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ETHER STUDIES
III. THE QUANTITATIVE DETERMINATION OF ALDEHYDE AS A CONTAMINANT

BY EDWARD PARKHURST PHELPS AND ALLAN WINTER ROWE

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In a previous communication[1] the authors have described a method for the quantitation of peroxide in anesthetic ether. The present paper deals with the details of a method for evaluating aldehyde, the other principal contaminant[2] of such ether.

Qualitative Tests for Aldehyde.—The observation by Weidenbusch[3] that aqueous potassium hydroxide and aldehyde form a brown resin, has been the basis of a generally accepted test. Traub,[4] White[5] and Krauch and Merck[6] have all specified procedures for the application of this test to ethers, and in one or another form it is officinal in most countries. That other substances such as vinyl alcohol,[7] hydrogen dioxide[8] and ozone[9] will produce like results, has frequently been observed. Baskerville and Hamor[10] reinvestigated the question and reached the conclusion that peroxides do not produce a yellow or brown color, but that alcohol might.[11] Baskerville and Hamor also observe the possible error introduced by contact of the ether with cork and ascribe it to the presence of extractives.[12]

Fuchsin decolorized with sulfurous acid or a sulfite, originally proposed by Schiff,[13] has been frequently investigated with varying results.

Adrian's[14] modifications of the Liebig[15] aldehyde ammonia test and the alkaline silver nitrate test, as applied to ether, are relatively insensitive and unreliable.

[1] THIS JOURNAL, **46**, 2078 (1924).

[2] See Rowe, *Ind. Eng. Chem.*, **16**, 896 (1924).

[3] Weidenbusch, *Ann.*, **66**, 153 (1848).

[4] Traub, *Pharm. Z. Russ.*, **31**, 504 (1909).

[5] White, *Pharm. J.*, [4] **25**, 780 (1907).

[6] Krauch and Merck, "Chemical Reagents," D. Van Nostrand Co., **1907**, p. 101.

[7] Poleck and Thümmel, *Z. anal. Chem.*, **29**, 717 (1890).

[8] Schoenbein and Börrigter, *Chem. News*, **53**, 69 (1886).

[9] Baeyer and Villiger, *Ber.*, **35**, 3038 (1902). Bach, *ibid.*, **35**, 3424 (1902).

[10] Baskerville and Hamor, *J. Ind. Eng. Chem.*, **3**, 301, 378 (1911). Many other references in these papers.

[11] The present authors, in the light of their own experience, feel that the results ascribed to alcohol were probably due to an aldehyde contamination. Pure alcohol produces a white turbidity, never a brown.

[12] In this connection see Feist, *Apot. Zeit.*, **25**, 104 (1910). Herzog, *ibid.*, **29**, 68 (1914). Schenk, *ibid.*, **31**, 290 (1916). Richter, *ibid.*, **33**, 191 (1919).

[13] Schiff, *Compt. rend.*, **61**, 45 (1865).

[14] Adrian, *Mon. Sci.*, **44**, 835 (1894).

[15] Liebig, *Pharm. Centr.*, **6**, 639 (1908).

Nessler's reagent has been thoroughly investigated and is today officinal in several countries. The use of *m*-phenylenediamine hydrochloride was re-studied by Baskerville and Hamor[10] who extended their investigation to embrace the *ortho* and *para* modifications. All these are susceptible to the influence of peroxides and the *para* compound was shown to be insensitive and unreliable. The present authors have used the *meta* compound as a means of purifying alcohol.

Quantitative Methods for Aldehyde.—Several methods have been described in the literature, chiefly adaptations of Schiff's reagent.[16] Of these the most involved but probably most exact is that of Francois.[17] In a personal communication from the E. I. du Pont de Nemours Experiment Station[18] Andreau and Gawthorp give the details of a contact test with Schiff's reagent which yields roughly quantitative results.

With the great sensitivity of the color reactions of aldehyde, a method based upon this property is one of election. The choice of a complementary reagent is a wide one, but the proved efficacy of Schiff's reagent made it the initial choice.

The method as finally adopted calls for the following materials.

1. **Schiff's Reagent.**—This was prepared by the method of Francois, as follows. Mix 30 cc. of 0.1% aqueous fuchsin solution and 200 cc. of a saturated solution of sulfur dioxide. After the mixture has been thoroughly shaken, 3 cc. of concd. sulfuric acid is added. After standing for 24 hours, the solution is filtered if a precipitate is present. It should be colorless or a faint lemon color. The method involves the use of a one-phase system, two standards and successive dilutions of the unknown to a final equality of color with one of them.

2. **Aldehyde-Free Alcohol.**—This is purified by *m*-phenylenediamine, as already described.[1]

3. **Absolute Ether.**—This was prepared by the method already given.[1]

4. **Pure Acetaldehyde for Standard.**—This was first prepared from aldehyde ammonia and subsequent distillation with dil. sulfuric acid, collecting in an ice-bath. Later, paraldehyde depolymerized with dil. sulfuric acid[19] was substituted using a Hempel distilling head, 90 cm. long. Temperature control of the distilling system is important. It is believed that this method produces fairly pure aldehyde. The possibility both of traces of volatile substances and of substances which may form constant-

[16] Girard and Rocques [*Compt. rend.*, **107**, 1158 (1888)] detail a method using *m*-phenylenediamine hydrochloride.

[17] Francois, *Chem. News*, **76**, 7 (1897); *J. pharm. chim.*, [6] **5**, 521 (1897).

[18] The authors take pleasure in expressing their thanks to the Company for its courteous coöperation.

[19] Dil. orthophosphoric acid is probably better. The point has not been thoroughly investigated by us.

boiling mixtures with the aldehyde, is of course, not excluded. The fact remains, however, that standard solutions made up from aldehyde distilled on different days, with reagents in somewhat different proportions and under slightly different conditions, check one another satisfactorily. This seems to be fairly good evidence that the aldehyde is reasonably pure, or that the impurities are not disturbing factors. In preparing a standard, certain criteria exist governing the choice of a menstruum among which are (1) a moderately high boiling point, (2) complete miscibility with ether and with Schiff's reagent, (3) complete freedom from aldehyde, (4) chemical stability and structure not forming a precursor of aldehyde. A variety of compounds were investigated, complying in the main with the above criteria. Among these were glacial acetic and lactic acids, ethyl acetate and other esters, alcohol and ether. Preliminary comparisons showed the last two to be easily the best although the alcohol does not comply with (4) and the ether violates (1) and requires some alcohol in the system to produce a single phase. Standards were prepared by adding weighed[20] amounts of the aldehyde to definite volumes of the respective solvents.

It is obvious that there are three primary factors of variation, namely, the amount of Schiff's reagent, the relative amounts of alcohol and of ether in the system and the time allowed for color development. Further, a secondary factor lies in the observation of Francois, that the amount of color is not proportional to the concentration of the aldehyde. A few comparisons of standards of various concentrations indicated sharply this limitation of the method.

With a Duboscq colorimeter and 15-minute period of color development, a solution of 1% acetaldehyde in alcohol gave a reading of 10 mm. in comparison with a reading of 7.7 mm. for a solution of twice this strength. Further, with a 0.1% solution reading 20 mm., one of 0.4% concentration read 10 mm. instead of the calculated 5 mm. There is an apparent rough exponential proportionality between the differences of observed and calculated readings on the one hand, and actual ratios of solution concentrations on the other. Interpolation on this basis, however, is at best uncertain and the authors feel that the standard and unknown must be of approximately equal concentration if results are to be dependable.

Turning to the primary factors, the influence of variation in the amount of Schiff's reagent can best be shown in tabular form. It is apparent that use of the larger amount of reagent produces no advantage. On the other hand, it entails the addition of an increased amount of the homogenizing material. The small quantity (5 cc.) was adopted as standard for the procedure.

[20] Sealed thin glass capsules of known weight used as containers permit transference and solution without loss of this highly volatile material. By using chilled apparatus and aldehyde at 7° pipets can be substituted without introducing serious error; $d^{20} = 0.80$.

TABLE I

INFLUENCE OF AMOUNT OF REAGENT

Schiff's reagent, cc.	Colorimeter reading 5	10
Standard	70.0	70.0
Sample A	70.2	71.5
Sample B	69.4	68.6

The relative influence of the proportions of the two menstrua is shown in a typical series collated in Table II.

TABLE II

INFLUENCE OF ALCOHOL AND ETHER

Expt.	Composition Standard Alcohol	Standard Ether	Test Alcohol	Test Ether	Readings Standard	Test
1	25	5	25	5	80.0	80.2
2						80.5
3	25	5	20	10	80.0	80.0
4						80.4
5						88.8
6						86.1
7	25	5	15	15	80.0	81.4
8						84.9
9						87.8

The presence of the ether seems to catalyze the color development in a negative sense or at least to inhibit uniformity of reaction velocity.[21]

As the 5cc. test sample of ether is a constant component of all analytical mixtures, to secure an absolute parity the later standards were all prepared with pure ether as the solvent and the volume taken adjusted to equate with that of the ether to be analyzed.

The influence of the time element is shown in the data included in Table III.

TABLE III

INFLUENCE OF TIME

	Standard: 5 cc. of 0.1% aldehyde (in ether), 10 cc. of pure alcohol, 5 cc. of Schiff's reagent	Test specimen: 5 cc. of contaminated ether, 10 cc. of pure alcohol (CHO free), 5 cc. of Schiff's reagent							
Time in minutes	5	10	15	20	30	35	50	60	
	Colorimeter readings								
Sample	Standard	Unknown							
A	55.0	55.2	55.3	..	55.9	..	56.2	56.6	56.4
B	30.0	..	40.4	..	40.1	..	39.6	38.8	38.6
C	30.0	..	..	34.5	..	32.2	..	32.3	32.5
D	55.0	..	54.2	..	54.7	54.6	..	54.5	55.3

[21] Other factors, such as increased volatility, possible contamination, etc., might equally well account for the discrepancies.

Such variations as are observed are of the magnitude of the observation errors. The two series where the longer column of liquid was read seem to have a slight upward, the other sets, a downward tendency. In no case is the change really significant. The time selected for the standard procedure was from 10 to 20 minutes and was conditioned largely by convenience.

Procedure.—A Duboscq colorimeter (Bausch and Lomb type) with 10cm. cups is used for the majority of the color comparisons. Where color development is slight, narrow flat-bottom tubes of the standard Nessler type should be substituted.

To each of two cylindrical containers 10 cc. of alcohol is added, followed by 1 cc. of the aldehyde (in ether) solution plus 4 cc. of pure ether to one, and 5 cc. of the ether sample to the other; 5 cc. of Schiff's reagent is now added to each of the two containers simultaneously. They are allowed to stand for 15 minutes and the colors are compared. If the colors in the two containers do not very nearly match each other in intensity, the procedure must be repeated, using more or less than 1 cc. of the most suitable aldehyde (in ether) standard (plus enough pure ether to make 5 cc.) until the colors match or nearly match.[22] As was previously stated, this repetition is essential as the color production is *not* proportional to the aldehyde concentration. The weight of aldehyde present in the standard represents the weight of aldehyde in 5 cc. of the ether sample. From this value the percentage of aldehyde can be computed.

A few sample results are collated in Table IV.

TABLE IV

SAMPLE RESULTS

5 cc. of aldehyde in ether standard	5 cc. of unknown
10 cc. of alcohol	10 cc. of alcohol
5 cc. of Schiff's reagent	5 cc. of Schiff's reagent

Time, 15 minutes

READINGS

	A	B	C	D	E	F
Standard.....	55.0	50.0	55.0	50.0	50.0	55.0
Test specimen....	55.5	56.5	60.4	54.0	42.3	39.4
Aldehyde, %....	0.106	0.163	0.255	1.70	0.052	> 1.100[a]

[a] About 1.47%.

Summary

A method based on the use of Schiff's reagent is described for the quantitative determination of aldehyde in ether which allows the estimation of minimum amounts of the order of 0.003%.

[22] Oftentimes, through qualitative testing or other evidence, the procedure for the first trial is varied from that just given in order to decrease the number of trials necessary to make the colors match in the standard and sample.