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717. *Submicro-methods for the Analysis of Organic Compounds. Part X.** *Determination of Fluorine.*

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Fluorine is determined in organic compounds on the submicro-scale by combustion in an oxygen-filled flask. The fluoride ion is then determined by a new reaction. Cerium(III) alizarin complexone forms a blue complex with fluoride ion which can be measured spectrophotometrically. There is no interference from other halides, sulphate, or nitrate. Phosphate or arsenate in amounts equivalent to fluoride has little effect.

The accuracy of the results is equivalent to that of the micro-procedure.

The determination of fluorine provides difficulties on any scale. The two most widely used methods, precipitation as lead chlorofluoride and titration with thorium nitrate, are not suitable for application on the submicro-scale. The solubility of lead chlorofluoride is too great and in any case only the titrimetric procedure, which is less satisfactory than the gravimetric procedure, could be applied; although the thorium nitrate titration is very sensitive, it is necessary to make control titrations on aliquot portions of the solution to establish the electrolyte concentration;[1] this is inconvenient on the submicro-scale. Attempts were made to precipitate calcium fluoride quantitatively so that a final complexometric titration could be made, but even in the presence of organic solvents, precipitation was incomplete in the minimum volume of solution which could be used.[2] Spectrophotometric methods were considered, but those which existed depend on the bleaching effect of fluoride ion on a suitably coloured metal complex and are subject to interference by anions which could be present after mineralisation of an organic compound.

Fortunately, studies in another field revealed a new reaction of the fluoride ion. Alizarin complexone (1,2-dihydroxyanthraquinon-3-ylmethylamine-*NN*-diacetic acid) [3] forms a red chelate with cerium(III); in the presence of fluoride ion, a new blue complex is formed,[4] whose nature is being investigated. As far as we know, this is the first known positive colour reaction of the fluoride ion. It is very sensitive and, unlike the common bleaching reactions, unaffected by sulphate ions. Other halides do not interfere, nor do phosphate and arsenate ions in moderate amounts. Hence this reaction appears ideal for the determination of fluorine in organic compounds, for the usually associated elements form anions which have little or no influence on it.

Within the range 15—50 μg. an absolute accuracy of ±0·5% can be achieved.

In qualitative tests, phosphate did not interfere unless amounts six-fold those of the fluoride ion were present. Only two compounds containing both phosphorus and fluoride were available; the results were as satisfactory as with the other compounds examined (Table 1).

Decomposition of the Sample.—Although there appears no reason why the conventional sodium fusion method could not be applied, the " oxygen-flask " method, first used by Hempel [5] in 1892 and revived in recent years by Mikl and Pech [6] and Schöniger,[7] was tried because of its speed and simplicity. Excellent results were obtained.

The sample is wrapped in filter-paper and clamped in a platinum wire attached to the stopper of a 250 ml. conical flask. Water is placed in the flask to absorb acid gases and the flask is filled with oxygen. The paper is lighted and the stopper immediately replaced. Combustion is complete in a few seconds. When absorption of acid gases is complete the fluoride ion is determined spectrophotometrically as the blue complex of cerium(III) alizarin complexone.

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Some compounds which contained $-CF_3$ gave low results. This has been noted previously by other investigators who have used the " oxygen-flask " method on the microscale[8] and was attributed to formation of carbon tetrafluoride; when they mixed the sample with sodium peroxide, effective decomposition was obtained. This was tried in the present instance, but the results were little better. However, when potassium chlorate was used the combustion proceeded satisfactorily.

A disadvantage of this method is that the paper can only be reduced to a certain size to allow convenient handling. This restricts reduction of the volume of the flask; it is essential that enough oxygen be present to ensure complete combustion of the paper and compound. A 250-ml. flask was the minimum size which could be used and the subsequent rinsing so diluted the solution that it was necessary to take about twice as much sample as is usual on the submicro-scale (100 µg). When this problem has been solved it should be possible to use 50 µg. or even smaller sample weights. The sodium fusion method would not have these limitations, but is far less convenient. More refined methods of spectrophotometry should also repay investigation.

Selection of pH *and Wavelength.*—At pH 4·3 alizarin complexone, which behaves as an acid–base indicator, just begins its transition from yellow to red; this pH was used throughout; the effect of using higher pH ranges was not studied. Determination of the optical density at varying wavelengths showed that 610 mµ was the most suitable wavelength for measurement of the fluoride complex. The calibration curve is linear over the range 8 to 35 µg. of fluoride, but its projection does not pass through the origin.

Results are included in the Table. Amounts of sample of the order of 100 µg. were used.

Compound	Fluorine (%) Calc.	Fluorine (%) Found	Error (%)	No. of detns.	Range of errors (%) Max.	Range of errors (%) Min.
Sodium fluoride	45·30	45·26	−0·04	24	−0·90	0·0
p-Fluorobenzoic acid	13·6	13·9	−0·30	9	±0·50	0·0
S-Benzylthiuronium heptafluoroadipate	22·0	21·7	−0·30	5	−0·60	−0·10
Research compound A	18·7	18·4	−0·30	7	−0·8	−0·10
Research compound B	9·49	9·36	−0·13	5	−0·24	+0·11
Research compound C	24·45	24·47	−0·03	3	−0·25	−0·05
Tetra-*p*-fluorophenylethylene	18·80	18·77	−0·03	7	−0·60	0·0
Trifluoroacetanilide	30·10	30·23	+0·13	4	+0·30	±0·20
S-Benzylthiuronium hexafluoroadipate	19·4	19·3	−0·10	5	+0·20	−0·60
$[CF_3{\cdot}C_6H_4{\cdot}P(C_2H_5)_2]_3CuI$	19·2	19·5	+0·30	3	−0·20	+0·60
$CF_3{\cdot}C_6H_4{\cdot}P(C_2H_5)_2CdI_2$	9·49	9·36	−0·13	4	−0·24	+0·11
m-Trifluoromethylbenzoic acid	30·00	29·81	−0·19	6	+0·10	−0·60

EXPERIMENTAL

Apparatus.—Optical density was measured on a Unicam SP.600 visual-range spectrophotometer. A 12v heavy duty battery was used to supply the current, since fluctuations of the A.C. mains were not eliminated sufficiently by the 12v transformer normally used.

Conical flasks (250 ml.) with B24 joints and stoppers were used for decomposition of the sample. The stoppers were fitted with 1 mm. diameter platinum wire for clamping the sample in position. These flasks are standard equipment and have been described in detail elsewhere.[7]

Solutions.—(1) 0·0005M-*Alizarin complexone.* 0·481 g. of pure alizarin complexone was transferred to a standard 2 l. flask, suspended in *ca.* 100 ml. of water, and dissolved by the addition of a minimum of fresh dilute sodium hydroxide solution. The solution was diluted to 1 l. and 0·5 g. of sodium acetate was added. Dilute hydrochloric acid was carefully added to bring the pH to *ca.* 5·0 (thin layer of solution pink). The solution was then diluted to the mark and transferred to a clean, dry, brown-glass vessel together with a further 500 ml. of water.

(2) 0·0005M-*Cerous nitrate.* 0·02M-Cerous nitrate solution was standardised by direct titration at pH *ca.* 6·0 with standard EDTA; Xylenol Orange was used as indicator. The correct volume of this solution was diluted to yield 2·5 l. of 0·0005M-Ce^{III}. The solution was transferred to a clean, dry vessel together with *ca.* 5·0 mg. of hydroxylamine hydrochloride.

(3) pH 4·3 *Acetate buffer.* 105 g. of hydrated sodium acetate and 100 ml. of glacial acetic acid were diluted to 1 l.

(4) *Fluoride solution*, 100 *μg. per ml.* 0·2211 g. of B.D.H. sodium fluoride (extra pure) was dissolved in water, diluted to 1 l., and stored in a Polythene bottle.

(5) *Fluoride solution*, 5·0 *μg. per ml.* 50 ml. of solution (4) were diluted to 1 l. and stored in a Polythene bottle.

Standard Curve.—A standard curve was constructed by weighing, on the submicro-balance, samples of pure, dry sodium fluoride whose weights lay between the limits of 20 and 90 μg. This gave a range of fluoride 10—40 μg. The samples were transferred to clean six-inch test tubes and dissolved in a little water.

Into a 100 ml. standard flask were introduced 10 ml. of 0·0005M-alizarin complexone solution, the fluoride solution, and washings from the tube; 2 ml. of pH 4·3 buffer were added and the solution diluted to *ca.* 75 ml. 10 ml. of 0·0005M-Ce^{III} were added with swirling; the solution was diluted to 100 ml., and was stored for 1 hr. in a box to protect it from light and draughts.

The optical densities of these solutions were measured in 4 cm. cells at a wavelength of 610 mμ by use of the blue-sensitive photo-cell against a blank solution containing only reagents. The standard curve was reproducible, but as a precaution against instrumental variation was checked against sodium fluoride with each series of determinations.

Procedure.—Samples of the compound previously dried over phosphoric oxide and sufficient to give 10—40 μg. of fluorine on combustion was transferred to a piece of ashless filter paper of the usual shape and size.[5] After deposition of the solid the paper was folded completely, doubled at right angles to the original folds, and rolled up into a cylinder to fit into the platinum spiral. The paper was lighted and burned off in a 250 ml. flask containing *ca.* 30 ml. of distilled water and an atmosphere of oxygen. After combustion, which should leave no carbonaceous residue, the solution was kept with occasional shaking for 10 min. The resulting solution was then treated as described in the preparation of the standard curve.

When the compound contains $-CF_3$ groups, the sample should be covered with 1 mg. of potassium chlorate before it is folded in the paper.

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