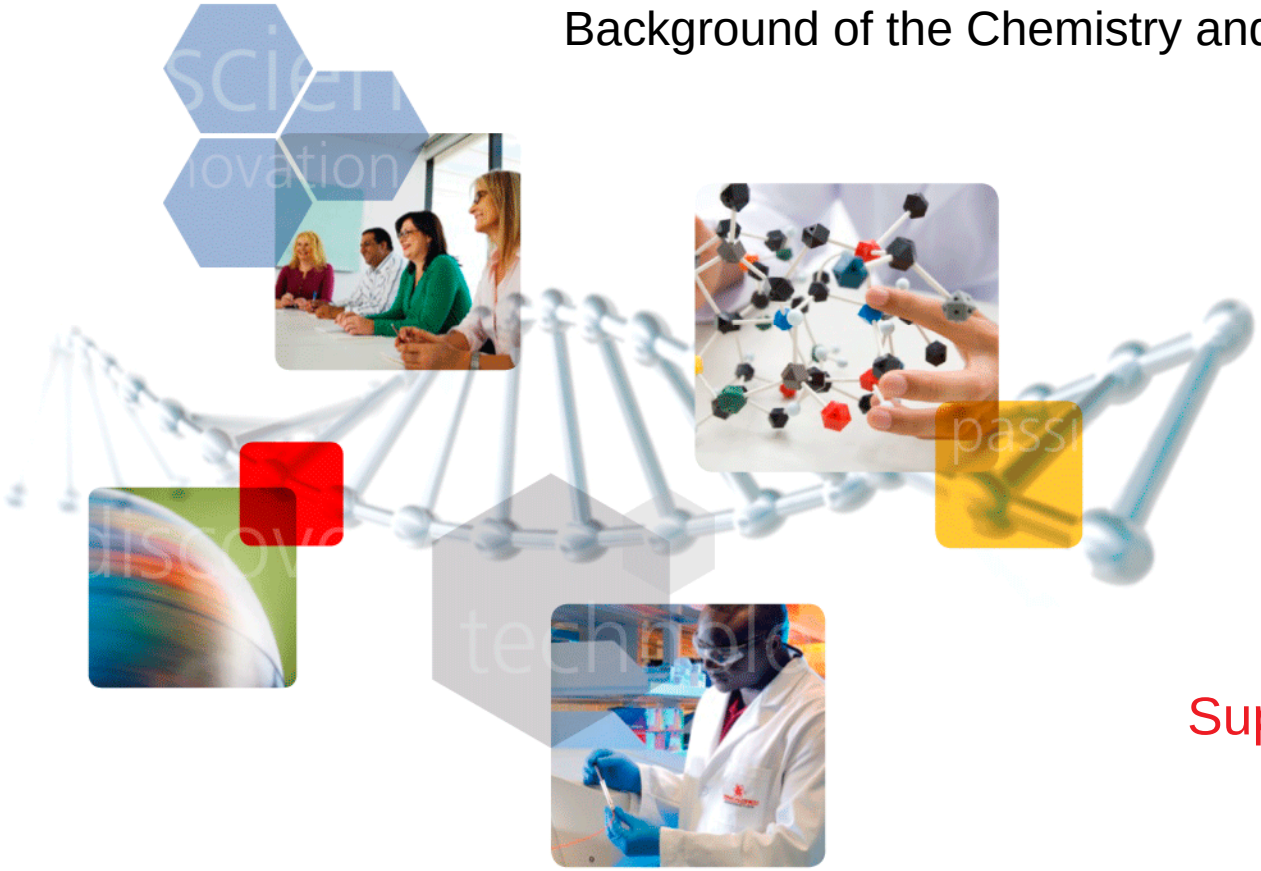
Moisture Determination by Karl Fischer Titration

Background of the Chemistry and Recent Developments



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Overview

Karl Fischer History

Pyridine vs. HYDRANAL®

Instrumentation Types- Coulometric or Volumetric

Sample Solubility

Control of pH

Side Reactions

Quality Control-Water Standards

Instrument Maintenance

What is Karl Fischer titration?

- **Karl Fischer is an analytical technique used to measure the moisture (water) content in solids, liquids or gases.**
- **Karl Fischer was a chemist working at a petrochemical company in Germany in the 1930's. He developed the technique. Sigma-Aldrich's Riedel-de Haën chemists Eugen Scholz and Helga Hoffmann improved upon it.**
- **Titration is defined as:**
  - "A technique to determine the concentration of a substance in solution by adding to it a standard reagent of known concentration in carefully measured amounts until a reaction of definite and known proportion is completed, as shown by a color change or by electrical measurement, and then calculating the unknown concentration."

How does K-F titration work?

In general, K-F titration can be summarized into a series of steps:

Add reagent ("titrant") to a burette

- The reagents include alcohol, SO_2, a base and I_2

Add sample solvent to the titration vessel

Begin stirring the vessel

Zero the instrument by titrating unwanted moisture in the system

Add the weighed sample to the titration vessel

Begin adding reagent from the burette while stirring

When the endpoint is reached, the electrode will detect no change in current upon addition of more reagent

By knowing how much titrant was added, the water content can be calculated

Normally, the K-F instrument does the calculations and reports the results as "% water" or "ppm water."

The Karl Fischer reaction

K-F titration involves two reactions:

In the first reaction, an alcohol (usually methanol or ethanol), sulfur dioxide (SO_2) and a base (RN) react to form an alkylsulfite intermediate:

(rxn. 1) $CH_3OH + SO_2 + RN \leftrightarrow [RNH]SO_3CH_3$

In the second reaction, the alkylsulfite reacts with iodine (I_2) and the water from the sample:

(rxn. 2) $[RNH]SO_3CH_3 + I_2 + \mathbf{H_2O} + 2RN \leftrightarrow [RNH]SO_4CH_3 + 2[RNH]I$

Since water and I_2 are consumed in equimolar amounts in reaction 2, if you know the amount of I_2 consumed, you know the amount of water that was present in the sample.

Types of K-F titration

There are 2 types of K-F titration: Volumetric & Coulometric

Although the endpoint of the reaction is marked by a persistence of the yellow (I_2) color, using the eyes is not very accurate. Both methods use bipotentiometric titration to measure the amount of I_2 consumed by the water

Bipotentiometric titration is simply monitoring the extent of reaction by measuring changes in electrical conductivity of the reaction solution

The difference between them is primarily in the way the I_2 is generated:

- In volumetric titration, the I_2 is included with the reagents
- In coulometric titration, the I_2 is generated at an electrode

Which one the customer chooses depends on:

- The method they are following or personal preferences (if any)
- The titration equipment they currently have in their lab
- The water levels in the sample, generally:
  - Volumetric: 0.1 – 100% H_2O
  - Coulometric: 0.001 – 0.1% H_2O

Bipotentiometric titration: Measuring I_2

The second reaction in the K-F titration – the one that actually consumes the water – is a redox reaction:

$$[RNH]SO_3CH_3 + I_2 + H_2O + 2RN \leftrightarrow [RNH]SO_4CH_3 + 2[RNH]I$$

Sulfur is oxidized from alkylsulfite (oxidation number +4) to alkylsulfate (oxidation number +6):

$$SO_3CH_3^{-2} \rightarrow SO_4CH_3^{-2} + 2e^-$$

Iodine is reduced:

$$I_2 + 2e^- \rightarrow 2I^- \quad (E^0 = 0.54\ V)$$

The reduction of iodine consumes electrons generated by the oxidation of sulfur, which changes the electrical potential of the system.

The change in potential is detected by an electrode (a double platinum electrode).

Instrumentation Types

Coulometric or Volumetric

- **While both techniques are based on the same two step reaction mechanism, they differ in the way that Iodine is introduced to the reaction**

- **The same K-F reactions occur in Coulometric titration as do in Volumetric titration**

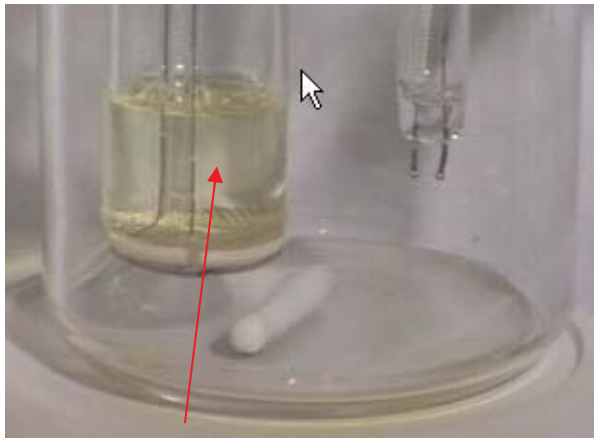
- **However, in the Coulometric system, the I_2 is generated *in situ* rather than added as a reagent**
  - It is generally considered more sensitive to lower water levels
  - The I_2 is generated at the anode: $2\ I^- \rightarrow I_2 + 2e^-$
  - The cathode reaction is: $2RNH + 2e^- \rightarrow H_2 + 2RN$

The Coulometric System

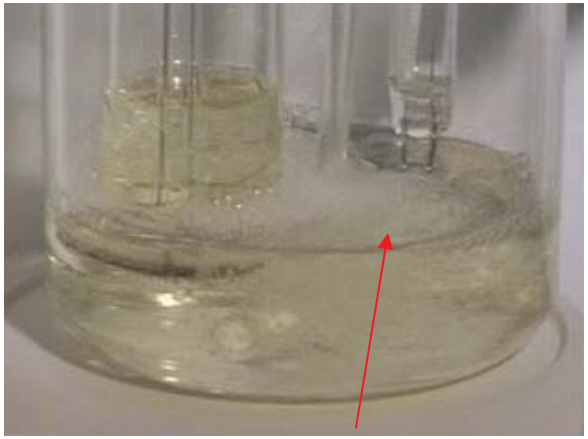
- Micro Detection System
- “Absolute Method”
- High Water Capacity Reagents
- Designed for Titration of Liquids & Gases Only
- Less System Flexibility
- Co-Solvents are limited
- No Option for Temperature Modification
- No Option for Homogenizer

Cell with diaphragm

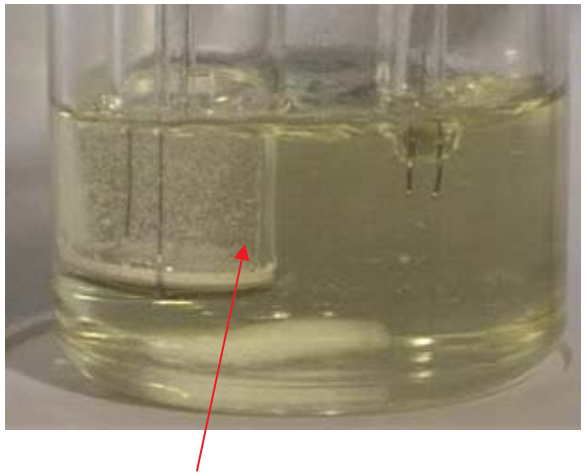
The cell with the diaphragm uses two solutions, one in the cathode chamber the other in the anode chamber.



Cathode compartment filled with catholyte solution (e.g. HYDRANAL®- Coulomat CG)



Anode compartment filled with anolyte solution (e.g. HYDRANAL®- Coulomat AG)
I_2 formation occurs at the anode:
$2I^- \rightarrow I_2 + 2e^-$



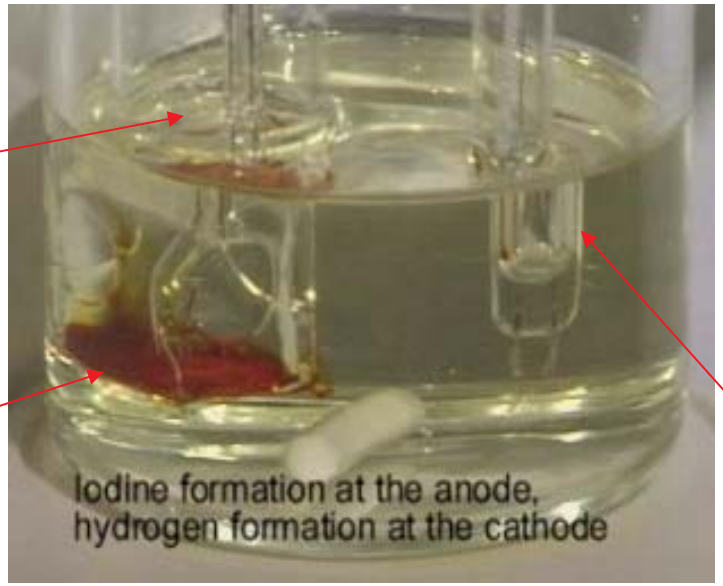
Titration begins. Note H_2 formation (bubbles) at the cathode:
$2H^+ + 2e^- \rightarrow H_2(g)$

Cell without diaphragm

The diaphragmless cell uses one solution that has all reagents needed for K-F titration (e.g. HYDRANAL®- Coulomat AG).

Cathode (reduction)
H_2 formation:
$2H^+ + 2e^- \rightarrow H_2$
(cathode not visible in this picture)

Anode (oxidation)
I_2 formation:
$2I^- \rightarrow I_2 + 2e^-$
note brown color



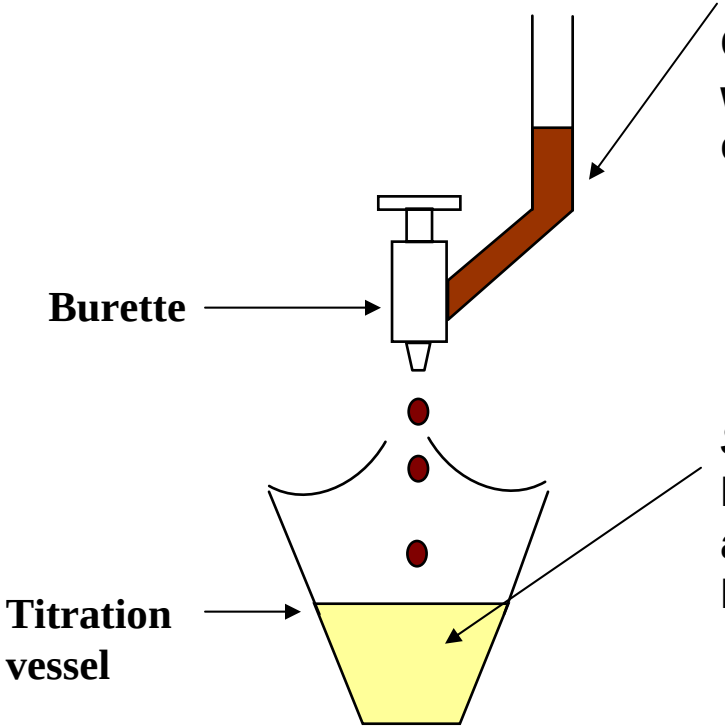
Double platinum indicator electrode

The Volumetric System

- **Designed for Higher Water Concentrations**
- **Fast Titration (30 mg Water per minute)**
- **Designed for Titration of Solids, Liquids & Gases**
- **System Flexibility**
  - Modified Solvent Systems
  - Temperature Adjustment
  - Peripheral Equipment (Homogenizer, Oven)

One Component System

The one component systems are the most popular.
The benefit of a one component volumetric titration is that it has almost unlimited water capacity.



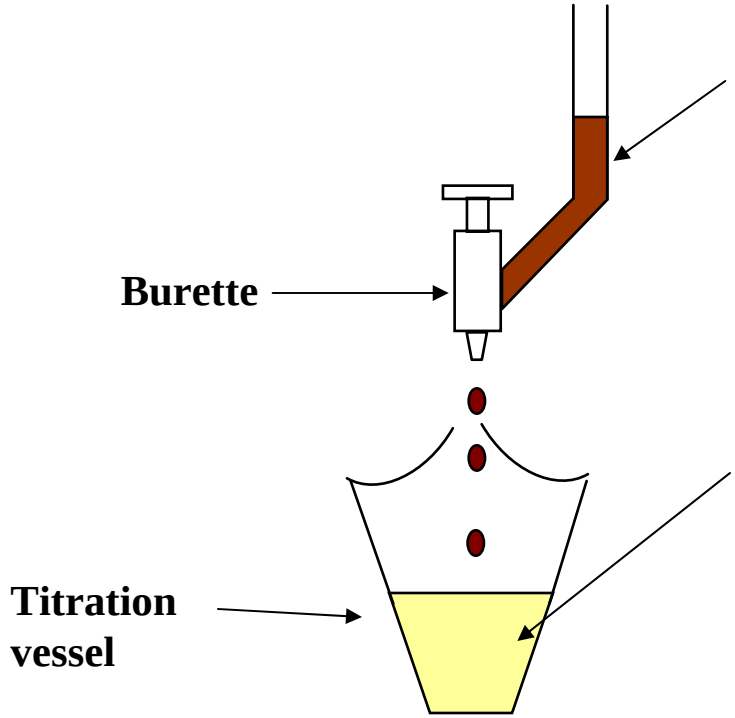
Titrant
Contains all reactants (SO_2, I_2 and base) except the water, dissolved in diethyleneglycol monoethyl ether (DEGEE) (e.g. HYDRANAL®- Composite)

Sample solvent
Methanol or other solvent to which sample is added (e.g. HYDRANAL®- Methanol Dry/ Methanol Rapid or CompoSolver E)

Two Component System

The benefits of a two component volumetric titration are:

- **Higher titration speed**
- **Greater accuracy for small amounts of water**
- **Higher buffer capacity**
- **Exact and stable titer**



Titrant
Contains I_2 in methanol or ethanol
(e.g. HYDRANAL®- Titrant or Titrant E)

Sample solvent
Contains SO_2 and base in methanol or ethanol
(e.g. HYDRANAL®- Solvent or Solvent E)

Volumetric System

Different Burette systems

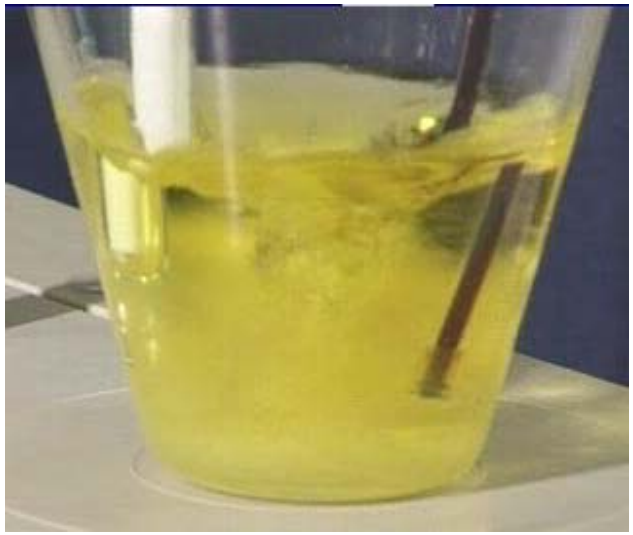
Older style burette

New style burette

Sample Solubility

Sample Solubility is Extremely Important to Obtain Total Water Content

- **Total Water = Surface Water + Bound Water**
- **Methods to Improve Sample Solubility**
- **Co-Solvent Additions**
- **Elevate Solvent System Temperature**
- **Add Homogenizer to System**



Sample Solubility

Co-Solvent Addition - *Chloroform*

- **Dissolution of fats, oils, and long-chained hydrocarbons is poor in Methanol**
- **Increases the solubility of long chain Carboxylic Acids,Ethers, Hydrocarbons**
- **Inhibits the dissolution of inorganic salts, and some sugars**
- **Changes the KF reaction stoichiometry...**

Sample Solubility

Co-Solvent Addition - *Chloroform*

Reagents Containing Chloroform

HYDRANAL®- Coulomat A
General use for a system with a diaphragm, contains methanol and chloroform

HYDRANAL®- Coulomat Oil
Anolyte for analysis of oils, contains methanol, chloroform and xylene

HYDRANAL®- Chloroform
Use as co-solvent for Karl Fischer
Max Water 0.01%

HYDRANAL®- Solvent CM
Solvent for use with oils; mix of chloroform and methanol

HYDRANAL®- LipoSolver CM
Solvent for use with Lipids; mix of chloroform and methanol

HYDRANAL®- Solver (Crude) Oil
Solvent for use with oils; mix of methanol, chloroform and xylene

Sample Solubility

Co-Solvent Addition - *Alcohol*

- **Dissolution of long-chained hydrocarbons is poor in Methanol**
- **Increases the solubility of long chain Carboxylic Acids,Ethers, Hydrocarbons**
- **Suitable alcohols include: 1-Propanol, 1-Pentanol, and 1-Hexanol**

Sample Solubility

Co-Solvent Addition - *Alcohol*

Reagents Containing Alcohol

HYDRANAL®- Coulomat AG
General use with or without a diaphragm, methanol based

HYDRANAL®- Coulomat AG-H
Specially manufactured for use with long-chained hydrocarbons and oils in a system with or without a diaphragm,contains methanol and 1-pentanol

HYDRANAL®- Coulomat E
Ethanol based anolyte, safer less toxic formulation. Contains Methanol.

HYDRANAL®- Solvent Oil

Solvent for use with oils; free of halogenated hydrocarbons

HYDRANAL®- LipoSolver MH
Solvent for use with Lipids; mix of 1-Hexanol and methanol

HYDRANAL®- CompoSolver E

Ethanol based solvent for one component titration. Replaces Methanol

Sample Solubility

Co-Solvent Addition - *Formamide*

- **Formamide improves solubility of polar substances in Methanol**
- **Addition of Formamide is preferred for analysis of carbohydrates, proteins, and inorganic salts**
- **Increases the speed of the Karl Fischer reaction**
- **Incompatible in a coulometric cell with a diaphragm**

Sample Solubility

Co-Solvent Addition - *Organic Solvents*

- **Acetonitrile good polar solvent**
- **N-Methylpyrrolidone dissolves polymer**
- **Pyridine good polar solvent, also basic for neutralization of acids**
- **Toluene, Xylene improve solubility of dirty oils**

Sample Solubility

Co-Solvent Addition - *Solvents to Avoid*

- **Dimethylformamide delays KF reaction (Lab Report L424)**
- **Dimethylsulfoxide recovery rates are too low (Lab Report L141)**
- **Secondary and Tertiary Alcohols cause increase in titer values**

Sample Solubility

Co-Solvent Addition Recommendations

Co-Solvent	Addition Limit Volumetric	Addition Limit Coulometric W/D	Addition Limit Coulometric WO/D
Chloroform	70%	25%	0%
Alcohol	70%	30%	20%
Formamide	50%	0%	20%
N-Methylpyrrolidone	50%	0%	0%
Pyridine	70%	30%	20%
Toluene	70%	30%	20%
Xylene	70%	30%	20%

W/D = With Diaphragm WO/D = Without Diaphragm

Titration at Elevated Temperature

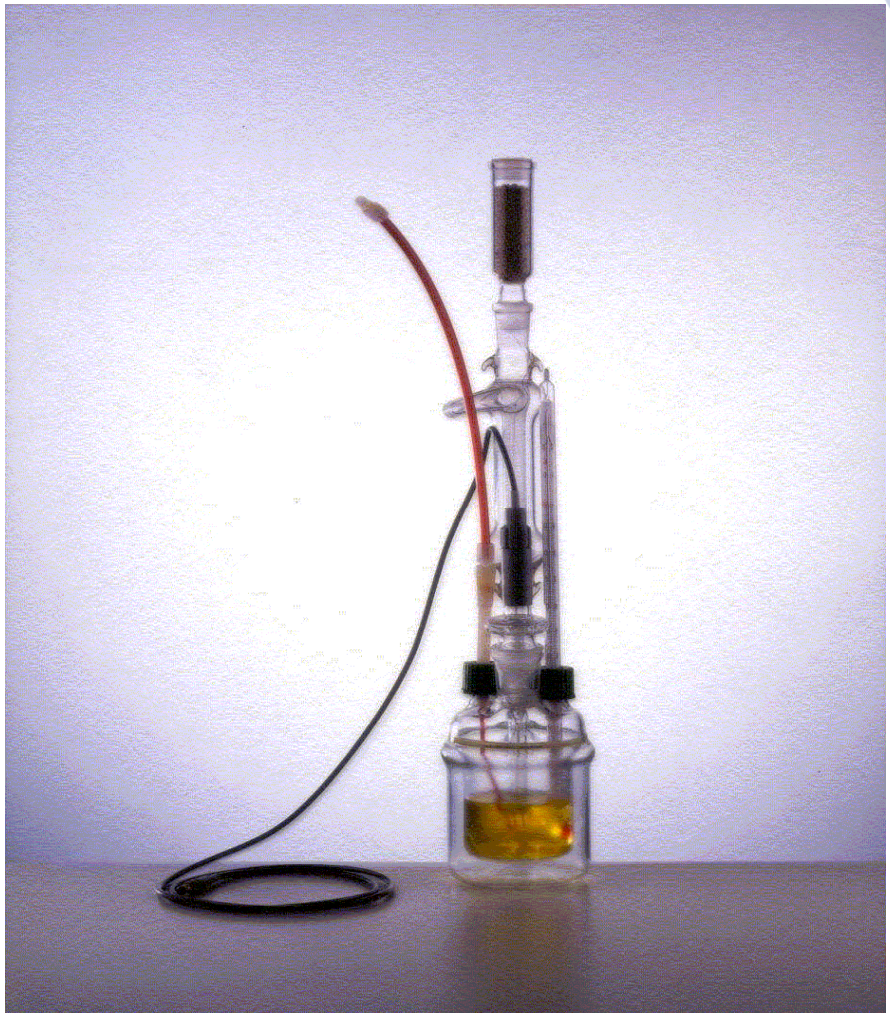
Sluggish Titrations

- **Sample is slow to dissolve**
- **Sample releases water slowly**

Titration at 50° C

- **Use Thermostatically Controlled Vessel**
- **Co-Solvent addition acceptable**

Change of titrator parameters not necessary



Addition of the Homogenizer

- **Used directly in the titration cell**
- **Volumetric system only**
- **Increases surface area and water extraction of the sample**
- **Ideal for solid samples and viscous liquids**
  - **Pharmaceutical tablets**
  - **Foodstuffs**
  - **Paints and Oils**

Influence of the base

Both K-F reactions:

(rxn. 1) $CH_3OH + SO_2 + RN \leftrightarrow [RNH]SO_3CH_3$

(rxn. 2) $[RNH]SO_3CH_3 + I_2 + H_2O + 2RN \leftrightarrow [RNH]SO_4CH_3 + 2[RNH]I$

pyridine

imidazole

depend on a base (RN).

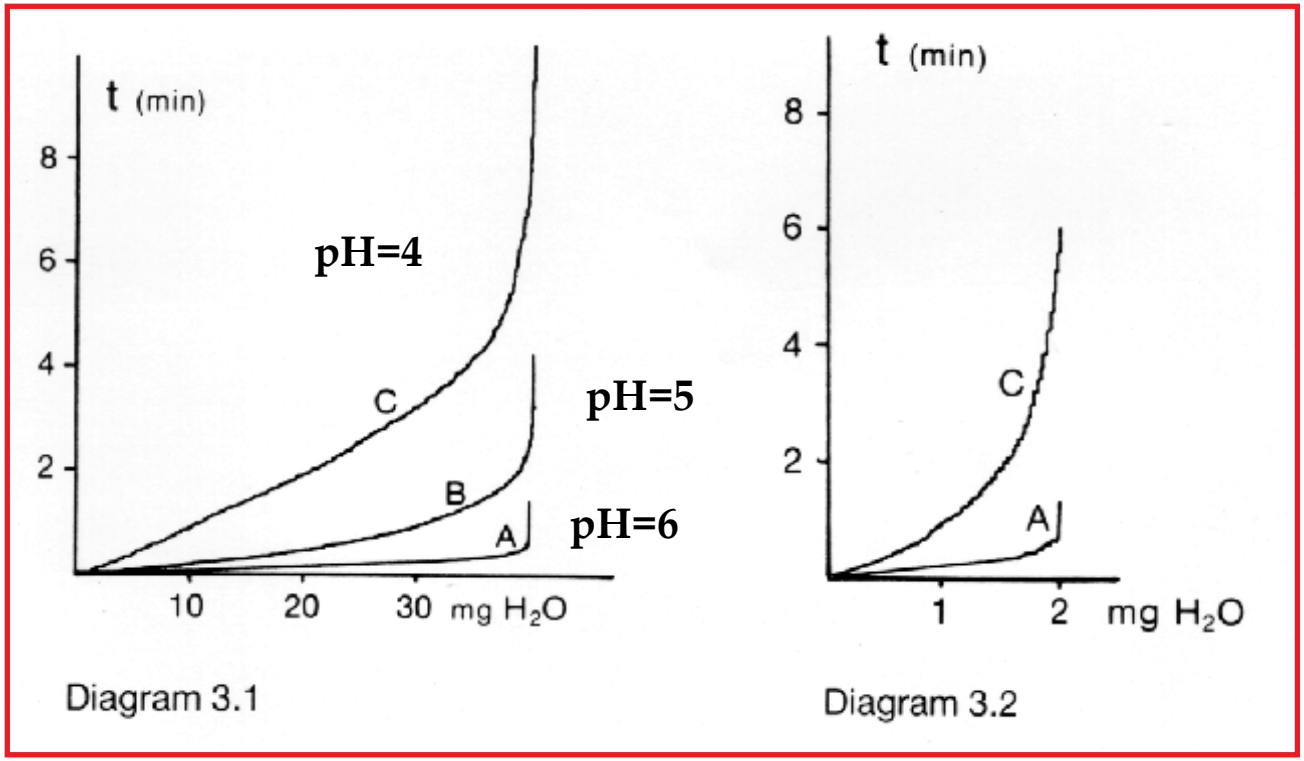
Pyridine was the original K-F base.

- pyridine, because of its weak basicity, cannot totally neutralize the methylsulfurous acid.
- The equilibrium in rxn. 1 is not completely shifted to the right. The reaction with pyridine is therefore slow and the endpoint is not stable, often making the repeatability using pyridine very poor.

Imidazole was chosen to replace pyridine.

- Imidazole shifts the rxn. 1 completely to the right, reaction is swift and endpoints clear and stable.
- Imidazole also does not have the unpleasant odor and toxicity of pyridine.
- imidazole is the patented foundation of the HYDRANAL® line

Pyridine vs. HYDRANAL® Titration Speed



Key: A=Titrant/Solvent, B=Composite/Methanol, C=Pyridine/Methanol

Control of pH
Neutralization of Acids

Low pH decreases the KF reaction rate

Neutralize acids using:

HYDRANAL®- Buffer Acid - Volumetric system only

Imidazole Coulometric system

Recommended amount of Imidazole

Volumetry: 7g of Imidazole per 30 ml solvent

Coulometry: 20g of Imidazole per 100ml anolyte

HYDRANAL®- Buffer Acid not compatible with Methanol reactive compounds.

Control of pH
Neutralization of Acids

Acids can shift working pH of the Karl Fischer system

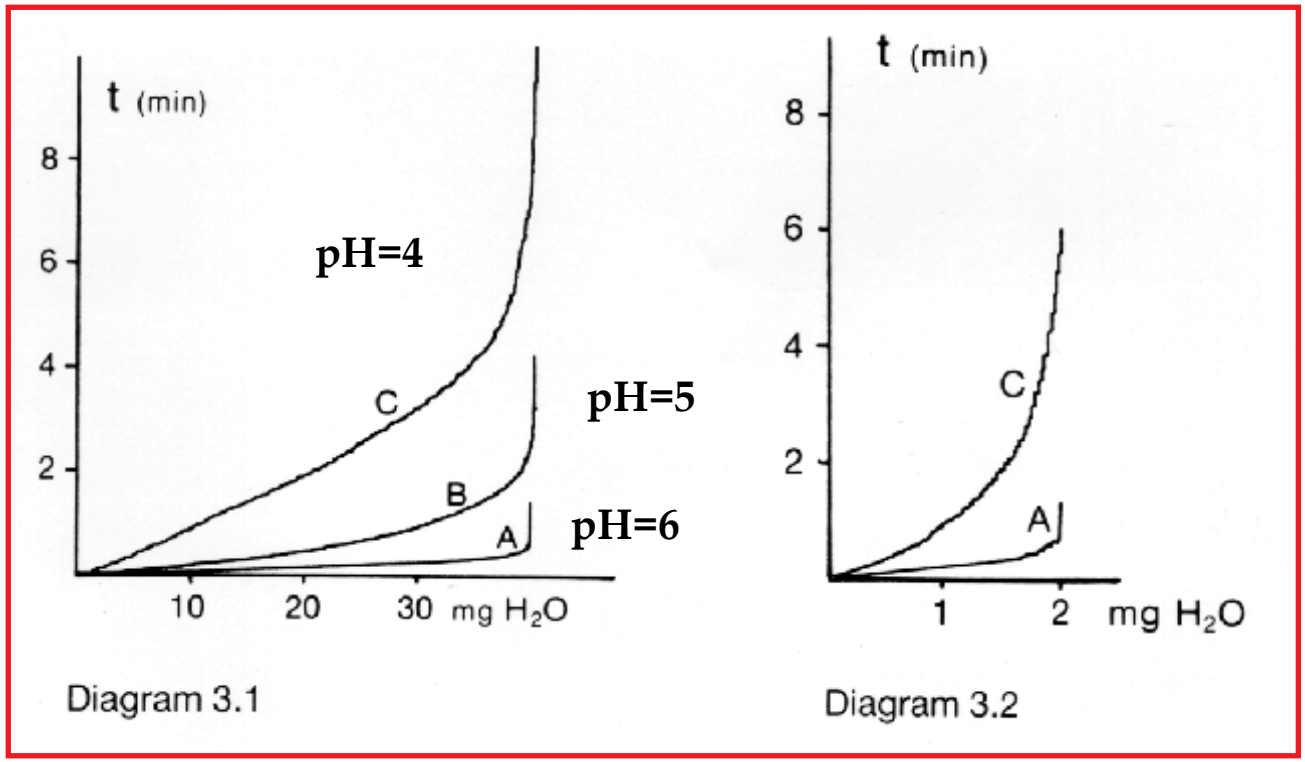
Aqueous Acids-neutralize in titration vessel with HYDRANAL® - Imidazole or HYDRANAL®- Buffer Acid

Concentrated Acids-neutralize in methanol free medium before titration.

HYDRANAL® - Buffer Acid should not be used in this case, because it contains Methanol.

Strong Carboxylic Acids-must be neutralized

Effect of pH on Equivalent Potential

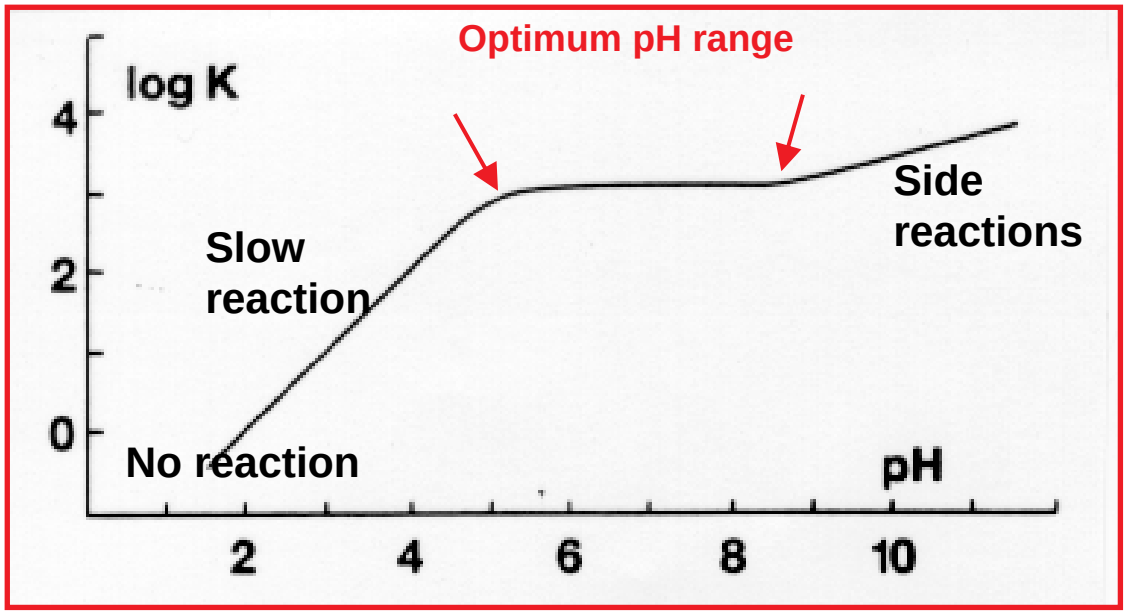


Key: A=Titrant/Solvent, B=Composite/Methanol, C=Pyridine/Methanol

pH influence on Karl Fischer

A pH between 5 and 7.5 is the optimum range for a Karl Fischer titration. Below a pH of 2, the reaction will not run. From pH 2 – 5, reaction is slow. Above a pH of 8, the iodine is consumed by side reactions causing false high results

Our K-F reagents are designed to give optimum pH control



pH dependence of the Karl Fischer reaction

Control of pH
Neutralization of Bases

High pH will slowly consume iodine

Neutralize bases using:

- **HYDRANAL®-Buffer Base**
- **Benzoic Acid**
- **Salicylic Acid**

Recommended amount of Benzoic or Salicylic

- **Volumetry: 7g of Acid per 30 ml solvent**
- **Coulometry: 20g of Acid per 100ml anolyte**

Control of pH
Neutralization of Bases

Bases can shift working pH of KF system

Weak basic amines (heterocycles)- no system modifications required

Strong basic amines (aliphatic amines)-require
HYDRANAL®- Benzoic Acid or
HYDRANAL®- Buffer Base

Irregular amines-require
HYDRANAL®- Benzoic acid and methanol-free solvent system

Side Reactions

Side Reactions Classified as…

Reactions Influenced by Methanol

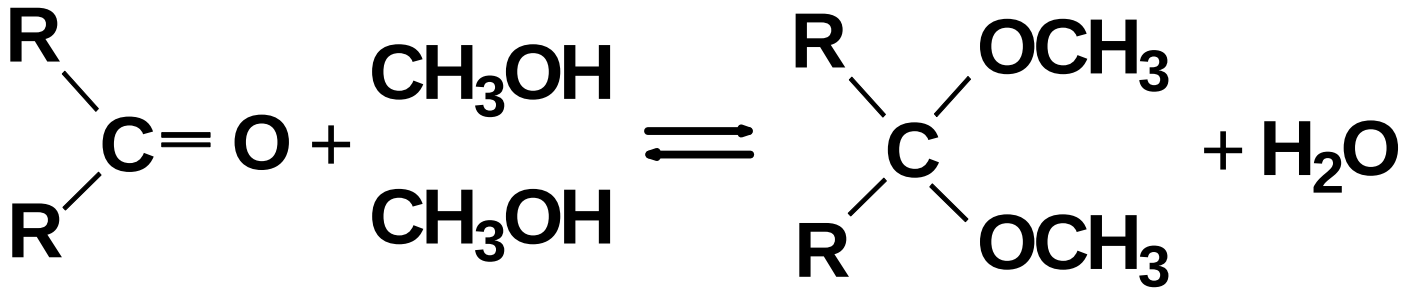
- Aldehydes react to form acetals, also undergo Bisulfite addition
- Ketones react to form ketals
- Amines undergo methylation
- Siloxanes undergo esterification

Reactions with Iodine

- Halogenated Hydrocarbons containing free halogens
- Mercaptans (Thiols)
- Phenols
- Peroxides

Methanol Side Reactions

Aldehyes and Ketones React with Methanol forming acetal



Water is the by-product

Methanol Free Reagents

Volumetric Reagents

- ***HYDRANAL®- Composite 5K***
  Titrating reagent for water determination of Aldehydes and Ketones
- ***HYDRANAL®- Working Medium K***
  Working medium for water determination of Aldehydes and Ketones. Contains Chloroform and Chloroethanol.
- ***HYDRANAL®- Medium K***
  Working medium for water determination of Aldehydes and Ketones. Contains Chloroform and 2,2,2-Trifluroethanol.
- ***HYDRANAL®- KetoSolver***
  Working medium for water determination of Aldehydes and Ketones. Free of halogenated hydrocarbons.

Coulometric Reagents

- **HYDRANAL®- Coulomat AK**
  Anolyte for the water determination of Ketones.
- **HYDRANAL®- Coulomat CG-K**
  Catholyte for the water determination of Ketones

Iodine Side Reactions

Testing for Iodine Reactivity

- **Dissolve a few Iodine Crystals in Methanol and Introduce Sample**
- **Watch for Solution to Change Color, if Clear Iodine Reaction is Present**

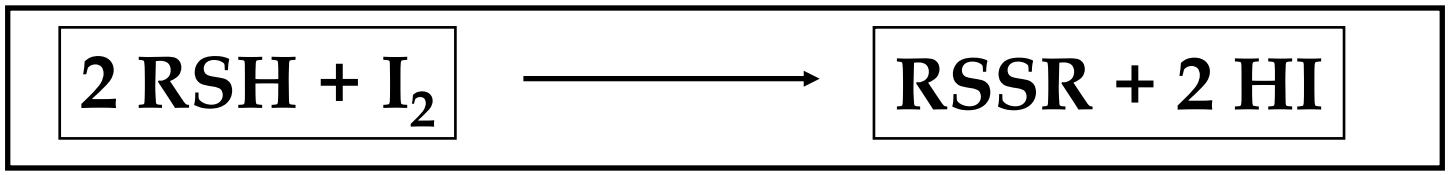
Reactions with Iodine

- **Halogenated Hydrocarbons containing free halogens require reducing the free halogen**
  - Reducing agent contains 10 g Imidazole + 5g SO_2 in 100 ml MeOH
  - Requires a blank of the reducing agent
  - HYDRANAL® Solvent can be used as Reducing Agent

Iodine Side Reactions

Reactions with Iodine

Mercaptans (Thiols) are oxidized by iodine

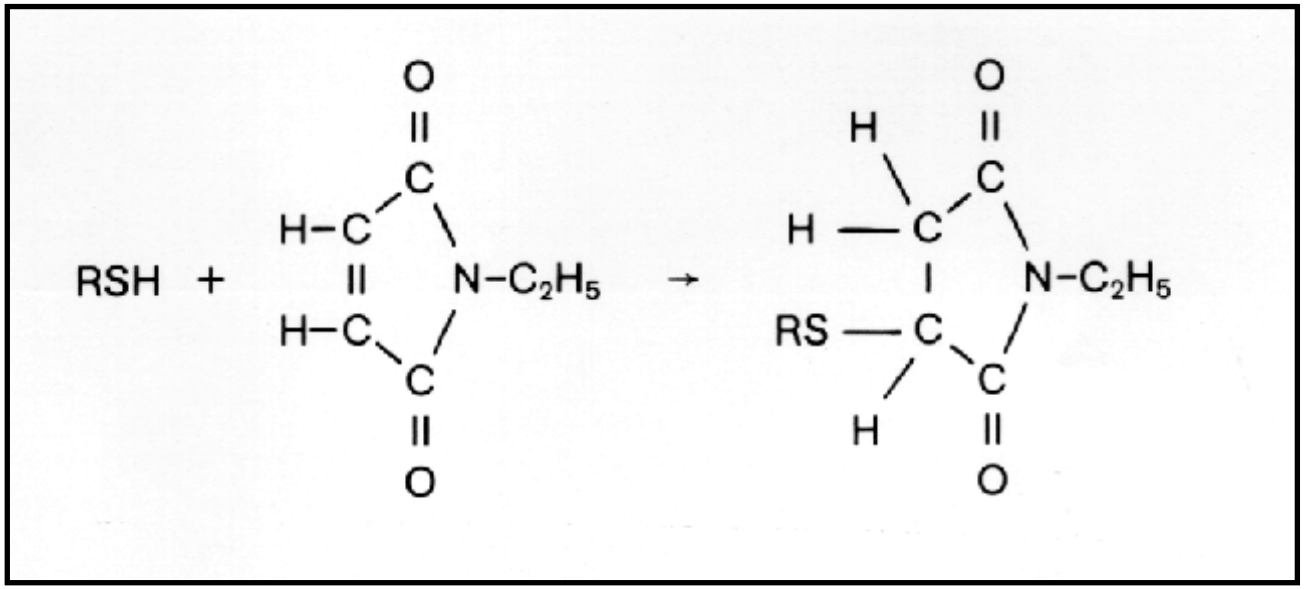


Suppress the side reaction by treating sample with N-ethylmaleimide in a buffered solvent system using HYDRANAL®- Buffer Acid

Iodine Side Reactions

Reactions with Iodine

Inhibition of Thiol Oxidation by Iodine



Volumetric Thiol Reduction

Composite 5 + (5:1) MeOH/ Buffer with 1 g N-ethylmaleimide

Sample introduced to solvent allowing 5 min pre-stir time

Iodine Side Reactions

Reactions with Iodine

- **Most Phenols do not react with KF reagents, higher molecular weight phenols and amino-phenols are most problematic**
- **Volumetric method is most suitable since the Oxidation potential is high in coulometry**
- **Acidify Solvent system to reduce interference**

Quality Control

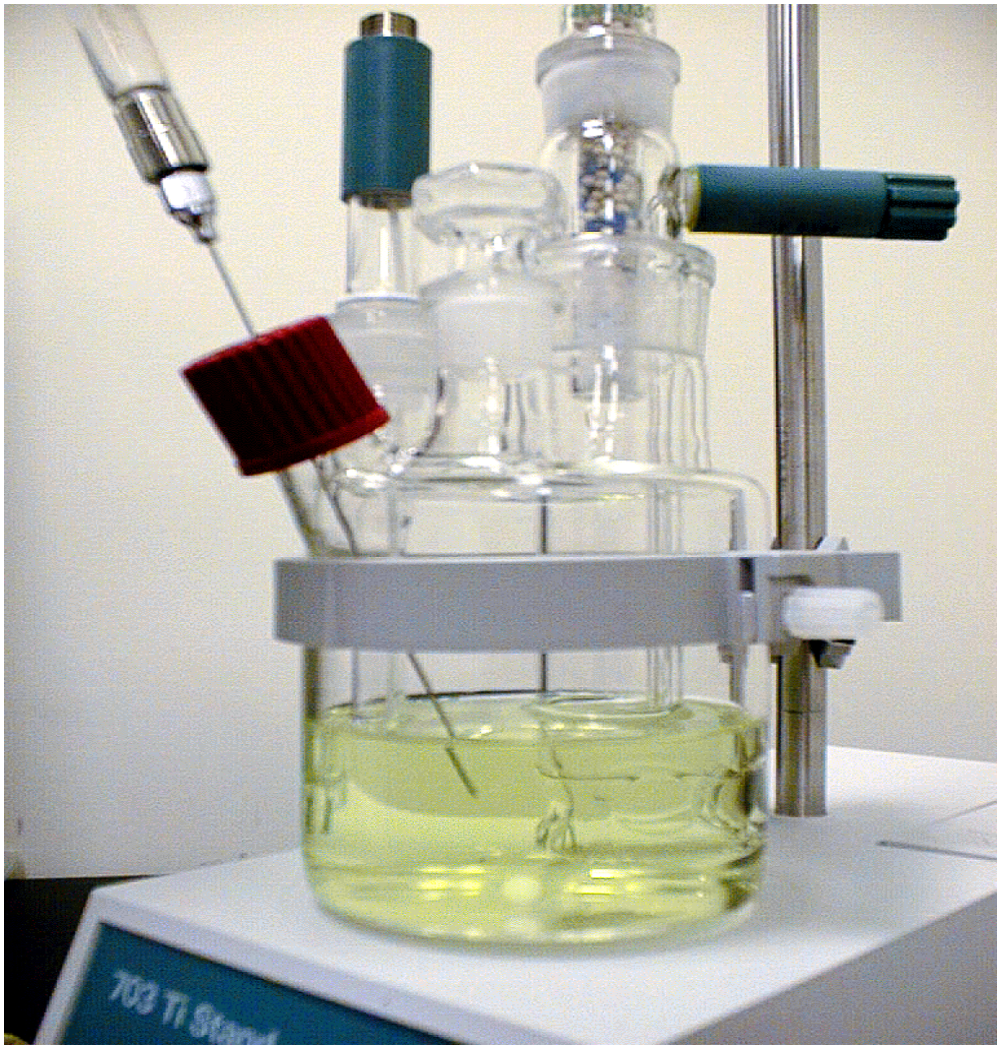
Water

- **First standard that comes to mind**
- **May be appropriate for certain applications**
- **Sample Size determines suitability**

Quality Control

Standard/Sample Introduction

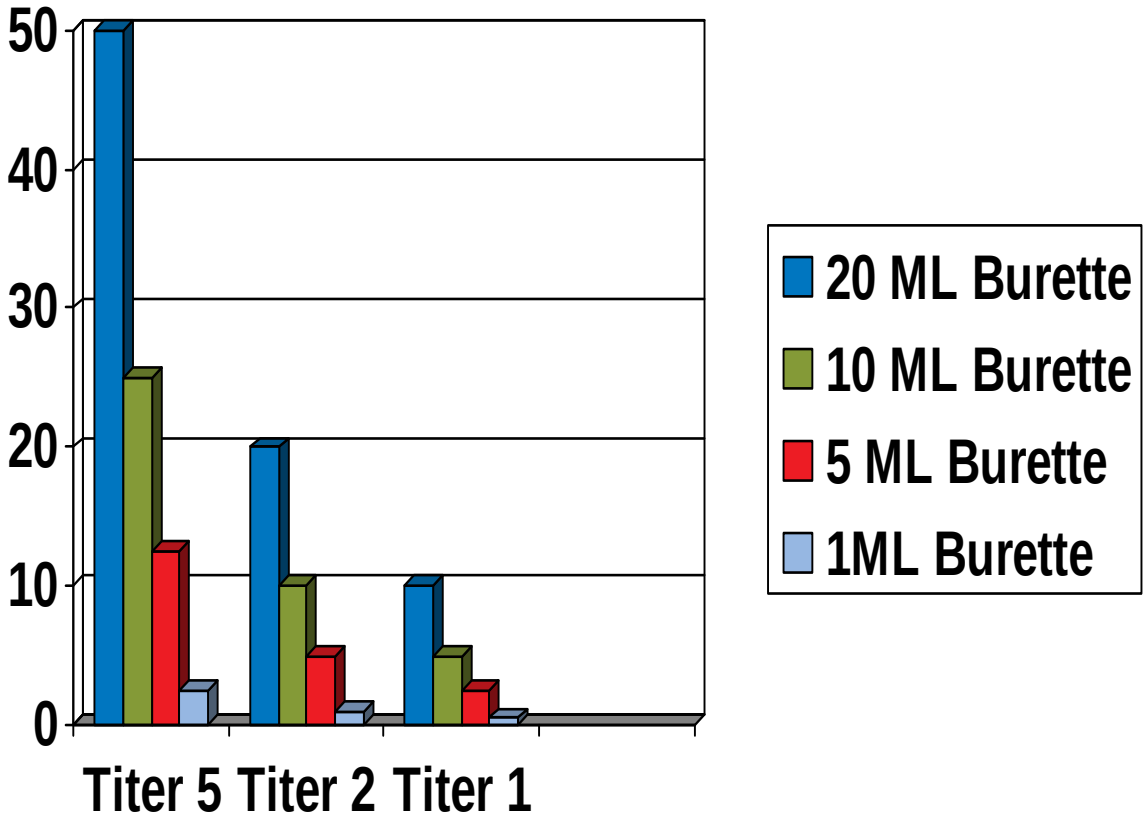
Inject below the surface of the solution



Quality Control

Water

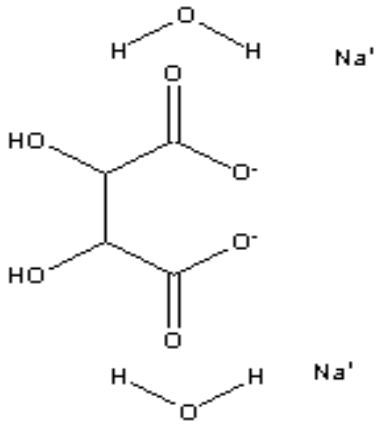
Sample Size in Milligrams of Water



Quality Control

Sodium Tartrate dihydrate

- **Solid Standard for Volumetric system**
- **Stable Water Content 15.66% ± 0.05%**
- **Solubility in Methanol limited**
- **Also available as NIST Traceable Product Number 34696**



Quality Control

HYDRANAL® - Standard 5.00

- Liquid standard for volumetric system
- Contains 5.00 ± 0.02mg/ml at 20°C
- Packaged in 100 ML and 500 ML Bottles

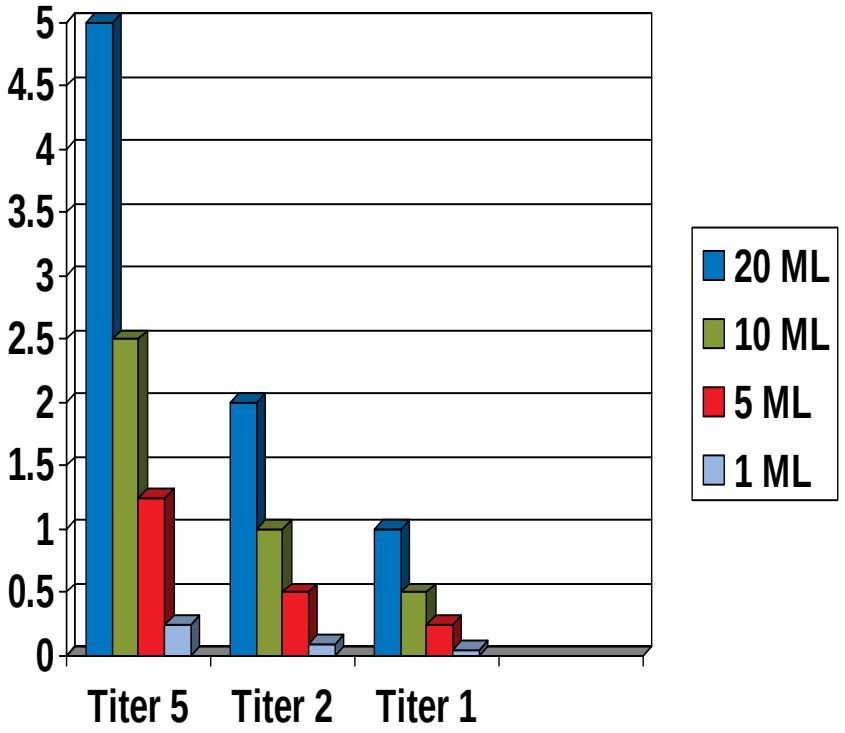
HYDRANAL® - Water Standard 10.0

- Liquid Standard Contains 10.0mg water per gram
- Packaged in 8 ml Glass Ampoules to insure integrity
- Standard is Traceable to NIST SRM 2890
- Certificate of Analysis in each package

Quality Control

Water Standard 10.0

Sample Size In Grams



Quality Control

	Test #1	Test #2	Test #3	Mean	Absolute Standard Deviation	Relative Standard Deviation
Water	**100.80%**	**98.84%**	**100.48%**	**99.81%**	**1.1%**	**1.1%**
Sodium Tartrate Dihydrate	**15.53%**	**15.38%**	**15.62%**	**15.51%**	**0.12%**	**0.8%**
Ampoule Standard with 0.1% water	**0.099%**	**0.100%**	**0.100%**	**0.0997%**	**0.0006%**	**0.6%**
Ampoule Standard with 1% water	**0.9999%**	**0.9992%**	**1.0010%**	**1.0000%**	**0.0009%**	**0.09%**

Quality Control

Handling Standards

- **Use dry glass gas-tight syringe (5ml or 10ml)**
- **Rinse syringe with standard**
- **Minimize exposure of standard to atmospheric m**
- **Weigh all samples using “weight by difference” T**

Quality Control

Instrument Maintenance

- **Clean Titration Vessel with Appropriate Solvent**
- **Replace Septum regularly**
- **Change desiccant regularly (New HYDRANAL® Molecular Sieve)**
- **Replace Volumetric unit's seals**
- **Coulometric units should use Teflon sleeves not grease**
- **When necessary perform Nitric Acid Cleaning**

Quality Control

Nitric Acid Cleaning

- **Rinse electrodes with methanol to remove reagents**
- **Use Concentrated Nitric Acid to soak electrodes**
- **Rinse with copious amount of water to remove acid**
- **Rinse with methanol**
- **Dry in low temperature (50° to 75° C) Oven**

HYDRANAL® Technical Center Your Source for Help with Karl Fischer

Technical Support 800-HYDRANAL(493-7262)

- **Application Assistance**
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- **Technical Literature on Karl Fischer**
- **Technical Training Seminars**
- **Web site www.sigmaaldrich.com**