[CONTRIBUTION FROM THE AMMONIA DEPARTMENT OF E. I. DU PONT DE NEMOURS AND COMPANY, INC.]

Analytical Procedures Employing Karl Fischer Reagent.[1] VI. The Determination of Carbonyl Compounds

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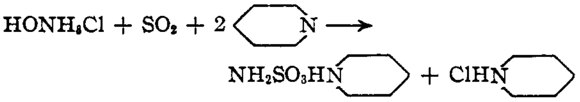
Hydroxylamine hydrochloride is widely used as a quantitative reagent for the determination of aldehydes and ketones. Most of the analytical procedures employing this reagent are acidimetric in nature[2] and, as such, are subject to interference from other acidic and basic substances. Also in such procedures the concentrations of organic solvents employed cannot be varied widely for fear of adversely affecting the indicator.

The present method, instead of employing acidimetry, determines the water formed in the reactions[2] by titration with the Karl Fischer reagent. This reagent requires no indicator and is not affected by large amounts of inert solvents. However, the amount of water initially present must be curtailed to avoid excessive blanks, so that solutions of hydroxylamine hydrochloride in anhydrous methanol, rather than in aqueous alcohol, are employed. The initial water content of the carbonyl compound must also be known, but this is now a simple matter since it is possible to eliminate the interference of these compounds with the reagent.[3]

Fischer reagent reacts in some unknown manner with hydroxylamine salts, to produce water; oximes on the other hand, are not affected by this reagent. Consequently all hydroxylammonium ions remaining after oxime formation must be stabilized prior to titration. This is done by adding an excess of a solution of sulfur dioxide and pyridine in methanol to the mixture ten minutes before titration to convert hydroxylamine to the pyridine salt of sulfamic acid



This is a modification of Raschig's synthesis of sulfamic acid from hydroxylamine and sulfur dioxide.[4] Pyridine accelerates this reaction.

Reagents.—Approximately 0.5 *N* hydroxylamine solution is prepared by dissolving 35 g. of finely powdered Eastman Kodak Company hydroxylamine hydrochloride in dry du Pont synthetic methanol (<0.1% water) to make 1 liter of solution. Other reagents include J. T. Baker C. P. pyridine and a 1 *M* solution of sulfur dioxide and pyridine in methanol, prepared by adding 45 ml. of liquid sulfur dioxide to a chilled solution of 80 ml. of pyridine and 875 ml. of methanol.

Most of the carbonyl compounds investigated were Eastman Kodak Co. chemicals. Formaldehyde was Mallinckrodt 37% aqueous solution; 2-methylpentanone-4 and 2,6-dimethylheptanone-4 were from Carbide and Carbon Chemicals Corporation.

Analytical Procedure.—A five to ten ml. sample (containing not more than 0.1 mole of carbonyl or water) is weighed into a 100 ml. g. s. volumetric flask and diluted to the mark with dry methanol at 25° (thermostat). Using rapid delivery pipets or burets, 30 ml. of hydroxylamine hydrochloride reagent and 5 ml. of pyridine are run into a 250 ml. glass stoppered volumetric flask. Using a precision pipet, 10 ml. of the sample in methanol solution is added to this mixture. The flask is placed in a water-bath at 60 ± 1° the stopper loosened momentarily for the expulsion of included air, then tightened, and the mixture heated for two hours. The flask is then removed and allowed to cool to room temperature. Twenty-five ml. of 1 *M* sulfur dioxide and pyridine in methanol is now added. After standing at room temperature for from ten minutes to one hour, the solution is titrated for water with Karl Fischer reagent.[5]

At least one blank containing 10 ml. of the same dry methanol employed above, in addition to the other reagents, is run with each set of samples. Initial water in the sample is determined after adding a 2% solution of hydrogen cyanide in pyridine to protect the carbonyl compound as outlined in the preceding paper of this series.[3]

The titer of the sample less that of the blank is calculated to millimoles of water. From this is now deducted the millimoles of water originally present in the sample. The net result is equivalent mole for mole to the carbonyl present.

Results.—Table I shows the results obtained with a number of aldehydes and ketones. In most cases the corresponding acidimetric values are tabulated.[2] Except where noted the results are for a heating period of two hours at 60° for the Karl Fischer procedure, two hours at 100° for the acidimetric method.

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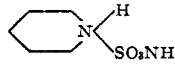
[1] This reagent discussed in detail in the first paper of the series (Smith, Bryant and Mitchell, THIS JOURNAL, **61**, 2407 (1939)) consists of a solution of iodine, sulfur dioxide and pyridine in methanol. It is specific for water.

[2] Bryant and Smith, *ibid.*, **57**, 57 (1935), includes reactions and references to other procedures.

[3] Bryant. Mitchell and Smith, *ibid.*, **62**, 3504 (1940).

[4] Raschig, *Ber.*, **20**, 588 (1887).

[5] Crystals of pyridinium sulfamate, 

, (m. p. 117° (dec.)) may appear before or during the titration. This material is without action upon the reagent. The end-point is matched by observing the supernatant liquid.

TABLE I

ANALYTICAL DATA FOR ALDEHYDES AND KETONES

Substance	% H_2O	% Recovery of carbonyl compound[b] Karl Fischer	 Acidimetric
Formaldehyde	50.6	(4)[a] 37.1 ± 0.2[c]	
n-Butyraldehyde	0.2	(2) 94.2 ± 0.2	93.9 ± 0.5
2-Ethylbutyraldehyde	.2	(6) 83.5 ± 0.6	83.2 ± 0.8
2-Ethylhexanal	.1	(2) 98.3 ± 0.2	95.8 ± 0.4
Dextrose	.0	(4) 102.2 ± 1.0	
Benzaldehyde	.1	(4) 98.6 ± 0.1[c]	98.6
Dimethylbenzaldehyde	.05	(4) 98.6 ± 0.2	98.5 ± 0.5
Salicylaldehyde	.1	(2) 99.7 ± 0.2	98.1 ± 0.1
Cinnamaldehyde	.1	(2) 99.1 ± 0.2	99.2
Vanillin	.05	(2) 99.8 ± 0.2	
Acetone	.04	(6) 98.9 ± 0.2	
		(2) 99.6 ± 0.2[c]	
2-Methylbutanone-3	1.2	(4) 83.5 ± 0.3	83.4 ± 0.4
2-Methylpentanone-4	0.1	(4) 97.5 ± 0.2	96.9 ± 0.6
2,4-Dimethylpentanone-3	.05	(4) 99.5 ± 0.2	
2,6-Dimethylheptanone-4	.1	(10) 99.4 ± 0.3	
Cyclopentanone	.2	(6) 98.6 ± 0.1	97.6 ± 0.2
Cyclohexanone	.1	(8) 99.0 ± 0.3[c]	99.0 ± 0.2
d-*l*-camphor	.0	(2) 84.6 ± 0.2	98.8[d]
		(2) 96.1 ± 0.0[e]	
Benzophenone	.0	(2) 100.3 ± 0.0	100.9[f]
Benzoin	.0	(3) 102.7 ± 1.2	102.4[g]
Carvone	.0	(4) 96.5 ± 0.5	95.5

[a] Figures in parentheses represent number of individual determinations. [b] Including maximum deviation from the mean. [c] 1/2 hr. in cold. [d] 5 hrs. at 100°. [e] 4 hrs. at 60°. [f] 3 hrs. at 100°. [g] 1 hr. at 100°.

The above method is applicable to aldehydes and ketones of the aliphatic, alicyclic and aromatic series. Camphor was the only substance of the group studied that failed to react completely. Mixtures of carbonyl compounds with acids, hydrocarbons or water were analyzed without loss of precision or accuracy. The results are in general more nearly quantitative than those of the earlier method. The average precision of the present procedure is about ±0.3%.

Interfering Substances.—Organic acids in the presence of an esterification catalyst react with the methanol to form water.[6] This interference can be eliminated by substituting pyridine for the methanol in preparing the sample dilution. Under these conditions the calculation must be modified to take account of the difference (up to 10%) between the pyridine content of the sample and the 10 ml. added to the blank. The water content of C. P. pyridine is usually large enough to make this difference significant. Free alkali titrates mole for mole as water, so that quantitative corrections readily can be made. The effects of large concentrations of such amines as do not react with the carbonyl group can be eliminated by the addition of excess acetic acid.

No interference has been observed in the presence of acids, ethers, esters or hydrocarbons.[7] High concentrations of water reduce the sensitivity of the method.

The authors wish to thank Mr. J. M. Lupton of this Laboratory for first suggesting the adaptation of the acidimetric procedure for use with Karl Fischer reagent.

Summary

1. A new analytical procedure for aldehydes and ketones is presented. The water formed in the reaction between carbonyl compounds and hydroxylamine hydrochloride, in the presence of pyridine, is determined by titration with Karl Fischer reagent. The method is applicable to aliphatic, alicyclic and aromatic carbonyl compounds.

2. Results obtained with a group of twenty-one aldehydes and ketones are tabulated.

3. The subject of interfering substances is discussed.

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(6) Mitchell, Smith and Bryant, THIS JOURNAL, 62, 4 (1940).

(7) The determination of carbonyl in the presence of anhydride is being investigated.