

609. *Submicro-methods for the Analysis of Organic Compounds.*
Part IV. The Determination of Iodine and Bromine.*

By R. BELCHER, R. A. SHAH, and T. S. WEST.

Bromine or iodine in organic compounds is determined by decomposing a 50 μg . sample in a sealed tube with molten metallic sodium. The iodide is oxidised with bromine-water to iodate and bromide is oxidised to bromate with hypochlorite; the determinations are completed iodometrically. The sharpness of the end-point and the amplification thus achieved yield results accurate to about $\pm 0.4\%$ absolute.

BROMINE and iodine in organic compounds are generally determined through the formation of iodate or bromate, since a six-fold amplification of the original bromine or iodine is thus obtained. Several procedures are available for decomposition of the organic compounds, but of two widely used procedures, *viz.*, combustion in a stream of air or oxygen, and fusion in a bomb with peroxide or metallic sodium, the latter was selected; absorption of microgram amounts of vapour by a small amount of liquid from a gas stream is difficult and the bomb technique eliminates possible loss of material by effecting both mineralisation and absorption in one sealed vessel.

Initially we explored both the peroxide and the sodium-fusion technique, specially designed metal bombs made from pure nickel being used.

The relatively large amount of sodium peroxide necessary for decomposition, leading to trouble in destroying the excess and difficulty in end-point detection owing to high electrolyte concentration, and the presence of impurities in this material, led us to abandon it. Superior results were obtained by sodium-fusion except that the higher temperatures caused heavy wear of the bombs. Subsequently, it was found possible to carry out the fusion in sealed borosilicate-glass tubes. The method thus offered the advantages of (a) requiring no special decomposition or absorption apparatus, (b) avoiding large volumes of solution, and (c) yielding a sample solution containing low concentrations of indifferent electrolyte. The fusion procedure efficiently decomposed all the compounds we have so far examined.

*Determination of Iodine and Bromine in Pure Solution.*¹—Iodine is converted from iodide into iodate by oxidation with bromine water; the iodate is determined by conversion into free iodine and titration with thiosulphate after destruction of the excess of bromine with formic acid. The excess of sulphuric acid used in the acidification must be carefully controlled to minimise "after-blueing." Bromide is oxidised to bromate at pH 6.2 by hypochlorite. The excess of hypochlorite is partly destroyed by keeping the solution at 95° for 10 min. and by subsequent addition of sodium formate. Finally, potassium iodide, sulphuric acid, and a small amount of ammonium molybdate catalyst are added whereby the bromate liberates a six-fold amount of iodine. This is then titrated as described above.

Decomposition of Organic Compounds.—The sodium was purified by Bürger's procedure.² Uniform lengths (7 mm. for 50 μg . samples) of the sodium wire were cut with a special tool and were carefully freed as far as possible from organic solvents to minimise the formation of colloidal carbon and unknown organic products. A fusion temperature of 350° for 15 min. gave complete recovery of iodine and yielded the colloidal carbon in a tractable form. For bromine compounds, a temperature of 350–380° was used. Temperatures much above 380° produce finely divided carbon which is difficult to filter off.

Destruction of Excess of Sodium.—In most fusion procedures, ethanol is added to ensure smooth destruction of the excess of sodium metal, but we found it advisable to destroy it

* Part III, *J.*, 1958, 2393.

¹ See R. A. Shah, Ph.D. Thesis, Birmingham University, 1957.

² Bürger, *Angew. Chem.*, 1941, **54**, 149; cf. also *Die Chemie*, 1942, **55**, 245; 1944, **57**, 25.

with the minimum amount of water, since this caused no risk of the formation of organic by-products which interfere in the iodometric titration.

Removal of Colloidal Carbon.—The fusion of organic compounds with metallic sodium usually produces colloidal carbon. The most particulate form was obtained within the temperature range specified; it was filtered off on paper pulp in the apparatus shown in the Figure. Failure to remove the carbon leads to errors owing to adsorption of oxidant on its surface, resulting in high consumption of hypochlorite, and obscuring of the end-point during titration. In the determination of bromine considerable amounts of hypochlorite were consumed even by the filtered solution. It is not certain whether this is caused by colloidal carbon passing through the filter or by water-soluble compounds formed during decomposition. An excess of hypochlorite considerably larger than the amount found adequate for work with pure solutions was therefore necessary to ensure complete oxidation of bromide in solutions obtained after fusion of organic bromo-compounds with sodium metal.

Determination of Iodine in Nitrogenous Compounds.—In determining iodine in nitrogen-containing compounds, cyanide formed during the fusion interfered by reacting with bromine to form cyanogen bromide which subsequently liberated iodine from potassium iodide, thus causing high recoveries. Several methods of removing cyanide were examined. The most effective involved boiling with hydrogen peroxide, with expulsion by boiling the solution just acidified with acetic acid; the latter was preferred since it is simpler and quicker. It is essential, however, that strict adherence to time, temperature, and conditions of acidity be maintained, as prolonged boiling at too high an acidity may cause serious loss of iodine as hydriodic acid. Cyanide was expelled from the fusion solution immediately after filtration. No modification of the bromine procedure was necessary for nitrogenous compounds, presumably because of the oxidation of cyanide ion by the hypochlorite.

Standardisation of Reagents.—For the determination of iodine, the thiosulphate was standardised in the normal way on the submicro-scale, a standard solution of potassium iodate being used. A similar procedure was used for bromine, but a slight tendency for low results to be obtained can be avoided by standardisation against pure potassium bromide (prepared by ignition of recrystallised potassium bromate) by oxidising it in the specified manner and taking it through the whole procedure. The improvement thus obtained is, however, slight.

Effects of Time and Temperature on the Oxidations.—Iodide is oxidised to iodate by bromine-water smoothly and rapidly at room temperature, but *ca.* 30 sec. should elapse before adding formic acid to destroy the excess of bromine. Considerably more care is needed in oxidising bromide to bromate by hypochlorite. The pH must be adjusted to *ca.* 6–6.2. It does not appear to matter whether the temperature is 90° or 95° provided that it is kept constant and that the blanks are determined at the same temperature. We controlled the temperature at 94° ± 1.0°.

The results obtained for several iodo- and bromo-compounds are given in Tables 1 and 2. With samples weighing *ca.* 50 µg. the results are generally accurate to within ±0.4% in both methods. The maximum deviation from the true analysis obtained in each series of analyses is given in col. 6. These give a true idea of the *worst* results that may be expected in using these methods, since the results reported are not selected and none was rejected. A truer picture of the accuracy is obtainable from col. 4 (average result) and col. 5 (standard deviation, "S.d."). The samples analysed range from relatively simple compounds to the more "difficult" heterocyclic materials; fluorine and chlorine do not interfere.

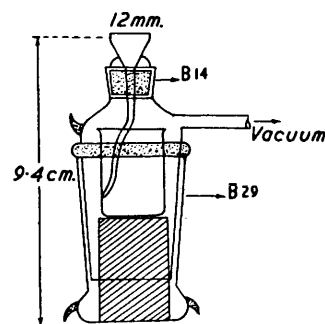


TABLE I. Analysis of iodine-containing compounds.

Compound	Range of sample wts. ($\mu\text{g.}$)	I content (%)			No. of dtmns.	Range of errors (%)	
		Calc.	Found (mean)	S.d.		Max.	Min.
<i>o</i> -Iodobenzoic acid	50—56	51.17	51.14	0.17	8	+0.30	-0.02
6-Deoxy-1 : 3-2 : 4-diethylidene-6-iodo-sorbitol	52—59	36.2 *	36.2	0.33	5	-0.49	+0.08
6-Deoxy-1 : 2-3 : 4-diethylidene-5- <i>O</i> -trichloroacetyl-6-iodosorbitol	49—53	25.97	25.62	—	4	-0.41	-0.2
<i>p</i> -Iodoacetanilide	41—57	48.61	48.7	0.25	6	-0.41	+0.06
Phenyltrimethylammonium iodide	43—51	48.26	48.36	0.28	5	+0.44	-0.08
" Ferron "	52—56	36.14	35.97	—	3	-0.42	+0.28
1-(2-Ethylphenyl)ethyltrimethylammonium iodide	47—61	39.79	39.84	0.11	6	+0.36	-0.02
5-Iodo-2-nitrobenzotrifluoride	41—53	40.04	39.92	0.32	6	+0.37	-0.03
Methyl 2-benzyloxycarbonylamino-6-iodo- α - <i>D</i> -glucoside	53—56	29.04	28.87	—	4	-0.48	+0.13

* Result by routine micromethod; theory 36.9.

TABLE 2. Analysis of bromine-containing compounds.

Compound	Range of sample wts. ($\mu\text{g.}$)	Br content (%)			No. of dtmns.	Range of errors (%)	
		Calc.	Found (mean)	S.d.		Max.	Min.
<i>p</i> -Bromobenzoic acid	49—60	39.75	39.74	0.43	7	+0.46	+0.2
Bromomethyl-triphenylpyrrolone	38—62	19.78	19.71	0.19	6	-0.26	-0.01
<i>p</i> -Nitrobenzyl bromide	56—69	36.99	36.95	0.36	5	+0.57	-0.08
6-Deoxy-1 : 3-2 : 4-diethylidene-6-bromo- <i>D</i> -sorbitol	38—70	26.3 *	26.21	—	4	-0.49	-0.07
<i>p</i> -Bromophenacyl bromide	55—59	57.50	57.54	—	3	-0.13	+0.03
<i>p</i> -Bromonitrobenzene	50—60	39.56	39.56	—	4	+0.58	-0.05
β -(2-Bromo-4 : 5-dibenzyloxyphenyl)-propionamide	50—53	18.16	18.21	—	4	-0.33	-0.05

* Result by routine micromethod; theory 26.9.

EXPERIMENTAL

Determination of Iodine.—(A) *Reagents.* (1) 0.02*N*-Potassium iodate prepared from "AnalaR" salt. (2) 10% Aqueous potassium iodide freshly prepared daily. (3) 2*N*-Sulphuric acid by dilution of "M.A.R." acid. (4) 90% Formic acid, "M.A.R." (5) Bromine water (saturated) prepared from "M.A.R." bromine. (6) 0.01*N*-Sodium thiosulphate prepared from "AnalaR" salt and containing 100 mg. of Na_2CO_3 per l. of solution; this solution was standardised on the submicro-scale against the 0.02*N*-potassium iodate. (7) Sodium metal, purified by Bürger's procedure,³ drawn into 1-mm. wire form, and stored under light petroleum (b. p. 80—100°) containing a little pentyl alcohol in a tightly stoppered bottle. (8) "Thyodene" indicator. (9) Methyl Red indicator, 0.05% aqueous.

(B) *Apparatus.*—(1) "Aglá" micrometer syringe burettes, used as described previously.³ (2) Electrically heated "Dural" block bored to hold the fusion tubes, used at 300—450°. The flat circular heating element was rated at 800 w/230 v. The block was well insulated in asbestos-cement tubing. (3) Magnetic stirrer. (4) Submicro-filtration device (see Figure). (5) Transference pipette. (6) Fusion tubes. These were made of borosilicate-glass tubing (8 mm. internal diam., 11—12 mm. outside diam., 7 cm. long) with a hemispherical seal at one end. They were cleaned with chromic acid.³ (7) Sodium cutting tool. This was fashioned like a pair of forceps with the gap between the blades adjusted to 7 mm. (8) Submicro-balance, as described elsewhere.⁴

(C) *Recommended Procedures.*—A 50 $\mu\text{g.}$ sample was weighed into the fusion tube by tapping the inverted weighing boat held in a pair of tweezers over its mouth. The boat was then reweighed. In each case the mean of three consecutive balance readings was taken. The tube was tapped gently to ensure transference of the sample to the bottom of the tube. Some sodium wire was then dried between Whatman No. 42 filter-papers, and a 7 mm. length then immersed briefly in ethanol, pressed once more between filter-papers, and put in the fusion

³ Belcher, West, and Williams, *J.*, 1957, 4323.⁴ Asbury, Belcher, and West, *Mikrochim. Acta*, 1956, 598.

tube. The tube was held in forceps by its upper end while being sealed about 2 cm. lower down; it was then placed in the heating block for 15 min. at 350°, then removed and allowed to cool. Tubes were opened by making a scratch some 2 cm. below the point recently sealed, and placing a molten soft-glass rod against it. A micro-drop of water was placed on the walls of the opened fusion tube by means of a transference pipette. The tube was gently tapped till the water made gradual contact with the sodium. When reaction had ceased a second drop was added similarly to ensure complete destruction of the metal. 0.2 ml. of water was added and the tube was set aside for *ca.* 2 min. to permit the sodium salts to dissolve. Meanwhile a little paper pulp was placed in the filtration device and washed 5 or 6 times with distilled water. The liquid in the fusion tube was filtered carefully into a clean micro-beaker under gentle suction, a transference pipette being used to deliver the liquid to the filter funnel. When all the liquid had been filtered, 0.2 ml. of distilled water was washed down the sides of the fusion tube and the liquid again filtered. The washing was repeated four times in all with 0.2 ml. portions of water. Several more washings with 0.1 ml. portions were then done to ensure quantitative transference of the sodium salts. (A fresh filter pad was used for each determination.)

The contents of the beaker were then stirred magnetically, a drop of Methyl Red indicator added, and the solution neutralised with 2*N*-sulphuric acid from a syringe burette. Two drops of bromine-water were added, and after 30 sec., two drops of formic acid. After 7 minutes' more stirring, the air above the liquid in the titration beaker was pumped away to remove traces of bromine. A drop of 2*N*-sulphuric acid and 3 drops of 10% potassium iodide solution were added, and the liberated iodine was titrated within $\frac{1}{2}$ min., standard thiosulphate and "Thyodene" indicator being used. The solid indicator was added from a micro-spatula when the yellow colour of iodine had almost vanished. A similar beaker filled to the same level with distilled water was used for comparison in locating the end-point. Lighting conditions similar to those described earlier were used.³

Blank (Control) Determination.—These were carried out simultaneously with the actual analyses. It was sometimes found useful to check the accuracy of the blank value by adding a known amount (say 100 μ l.) of standard 0.02*N*-iodate to the filtered "blank" solution and comparing the recovery with the known equivalence, particularly in assessing very small blank values. A normal blank value was 2–6 μ l. of 0.01*N*-thiosulphate.

1 μ l. of 0.01*N*-Na₂S₂O₃ \equiv 0.2115 μ g. of I.

Determination of Iodine in Nitrogenous Compounds.—Reagents and apparatus. These were as above, with the addition of 4*N*-acetic acid, and boiling-tubes of borosilicate glass of similar shape to fusion tubes but of 1.6 cm. diam. and having platinum ribbon (*ca.* 1 cm. long) fused through the bottom. By heating the outer end of the platinum strip with a micro-burner, heat is transferred smoothly to the liquid, thus ensuring boiling without "bumping."

Procedure. As before, but the filtrate was collected in a boiling tube (as above) instead of a 5 ml. beaker. The cyanide was removed by neutralisation to Methyl Red with 4*N*-acetic acid, addition of 30 μ l. in excess, dilution to 3 ml., and gentle boiling as described above for 2 min. The tube was then cooled under the tap, the inner surface carefully washed with 2 or 3 drops of water, and the determination carried out as described for non-nitrogenous compounds after oxidation with bromine, etc.

N.B. If the excess of acetic acid, volume of solution, and recommended boiling time are not adhered to, there is serious danger of loss of hydriodic acid at this stage.

Blanks were determined as before.

Determination of Bromine.—Reagents. (1) 1*N*-Sodium hypochlorite, prepared from bromine-free sodium hypochlorite solution (14–15% available chlorine; from Imperial Chemical Industries Limited). (2) 20% Sodium dihydrogen phosphate prepared from "AnalaR" salt. (3) 50% Aqueous sodium formate. (4) 2*N*-Hydrochloric acid prepared by dilution of "M.A.R." acid. (5) 12*N*-Sulphuric acid prepared by dilution from "M.A.R." acid. (6) Ammonium molybdate solution prepared by dissolving 2.9 g. of "AnalaR" salt in 100 ml. of water. (7) Methyl Red indicator, (8) 0.01*N*-sodium thiosulphate, and (9) sodium metal, all as described above.

Apparatus.—As before, with the addition of an electrically heated "Dural" block to maintain the temperature of the solution at 90–95° \pm 1° during oxidation of the bromide to bromate.

Procedure.—The fusion procedure for iodine was used. The fusion tube and filter pad were tested with phenolphthalein for alkalinity to ensure complete transference and washing. The sodium hydroxide in the boiling-tube was neutralised with 2*N*-hydrochloric acid to a Methyl Red end-point, a micrometer syringe burette being used. The end of the burette tip was washed with 1 or 2 drops of water after removal from the liquid, the washings being collected in the tube. 300 μ l. of 1*N*-hypochlorite and 350 μ l. of sodium dihydrogen phosphate solution were then added to the tube to maintain a pH of *ca.* 6.2. The boiling-tube which now contained *ca.* 3 ml. of liquid was then placed in the heating block (temp. *ca.* 120°) for 15 min. With our apparatus, this ensured an equilibrium temperature of 94° \pm 1°. Then 3 drops of 50% sodium formate solution were added, and after 30 sec. the tube was set aside for another 5 min. to cool slowly. Finally it was cooled under the tap and the sides were washed down with 3 or 4 drops of water. The tube was then mounted on the magnetic stirrer, 6 drops of 12*N*-sulphuric acid, 3 drops of 10% potassium iodide, and a microdrop of ammonium molybdate catalyst solution were then added, and the liberated iodine was titrated. Uniform illumination was obtained from a 60 w "daylight" blue bulb; two similar tubes containing roughly the same amount of water were used for comparison in detecting the end-point.

A usual value for the blanks is 2—3 μ l. of 0.01*N*-thiosulphate.

Standardisation of Sodium Thiosulphate against Pure Potassium Bromide.—A slight tendency to low results can be corrected for by fusing weighed amounts of pure potassium bromide with sodium in tubes as above and carrying through the entire procedure. Pure potassium bromide can be obtained by strong ignition of doubly recrystallised "AnalaR" potassium bromate in a silica crucible. With this method of standardising the thiosulphate it is advisable to take the mean of at least six determinations; the improvement obtained is only slight.

We are grateful to Dr. J. Berger, of The Royal Danish School of Pharmacy, Copenhagen, for independently carrying out serial check determinations on both methods of analysis. One of us (R. A. S.) thanks the Commonwealth Relations Office and the Government of Pakistan for the award of a scholarship under the Colombo Plan.