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Determination of Methoxyl and Ethoxyl Groups in Organic Compounds*

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Determination of methoxyl and ethoxyl groups in organic compounds according to Zeisel's method frequently yielded somewhat higher analytical values. This usually occurred when the methyl or ethyl iodide was insufficiently purified from matters which hindered their determination. Liquid-filled washers are used for the elimination of these matters. When the liquids in the washer were replaced by solid ascarite, and the determination carried under a stream of nitrogen or air, no errors occurred. Besides, if a layer of anhydrous was added to the washer containing ascarite, the carbon and hydrogen content of the obtained methyl or ethyl iodide could be determined, and it could thus be ascertained whether the organic compound contained methoxyl groups, ethoxyl groups, or a mixture of both.

Determination of methoxyl and ethoxyl groups in organic compounds can be carried out according to the Zeisel¹ macro, Vieböck-Brecher² semimicro method, and the Pregl³ micro method. In these procedures, as well as in modified procedures⁴, the methoxyl and ethoxyl groups react with hydriodic acid, yielding methyl iodide and ethyl iodide respectively, which are purified by passing through a washer under a stream of carbon dioxide, and which are finally collected into a receiver. The determination of the obtained methyl or ethyl iodide is carried out by gravimetric or titrimetric methods. Unsatisfactory results in the determination of methoxyl and ethoxyl groups can result from the following reasons:

- a) incomplete reaction with hydriodic acid,
- b) insufficient purification of methyl or ethyl iodide,
- c) incomplete absorption of methyl or ethyl iodide in the receiver.

For the reaction to proceed quantitatively, it is necessary to use hydriodic acid of the density 1.7, but even if such an acid is used, the reaction may remain incomplete. This happens if the sample is not completely dissolved or if it is very volatile. The solubility can be increased by adding organic solvents. Herzig⁵ suggested acetic anhydride for this purpose, Baeyer and Villiger⁶ glacial acetic acid, Weishut⁷ phenol, and Bruckner⁸ propionic anhydride. With highly volatile substances or with those having highly volatile reaction products, a quantitative reaction with hydriodic acid can be obtained in appropriately closed systems. Such procedures have been described by Furter⁹, Kolka and Vogt¹⁰, Kirsten, and Sara Ehrlich-Rogozinsky⁴.

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Methyl and ethyl iodides are usually purified in washers containing various liquids. It is expected from these liquids to eliminate completely iodine, hydriodic acid and hydrogen sulphide from the gaseous mixture and on the other hand to permit quantitative elapsing of methyl and ethyl iodide. Exceptionally, by using the receiver following Vieböck-Brecher², elimination of hydrogen sulphide becomes unnecessary.

Franzen, Hegemann and Disse¹¹ have investigated a number of liquids in the light of the above mentioned requirements, and they came to the conclusion that sodium thiosulphate should not be used, as methyl iodide partially reacts with it, forming sodium thiosulphate methyl ester, and therefore the analytical results were considerably lower than expected. These authors have, furthermore, ascertained that the following liquids retain iodine and hydriodic acid and transmit methyl iodide: sodium antimony tartrate¹², hydroxylamine¹², *l*-ascorbic acid,¹³ hydrazine¹¹, and red phosphorus in aqueous suspension.¹³

The possibility of incomplete absorption of methyl or ethyl iodide in the receiver was completely eliminated in the method of Vieböck and Brecher,² in which a mixture of bromine, acetic acid and sodium acetate was used for absorption.

Since considerable errors may occur in the determination of methoxyl and ethoxyl groups on account of inadequate purification, we have attempted to eliminate these errors altogether by filling the washers with ascarite instead of liquids as beforehand.

Experimental results have shown that washers with ascarite are much more effective than those with liquids. They completely retain iodine, hydriodic acid and hydrogen sulphide, and have no action whatever on ethyl and methyl iodides, which are quantitatively recovered in the receiver.

Blank determinations with liquid-containing washers can vary a lot, depending on the flow rate. Stable blank values can only be obtained at a constant flow rate. This usually is one bubble per second. Moreover, it is necessary to maintain a constant flow rate during the determination as well, so as obtain correct analytical values. This is rather difficult to achieve, both in blank determinations and in actual analysis, especially if boiling-detention occurs.

Investigations have shown that notwithstanding considerable changes in flow rate, blank determination results remain constant. Actual analyses need not be carried out with the same flow rates as in the blank determination, and no special care need be taken of the constant flow rate during the experiments. It has been shown, furthermore, that boiling detention, and therefore changes in flow rates, have no effect on the results either of blank determinations or of analyses. Moreover the hydriodic acid of density 1.7 need not be quite colourless, but may be discoloured by iodine. One of the advantages of ascarite is this that the same washer can be used for a number of determinations without refilling, whereas liquids have to be renewed for each determination.

Another advantage of this filling is the possibility of adding a layer of anhydron, and then the washer can be attached to an apparatus for the determination of carbon and hydrogen contained in methoxyl or ethoxyl groups analogous to Friedrich's¹⁴ carbon determination. In a separate test,

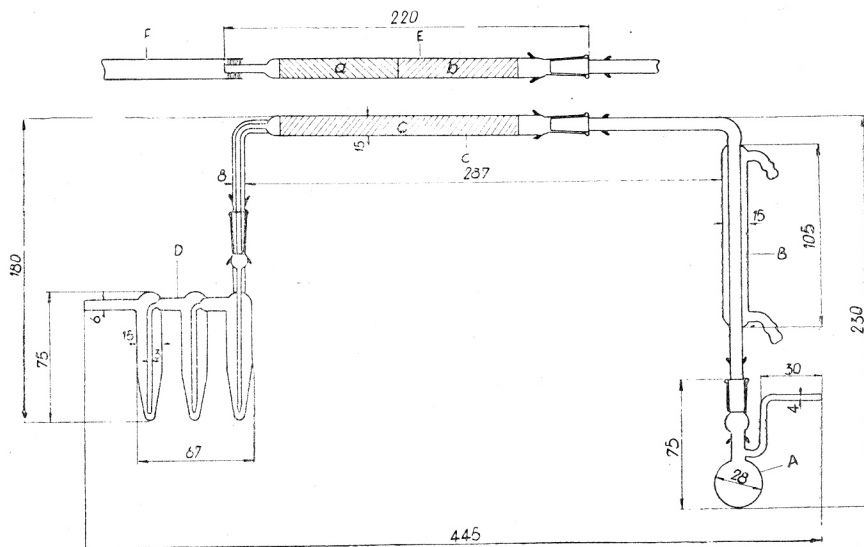
carbon and hydrogen can be quantitatively determined, and it can be thus ascertained whether the sample contains only methoxyl or ethoxyl groups, or determined the ratio of methoxyl v. ethoxyl in their mixture.

EXPERIMENTAL

Apparatus

The apparatus on Fig. 1. was used for the determinations. It consisted of a reaction flask (A), condenser (B), washer (C) and receiver (D). All parts are of Pyrex brand glass, connected by standard ground glass joints.

The reaction vessel with a side arm for the inlet of nitrogen is of 10 ml. capacity. It is connected to the condenser with a B10 joint. The side arm of the condenser, bent at 90°, is connected by means of a B10 joint to the washer, which is also connected with a side arm bent at 90° and B7 joint to the receiver. The receiver consists of three small vessels which are connected in a series. The exact dimensions of the parts are given in Fig. 1 in mms.

*Method of Determination*

Determinations of methyl and ethyl iodides are carried out by the iodometric method following Vieböck and Brecher and Leipert.²

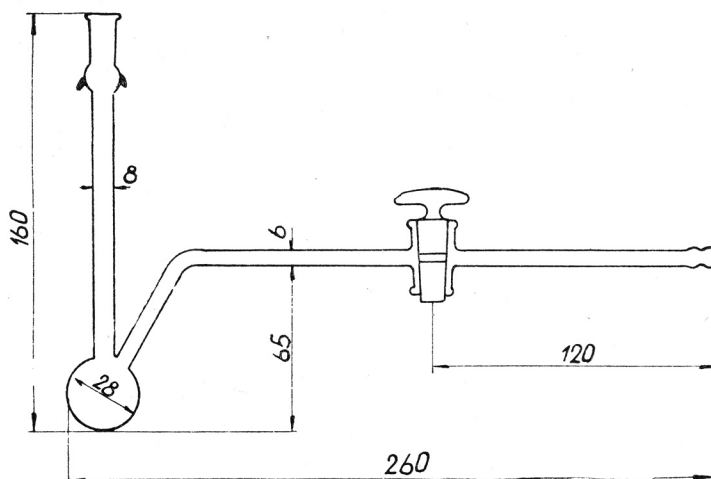
The Usefulness of Ascarite-Filled Washers

The purpose of these investigations was to ascertain whether ascarite-filled washers allow methyl and ethyl iodides to escape quantitatively into the receiver. Definite quantities of completely pure methyl or ethyl iodide are drawn through the ascarite-containing washer by aid of a stream of nitrogen into the receiver, and determinations have shown that ascarite had allowed the methyl or ethyl iodide to escape quantitatively.

Procedure

A sample of methyl iodide or ethyl iodide was weighed in a sealed glass capillary (the same kind of capillary as commonly used in carbon and hydrogen micro-determinations of volatile compounds). The capillary was transferred to the reaction flask so that the sealed end was at the bottom. In this determination

a reaction flask with a somewhat longer neck than usual was used (Fig. 2), and there was a side arm for nitrogen. The stopcock was closed, the capillary crushed with a glass rod which was left in the apparatus during the experiment, and the reaction flask quickly connected to the apparatus. All other parts should have been interconnected previously. The prescription for washer and receiver filling is given later. The stopcock on the reaction flask was open and a stream of nitrogen allowed to pass at the rate of 10–20 ml. per minute. The reaction flask was then



placed into a water bath, which was gradually heated to boiling point, and kept at that temperature until the end of the experiment. The stream of nitrogen was obtained from a steel cylinder, through a pressure regulator, bubble counter filled with distilled water, and a precision screw clamp. The pressure regulator, bubble counter and precision screw clamp are of the same construction as in the apparatus for the micro determination of carbon and hydrogen. The mentioned speed of 10–20 ml. of nitrogen per minute corresponded to 2–4 bubbles per second with the bubble counter used. With the more volatile methyl iodide each experiment took about 70 minutes, and with ethyl iodide about 90 minutes. After the experiment was completed the methyl or ethyl iodide was determined in the receiver by iodometric titration in the same way as in the determination of methoxyl or ethoxyl groups. 0.02 N sodium thiosulphate was used.

1 ml. 0.02 N $\text{Na}_2\text{S}_2\text{O}_3$ = 0.4732 mg CH_3J

1 ml. 0.02 N $\text{Na}_2\text{S}_2\text{O}_3$ = 0.5199 mg $\text{C}_2\text{H}_5\text{J}$

Results of these experiments are given on Tables I and II.

TABLE I

<i>Methyl iodide</i>		
mg.	Found mg.	Found %
15.180	15.148	99.79
25.735	25.692	99.83
9.425	9.406	99.80

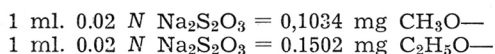
TABLE II

<i>Ethyl iodide</i>		
mg.	Found mg.	Found %
13.929	13.981	100.37
17.502	17.443	99.67
34.545	34.527	99.95
27.340	27.349	100.03

In all these experiments the value of the receiver was subtracted from the consumption of sodium thiosulphate. The value of the receiver is the quantity of sodium thiosulphate consumed for the titration of the glacial acetic acid solution of sodium acetate (10 ml.) with 10 drops of bromine. These values amounted to 0.12 ml. 0.02 *N* sodium thiosulphate in each of these determinations. The value of the receiver is the result of small quantities of iodine in the bromine used.

Micro determination of methoxyl and ethoxyl groups

For this determination the apparatus depicted in Fig. 1 was used. Prior to determinations the apparatus was washed with chrom-sulphuric acid and distilled water and dried at 110° C. The washing compartment (C) was filled with a 10 cm. layer of ascarite (c) protected at the ends by cotton or quartz wool. The tube was connected to the condenser (B), the ground glass joints lubricated with silicone lubricant. 10 ml. of sodium acetate in glacial acetic acid and 10 drops of bromine were put into the receiver (D). The receiver was attached to the washer, the ground glass joint of which was moistened with a drop of distilled water. The sample (3–10 mg.) was transferred to the reaction flask (A), 2–3 crystals of phenol and 3 drops of acetic anhydride added, and the mixture heated until completely dissolved. Into the cooled mixture a boiling capillary was placed and 3 ml. of hydriodic acid added. The reaction flask was attached at once to the condenser, the joint of which had been moistened with distilled water. A stream of nitrogen was passed through the system at a rate of 10–20 ml. per second. Water was allowed to flow through the condenser, and the reaction flask heated with a micro burner so that the solution boiled gently. This heating process, under a stream of nitrogen, took 40 minutes from the beginning of the boiling of the solution in the determination of the methoxyl group, and 60 minutes for the ethoxyl group. Afterwards, the contents of the receiver were transferred to a titration flask of 250 ml. capacity, with a ground glass neck, into which 5 ml. of aqueous sodium acetate had previously been added. The remainder of the solution in the receiver was washed into the titration flask with distilled water, to which formic acid was added dropwise with continuous stirring, until the colouring disappeared. To the colourless, odourless liquid a small drop of methyl red was added, with the aid of a glass thread, to ascertain the absence of free bromine. If no bromine is present, the solution remains coloured. Should free bromine be present more formic acid should be added. When the solution was definitely free of bromine, 2 ml. of 10 per cent potassium iodide solution and 5 ml. of 2 *N* sulphuric acid were added. The mixture was left in the titration flask for five minutes, and then titration with 0.02 *N* sodium thiosulphate was carried out, with addition of 4–6 drops of starch solution. Results are given in Tables III and IV.



The blank value was subtracted from the consumed 0.02 *N* solution of sodium thiosulphate in all these analyses. A constant blank value of 0.22 ml. of 0.02 *N* sodium thiosulphate resulted in all experiments with regard to reagents used.

The blank value is slightly higher than the value of the receiver, because of the impurity of the acetic anhydride employed.

The analyses were performed in series, without cleaning the cooler or changing the ascarite filling in the gas-purifying tube. Only the reaction flask and the receiver were washed and dried.

Microdetermination of the carbon and hydrogen of methoxyl and ethoxyl groups

A combination consisting of the apparatus for the determination of methoxyl and ethoxyl groups, and of the conventional apparatus for the micro determination of carbon and hydrogen, was used. The apparatus is assembled in such a way as to place the reaction flask, condenser and a slightly different washer containing a 6 cm. layer of anhydrone in addition to a 6 cm. layer of ascarite, between the air inlet and the combustion tube of the apparatus for the determination of carbon and hydrogen. The washer is first filled with a layer of ascarite (b), and then with

TABLE III

Substance	mg.	Found CH ₃ O- %	Calcu- lated CH ₃ O- %
Vanillin	7.367	20.30	20.40
C ₈ H ₈ O ₃	4.110	20.30	"
Quinine hydrochloride	8.912	8.63	8.60
C ₂₀ H ₂₄ O ₂ N ₂ · HCl	3.532	8.79	"
Guaiacol	7.792	24.74	25.00
C ₇ H ₈ O ₂	8.107	24.76	"
Brucine	7.710	15.63	15.74
C ₂₃ H ₂₆ O ₄ N ₂	4.058	15.60	"
Guaiacol carbonate	7.313	22.69	22.63
C ₁₅ H ₁₄ O ₅	4.666	22.27	"
Codein hydrochloride	6.657	9.23	9.24
C ₁₈ H ₂₁ O ₃ N · HCl	4.355	9.31	"
Papaverine hydro- chloride	7.714	32.92	33.02
C ₂₀ H ₂₁ O ₄ N · HCl	4.200	32.86	"
Chloroacetyl-methoxy serine	6.538	15.86	15.86
C ₆ H ₁₀ O ₄ NCl			
2-Methoxy-N-nitro- soethylurea	5.912	20.88	21.09
C ₄ H ₉ O ₃ N ₃			
3-Diazo-4-methoxy-1- phthalimido-butan- 2-one	7.798	11.33	11.36
C ₁₃ H ₁₁ O ₄ N ₃			

a layer of anhydron (a), considering the flow direction. These layers are separated from each other and protected at the ends by small wads of cotton or quartz wool. The reaction flask into which the substance (10—20 mg.) and all the other reagents listed in the methoxyl determination were put, was immediately connected with the cooler and a stream of air was passed through the apparatus at the rate of 10 ml./sec. With water flowing through the condenser the reaction flask was heated with a microbunsen burner to a gentle boil. The heating proces in the stream of air from the beginning of the boiling of the solution took about 60 minutes. The heating of the reaction flask was then omitted and a stream of air passed for 20 more minutes.

TABLE IV

Substance	mg.	Found C ₂ H ₅ O- %	Calcu- lated C ₂ H ₅ O- %
Phenacetin	7.720	25.00	25.15
C ₁₀ H ₁₃ O ₂ N	4.347	25.15	"

The results of these analyses can be seen on Table V.

TABLE V

Substance	mg.	Carbon and hydrogen content of methoxyl groups			
		Found H %	Found C %	Calculated H %	Calculated C %
Vanillin	9.788	1.95	7.82	1.98	7.89
	9.880	2.03	7.98	1.98	7.89
Guaiacol	11.089	2.42	9.76	2.44	9.68
Guaiacol carbonate	11.922	2.26	9.06	2.21	8.76
Papaverine hydrochloride	10.423	3.19	12.84	3.22	12.78
Brucine	10.716	1.58	6.30	1.53	6.09
Quinine hydrochloride	19.133	0.86	3.44	0.84	3.33
Codein hydrochloride	19.664	0.93	3.63	0.90	3.58
Substance	mg.	Carbon and hydrogen content of ethoxyl groups			
		Found H %	Found C %	Calculated H %	Calculated C %
Phenacetin	9.558	2.84	13.50	2.81	13.40

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IZVOD

Određivanje metoksilne i etoksilne skupine u organskim spojevima

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Opisana je poboljšana metoda mikroodređivanja metoksilne ili etoksilne skupine u organskim spojevima. Kod ove metode upotrebljena je ispiralica s krutim natronazbestom. Određivanje je vršeno u struji dušika. Ispiralica s krutim natronazbestom omogućava veći broj određivanja bez promjene natronazbesta i dozvoljava podešavanje brzine strujanja u većem rasponu od ispiralica sa tekućinama. Osim toga, u kombinaciji sa aparaturom za određivanje ugljika i vodika, ona dozvoljava određivanje ugljika i vodika metoksilnih ili etoksilnih skupina.

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