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THE PRESENT STATUS OF METHODS
FOR THE MICRODETERMINATION OF
FLUORINE IN ORGANIC COMPOUNDS

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The determination of fluorine in organic compounds poses several problems. The few laboratories which are continuously engaged in the analysis of fluorinated compounds each have their own procedural modification, by which they swear, but an analyst inexperienced in the field finds a bewildering array of procedures, the relative merits of which are difficult to assess without prolonged experimentation. This Report describes an attempt to provide guidance based on a survey of methods used and on collaborative testing of suitable compounds.

The survey described here was initiated by Dr. Al Steyermark in 1964 with the intention of extending on an international basis a survey of methods used in 1960 for the determination of fluorine in organic compounds in American laboratories.¹ Unfortunately, Dr. Steyermark had to abandon this work on account of ill health.

In 1965, the survey was resumed, and a series of six samples was submitted to collaborating laboratories. A total of 39 laboratories (25 European and 14 North American) engaged in this test, but the results of the test were quite unsuitable for statistical analysis. Although most of the laboratories (27) used the Schöniger oxygen-flask method² to decompose the samples, the diversity of absorbing solutions used for the decomposition products (water or varying concentrations of ammonia or sodium hydroxide) and of additives used to assist combustion (glucose, sucrose, paraffin, sodium peroxide, potassium nitrate) made it impossible to differentiate the essential from the trivial. The situation was not alleviated by the fact that there was also a great variety of spectrophotometric and titrimetric procedures for completing the determination: very few laboratories used even the same modification of the well-established titration with thorium nitrate solution to an alizarin red S end-point. The 1965 survey was further complicated by most participating American laboratories having changed their methods of determination between 1960 and 1965.

In general, this initial survey served simply to support the long-standing hypothesis that most analysts can produce reasonable results for most samples if they employ a method with which they are thoroughly familiar. It also served to prove that no particular method was widely regarded as superior to any other for organic fluorine analysis. The Commission is very grateful to the many workers who willingly donated their time and energy to this initial stage of the survey, which was reported at the 1967 Conference.*

In 1966, a new method for the determination of fluoride was introduced: the fluoride-selective electrode of Frant and Ross⁴ based on a single-crystal lanthanum fluoride membrane. This was originally proposed for direct potentiometric determinations of fluoride, but was also

studied in detail for potentiometric titrations of fluoride by Lingane.⁵ The early spectacular success of these methods in a few laboratories with heavy commitments in the routine analyses of fluorinated organic compounds suggested that any further international survey should be postponed until the application of the methods had become more widespread. Further tests were therefore delayed until 1971.

PRESENT SURVEY

In the recent stage of the survey reported here, thirteen laboratories finally participated (Table 1). The samples were distributed as unknowns except for the first standard compound; the purities of the samples distributed were checked in the Reporter's laboratory on the basis of melting points and analyses for carbon, hydrogen and nitrogen. The samples (Table 2) were selected as being representative of the types most likely to be encountered in practice: (1) a widely accepted standard material readily available in a pure form; (2) a sample containing only a moderate amount of fluorine and a possible interfering element (sulfur); (3) a fairly typical research sample; (4) a polymeric material of high fluorine content and high stability; (5) a mixture of compounds containing elements known to interfere with most methods of determining fluorine. Because of the difficulties of obtaining pure multielement compounds in sufficient quantity, collaborators were asked to analyse mixtures of

Table 1. Participating laboratories

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Dr. F. Ehrenberger, Analytisches Laboratorium, Farbwerke Hoechst AG, Frankfurt/Main-Hoechst, West Germany.
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Dr. R. Levy, Service Centrale de Microanalyse, C.N.R.S., 2 rue Henri Dunant, 94 Thiais, France.
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Dr. L. Mazor, Institute for General Chemistry, Technical University, Budapest XI Gellert-ter 4, Hungary.
Dr. Satoshi Mizukami, Shionogi Research Laboratory, Shionogi and Company Ltd., Kukushima-ku, Osaka, Japan.
Mr. George F. Morris, Analytical Research Service, Research Branch, Department of Agriculture, Ottawa, Canada.
Dr. A. M. G. Macdonald, Department of Chemistry, University of Birmingham, PO Box 363, Edgbaston, Birmingham B15 2TT, UK.
Mr. D. B. Ratcliffe, Marchwood Engineering Laboratories, C.E.G.B. Marchwood, Southampton, Hants SO4 4ZB, UK.

*Copies of this report are available on request; the information is now too out of date to be worth describing in detail.

Table 2. The samples distributed in the second test

Sample	Source	% F	% C	Found	% H	Found	% N	Found
		Nominal	Nominal		Nominal		Nominal	
1. Trifluoroacetanilide	M.A.S. grade Hopkin & Williams Ltd.	30.13	50.80	—	3.19	—	7.40	—
2. 4-Fluorobenzenesulfonamide*	R. N. Emanuel	10.85	41.14	41.1 41.4	3.45	3.2 3.5	8.00	8.1 8.3
3. Trifluoromethylbenzimidazole	Research sample	30.62	51.62	51.8 51.3	2.71	2.9 2.9	15.05	15.3 15.2
4. Polytetrafluoroethylene†	Imperial Chemical Industries	75.98	24.02	24.3 24.1	— —	— —	— —	— —
5. A mixture of chlorobenzoic acid, triphenylphosphine and 2-arsanilic acid								

*S = 18.4.

†This sample of high-purity material was donated by Mr. A. G. Jones, Plastics Division, Imperial Chemical Industries, Ltd., to whom the Commission expresses its grateful thanks.

Table 3. Methods used in the participating laboratories

Laboratory	Decomposition	Determination	Remarks
I	Silica flask: 5 ml H ₂ O	Selig titration; photometric e.p.	Polyurethane foam added in all cases.
II	Polycarbonate flask: H ₂ O	Th(NO ₃) ₄ titration: fluoride electrode Thorium chloranilate spectrophotometry (for sample 2)	P interferes and sample 5 was not analysed. 40 mg of dodecanol added to sample 4.
III	Potassium fusion	Ion-exchange: titration ¹¹	Sample size: 20–30 mg. No precautions for interference.
IV	Silica flask: 4 ml H ₂ O	Horaček titration	No precautions for sample 4 or 5. With sample 2, S was titrated first with Ba(ClO ₄) ₂ solution.
V	Wickbold method	La(NO ₃) ₃ titration: fluoride electrode	
VI	Polypropylene flask: 10 ml 0.1 M NaOH	Direct measurement with fluoride electrode ¹²	Benzoic acid added to sample 4.
VII	Silica flask: H ₂ O	Iron sulfosalicylate spectrophotometry ¹³	Distillation before colorimetry for samples 2 and 5.
VIII	Silica flask: H ₂ O	Horaček titration	No precautions for any sample.
IX	A. Wickbold method	Th(NO ₃) ₄ titration: alizarin red S-methylene blue indicator	Poor end-point with sample 5.
	B. Wickbold method	Direct measurement with fluoride electrode	
	C. Silica flask: H ₂ O	Direct measurement with fluoride electrode	
X	Pyrex flask: H ₂ O	Selig titration	Na ₂ O ₂ added to all samples. Flasks were well conditioned by repeated prior determinations of fluorine. Standard addition method used to overcome interferences for samples 2 and 5.
XI	Silica flask: H ₂ O	Th(NO ₃) ₄ titration: fluoride electrode	Isopropanol (80%) as titration medium. Dodecanol added to sample in all cases. Prior separation with silver oxide for sample 5.
XII	Silica flask: 10 ml H ₂ O	Selig titration	Poor end-points for sample 5. Titrant standardized against sodium fluoride. 300-ml flask used.
XIII	Silica flask: 5 ml H ₂ O	Selig titration	No end-points for sample 5.

samples (1) and (5), in order to assess the effects of possible interfering elements.

In order to reduce the number of experimental variables which had made the previous survey impossible to interpret on any kind of statistical basis, collaborators were asked to use the following procedures:

(a) decomposition by the Schöniger oxygen-flask technique, with either silica or polypropylene flasks, and absorption of the combustion products in water; or decomposition by the Wickbold oxyhydrogen method;⁶

(b) titration with lanthanum(III)⁷ or thorium(IV)⁸ solution to a potentiometric end-point at the Orion fluoride-electrode; or titration with lanthanum(III) solution to a hematoxylin end-point;⁹ or titration with thorium(IV) solution to a methylthymol blue end-point.¹⁰

The methods which were actually used in the test are

summarized in Table 3. The results which were reported are listed in Table 4. Collaborators were asked to do two or three determinations on each sample. It is well known in collaborative testing that results from different laboratories vary more than results obtained within one laboratory,¹⁴ therefore the additional labour involved in providing more results from each laboratory seemed pointless. A survey of the results is given in Table 5.

INTERPRETATION OF RESULTS

Trifluoroacetanilide

Initial scanning of the results indicated that Method C of Laboratory IX possessed a large negative bias for all the samples tested. The only apparent difference in procedure from other methods which gave acceptable results lies in the addition of sodium peroxide as an

Table 4. Details of results obtained

Laboratory	Sample 1		Sample 2		Sample 3		Sample 4		Sample 5		
	% F	Av.% F	% F	Av.% F	% F	Av.% F	% F	Av.% F	% F	Av.% F	
I	30.27		11.48		30.69		74.55		—	—	
	30.85	30.45	11.44	11.42	31.30	30.84	73.74*	74.15			
	30.24		11.36		30.53						
II	30.1	30.05	10.8	10.63	30.5	30.4	75.8	76.34	—	—	
	30.0		10.5		30.3		76.6				
			10.6		30.4		76.0				
							76.6				
III	32.76	30.97	12.13	12.01	30.27	30.03	74.15	74.35	68.70	—	
	29.95		11.90		29.80		74.56		69.60		
	30.20										
IV	29.98	30.09	11.55	11.60	30.41	30.48	75.99	76.20	37.71	—	
	29.95		11.56		30.37		76.20		40.94		
	30.35		11.69		30.67		76.43		42.64		
V	30.32	30.50	11.39	11.26	30.76	30.62	76.23	76.01	30.84	30.56	
	30.38		11.08		30.58		75.59		30.69		
	30.87		11.11		30.51		76.20		30.15		
	30.43		11.47				76.03				
VI	29.74	29.93	10.70	10.61	29.16	29.78	71.07†				
	30.18		10.90		30.08		76.90		29.05		
	29.87		10.23 ^b		29.80		75.19				
							75.54				
VII	30.10	29.99	11.57	11.57	30.42	30.39	76.05	76.03	29.93	29.92	
	29.91		11.66		30.38		75.92		29.59		
	29.95		11.48		30.38		76.32		30.24		
							75.86				
VIII	30.14	30.11	10.21	10.20	30.13	30.23	76.37	76.24	30.32	—	
	30.08		10.19		30.25		76.12				
					30.32						
IX	A	30.20	30.16	10.80	10.65	30.3	30.47	75.8	76.20	32.6	—
		30.10		10.50		30.4		75.8		32.0	
		30.20				30.7		77.0			
	B	30.3	30.06	10.7	10.70	30.4	30.40	75.7	75.75	29.9	29.95
		30.0		10.7		30.4		75.8		30.0	
		29.9		10.7							
	C	29.3	29.15	10.7	10.45	29.9	29.50	69.8	69.5	—	—
		29.0		10.2		29.1		69.2			
X	30.05	30.25	11.03	10.81	30.44	30.38	75.91	76.14	30.51	30.36	
	30.38		10.76		30.57		76.22		30.26		
	30.15		10.64		30.27		76.33		30.62		
	30.41		10.81		30.24		76.11		30.05		
XI	29.53	29.93	—	—	31.03	30.96	75.82	76.40	30.85	30.60	
	29.90				30.79		76.99		30.36		
	29.99				31.06						
	30.30										
XII	29.82	29.29	10.09	10.85	29.96	29.76	71.19	71.92	30.01	—	
	28.34		11.31		30.01		71.20		32.52		
	28.82		10.56		29.56		72.14		34.88		
	29.23		11.34		29.69		73.11		32.33		
	30.26		10.97		29.60		71.98		30.10		
XIII	29.78	30.01	10.80	10.86	30.30	30.55	—	—	—	—	
	30.24		10.92		30.80						

*A third result of 51.96% F was obtained, but this was due to the sample not igniting properly.

†Charring was noted, hence this result was discarded.

auxiliary source of oxygen for the combustion; this auxiliary oxidant has been recommended in the literature, and was in fact applied by one collaborator in the initial survey without ill-effect, but it appears that this additive conveys no benefit and may be deleterious to accuracy. Results obtained by this method were therefore omitted from all further consideration.

The overall mean result for all other results corresponded exactly to the theoretical result, but the standard deviation was excessive (0.595). The obvious outliers

were the results from laboratories III and XII; the causes for these outliers are not clear. Possibly the flasks used in Laboratory XII were too small (300 ml) or were of impure silica. When these results were omitted, the standard deviation on all results improved to 0.280.

Insufficient results are available for the application of standard statistical tests for significant differences between the various other procedures which were used. The excellent standard deviation for the Horaček titration probably signifies technical skill in the two laboratories

Table 5. Survey of results

Sample	1				2				3				4			
	Mean %	s	n*	L†	Mean %	s	n	L	Mean %	s	n	L	Mean %	s	n	L
Overall	30.13	0.595	44	13	11.00			13	30.32			13	75.4			12
Overall w/o III and XII	30.13	0.28	36	11	10.95	0.46	31	11	30.52‡	0.29	32	10	75.94	0.625	34	10
Flask decomposition¶	30.09	0.25	26	9	10.96	0.51	22	8	30.53	0.32	24	8	76.18§	0.47	23	8
Wickbold decomposition	30.24	0.31	10	2	10.94	0.35	9	2	30.50	0.21	8	2	75.99	0.43	9	2
Selig titration¶	30.23	0.33	6	3	10.98	0.37	9	3	30.59	0.32	9	3	76.14¶	0.26	3	1
Horaček titration	30.10	0.16	5	2	10.90	0.80	5	2	30.35	0.34	6	2	76.22	0.33	5	2
Potentiometric titration	30.16	0.35	12	3	10.94	0.41	7	2	30.66	0.31	9	3	76.25	0.51	10	3
Potentiometric measurement	30.00	0.25	6	2	10.71	0.15	5	2	30.40	0.31	2	1	75.82	0.665	5	2

*Number of results.

†Number of laboratories.

‡Results from Lab. VI also omitted as outliers.

§Results from Lab. I also omitted as outliers.

¶Results from Labs III and XII omitted on the basis of unsatisfactory performance on the standard sample.

which used it, as much as clarity of end-points. Potentiometric titrations with lanthanum(III) and thorium(IV) solutions were applied; both seemed equally satisfactory and these methods were grouped together in the statistical analysis.

On the basis of these results, any of the methods used seems satisfactory. For the oxygen-flask decomposition, the flasks may be made of silica or plastic material; even pyrex glass may be used provided that it has been thoroughly conditioned by burning many fluorinated compounds in it (Lab. X).

4-Fluorobenzenesulfonamide

This sample was selected as having a moderate amount of fluorine (10.85%) with a larger amount of a possible interfering element (18.4% S), a situation typical of much drug analysis. The first problem in analyzing the results for this compound was to decide whether to calculate standard deviations from the mean result found or from the theoretical value for the compound. The latter course was taken because the purity of the sample was satisfactory, judged from other elemental analyses (Table 2), and because the overall mean result could have been affected by interference of sulfate or sulfite ion.

With regard to the decomposition method, both the oxygen flask and oxyhydrogen flame methods are satisfactory (Table 5). Potassium fusion followed by ion-exchange leads to high results, probably because of interference from sulfide.

With regard to the method of completing the determination the most accurate results were obtained by the Selig titration (Labs X, XII, XIII), and by direct potentiometric measurement; spectrophotometry with thorium chloranilate (Lab. II) was also satisfactory. The excellent accuracy of the mean result from Laboratory XII suggests that the low results for other compounds may have been caused by standardization errors, because the amounts of fluorine taken for the analysis of the compounds lay over a wide range. The good mean value obtained by the Horaček titration conceals a wide interlaboratory range which is evident in the standard deviation; this titration should be applied to sulfur-containing compounds with caution, but it should be noted that Laboratory IV carried out a prior titration of sulfate, which may have affected the fluoride value. The results indicate that optimal precision for fluorine in the presence of sulfur is achieved by direct potentiometric measurement, but many more results would be necessary to prove this conclusively.

Trifluoromethylbenzimidazole

In general, the results reported for this sample reflect those already discussed for trifluoroacetanilide. The reasons for the low results obtained by Laboratory VI are unclear. On the basis of the analysis of the standard sample (1), results submitted from Laboratories III and XII were also omitted from the calculations. The general results confirm that nitrogen in the organic sample does not affect any of the methods of determination.

Polytetrafluoroethylene

This sample was of guaranteed high purity, therefore all deviations were calculated from the theoretical fluorine content. There is surprisingly little difference between the mean results (and deviations) for the flask and Wickbold decomposition methods. There was also no clear difference between the results obtained by straightforward oxygen flask combustion (Labs IV, VII, VIII, IX) and by this combustion in the presence of additives such as dodecanol (Labs II, XI) or benzoic acid (Lab VI) which are supposed to aid the decomposition of highly fluorinated organic compounds. It should, however, be noted that from the whole set, two results by the flask decomposition method were discarded because of obvious charring.

There seem no significant differences between the methods of completing the determination for this compound.

The effect of interfering elements

Collaborators were requested to analyse sample 1 after the addition of 5–10 mg of an organic mixture containing chlorine, phosphorus and arsenic as likely interfering elements.

As can be seen from Table 4, some collaborators did not submit results for this part of the test. Laboratories I, II and XIII stated that they knew phosphorus interfered with their methods of determination. The point was adequately proved by the results submitted by Laboratories III, IV, IX and XII who took no precautions against interference. Satisfactory results were obtained by means of a Wickbold decomposition followed by either a direct electrometric measurement of fluoride (Lab IX, method B) or a potentiometric titration with lanthanum(III) solution (Lab V), but not in conjunction with a visual titration with thorium(IV) (Lab IX, method A). However, direct electrometric measurement after an oxygen flask combustion yielded rather low results (Lab.

VI); this may be due to the effects of partially oxidized states of phosphorus or arsenic, for it seems unlikely that the amounts of interfering elements present would affect the buffering capacity of the TISAB used.

A statistical survey of the satisfactory results does not seem of value, because of the paucity of results and the variety of methods used to overcome interference. However, it should be noted that satisfactory results were also achieved by oxygen flask combustion in conjunction with distillation and spectrophotometry (Lab. VII), or with a standard addition titration to compensate for interfering effects (Lab. X). Separation of interferences by precipitation with silver oxide gave rather high results, which would still be acceptable for many purposes (Lab. XI).

CONCLUSIONS

The results of this survey have not proved that any one procedure is greatly preferable to another for the determination of fluorine in organic compounds.

With respect to the popular oxygen flask method, however, it seems that several factors can be regarded as proven: (1) water is an efficient absorbing solution, so that there is no need to complicate matters by introducing alkaline absorbents, and (2) the method is efficient for the decomposition of highly fluorinated polymers with or without organic additives. Auxiliary oxidants in the flask method should be used with caution. The problem of how best to deal with highly fluorinated volatiles has not been solved in this survey, although it was touched on in the initial survey.

The Wickbold method of decomposition appears to be satisfactory and to be particularly suitable for materials containing interfering elements. It is doubtful if the potential of this method in routine analysis for fluorine has been fully realized. Decomposition by fusion with potassium accompanied by ion exchange should, apparently, be applied with some caution.

With regard to the method of completing the determination, none of the electrometric, titrimetric or spectrophotometric procedures used in this survey shows any particular virtue that should give it preference to another.

It should, however, be stressed that most collaborators stated that the amount of compound taken for analysis should be adjusted so that the amount of fluoride ion finally determined lies within a quite narrow range. In all cases mentioned in this Report, with the exception of the potassium fusion method, the sample sizes lay in the range 1–10 mg, varying in actual size with the method and sample used. It is of considerable importance for accuracy that whichever procedure is selected should be standardised against a similar quantity of fluoride to that expected from the routine samples.

The potentiometric titration methods do not show any particular gain in accuracy or precision over the best visual titration methods, and their application should probably be decided on economic rather than chemical grounds. The direct potentiometric measurements with the fluoride-selective electrode appear to convey certain benefits, but a larger sampling of laboratories is necessary before a definite conclusion can be reached.

The Commission is greatly indebted to the many analysts who participated in the various stages of this survey. Both the good and the bad results have been essential to make it worthwhile.

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