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# Analytical Procedures Employing Karl Fischer Reagent.[1] III. The Determination of Organic Acids

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The most obvious procedures for the quantitative determination of carboxylic acids are those based on neutralization by strong alkalies. These methods, however, are so general as to be subject to interference from many other types of compounds producing hydrogen ions. For example, where inorganic acids are present, these must be separated or determined separately by specific methods before a measure of the carboxyl group can be obtained by the usual titration with standard base.

In the present investigation a carboxyl procedure independent of ordinary acid–base titrimetry was devised. Its basis is the estimation of water liberated by the reaction $RCOOH + CH_3OH \longrightarrow RCOOCH_3 + H_2O$. This reaction is almost identical with the one used in the authors' hydroxyl procedure.[2] It proved possible to obtain practically stoichiometric conversions of a large number of organic acids to the corresponding esters and water by using a large excess of methanol containing boron fluoride. Nieuwland and his collaborators found the latter substance to be an efficient esterification catalyst.[3] Inasmuch as one mole of water is formed for each equivalent of carboxyl esterified, the water found by titration with Karl Fischer reagent, less that originally present, becomes a measure of the carboxyl content. Strong inorganic acids, with the exception of sulfuric, are not esterified by this procedure. The apparatus requirements are very simple, the entire analysis including the esterification and titration steps being carried out in glass-stoppered flasks.

The new carboxyl procedure is applicable to aliphatic acids generally, including branched chain and hydroxyl substituted types, and also aromatic acids having the carboxyl attached to an aliphatic side-chain. Typical aromatic acids having the carboxyl group attached directly to the ring do not react quantitatively. The heterocyclic furoic acid and the sterically hindered alicyclic camphoric acid also fail to react completely.

Changes in the concentration of the catalyst solution have a marked effect on the esterification of strictly aromatic acids.[3d] An increase, for example, gave results more nearly quantitative. By careful control of this variable it was possible to esterify aliphatic acids without appreciably affecting aromatic acids.

The average precision and accuracy based on comparisons with alkali titration are about ±0.3%.

## Experimental

**Analytical Procedure.**—Five to 10 ml. of sample is weighed into a 100-ml. g. s. volumetric flask half-filled with dioxane. The mixture is made up to volume with more dioxane, shaken until homogeneous and allowed to stand at least thirty minutes in a water-bath at 25 ± 1°. Five ml. (using calibrated pipet) of the dioxane solution is placed in a 250-ml. g. s. volumetric flask. To this is added exactly 20 ml. of the catalyst solution.[4] The flask is then placed in a water-bath[5] at 60 ± 1°, and after momentarily raising the stopper to allow for expansion of the included air, is firmly stoppered and maintained at that temperature for one hour.[6] At the end of this period the sample is removed, allowed to cool to room temperature spontaneously, and then titrated with Karl Fischer reagent.[7] A blank is run using 5 ml. of dioxane and 20 ml. of catalyst solution. After correction for water in the dioxane and catalyst, the millimoles of water present after treatment, less the water originally present, are equal to the milliequivalents of free carboxyl in the sample.

The water originally present may be obtained by titrating 5 ml. of the original dioxane solution with Fischer reagent. A correction must be made for the water initially present in the dioxane as this quantity is usually apprecia-

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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, Mitchell and Smith, This Journal, **62**, 1 (1940).

[3] (a) Bowlus and Nieuwland, *ibid.*, **53**, 3837 (1931); (b) Hinton and Nieuwland, *ibid.*, **54**, 2017 (1932); (c) Hennion, Hinton and Nieuwland, *ibid.*, **55**, 2857 (1933); (d) Sowa and Nieuwland, *ibid.*, **58**, 271 (1936).

[4] This solution is prepared by dissolving 100 g. of boron trifluoride gas and 2 ml. of water in sufficient du Pont synthetic methanol (water content 0.15% or less) to make a final volume of one liter. Boron fluoride of suitable quality may be obtained in cylinders from the Ohio Chemical Co., Cleveland, Ohio.

[5] Smith and Bryant, This Journal, **57**, 62 (1935), describe a convenient water-bath.

[6] Acetic and propionic acids react to completion at 25° in one hour, while formic acid requires two hours.

[7] In the presence of the catalyst solution, the iodine color of the reagent may persist during the addition of about the first 15 ml., producing a false end-point. The water included in the catalyst solution is sufficient to permit the addition of 15 ml. of reagent directly. Further addition of reagent produces a normal discharge of the brown color until the true end-point is reached. The false end-point may be avoided altogether if 5 ml. of pyridine of known water content is added just before titration. Unlike the hydroxyl method,[2] this procedure is reliable without the extra pyridine.

ble. The correction is made on the basis of the volume of dioxane in the aliquot, figured with sufficient precision as the difference between the total volume of solution and the volume of concentrated sample employed, neglecting volume changes on mixing.

## Analytical Results

The experimental results obtained with a group of organic acids are given in Table I. In most cases the results are within 0.3% of those obtained by aqueous caustic titration.

Benzoic and salicylic acids reacted only to the extent of 58 and 19%, respectively; furoic and camphoric, 35 and 75%. Benzilic acid, which should esterify as an aliphatic, reacted only 45%, probably due to steric hindrance.[8]

The solid acids studied in the present research, with the exception of glycolic, phenylacetic and cinnamic acids are not very soluble in dioxane. The original sample should therefore be no larger than 2.5 g. per 100 ml. of dioxane solution.

TABLE I

ANALYTICAL DATA FOR ORGANIC ACIDS

| Acid[b] | % Acid (alkali titration) | | Complete analysis Using Karl Fischer reagent % Acid | % Water | Total |
|---|---|---|---|---|---|
| Formic | | (6)[a] | 97.2 ± 0.2 | 2.2 | 99.4 |
| Acetic[c] | | (2) | 99.6 ± .2 | 0.1 | 99.7 |
| Propionic | | (2) | 99.8 ± .1 | .2 | 100.0 |
| *n*-Butyric | 99.5 | (8) | 99.5 ± .4 | .5 | 100.0 |
| *i*-Butyric | 99.5 | (6) | 99.7 ± .2 | .5 | 100.2 |
| *dl*-Methylethyl acetic | | (2) | 95.1 ± .0 | .7 | 95.8 |
| Trimethylacetic | | (2) | 99.6 ± .0 | .4 | 100.0 |
| *n*-Caproic | 99.1 | (6) | 99.3 ± .3 | .4 | 99.7 |
| Stearic[d] | | (4) | 100.3 ± .1 | .0 | 100.3 |
| Succinic[g] | | (2) | 99.1 ± .5 | .7 | 99.8 |
| Oleic[d] | 99.5 | (2) | 99.2 ± .0 | .5 | 99.7 |
| Linoleic[d] | 98.2 | (2) | 96.5 ± .5 | 1.2 | 97.7 |
| Glycolic | 99.9 | (4) | 99.6 ± .2 | 0.0 | 99.6 |
| α-Hydroxy-*i*-butyric[f] | 97.6 | (4) | 97.9 ± .5 | .1 | 98.0 |
| Tartaric[g] | 94.5 | (4) | 94.3 ± .5 | .1 | 94.4 |
| Ricinoleic[e] | 58.3 | (4) | 58.4 ± .5 | 1.7 | 60.1 |
| Phenylacetic | | (2) | 100.0 ± .2 | 0.0 | 100.0 |
| Cinnamic | | (2) | 99.7 ± .3 | 0.0 | 99.7 |

[a] Figures in parentheses represent number of determinations. [b] Except where noted, above acids are Eastman Kodak Co. chemicals. [c] Merck glacial C. P. [d] Eimer and Amend pure. [e] Eimer and Amend technical. [f] American Cyanamid Company. [g] J. T. Baker Analyzed C. P.

An increase in catalyst concentration had a marked effect on the esterification of aromatic and heterocyclic acids. Table II shows this change from the regular catalyst solution to a solution three times as strong (300 g. per liter).

TABLE II

ESTERIFICATION USING HIGHER CONCENTRATIONS OF CATALYST

| Substance | % Acid esterified Regular catalyst concn. | High catalyst concn. |
|---|---|---|
| Benzoic | 58 | 98.5 ± 0.3 |
| Salicylic | 18 | 67 |
| Anisic | | 88.5 |
| Phthalic | | 88 |
| Camphoric | 40 | 46 |
| Furoic | 34 | 83 |

It is interesting to note that by substituting in the one case glycol and in the other di-isopropylcarbinol for methanol in the catalyst solution and following the conditions of the general procedure, the extent of reaction with benzoic acid was increased to 75% with the glycol solution and decreased to 16% with the di-isopropylcarbinol solution.

A decrease in the concentration of the catalyst solution (25 and 50 g. per liter), while having little effect on the esterification of aliphatic acids, reduced considerably the reaction of aromatic and heterocyclic acids and the sterically hindered camphoric acid. These results are noted in Table III.

TABLE III

ESTERIFICATION USING LOWER CONCENTRATIONS OF CATALYST

| Substance | % Acid esterified Catalyst, 25 g./liter *a* | *b* | Catalyst, 50 g./liter *a* | *b* |
|---|---|---|---|---|
| Formic | 96.9 ± 0.1 | 97.7 ± 0.0 | 97.7 ± 0.0 | |
| Acetic | 98.8 ± .0 | 98.8 ± .0 | 99.1 ± .2 | 99.8 ± 0.1 |
| Isobutyric | 96.2 ± .0 | 99.0 ± .2 | 98.9 ± .2 | |
| Trimethylacetic | 31.7 ± .0 | 95.8 ± .3 | 52.9 ± .0 | 96.5 ± 0.3 |
| *n*-Caproic | 98.6 ± .0 | | | |
| Oleic | 95.6 ± .0 | | | |
| Stearic | 100.3 ± .1 | | | |
| Succinic | 87.6 ± .6 | 99.1 ± .3 | | |
| Camphoric | 1.3 ± .5 | | | |
| Benzoic | 1.4 ± .8 | 34.9 ± .3 | 6.2 ± .0 | 52.5 ± 0.3 |
| Salicylic | 0.0 ± .6 | 8.4 ± .0 | 1.1 ± .5 | 18.4 |
| Furoic | 0.9 ± .3 | | | |

[a] Conditions: 1 hour at room temperature (26 ± 1°).
[b] Conditions: 1 hour at 60°.

Examination of the results in Table III suggests that mixtures of aliphatic and aromatic acids should behave in the same manner as the pure substances. Mixtures of acetic–benzoic and acetic–salicylic acids were analyzed, following the conditions of column 1; *i. e.*, 25 g./l. of catalyst for one hour at room temperature. These results are given in Table IV.

On the basis of Table III, the above procedure may be modified for other mixtures, taking into account the behavior of the pure acids.

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(8) Citric acid is about 92% esterified.

TABLE IV

ANALYSIS FOR ACETIC ACID IN THE PRESENCE OF BENZOIC AND SALICYLIC ACIDS

| Nature of mixture | % Aromatic acid added | % $CH_3COOH$ added | % $CH_3COOH$ found |
|---|---|---|---|
| Acetic and benzoic acids | 89.6 | 10.4 | 12.6 ± 0.0 |
| | 50.8 | 49.2 | 50.1 ± .1 |
| | 11.8 | 88.2 | 88.1 ± .1 |
| Acetic and salicylic acids | 91.3 | 8.7 | 9.0 ± .0 |
| | 47.1 | 52.9 | 52.9 ± .0 |
| | 11.7 | 88.3 | 87.7 ± .1 |

**Interfering Substances.**—Aldehydes and ketones react with the methanol of the catalyst solution presumably to form acetals and ketals:

$$RCHO + 2CH_3OH \longrightarrow RCH(OCH_3)_2 + H_2O$$
$$RCOR' + 2CH_3OH \longrightarrow RR'C(OCH_3)_2 + H_2O$$

In all observed cases, however, the reaction was stoichiometric, so that suitable corrections could readily be made. It is self-evident that substances easily dehydrated interfere with the analysis. Of several classes of substances tried, tertiary alcohols were the only chemicals that were dehydrated sufficiently to affect the method. Tertiary butanol was dehydrated 37% by the above catalyst solution.

Among the strong inorganic acids tried, sulfuric acid was the only one esterified by the catalyst solution. The reaction is quantitative, however, in that one mole of water is formed per mole of the acid: $H_2SO_4 + CH_3OH \longrightarrow CH_3HSO_4 + H_2O$. Other acids, such as benzenesulfonic, phosphoric and hydrochloric, do not interfere with the method.

In the titration of sulfuric acid for water a dioxane solution of the acid should be used. Apparently some charring occurs when concentrated sulfuric acid is titrated directly with Karl Fischer reagent.

Those compounds which fume or volatilize readily, such as hydrochloric acid, are best titrated for water in the presence of an inert solvent.

Boric acid reacts stoichiometrically with the methanol in Karl Fischer reagent, even in the absence of catalyst solution: $H_3BO_3 + 3CH_3OH \longrightarrow (CH_3)_3BO_3 + 3H_2O$.

Anhydrides also interfere with the procedure, probably as follows

$$(RCO)_2O + CH_3OH \longrightarrow RCOOCH_3 + RCOOH$$
$$RCOOH + CH_3OH \longrightarrow RCOOCH_3 + H_2O$$

On this basis the extent of reaction with acetic anhydride was 61% in dioxane solution, but essentially quantitative in methanol solution.

Unsaturated alcohols and hydrocarbons do not interfere with the procedure, as indicated particularly by experiments with allyl alcohol and amylene.

## Summary

1. A specific quantitative method for the determination of organic carboxylic acids has been described. The method is based on complete esterification and subsequent titration of the water liberated, using the highly specific Karl Fischer reagent.

2. Analytical results for eighteen acids, principally aliphatic, are tabulated.

3. The effect of changes of catalyst concentration upon esterification has been noted.

4. A method for the estimation of aliphatic acids in the presence of aromatic acids, based on large differences in esterification rate, has been demonstrated for selected cases.

WILMINGTON, DELAWARE RECEIVED SEPTEMBER 26, 1939