and nearly free from blank; there is no possibility of loss of iodine

through volatilization or incomplete extraction from ash, and samples containing alkali metals do not damage the combustion tubes; the iodometric method used to measure the iodine is one of the most exact and precise volumetric methods known; the volumetric factor is favorable; the working time for both digestion and titration is favorable; and the techniques required are simple and well known and the reagents are essentially the same as those commonly used in many laboratories for the Leipter iodometric method for iodine and the Vieböck method for methoxyl (11, pp. 172 and 239; 12).

APPARATUS AND REAGENTS

Carius tubes are made from borosilicate glass tubing 0.5 inch in outside diameter, $\frac{3}{32}$ -inch wall, and approximately 7 inches long. This tubing is also sold as Pyrex Brand high pressure gage glass, and is usually available from boiler supply or mill supply companies.

Carius Furnace. Any suitable tube furnace capable of heating the sealed combustion tubes to 300° C.

Nitric Acid-Mercuric Nitrate Reagent. Dissolve 20 grams of reagent grade mercuric nitrate [$\text{Hg}(\text{NO}_3)_2 \cdot x\text{H}_2\text{O}$] in 100 ml. of nitric acid, conforming to AMERICAN CHEMICAL SOCIETY specifications, specific gravity 1.42. (The solution should assay approximately 13 grams of mercury per 100 ml.)

Alkaline Sulfite-Sulfamic Acid Reagent. Dissolve 10 grams of sodium sulfite, A.C.S., and 5 grams of pure aminosulfonic acid (sulfamic acid) in 300 ml. of 15% w./v. cool sodium hydroxide. The reagent is stable at least one month.

Sodium acetate (trihydrate), A.C.S., 20% aqueous solution.

Solution of sodium acetate (trihydrate), A.C.S., in glacial acetic acid, 10%.

Bromine, A.C.S., free from iodine (traces of iodine may be removed from the bromine by shaking it cautiously in a separatory funnel with several small portions of water).

Formic acid, A.C.S., 90%.

Potassium iodide, A.C.S., granulated, free from iodate.

Sulfuric Acid, Dilute. Add 1 volume of concentrated A.C.S. sulfuric acid to 9 volumes of distilled water.

Sodium thiosulfate, 0.01 N, is standardized against potassium biiodate under the conditions of the method, using all the reagents.

Starch Indicator. Dissolve approximately 5 grams of 20% amylose (G. Frederick Smith Chemical Company) in 100 ml. of boiling water and allow to cool to room temperature. Filter through glass wool and add a few drops of mercury as preservative. The end point is sharper with the amylose indicator than with the usual soluble-starch indicator, but the latter may be used.

Potassium biiodate, 0.0008 M (0.3249 gram of the pure dry salt per liter), for standardizing the thiosulfate.

PROCEDURE

Weigh a 5- to 10-mg. sample containing not more than 4 mg. of iodine into a Carius tube and add 0.3 ml. of nitric acid-mercuric nitrate reagent. Seal the tube as usual and digest 3 hours at 300° C. Allow to cool to room temperature in the furnace and then heat the tip of the tube with a soft flame to drive out the condensed acid. Cool the lower half of the tube in ice water. Apply a sharp, small flame to the capillary until it opens as a result of slight internal pressure. Make a file scratch near the constriction and open the tube with a hot glass rod as usual.

Wash the contents of the tube into a 125-ml. iodine flask containing 3 ml. of alkaline sulfite-sulfamic acid reagent and 5 ml. of aqueous sodium acetate solution. Use approximately 20 ml. of water to wash out the tube and the tip. Add 5 ml. of glacial acetic acid-sodium acetate solution and mix well. Add bromine (approximately 0.12 ml.) until the solution is clear and a strong yellow-brown color remains after thorough shaking. Allow to stand at least 2 minutes to permit complete oxidation, then add formic acid (approximately 0.25 ml.) down the side of the flask. Shake the stoppered flask cautiously until no more pressure develops. If the solution is not perfectly

colorless, add a few more drops of formic acid. Wash down the neck of the flask and draw a current of air over the liquid (14) to sweep all bromine fumes from the flask. Add 0.5 gram of potassium iodide and 4.5 ml. of the dilute sulfuric acid, and swirl the stoppered flask gently to dissolve the iodide. Allow to stand 5 minutes; then titrate the liberated iodine rapidly with 0.01 N sodium thiosulfate to a pale yellow color, add 2 drops of the amylose indicator solution, and continue the titration to a colorless end point.

A blank determination should be made using all reagents; however, the blank need not be digested. The blank titration is usually about 0.02 ml. of 0.01 N sodium thiosulfate.

The calculations are made as follows:

$$\frac{\text{Net ml. of } 0.01 \text{ N Na}_2\text{S}_2\text{O}_3 \times 0.21153 \times 100}{\text{sample wt. (mg.)}} = \% \text{I}$$

RESULTS

National Bureau of Standards No. 145 2-iodobenzoic acid, pure potassium iodobenzoate, and a group of commercial organic chemicals of unknown purity containing a variety of elements and functional groups were analyzed by this method and by the Grote method as described by Sundberg and Royer (17), modified to give a more dilute acid solution for the liberation of the iodine.

For the eleven samples analyzed by both methods (Table I) the difference between the high and low value for the Carius method averaged 0.14% and for the Grote method, 0.15%. Results by the Carius method averaged higher than did those by the Grote method for five of the samples. The average values obtained by the two methods agreed within 0.1% for four of the samples and in no case was the difference more than 0.2%. The average difference between results by the two methods was 0.12% (equivalent to 0.03 ml. of 0.01 N sodium thiosulfate for a 5-mg. sample). Because of the high percentage of iodine in the samples, this discrepancy amounted to an average difference of only 2.3 parts per thousand.

These data show that the accuracy and precision of the proposed method are good.

DISCUSSION OF METHOD

All Carius microtubes used in this laboratory are made from heavy-walled borosilicate glass tubing 0.5 inch in outside diameter. As a safety precaution, commercial thin-walled Carius tubes should not be used for this method. Explosions with the heavy-walled tubes are exceedingly rare and no such tube has ever exploded in this laboratory after it was cool. The tubes may be re-used as long as they are of sufficient length. Dried samples may be conveniently placed in the tubes with A.C.S. specification (15) capped weighing tubes. Materials that react with cold

Table I. Recovery of Iodine from Organic Compounds

Sample	Carius-Iodometric Method			Grote Method		
	Av. %	Replicates %		Av. %	Replicates %	
2-Iodobenzoic acid, N.B.S. No. 145	51.09 ^a	...		51.15	51.18, 51.18, 51.10	
<i>o</i> -Iodophenol	57.54	57.62, 57.55, 57.44		57.36	57.45, 57.37, 57.27	
<i>p</i> -Chloriodobenzene	53.05	53.12, 53.02, 53.00		52.91	52.92, 52.90	
<i>p</i> -Bromiodobenzene	44.53	44.60, 44.52, 44.46		44.34	44.45, 44.33, 44.23	
<i>p</i> -Diiodobenzene	76.84	76.71, 76.61, 76.61		76.75	76.85, 76.76, 76.63	
<i>p</i> -Nitroiodobenzene	50.75	50.77, 50.77, 50.71		50.83	50.88, 50.82, 50.80, 50.80	
<i>p</i> -Iodoaniline	58.67	58.76, 58.73, 58.71, 58.47		58.58	58.78, 58.55, 58.42	
<i>g</i> -Iodopropionic acid	63.08	63.17, 63.04, 63.02		63.24	63.29, 63.28, 63.26, 63.11	
Hexamethylenetetramine ethiodide	42.74	42.80, 42.74, 42.68		42.89	42.91, 42.88, 42.87	
7-Iodo-8-hydroxyquinoline- 5-sulfonic acid	35.70	35.76, 35.74, 35.70, 35.61		35.65	35.72, 35.67, 35.55	
Potassium iodobenzoate	44.29	44.32, 44.25		^b		
3,5-Diiodo-L-tyrosine (air- dry sample)	57.87	57.88, 57.86, 57.86		57.99	58.04, 57.97, 57.96	
3,5-Diiodo-L-tyrosine (lyophilized in Carius tube)	57.91	57.99, 57.91, 57.84		

^a Average of 12 analyses: maximum, 51.17%; minimum, 50.99%; standard deviation, 0.057%. Theory, 51.17% I.

^b Not susceptible to analysis by Grote method. Theory, 44.36% I.

nitric acid should be kept from contact with the acid until the tube is sealed; either the sample or the acid may be introduced into the tube in a small, thin-walled vial. In some cases aqueous solutions of organic compounds or biological preparations may be aliquoted into the tube, shell-frozen in a dry ice-acetone bath, and vacuum-dried from the frozen state (lyophilized).

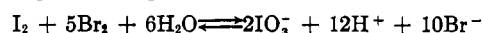
All digestions made in this study were carried out at 300° C. for 3 hours. Three hundred degrees is the maximum temperature usually recommended for the Carius digestion and the 3 hours' duration of heating is considerably greater than the 1-hour period recommended by Niederl *et al.* (10; 11, p. 156). Other workers have recommended longer times, and for certain unusual samples extended digestions may be necessary. No study was made to determine whether the digestions could be carried out satisfactorily at lower temperature or for a shorter time, or whether fuming nitric acid could be used.

The application of this method to the determination of traces of iodine in organic materials was not attempted, for sample weights beyond the scope of the method would probably be required. The method described here has been used, however, for 12- to 15-mg. samples of iodinated proteins containing as little as 0.5% iodine.

The alkaline sulfite-sulfamic acid reagent is used to neutralize the nitric acid and to eliminate the nitrites formed during the digestion. Nitrite must be removed, because it will liberate free iodine from an acid iodide solution. The chlorine used as oxidant by Doering (3) completely oxidizes the nitrites, but the bromine used in this method will not completely perform the oxidation (5, 9). Other workers have destroyed traces of nitrites formed during dry combustion of nitrogenous substances with such reagents as ammonium chloride, bisulfite, urea, and sodium azide (5). The authors have found that the combination of sulfite and sulfamic acid used as described herein is entirely effective in removing the relatively large amount of nitrites formed during the digestion. The other reagents, particularly sodium azide, could probably be used for this purpose; however, Baumgarten and Marggraff (1) report that sulfamic acid is more effective than sodium azide.

Bromination and removal of the excess bromine should be

carried out at room temperature, because elevated temperatures tend to displace the equilibrium



toward the left (6, 13). For the same reason, the iodide and acid should be added to form the iodine soon after the excess bromine is discharged.

Aside from weighing, the working time per sample is about 30 to 35 minutes.

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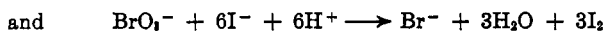
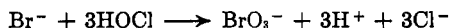
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Carius Iodometric Microdetermination of Bromine in Organic Compounds

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THE classical Carius method offers the simplest and most direct means for the determination of bromine in organic compounds. However, the gravimetric factor is rather unfavorable, chlorine and iodine interfere, and, because the bromine is measured gravimetrically, the procedure is time-consuming. Although argentometric, acidimetric, and iodometric methods have been used for the volumetric estimation of bromine following certain wet and dry combustions of the sample, no simple volumetric method employing the favored Carius digestion has been proposed for the determination of this halogen. The iodometric measurement of bromine, which is based on the reactions



is preferred over other volumetric methods (4) because of freedom from interference by chloride and nitrogen, the sharpness of the end point, and the favorable volumetric factor.

The work reported herein was undertaken to develop a simple method that would combine the excellent Carius digestion and the preferred iodometric estimation of the bromine.

EXPERIMENTAL

Silver is commonly used to fix in the nonvolatile state the halogen formed during the Carius digestion. Mercury has been used for this same purpose by Doering (2), Weygand and Werner (6), and White and Secor (7) in methods for the Carius-iodometric determination of iodine. Silver and mercury interfere with the quantitative oxidation of bromide to bromate and/or with the subsequent removal of the excess oxidant. No simple way could be found to eliminate this interference. No other chemical means was found which would render nonvolatile the halogen in the digest and would not interfere with the subsequent operations.

The vapor pressures of bromine and of hydrobromic acid are