

Degree Course Life Technologies

Option Analytical Chemistry

Diploma 2008

Julien Fardel

*Application of thermometric
titration methods*

Professor

Romolo Cicciarelli

Experts

Dr Rudolf Pock
Daniela Rentsch

Sion, 21 November 2008

HES-SO Valais

SI	TV	EE	IG	EST
X	X			

Données du travail de diplôme
Daten der Diplomarbeit

FO 1.2.02.07.DB
mam/30/06/2008

Confidentiel / Vertraulich

☐ oui / ja ☐ non / nein

<input type="checkbox"/> FSI <input checked="" type="checkbox"/> FTV	Année académique / Studienjahr 2007/2008	No PS / Nr. PS ca/2008/70
Mandant / Auftraggeber <input type="checkbox"/> HES—SO Valais <input checked="" type="checkbox"/> Industrie Lonza AG Visp <input type="checkbox"/> Ecole hôte	Etudiant / Student Julien Fardel	Lieu d'exécution / Ausführungsort <input type="checkbox"/> HES—SO Valais <input type="checkbox"/> Industrie <input type="checkbox"/> Ecole hôte
Professeur / Dozent Romolo Ciciarelli	Expert / Experte (données complètes) Rudolf Pock	

Titre / Titel

Anwendung von Thermometrischen Titrationen

Description et Objectifs / Beschreibung und Ziele

Die thermometrische Titration ist Dank technologischer Fortschritte wieder aktuell geworden.

Die Fa. Metrohm hat ein neues Titrationsgerät auf der Markt gebracht. Die Einsatzmöglichkeiten dieses Gerätes in einem Kontrolllabor sollen evaluiert werden indem die Vor- und Nachteile gegenüber der verwendeten Methode vermittelt werden.

Diese Untersuchungen sollen, wie auf der Seite 15 der Semesterarbeit vorgeschlagen wurde, folgendes umfassen:

Vergleich der folgenden Titrationen

- Säure-Base Titration: Selektivität der Titration von 5-Ethyl-2-methylpyridin und Nicotinsäure
- Bestimmung von Aldehyden
- Bestimmung von Grignard-Reagenzien
- Bestimmung von Wasser: Vergleich mit Karl Fischer Titration.

Signature ou visa / Unterschrift oder Visum

Resp. de filière
Studiengangsleiter:

Etudiant/Student:



Délais / Termine

Attribution du thème / Ausgabe des Auftrags:
01.09.2008

Remise du rapport / Abgabe des Schlussberichts:
21.11.2008 — 12.00

Exposition publique / Ausstellung Diplomarbeiten:
28.11.2008

Défense orale / Mündliche Verfechtung:
semaine/Woche 49

Rapport reçu le / Schlussbericht erhalten am Visa du secrétariat / Visum des Sekretariats

Application de méthode de titrage thermométrique Anwendung von Thermometrischen Titrationen

Objectif

Le titrage thermométrique est une méthode datant des années 70 qui est redevenue actuelle grâce, entre autre à l'appareil de la fabrique Metrohm. L'entreprise Lonza A.G. Viège s'intéresse à cet appareil afin de l'inclure dans leurs outils analytiques pour résoudre certains problèmes d'autre appareil de titrage disponible. C'est pourquoi ce travail de diplôme a été réalisé, afin de connaître cet appareil, ses forces et ses faiblesses.

Résultats

Les essais suivants ont été testés lors de ce travail de diplôme et les résultats suivants ont été obtenus :

- ° Titrage thermométrique acide – base contre titrage potentiométrique dynamique acide – base
Les deux méthodes ont une précision identique et une utilisation simple.
- ° Détermination des aldéhydes, cétone et alcool par titrage thermométrique
Aucune méthode n'a pu être trouvée pour les aldéhydes et cétones sans préparation spéciale d'échantillon. Mais par contre une méthode a été trouvée pour les alcools secondaires.
- ° Détermination de l'eau par titrage Karl Fischer versus thermométrique.
Les faiblesses du titrage thermométrique font qu'il est recommandé uniquement pour les cas où un titrage Karl Fischer n'est pas réalisable.
- ° Détermination des réactifs de Grignard.
Une méthode thermométrique a pu être établie pour la détermination du nombre de mol de Grignard dans une solution concentrée ~3M sans préparation d'échantillon.
- ° Permanganométrie potentiométrique contre Permanganométrie thermométrique.
Le standard utilisé en potentiométrie à savoir l'oxalate de sodium n'est pas un standard conseillé en thermométrique. D'autre standard ont été cherchés.

Mots-clés

Analytique, thermotitration, titrage, thermométrique, acide-base, Karl Fischer, alcool secondaire, aldéhyde, cétone, Grignard, permanganométrie, KMnO_4 , NBS, potentiométrique, Titrotherm 859, enthalpie

Ziel

Die Thermometrische Titration ist eine Methode von 30 Jahren, die wieder aktuell geworden ist durch das Metrohms Gerät. Die Firma Lonza AG Visp interessiert sich über dieses neue Gerät, und für eine neue analytische Instrumente zu kaufen. Dieser Apparat ist für einige Probleme zu lösen, für die sie keine andere Lösung haben. Deshalb wurde die Diplomarbeit gemacht um die Stärke und die Schwäche des Gerätes kennen zu lernen.

Resultate

Teste während die Diplomarbeiten gemacht und gaben folgende Resultate :

- ° Thermometrische Titration Sauer – Basen gegen Potentiometrische Titration Sauer – Basen
Die zwei Methoden haben ganz gleiche Genauigkeit und sind einfach.
- ° Bestimmung von Aldehyden, Ketone und Alkohol mit Thermotitration.
Keine Methoden wurde für Aldehyden und Ketone gefunden ohne Vorbereitung der Probe. Aber eine Methode wurde gefunden für Sekundäre Alkohol.
- ° Bestimmung von Wasser mit Karl Fischer oder mit Thermotitration
Die Schwächen der Thermometrischen Titration sind gross, aber sie können gebraucht werden wenn eine Karl Fischer Titration nicht möglich ist
- ° Bestimmung von Grignard Reagenzien
Eine Thermometrische Methode konnte festgestellt werden, für die Bestimmung der Anzahl mol Grignard in einer konzentrierten Lösung ~ 3M ohne Vorbereitung der Probe.
- ° Potentiometrische Manganometrie gegen Thermometrische Manganometrie.
Der wie verwendete Standard in der potentiometrischen Natrium-Oxalate wird nicht als thermometrischer Standard empfohlen. Andere Standards wurden versucht..

Schlüsselwörter

Analytische, Thermotitration, Titration, Thermometrische, Sauer – Basen, Karl Fischer, Sekundäre Alkohol, Aldehyden, Ketone, Grignard, Manganometrie, KMnO_4 , NBS, Potentiometrische, Titrotherm 859, Enthalpie

Application of thermometric titration methods

Goal :

The thermometric titration is a method that exist by 70s but which was updated with a new product from Metrohm factory. The company Lonza AG Visp is interested in this device to include it in their analytical tools to solve some problems of other titration devices available. That is why this work diploma was designed to know this product and these strengths and weaknesses.

Results :

The tests made during the diploma work and the results obtained follow.

° Thermometric acid - base titration compared to potentiometric dynamic acid - base titration.

Both methods have the same precision and are both easy to use .

° Determination of aldehydes, ketones and alcohol by thermometric titration.

None could be found for aldehydes and ketones, but a method has been found for secondary alcohol.

° Determination of water by Karl Fischer titration versus thermometric titration.

The weaknesses of thermometric titration makes it only recommended for cases where a Karl Fischer titration is not feasible.

° Determination of Grignard reagents.

A thermometric method is established for determining the number of moles in a Grignard ~ 3M solution without sample preparation.

° Potentiometric permanganometrie compared to Thermometric permanganometrie.

The standard used in potentiometric, named sodium oxalate, is not a standard recommended by thermometric titration. Also other standard were searched.

Keywords :

Analytical, Thermotitration, Titration, thermometric, acid – base, Karl Fischer, secondary alcohol, aldehyde, ketone, Grignard, Permanganometrie, KMnO_4 , NBS, Potentiometric, Titrotherm 859, Enthalpy

Contents

1	Theoretical part.....	6
1.1	Potentiometric Titration	6
1.1.1	Acid base titration	6
1.1.2	Titration Redox.....	8
1.2	Titration of water (Karl Fischer)	8
1.3	Thermochemistry	9
1.4	Themometric Titration	12
1.4.1	Different uses of thermometric titration	13
2	Materials and methods.....	15
2.1	Materials	15
2.2	Reagents	16
2.3	Methods	19
2.3.1	Acid base titration	19
2.3.2	Titration of Aldehyde, Ketone and Alcohol	21
2.3.3	Titration of Water	23
2.3.4	Titration of Grignard	24
2.3.5	Titration with KMnO_4	25
3	Practical Part.....	26
3.1	Critical points of thermometric titration	26
3.2	Acid base titration	29
3.2.1	Determination of titer NaOH 1M	29
3.2.2	Typical crytical solution for acid base titration.	30
3.3	Titration of Aldehyde, Ketone and Alcohol	35
3.3.1	Aldehyde and Ketone	35
3.3.2	Alcohol	36
3.4	Titration of Water.....	39
3.4.1	Determination of water equivalent of titrant	40
3.4.1	Water content of conc. Sulfuric acid.....	41
3.4.1	Water content of Ascorbic acid.....	42
3.5	Titration of Grignard	44
3.6	Titration with KMnO_4	47
3.6.1	Determination of the titer of KMnO_4	47
3.6.2	Titration of Fe^{2+}	49
3.6.3	Titration of KI	49
3.6.4	Titration of Ascorbic acid	50
4	Conclusions.....	53
5	Bibliography	54
6	Annexes.....	55

1 Theoretical part

What is acid base?

Several definitions are used for acid and base following the field of use. The definition will be taken from Brönsted and Lowry (1923) is as follows [3,4]: We call acid a kind likely to yield a proton (H^+) and base a kind capable of capturing a proton. Hence the concept of couple acid base.

Why the titration?

This allows for quick results, a detection limit in ppm with any analyses (Cl), an easy automation, excellent reproducibility ($\approx 0.2\%$) and a low-cost analysis.

1.1 Potentiometric Titration

The titration is a basis quantitative analytical method. It allows a simple analysis to determine the amount of product in the sample following a chemical reaction without need do a comparison with a standard. The potentiometric titration following the potential of a solution also it is a differential method between a reference and a measurement electrodes. This potential can be interpret as a pH or a potential redox par example.

1.1.1 Acid base titration

This titration is a very common way of determining easily the presence and quantity of a base or an acid in a solution. There are two main types of acid base titration, the first in water, and the second in non-aqueous environment.

The method in non-aqueous environment allows greater flexibility of analyses because the detestability of weaker acids in water is rendered difficult or impossible by the self proteolyses of water. The equation used to determine the amount of acid or base is none other than the equation of Henderson-Hassel Balch.

$$pH = pK_a + \text{Log} \left(\frac{[A^-]^* \gamma_{A^-}}{[HA]^* \gamma_{HA}} \right) \quad \text{Eq. 1}$$

γ = Activity factor of the species desired

In the equation of Henderson-Hassel Balch activity is taken into account, not just the concentration of species, we must then get this activity. So here is the formula extracted from [2] to calculate this factor.

$$\gamma = e^{\left(\frac{-0.51 * Z^2 * \sqrt{\mu}}{1 + \frac{\alpha * \sqrt{\mu}}{305}} \right)}$$
Eq. 2

$$\mu = \text{Ionic strength} = \frac{1}{2} \sum_i (C_i * Z_i^2) \text{ [mol/l]}$$

$$Z = \text{Charge of the compound}$$

$$\alpha = \text{Ionic radius of the ion hydrated [\AA]}$$

The acid base titration uses electrodes based on the potential of the solution.

For a pH sensor, for example, the potential of the latter follows the law in equation 3 at 25° C [1].

$$E = CTe + \beta(0.05916) \log \frac{a_{H^+} (ext.)}{a_{H^+} (int.)}$$
Eq. 3

$$\beta = \text{Effectiveness of electromotive value between 0.98 - 1.00}$$

$$a_{H^+} = \text{Ion activity } H^+_{(ext.)} = \text{externe }_{(int.)} = \text{interne}$$

The major problem of pH electrodes according to [1] is the crystallization or deposit residue on the junction : external electrode - solution to measure. The problem is that in doubtful cases two electrodes should be used instead of one to verify the results. It is important to look at the pH range over which the electrode is usable, because not all the electrodes have the same application ranges. The error of pH electrode measurement is very pronounced in the very low and high pH [1]. For an ionone densities measurement we always use a reference electrode. The selectivity is influenced by Na⁺ ion because this ion makes an interference with H⁺ ion

The acid base titration has some limitations, first a base with a pKa greater than 9 is very difficult to titrate except through a non-aqueous environment. Secondly a difference of less than 3 or 4 pKa makes indistinguishable the two potential jumps and a minimum of 10⁻⁴ mol/liter is needed for many of analyses [1,2]. Here are some of the biggest and main problems of acid basic titration in potentiometry.

1.1.2 Redox Titration

The redox titration is a titration that allows the following of a solution's potential (also called oxidation-reduction titration), it is a type of titration based on a redox reaction between the analyte and titrant. Redox titration may involve the use of a redox indicator and/or a potentiometer.

Oxidation describes the loss of electrons by a molecule, atom or ion.

Reduction describes the gain of electrons by a molecule, atom or ion.

Oxidation and reduction properly refer to a change in oxidation number.

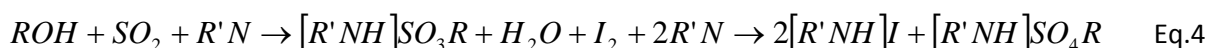
For example: $2\text{Fe}^{2+} + \text{H}_2\text{O}_2 + 2\text{H}^+ \rightarrow 2\text{Fe}^{3+} + 2\text{H}_2\text{O}$

The reduction is done by Fe and the oxidation by O.

The redox can have indicator too the acid base titration, an indicator that undergoes a definite color change at a specific electrode potential.

1.2 Titration of water (Karl Fischer)

This titration method has been developed by a German chemist in 1935. Karl Fischer titration is a widely used analytical method for quantifying water content in a variety of products. The fundamental principle behind it is based on the Bunsen Reaction between iodine and sulfur dioxide in an aqueous medium. Karl Fischer discovered that this reaction could be modified to be used for the determination of water in a non-aqueous system containing an excess of sulfur dioxide. To carry out this titration he used a primary alcohol (typical alcohol used is Methanol or diethylene glycol monomethyl ether (DEGEE)) and a base (pyridine or imidazole) as the buffering agent. [11]



Water and iodine are consumed in a 1:1 ratio in the reaction 4. [11-14]

There are two types of Karl Fischer Titration : the first is volumetric and the second coulometric.

The result of a titration of water is oft given in WE = water equivalent; it means : weight of water in [mg] / how much reagent used in [ml]. [14] It exists a product often used to determine the titer of a blank is the Sodium tartrate-2-hydrate, because he is a not so hygroscopic product with a standard hydration. [14]

1) Volumetric

In Karl Fischer volumetric, iodine solution is added mechanically to a solvent containing the sample by the titrator's burette during the titration. Water is quantified on the basis of volume of Karl Fischer reagent consumed.

Also 1 mole of iodine is consumed for each mol of H_2O and the rest of iodine is titred after the reaction.

Volumetric is best suited for the determination of water content in a range of 100 ppm to 100%. [11]

2) Coulometric

In Karl Fischer coulometric, iodine is generated electrochemically in situ during the titration. Water is quantified on the basis of the total charge passed (Q), which is measured by current (amperes) and time (seconds), according to the following relationship $1 \text{ mg } H_2O = 10.72 \text{ C}$

Also 2 moles of electrons are consumed per mole of water and at the equivalence point, an excess of I_2 appears and an abrupt voltage drop marks the endpoint.

Coulometric is best suited for the determination of water content in a range of 1 ppm to 5%. [11]

This titration has a pH limitation because when it is lower than 5 the titration speed is very slow. And on the other hand, when pH is higher than 8, titration rate is fast, but only due to an interfering esterification side reaction which produces water, resulting in a vanishing endpoint.

Beware of the possible reaction between alcohol and the compound that may react like water with iodine (aldehyde ketone, ether). Aldehydes and ketones must be modified before titration by the addition of HCN or with another sort of reaction. A very acidic or basic compound may change the pH and stop or reduce the Karl Fischer titration. [14]

1.3 Thermochemistry

Thermochemistry is built on the first law of thermodynamics, adapted more generally by the law of J.R. Mayer and J.P. Joule :

« The energy of an isolated system remains constant. ».

The thermochemistry is, among other things, the study of the difference in heat released by a chemical reaction. This difference, at constant pressure, is called enthalpy and is written ΔH and is defined in [kJ/ mol], it represents an exothermic reaction if it is negative and an endothermic reaction if this difference is positive. The state function is as follows :

$$\Delta H = \Delta U + P\Delta V \quad \text{Eq. 5}$$

ΔU = Internal energy difference (work + heat)

P = Pressure

ΔV = Volume difference

The law of Hess allows to deduct the standard enthalpy reaction ($\Delta_r H_{298}^0$) from the standard enthalpy formation ($\Delta_f H_{298}^0$) of the reactants. The usual convention: $\nu_i > 0$ for products and < 0 for reagents applies here.

$$\Delta_r H_{298}^0 = \sum_i \nu_i \Delta_f H_{298}^0(i) \quad \text{Eq. 6}$$

The equation 7, derived from the law of Kirchhoff, can calculate the standard enthalpy reaction of a compound at the desired temperature

$$\Delta_r H_T^0 = \Delta_r H_{298}^0 + \Delta C_p \cdot (T - 298) \quad \text{Eq. 7}$$

$\Delta_r H_{298}^0$ = Enthalpy reaction at standard condition (25°C and 1 atm)

ΔC_p = Difference in calorific capacity at constant pressure

T = Temperature in Kelvin

The equations 6 and 7 may also be applied to standard entropies reaction ($\Delta_r S_{298}^0$), which is a measure of the disorder caused by the reaction.

All these concepts can put in place the main that combines them all, the free energy of Gibbs or free enthalpy (ΔG). Which is defined as follows :

$$\Delta G = \Delta H - T\Delta S = \Delta U + P\Delta V - T\Delta S \quad \text{Eq.8}$$

The equation 8 lets say that if the reaction is going with T and P as constants, a $\Delta G < 0$ for this reaction means that it is spontaneous and conversely if $\Delta G > 0$ the reaction is impossible. A balanced response is obtained when the $\Delta G = 0$ which is what any system tends to achieve. At this point the chemical potential (μ) of all species is equal. For each reaction where the free energy is not opposed to entropy, enthalpy is significantly larger than the free energy.

$$\Delta G_T^0 = \sum \nu_i \mu_i^0 = 0 \quad \text{Eq.9}$$

The chemical potential is defined as follows

$$\mu_i = \mu_i^0 + RT \ln(a_i) \quad \text{Eq.10}$$

a_i = Activity of the compound i

R = Constant of ideal gas

T = Temperature in Kelvin

The equation 11 allows to get the equilibrium constant at a fixed temperature ($K(T)$) of a reaction, knowing the Gibbs free energy of the system.

$$\Delta G_T^0 = -RT \ln\{K(T)\} \quad \text{Eq.11}$$

The van t'Hoff equation which is derived from the equation 11 makes it possible to link the balance constant and the enthalpy of a system.

$$\frac{d \ln K}{dT} = \frac{\Delta_r H_T^0}{RT^2} \quad \text{Eq.12}$$

Assuming that $\Delta_r H_T^0$ is constant in the interval T considered, we have :

$$\ln K = \left(\frac{\Delta_r H_T^0}{R} \right) \left(-\frac{1}{T} \right) + \text{constante} \quad \text{Eq.13}$$

This allows linking K with 1/T by a straight line, whose slope is the standard reaction enthalpy on the constant of perfect gas.

Another part of the thermochemistry interesting for this work is the equation 14 that allows reporting the amount of energy supplied and the change in temperature reached.

$$Q = \frac{m}{M} * \Delta(C_p * T) \quad \text{Eq.14}$$

Q = Quantity of Joule [J/mol]

m = Masse [g]

M = Molar weight [g/mol]

T = Temperature in Kelvin

C_p = Calorific capacity at constant pressure

1.4 Themometric Titration

In a thermometric titration, the reaction produces molar heat reaction, which is presented as a measurable change. According to the equation 8, a detector based on the change in temperature show greater inflection than a detector based on the change of free energy only.

The thermometric titration demands, as the potentiometric titration, fast reactions to obtain titration endpoints reproducible. It is possible to add catalysts to bring a faster response.

The volumetric solution is added constantly and the end of the reaction is indicated by a change in temperature. The display of the results is shown by a temperature curve [$^{\circ}\text{C}$] / volume [ml]. The derivative of this curve can get, where a break is, a peak indicating the titration endpoint.

The system, in which the reaction takes place, should ideally be adiabatic. The external influences are serious pests, here are the most cited:

- Heat acquired and lost by the container.
- The difference in temperature between the titrant solution and the titred solution.
- Temperature change due do evaporation of the solution on the surface.
- Heat of the solubilization reagent in the volumetric solution of the titred solution.
- Heat of friction due to stirring due to mechanical actions (minor influence [7])
- Heat produced by the internal thermistor (really minor influence [7])

The system Metrohm 859 Titrotherme is capable of resolving temperature differences through the thermistor of 10^{-5} [K] with a response time of 0.3 [s] and a frequency of 50 [Hz] [7].

As seen in the equation 14, the molar heat capacity of solvent used influence the amount of energy needed in order to obtain a perceptible change in the temperature of the device. Since water is the primary solvent used here is the report possible to establish whether a reaction is theoretically observable or not with an 859 Titrotherme, which is having a temperature difference of at least 10^{-5} [K]. Although this Q_{\min} is only theoretical because the influences of the factors mentioned above increases the background noise in the system.

Working with dilute solutions, it is possible to apply the equation 14 with :

$$C_{P(\text{H}_2\text{O})} (\text{l}) \text{ de } 0\text{-}100^{\circ}\text{C} = 75.4 \text{ [J/mol]} [3]$$

$$M = 18 \text{ [g/mol]}$$

$$\Delta T = \text{Temperature resolution of the thermistance } 10^{-5} \text{ [K]}$$

$$Q_{\min} = 4.184 * 10^{-5} * m[\text{g}] \quad \text{Eq.15}$$

The Cp of the Methanol is smaller as the Cp of water and this value is: 2.368[J/g] at 0[°C] and 2.578[J/g] at 40 [°C]. So in methanol the change of temperature get quickly visible as in water.

1.4.1 Different uses of thermometric titration

The thermometric titration is very versatile because it does not require electric or electrochemist interaction with the probe. The Titration may take place in environments totally non-conductive, non-polar, in troubles solutions, micellar suspensions or mixtures as well as being used to follow a precipitation reaction.

Acid/base

The reaction of a strong acid and a strong base gives approximately -56 [kJ / mol] that can be calculated from a portion of enthalpies formations in order to obtain reaction enthalpy, see equation 6 [7].

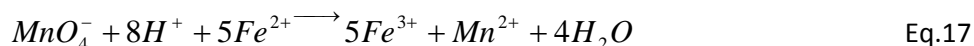


$$\Delta_f H_{298}^0 \quad 0 \quad -230.0 \quad -285.8 \quad \Delta_r H_{298}^0 = -55.8 \text{ [kJ/mol]}$$

The titration of weak base or weak acid works equally well, but their enthalpies are less important. The acid base titrations can be made in non-aqueous environment without problem. It is even possible to make the acid base titration in presence of a catalyst.

Redox

Redox reactions often have large reaction enthalpy making them reactions of choice for the thermometric titration. For example, the titration ion iron (II) by permanganate solution [7].



$$\Delta_f H_{298}^0 \quad -541.4 \quad 0 \quad 5x-89.1 \quad 5x-48.5 \quad -220.8 \quad 4x-285.8 \quad \Delta_r H_{298}^0 = 123.9 \text{ [kJ/mol]}$$

Other titrant used in redox titration as thiosulfat or hypochlorite can also be used in thermotitration.

Complexometric

The use of EDTA can be easily used for titration because it creates complexes, although the reaction

enthalpies are much lower than those of redox reactions. For example Ca^{2+} (-23.4 [kJ/mol]) and Mg^{2+} (+20.1 [kJ/mol]) can be titrated at the same time.

Precipitation

With precipitation, it is possible to titrate among other, sulfates, certain metals and cationic anionic and neutral surfactants. This method is used when the potentiometric titration does not produce satisfactory results.

Micellar

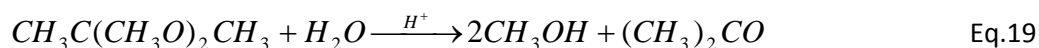
Is a very promising titration spoken by most of the publications listed in the bibliography. It uses a two-phase solution often mentioned in publications as being composed of water and octanol. This method allows the titration of compounds immiscible in water, with a solution that is still mostly water. To make a micellar titration, it is necessary to determine the coefficient partition also called logP. It is determined as follows: [18-21]

$$\log P_{\text{oct/wat}} = \text{Log} \left(\frac{[\text{solute}]_{\text{octanol}}}{[\text{solute}]_{\text{water}}} \right) \quad \text{Eq.18}$$

The logP is a concentration ratio of the non-ionized compound between the two solutions. There is also logD which is the distribution ratio and which is established on the same basis but take into account all forms, ionized and non-ionized.

Titration of water

Two main methods are used in thermometry. The first uses 2,2-dimethoxypropane (DMP) see equation 19 and the second triethyl orthoformate (TEOF) see equation 20 [7].



$$\Delta_f H_{298}^0 \quad -459.4 \quad -285.8 \quad 2 \times -239.2 \quad -239.2 \quad \Delta_r H_{298}^0 + 27.6 \text{ [kJ/mol]}$$



These methods allows working with stable non-hygroscopic products, which react with water only in presence of a catalyst H^+ and which do not require special storage. The method is applicable to a broad band of 0.02% to 67% of water [7]. On the contrary a high white limits precision, because there are possibilities of reactions with the water of the solvent or the installation.

2 Materials and methods

2.1 Materials

- Usual laboratory Material
- Metrohm, 859 Titrotherm technical data in[A1]
- Metrohm, 809 Titrando serial N° 15267
- Metrohm, 800 Dosino
- Metrohm 802 Stirrer
- Metrohm, titration vessel 6.1415.220
- Mettler, AE 240 analytical balance
- Mettler, AT 200 analytical balance
- Metrohm, 751 GPD Titrino
- Metrohm, 703 Ti Stand

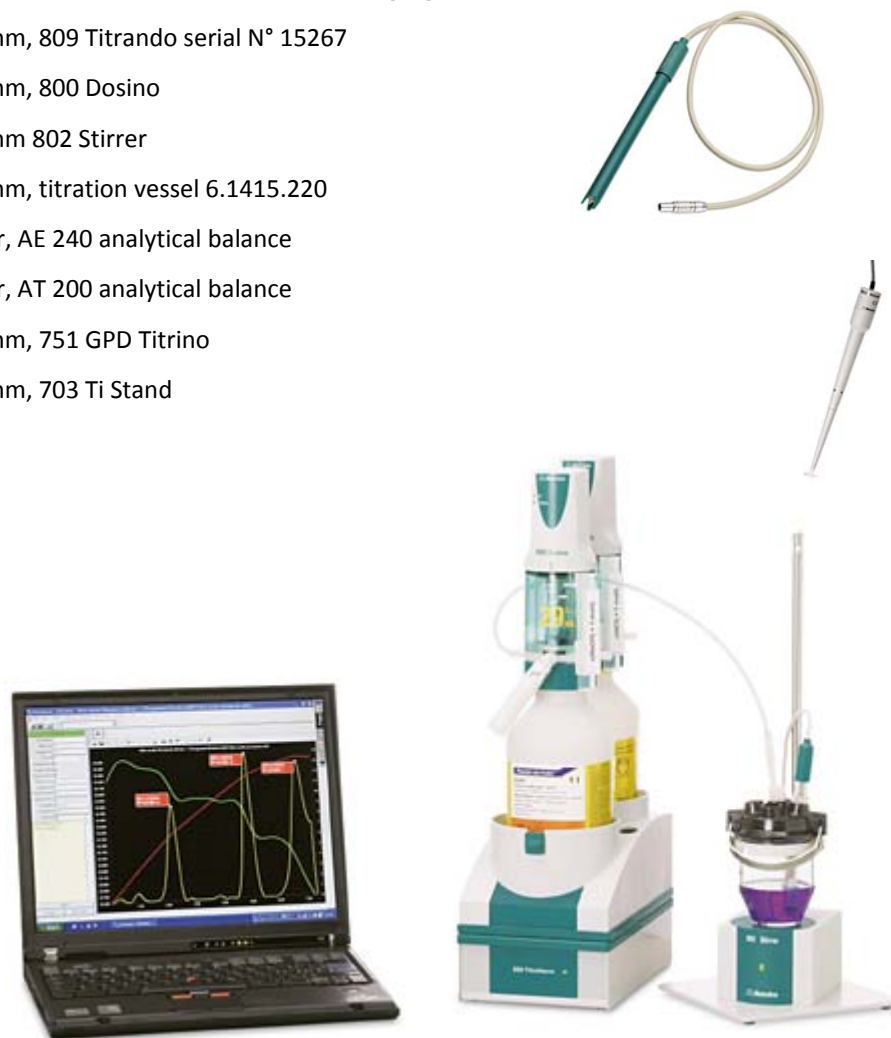













Figure 1 : Picture of the Titrotherm 859, of the temperature sensor for 859 Titrotherm and of the stirrer 802 [23]

2.2 Reagents

Table 1 : Toxicology reagents

Products / Purity	Supplier	Formulas	Molar Weight	Numbers R et S	Dangers
Phosphoric Acid 85% EP4	Schweizerhall Chemie AG Lot: 0000175090 UN 1805	H ₃ PO ₄	97.99	R : 34 S : 26, 45	
Sodium hydroxyde 1 [mol/l]	Scharlau chemie SA Ref: SO0441005P Batch: 94104	NaOH	40.00	R : 35, 36/38 S : 26, 37/39, 45	
5-Ethyl-2-Methyl pyridine	Labor Product A-1000 03.09.2008	C ₈ H ₁₁ N	121.18	R : 20/21/22, 34 S : 26, 36/37/39, 45	
Nitric Acid 65% extra pur	Scharlau chemie SA Ref: AC 1599 UN 2031	HNO ₃	63.01	R : 35 S : 23, 26, 36, 45	
Nicotinic Acid	Labor Product 03.09.2008	C ₆ H ₅ NO ₂	123.11	R : 36 S : 26, 39	
Potassium Hydrogen Phthalate 100%	Scharlau chemie SA Ref: SO0441005P UN 1924	C ₈ H ₅ KO ₄	204.22	R :- S : 24/25	-
Sodium Chloride p.a. purum > 99.5%	Fluka Lot: 449008/1 10204094	NaCl	58.44	R :- S :-	-
Ammonium Nitrate p.a. purum > 99%	Fluka Lot: 446337/1 31004036	NH ₄ NO ₃	80.04	R : 8 36/37/38 S : 17,26,37/39	 
2,4 Dinitrophenylhydrazine p.a. puriss >99.0%	Fluka Lot: 1331283 23807294	C ₆ H ₆ N ₄ O ₄	198.14	R : 1,11,22,40 S :16,36/37,45,48A	 
Ethyl acetate super puris solvant	Romil Batch: L533400 UN 1173	C ₄ H ₈ O ₂	88.11	R : 11,36,66,67 S : 16,26,33	 
Acetic acid p.a. puris pH Eur	Fluka Lot: 71990 UN 2789	C ₂ H ₄ O ₂	60.05	R : 10,35 S : 23,26,45	
Methanol p.a. puris	Fluka Lot: 1369395 50908337	CH ₄ O	32.04	R : 11,23/24/25,39/23/24/25 S : 7,16,36/37,45	 
Natrium borhydrid	ex Rohm&Hass ex Pilothalle Batch: 14385	NaBH ₄	37.83	R : 15,23/24/25,34 S : 22,26,36/37/39,43A,45	 
N-Bromosuccinimide purum > 95%	Fluka Lot: 454591/1 31004254	C ₄ H ₄ BrNO ₂	177.99	R : 22,34 S : 22,26,36/37/39,45t	
Potassium Iodide p.a.	Merck Lot: B938143 640	KI	166.00	R :- S : 24/25	-
Potassium Iodate w±2u = 99.9%±0.12%	Fluka Lot: 1137457 13804001	KIO ₃	214.00	R : 8,22 S : 17	
Sodium thiosulfate 0.1 [mol/l]	Scharlau chemie SA Ref: SO0731005P Batch: 85306	Na ₂ S ₂ O ₃	158.10	R : - S : 24/25	-

L-Carnitine <i>Cristaline</i>	Labor Product Batch: 4405 LIAS : 613333	$C_7H_{15}NO_3$	161.20	R : 36/37/38 S : 26,37/39	
Hydrochloric acid 32% p.a.	Merck Lot: z116819 820	HCl	36.46	R : 34,37 S : 26,45	
Ascorbic acid <i>Ph Eur</i>	Fluka Lot: 449163/1 31103256	$C_6H_8O_6$	176.13	R : - S : 24/25	-
Ascorbic acid <i>Ph Eur</i>	Fluka Lot: 1388851 11508P07	$C_6H_8O_6$	176.13	R : - S : 24/25	-
Hypophosphorous acid	Ex. Febex Batch: 08-23 CN Nr : 2930	H_3PO_2	66.00	R : 34 S : 26,36/37/39,45	
Tylosin derivate modified	Labor Product -	-	734.02	- -	-
Triethyl ortoformate 99%	Riedel-de Haën Lot: 71720	$C_7H_{16}O_3$	148.20	R : 10, 36 S : 16, 26, 39	
Aceton-dimetylacetal <i>Purum > 96%</i>	Fluka Lot: 1375579 43508249	$C_5H_{12}O_2$	104.15	R : 11, 36/37/38 S : 16, 26, 37/39	
Methansulfonic acid <i>Puriss > 99%</i>	Fluka Lot: 1245105 51806038	CH_4O_3S	96.10	R : 34 S : 26,36,45	
Propan-2-ol <i>SpS > 99.9%</i>	Romil Batch: A555457	$(CH_3)_2CHOH$	60.10	R : 11,36,67 S : 7,16,24/25,26	
Hydranal non hygroscopic standard 5.00	Riedel-de Haën Lot: 8072B	-	-	R : 10,20/21/22,37/39,41,67 S : 25,26,36/37/39	
Potassium phosphate	Labor Product ZS ADHOC01/015610/B-Sigma	K_3PO_4	212.27	R : 35 S : 26,36/37/39,45	
Molecular Sieve Dehydrate with indicator for drying solvents	Fluka Lot: 014742/1 30105187	-	-	R :- S :-	-
Hydranal Composite 5	Riedel- de Haën Lot: 8109A	-	-	R :- S :-	-
Tetrahydrofuran <i>Puriss</i>	Fluka Lot: 1332672 21907172	C_4H_8O	72.11	R : 11,19,36/37 S : 16 ;29 ;33	
Ethyl Acetate <i>SpS</i>	Romil Batch: L533400	$C_4H_8O_2$	88.11	R : 11,36,66,67 S : 16,26,33	
Ethyl magnesium Chloride <i>Sol 20% w/w</i>	Labor Product In THF and Dimethoxyethane	C_2H_5ClMg	88.82	R : 11,14/15,19,22,34 S : 6A,16,24/25,36/37/39,43A,45	
Diethyl ether <i>Analytical grade, Pheur</i>	Scharlau Batch: 58260	$C_4H_{10}O$	74.12	R : 12,19,22,66,67 S : 9,16,29,33	
Tert butyl-methyl ether <i>Purum</i>	Fluka Lot: 1215986 53405215	$C_5H_{12}O$	88.15	R : 11,38 S : 9,16,24	
Methyl magnesium bromide <i>3.0M in diethyl ether</i>	Aldrich Lot: 04520BH-388	CH_3BrMg	119.26	R : 11,14/15,19,34,48/20,63,65,67 S : 6A 8,16,33,36/37/39,43B,45,46,62	

Butyl magnesium chloride <i>2.0M in THF</i>	Aldrich Batch : 00126CE	C_4H_9ClMg	116.88	R : 11,15,19,34 S : 7/8,16,29,33,36/37/39,45	 
Xylene mixture of isomers <i>For Karl Fischer titration</i>	Scharlau N° X10059	C_8H_{10}	106.17	R : 10,20/21,38 S : 25	
2-Butanol <i>Puriss p.a.</i>	Fluka Lot: 385640/1 30799	$C_4H_{10}O$	74.12	R : 10,36/37,67 S : 7/9,13,24/25,26,46	
2,2'Biquinoline 96 %	Aldrich Lot: B3,540-7	$C_{18}H_{12}N_2$	251.31	R : 36/37/38 S : 26,37/39	
Potassium Permanganate <i>Solution 0.1N (0.02M)</i>	Scharlau Batch: 35612	$KMnO_4$	158.04	R : 8,22,50/53 S : 60,61	  
Oxalic acid Sodium <i>w±2u = 99.79%±0.26%</i>	Fluka N° 71804	$C_2O_4Na_2$	134.00	R : 21/22 S : 24/25	
Ammonium iron(II) sulfate hexahydrate <i>puriss</i>	Riedel-de Haën Lot:62200	$(NH_4)[Fe(SO_4)_2] \cdot 6H_2O$	392.14	R : - S : 24/25	-
Silver nitrate <i>Solution 0.1 N</i>	Scharlau Batch: 94797	$AgNO_3$	169.87	R : 34,50/53 S : 26,45,60,61	 

The source of the R and S Numbers and Dangers is ChemExper [24]

2.3 Methods

2.3.1 Acid base titration

A) The thermometric acid base titration method is after optimization:

Titrant: NaOH 1M

Sample weight precisely 0.8-1.0 [g] / Addition of dest. Water to 40 ml

Parameters:

- Stirrer of 11 (as Technical specification 1500-1650 [min⁻¹])
- Addition of 2 [ml/min]
- Filter factor of 40-60
- Position of the burette 3 / 4 of turn before the thermistance
- Delay time 15 [s]
- Selection Peak with the second derivative

To determine the NH₄NO₃ concentration, an addition of this product is making between 15 and 25 [mg].

B) The potentiometric acid base titration for solution Test method is as follows:

Titrant: NaOH 1M

Sample weight precisely 2.4-2.8 [g] / Addition of dest. water to 50 ml

DET pH Parameters:

- | | |
|---------------------------------|------------------------------|
| - Density measure 2 | - Temperature 25.0 [°C] |
| - Min. Increment 10.0 [μl] | - Stop Volume 20 [ml] |
| - Delivery rate 3 [ml/min] | - Stop pH 14 |
| - Measurement Drift 20 [mV/min] | - Stop EP 4 |
| - Waiting 38 [s] | - Filling speed max [ml/min] |
| - Start Volume 10 [ml] | - Statistic ON |
| - Dose speed max [ml/min] | - EP-Criteria 2 |
| - Pause 15 [s] | - EP-Anchored all |
| - Input 1 | |

For the determination of the NH₄NO₃ addition of this product is 5 ml of a 2M solution.

Calculation:

% mass 5-ethyl-2-methylpyridine (EMP) = (EP3 [ml]- EP2 [ml])*titer of NaOH*12.11/ Sample masse [g]

% mass Nicotinic acid (NS) = (EP2 [ml]- EP1 [ml])*titer of NaOH*12.31/ Sample masse [g]

% mass Nitric acid (HNO₃) = (EP4 [ml] - EP3 [ml] + EP1 [ml] -*Blanc*)*titer of NaOH*6.3/ Sample masse [g]

% mass Ammonium Nitrate (NH₄NO₃) = (EP4 [ml] - EP3 [ml])*titer of NaOH*8.004/ Sample masse [g]

C) The thermometric acid base titration NaOH 1M titer determination after optimization

Titrant: NaOH 1M

Sample weight precisely 0.6-1.4 [g] Potassium hydrogen phthalate / Addition of dest. Water to 40 ml

Parameters:

- Stirrer of 11 (as Technical specification 1500-1650 [min⁻¹])
- Addition of 2 [ml/min]
- Filter factor of 40-60
- Position of the burette ¾ of a turn before the thermistance
- Delay time 15 [s]
- Selection Peak with the second derivative

D) The potentiometric acid base titration for NaOH 1M titer determination

Titrant: NaOH 1M

Sample weight precisely 2.0-2.1 [g] Potassium hydrogen phthalate / Addition of dest. water to 60 ml

DET pH Parameters:

- | | |
|---------------------------------|-----------------------------|
| - Density measure 4 | - Temperature 25.0 [°C] |
| - Min. Increment 5.0 [µl] | - Stop Volume 6*masse [ml] |
| - Delivery rate 3 [ml/min] | - Stop pH OFF |
| - Measurement Drift 30 [mV/min] | - Stop EP OFF |
| - Waiting 26 [s] | - Filling speed 30 [ml/min] |
| - Start Volume 4*masse [ml] | - Statistic ON |
| - Dose speed max [ml/min] | - EP-Criteria 5 |
| - Pause 5 [s] | - EP-Anchored bigger |
| - Input 1 | |

Calculates:

Titer NaOH = (Sample size [g] * 1000) / ((EP1 [ml] - *Blanc*)*Concentration of NaOH) 204.22)

2.3.2 Titration of Aldehyde, Ketone and Alcohol

A) The thermometric titration method for $\text{Na}_2\text{S}_2\text{O}_3$ 0.1M titer determination is:

Titrant: $\text{Na}_2\text{S}_2\text{O}_3$ 0.1M

Sample : make a solution with precisely about 2.0 [g/l] KIO_3 in a solution 1:10 HCl 32% and dest. water.

Add 1-20 [ml] of this solution

Addition of dest. water to 40 ml

Parameters:

- Stirrer of 11 (as Technical specification 1500-1650 [min^{-1}])
- Addition of 2 [ml/min]
- Filter factor of 40-60
- Position of the burette 3 / 4 of turn before the thermistance
- Delay time 20 [s]
- Selection Peak with the second derivative

For the determination add 10 [ml] of a solution 5% (w/v) KI.

Calculates:

$\text{Titer Na}_2\text{S}_2\text{O}_3 = (\text{Sample size [g]} * 60 * \text{purity of KIO}_3[\%]) / ((\text{EP1 [ml]} - \text{Blanc}) * \text{Concentration of Na}_2\text{S}_2\text{O}_3) 214.00$

B) The thermometric titration method for N-Bromosuccinimide (NBS) powder titer determination is:

Titrant: $\text{Na}_2\text{S}_2\text{O}_3$ 0.1 M

Sample : weight precisely 0.015-0.100 [g] NBS / Addition of dest. water to 40 ml

Parameters:

- Stirrer of 11 (as Technical specification 1500-1650 [min^{-1}])
- Addition of 2 [ml/min]
- Filter factor of 40-60
- Position of the burette 3 / 4 of turn before the thermistance
- Delay time 20 [s]
- Selection Peak with the second derivative

For the determination add 5 [ml] of a solution of 3% (v/v) CH_3COOH and add 10 [ml] of a solution 4% (w/v) KI.

Calculates:

$\text{Titer NBS [\%]} = ((\text{EP1 [ml]} - \text{Blanc}) * \text{Concentration of Na}_2\text{S}_2\text{O}_3) 177.985 / (\text{Sample size [g]} * 1000 * 2)$

C) The thermometric titration method for NBS titer determination is:

Titrant: $\text{Na}_2\text{S}_2\text{O}_3$ 0.1 M

Sample : NBS 0.01M solution 10 - 18[ml]

Addition of dest. water to 40 ml

Parameters:

- Stirrer of 11 (as Technical specification 1500-1650 [min^{-1}])
- Addition of 2 [ml/min]
- Filter factor of 40-60
- Position of the burette 3 / 4 of turn before the thermistance
- Delay time 20 [s]
- Selection Peak with the second derivative

For this determination add 2 [ml] of a solution of 3% (v/v) CH_3COOH and add 5 [ml] of a solution 4% (w/v) KI.

Calculates:

Titer NBS solution = $((\text{EP1 [ml]} - \text{Blanc}) * \text{Concentration of } \text{Na}_2\text{S}_2\text{O}_3) / (\text{Sample volume [ml]} * 2)$

D) The thermometric titration method for Ascorbic acid and tested on different other product is:

Titrant: N-Bromosuccinimide (NBS) 0.01 M

Sample : make a solution with about 0.02 M of the compound to analyse.

Addition of dest. water to 40 ml

Parameters:

- Stirrer of 11 (as Technical specification 1500-1650 [min^{-1}])
- Addition of 2 [ml/min]
- Filter factor of 40-60
- Position of the burette 3 / 4 of turn before the thermistance
- Delay time 20 [s]
- Selection Peak with the second derivative

For the determination of certain compound add 5 [ml] of a solution of 3% (v/v) CH_3COOH and sometimes add 10 [ml] of a solution 4% (w/v) KI.

Calculates:

Ascorbic acid [g/l] = $((\text{EP1 [ml]} - \text{Blanc}) * \text{Concentration of NBS} * 176.13) / (\text{Sample volume [ml]})$

2.3.3 Titration of Water

A) The thermometric titration method for titer determination of Triethyl ortoformate (TEOF) is:

Titrant: TEOF 2M or DMP 2M

Sample : weight precisely 5.0-8.0 [g] of Hydranal non hygroscopic standard 5.00 %

Addition of 30 [ml] of solution ~1% v/v methansulfonic acid in iso propanol (with dosino 2x15 [ml])

Parameters:

- Stirrer of 11 (as Technical specification 1500-1650 [min⁻¹])
- Addition of 2 [ml/min]
- Filter factor of 70
- Position of the burette 3 / 4 of turn before the thermistance
- Delay time 30 [s]
- Selection Peak with the second derivative

For the determination of acetone-dimethylacetatal (DMP) titer makes the same method but the selection peak change to max and not min (endothermic reaction).

Calculates:

Titer TEOF solution = (Titer Hydranal solution*Sample [g]*1000) / ((EP1 [ml] - *Blanc*)*18.015*100)

B) The thermometric titration method for Ascorbic acid and tested on different other product is:

Titrant: TEOF 2M or DMP 2M

Sample : weight precisely 1.0-3.0 [g] of the sample not soluble substance

Addition of 30 [ml] of solution ~1% v/v methansulfonic acid in iso propanol (with dosino 2x15 [ml])

Parameters:

- Stirrer of 11 (as Technical specification 1500-1650 [min⁻¹])
- Addition of 2 [ml/min]
- Filter factor of 70
- Position of the burette 3 / 4 of turn before the thermistance
- Delay time 30 [s]
- Selection Peak with the second derivative

For the determination of soluble substance the weighing can increase.

Calculates:

Ascorbic acid water [%] = ((EP1 [ml] - *Blanc*)*18.015*100*Titer TEOF) / (Sample weight [g] *1000)

C) The Karl Fischer titration method is the method with titrant Hydranal composite 2 or 5 [A7]

2.3.4 Titration of Grignard

A) The thermometric titration method for Grignard concentration determination:

Titrant: Iso Propanol (dry) ~1.3 M in Tert butyl-methyl ethane (MTBE)(dry)

Addition of 40 [ml] of Tert butyl-methyl ethane (MTBE) (dry) in vessel

Sample : weight precisely 1.0-3.0 [g] of Grignard solution direct in vessel prepare.

Parameters:

- Stirrer of 11 (as Technical specification 1500-1650 [min⁻¹])
- Addition of 1 [ml/min]
- Filter factor of 80
- Position of the burette 3 / 4 of turn before the thermistance
- Delay time 10 [s]
- Selection Peak with the second derivative

First dry the stirring and vessel: add ~40ml MTBE dry in the vessel and stir 30[s].

Second the titration must be making in N₂ or Ar but a balloon or a constant flux can give some fresh in the system so you can only prepare this atmosphere before start.

Calculates:

Grignard [%] = ((EP 1[ml] – Blank)*Titer Solution isoPropanol*Molar weight [g/mol]) / (1000*Sample [g])

B) The Grignard titration method is the method present in [A8]

2.3.5 Titration with KMnO_4

A) The thermometric titration method Manganometri:

Titrant: KMnO_4 0.02 [mol/l]

Sample: weight precisely $2.0 \cdot 10^{-4}$ - $6.0 \cdot 10^{-4}$ [mol] equivalent* of Sample direct in vessel/ Add 10 [ml] of H_2SO_4 ~20% / Add 0.5 [g] $\text{MnSO}_4 \cdot \text{H}_2\text{O}$ / Add to 40 [ml] with H_2O dest.

* is mol used of KMnO_4

Parameters:

- Stirrer of 11 (as Technical specification 1500-1650 [min^{-1}])
- Addition of 0.5 [ml/min]
- Filter factor of 80
- Position of the burette 3 / 4 of turn before the thermistance
- Delay time 30 [s]
- Selection Peak with the second derivative

Calculates:

Sample [%] = Stochiometric Factor [-] * ((EP 1[ml] – Blank)*Titer Solution KMnO_4 *Molar weight sample [g/mol]) / (1000*Sample [g])

Titer KMnO_4 [-] = ((Sample [g])*1000*Purty of Standard [%]) / ((EP 1[ml] – Blank)* Titer Solution KMnO_4 *Molar weight sample [g/mol])) / Stochiometric Factor [-]

For example stochiometric factor for Ascorbic acid or Oxalic acid Sodium is 2.5 and for Ammonium iron(II) sulfate hexahydrate is 5.0

B) The KMnO_4 potentiometric titration method is the method present in [A9]

3 Practical Part

In this part you can read what it has been done, a summary of all results that were obtained and some opinions or discussions.

3.1 Critical points of thermometric titration

For optimizers we started with a method find in the metrohm website in annexes [A2] and with a solution with 3-4 EP (HNO_3 ~37%, Nicotinic acid ~4%, 5-Ethyl-2-Methylpyridine~8%, Ammonium nitrate ~0.4%) and a factorial designs $2^{(4-1)}$ was made as Table 2

Table 2 : Factors selection for factorial designs

		+	-
A:	Delivery rate [ml/min]	5	2
B:	Stirring	8	3
C:	Burette position [lap]*	3 / 4	2 / 4
D:	Delay time [s]**	10	2

* Shown as in Figure 2 A) is Stirring and the arrow give the sense of rotation B) Thermo detector 1, 2, 3) Position for burette in quarter turn

** Delay time is the stirring time before titration started.

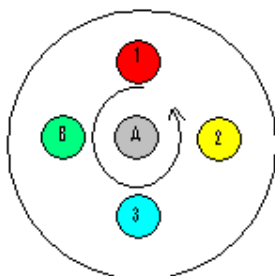


Figure 2 : Schematic drawing of the vessel holder

The results of the factorial designs $2^{(4-1)}$ were so bad that it was impossible to use them, because no response gave all the important information for this optimization. For example response EP1 [ml] or EP3 [ml] had different results and different important factors. But any of them gave all the important things for an analysis.

EP1 [ml] factor with influence were: C, AC+BD, BC, D or ABC ($S_{xy} = 0.0232$)

EP3 [ml] factor with influence were: D or ABC ($S_{xy} = 0.0416$)

Another response was tested: the difference between EP1 and EP2 [ml], it gave only one influent factor A ($S_{xy} = 0.2533$). To see the result : Annexes [A3]

In second time an ANOVA was made with these 4 factors but with different values. The value of some factors has been changed to test if another input gives easier results to interpret. See Table 3

Table 3 : Factors selection for ANOVA (analysis of variances)

		+	-
A:	Delivery rate [ml/min]	5	3
B:	Stirring	9	6
C:	Burette position [lap]	3 / 4	2 / 4
D:	Delay time [s]	10	5

For this analysis we had some problems because with EP2 [ml] EP3 [ml] all factors have more than 5% of signification with a residual deviation standard of 0.104[ml] and 0.059 [ml]. But with EP1 [ml] response , D, AB, BC, BD, ABC, ABD, BDC, have less than 5% of signification with an residual deviation standard of 0.063 [ml].

Also these results are useless for the rest of the optimization.

It can be seen that with this statistic method we have not good results. So we took all results and watched on each thermogramme which factor has what effect. These effects are given in Table 4.

Table 4 : factors of thermometric titration and effects

Factors	Effect / Influence
Delivery rate [ml/min]	More speed = peak second derivative spread Less speed = more point = more imperfection
Stirring	More rapidly = air bubble = disturbance Less rapidly = not mixed = disturbance
Burette position	1/4 = rapidly visible = not mixed = disturbance 2/4 = not totally mixed = less disturbance 3/4 = mixed good = even fewer disturbance
Delays time [s]	Too little = mixed not good = disturbance Too big = waste of time
Temperature solution	If solution > reagent, a part of Q is used to heat reagent and is not visible
Temperature reagent	If reagent > solution, a part of the temperature gain is for reagent and not for reaction.
Filter factor*	Too big filter factor consider everything as EP Much bigger filter factor mitigated the disturbance Less filter factor accentuated the visibility of EP Too less filter factor accentuated the disturbance

*Filter factor is a filter that selects how many points is average to make derivatives, to see effects of filter factor, see [A4]

With this observation we can make a “one by one” factors optimization. For that, all other parameter was blocked and only one changes.

First we have blocked delivery rate too 3 [ml/min], the burette position to 3/4, the delays time to 15 [s] and the filter factor to 40, and change the stirring between 8 and 15. After 11, bubbles are formed and with 9 and 8 the interference due to the bad mix appear. Also the best stirring find is 11. With

this best stirring fixed and the other factors not changed, we still need to change the delivery rate to 1-4 [ml/min]. The best delivery rate that has been found is 2 [ml/min] because with a slower rate the peaks of second derivatives is smaller and with a faster rate the disturbance is bigger. After that, with a found stirring and delivery rate, we need to search for the best filter factor. It is between 40 and 60 but that depend on the concentration of solution analysed. The burette position is chosen at $\frac{3}{4}$ because it is the best time to equilibrate the solution before the probe. The temperature of the titrant and the sample are the best when they are about the same. Also the dest. water used for analyses is taken at ambient temperature and the titrant solution too. In the end we obtain the method in 2.3.1 A. For have a idea of the possible look of thermogramme see Annex [A9-10]

The titrant is added at constant rate, to regroup all the following effect in the blank of this titration [7]:

- Inefficiencies in the mixing of the titration solution
- Reaction Kinetics (in the case of non ionic titration)
- Heat transfer delay across the solution and the thermistor
- Electronic and software processing delays.

To have the blank and in same time the titrant concentration, it is possible to make experiment with different sample weighing and report the sample [mmol] on X axis and the titrant [ml] on Y axis. The slope of this linear curve gives, when it is divided by the molarity factor, the titer of this solution. The intercept of this curve give the blank of this analysis. With this curve we can computed an LOD theoretic, for example for the determination of NaOH see Figure 3.

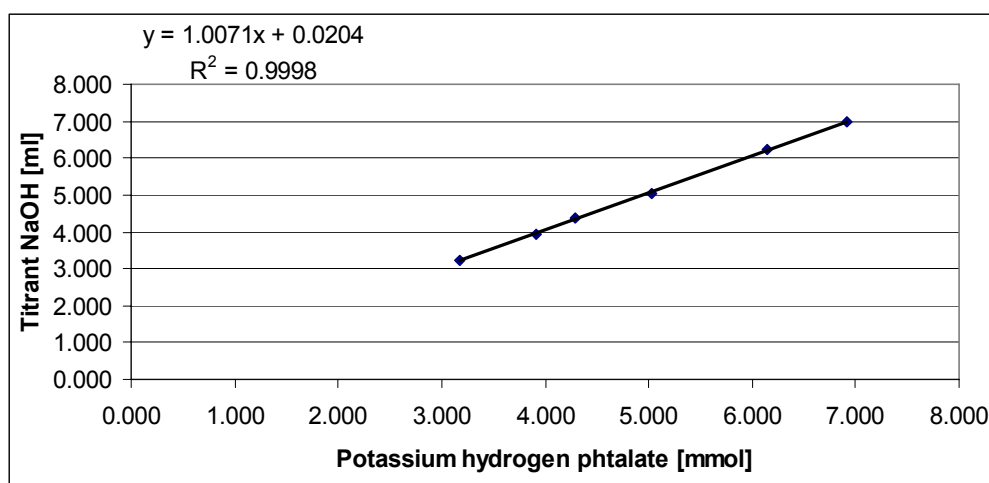


Figure 3 : Calibration and determination of titer of 1 M NaOH.

Titer NaOH = 1 (because 1 mol NaOH react with 1 mol KHP)/1.0071 (Slope) = 0.993

Blank of the analysis = 0.0204 [ml]

Theoretical LOD and LOQ: 0.5[ml]titrant (ending disturbances) -> 0.097 [g] $C_8H_5KO_4$

3.2 Acid base titration

This titration type is good for thermometric because it has strong enthalpies reaction.

In this part EMP = 5-Ethyl-2-Methylpyridine and NS =Nicotinic acid

3.2.1 Determination of titer NaOH 1M

Determination of NaOH titer is tested with dynamic potentiometric titration, monotone potentiometric titration, thermometric method find in annexes [A2] and thermometric optimized method. Results of the 4 determination is given on Table 5

Table 5 : Results of titer finder with different method

N°	Type	Average	Standard deviation	$\Sigma(y-\hat{y})^2$	Numbers analyses
1	Thermometric	0.987	0.008	4.57E-04	x6
2	Potentiometric	0.999	0.000	-	x3
3	Thermometric	0.999	0.001	9.14E-04	x6
4	Potentiometric	0.997	0.001	-	x3

The N° present on Table 5 say the order in which the analyses were made. 1 and 2 were made the same day and, 3 and 4, 5 day after. Method 1 is thermometric method find in annexes [A2], method 2 is DET pH (dynamic), method 3 is thermometric titration with best method found(stirring 11, addition 2 [ml/min], burette in ¼ turn place) method 4 is a potentiometric method MET pH (monotone).

The thermometric titration is a monotone titration it is for that reason that a comparison with the MET pH potentiometric was done. The comparison of the potentiometric DET pH titration is to see if with thermometric titration we have the same result than with a dynamic potentiometric titration. In Table 5 the $\Sigma(y-\hat{y})^2$ formula is the linearization of potassium hydrogen phthalate [g] to reagent [ml].

To see the difference between 1 and 3 see Figure 4 and the next one, the filter factor is not equal on this two figures but it is because the methods are not the same.



Figure 4 : Method 3 with filter factor 40

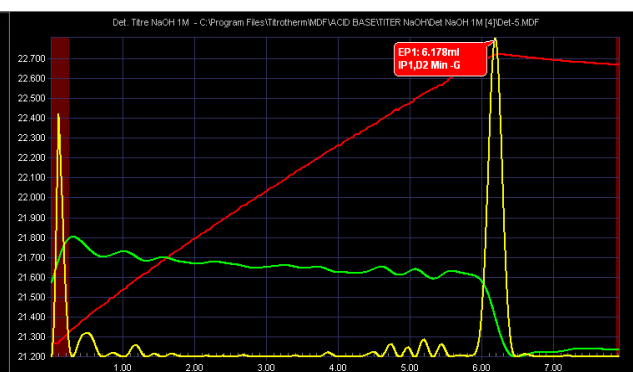


Figure 5 : Method 1 with filter factor 60

Statistic test T and F were used on these results and we can confirm the link between methods 2 and 3. Also a better titration give better result as the difference between DET en MET in potentiometric titration. To see that, look at annex [A5]

3.2.2 Typical crytical solution for acid base titration.

This typical solution is 36-39% HNO_3 , 8-9% 5-Ethyl-2-Methylpyridine, 4.0-4.2 % Nicotinic acid, 0.5-0.6% NH_4NO_3 . The first test is made with an artificial solution with only these compounds but the real solution contained many other reagents and is tested later in this document.

The comparative analyses are made with method 2.3.1 A for thermometric and 2.3.1 B for potentiometric titration.

On the Figure 6 and Figure 7 the order of the peaks is first HNO_3 (EP1) not used for protoning the other compound, second the Nicotinic acid (NS) (EP2), the third is 5-Ethyl-2-Methylpyridine (EMP) (EP3) and the last is NH_4NO_3 (EP4). This order is issued by their respective pK_a [5], -1.4, 2.0, between 6.4-7.4 (not found the exact value in [5]) and finally the last EP is found by adding ammonium nitrate.

To obtain the range of how many gram is the best weighing for thermotitration, we have make this analysis between 0.5-3.0 [g] of typical solution. After that, a visual scan have rapidly lay the limitation masse of the analysis. This part is important because too much mass is also not good. A bigger weighing corresponds to a bigger volume titrant and so a bigger volume to heat before the probe reacts for temperature change. The difference between the temperature at end of the titration and the temperature coming after get smaller as the titrant volume gets bigger. It is due to the form of the curve of temperature, this curve shows a logarithmic form. This form can be explained by the fact that there is a much bigger volume to heat and a less quantity of product that create heat, and that explain why we get smaller peak.

A second effect is that the last peak is often bigger because that is in this moment that the big change of temperature appeared. But that depend on many factor, fo example delta temperature titrant-solution and enthalpies of the last reaction.

A detection limit has been tested but when we want to make it with Nicotinic acid or with EMP, the problem is that both solutions need to be protonised in order to be soluble in the water. In a small concentration we can't split the acid used to protonise and the compound because they make only one peak. The two peaks are too close to distinguish them.

For HNO_3 the detection limit is limited because the 0.5 first ml of the titration in thermotitration have many problems due to mixing. Also for nitric acid the detection limit is $0.5 \cdot \text{NaOH}$ titers for this analysis but it depend to other factor as temperature of titrant or the analysed solution.

To see the NH_4NO_3 we must add a quantity of this product to the solution because otherwise we only have one peak with 5-ethyl-2-methylpyridine. Many additions have been tested between 0.12-5.1 [g] but the best result is obtained with smaller quantity as 12-25 [mg]. With more quantity the peak is very small and with less the peak is not good visible. See Figure 6 Figure 7.

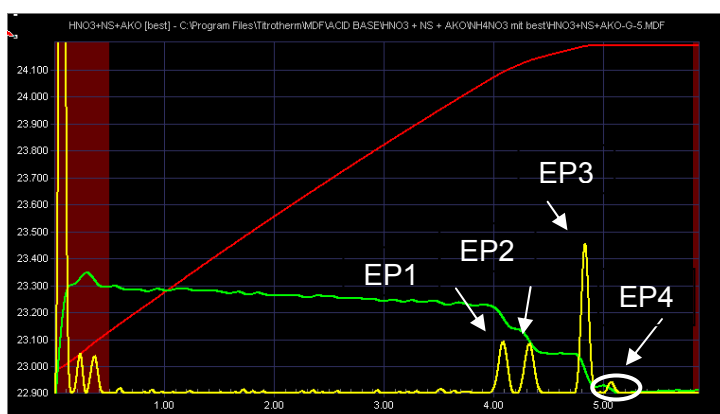


Figure 6 : 0.87 [g] solution and addition of 0.012 [g] NH_4NO_3 Filter factor 50

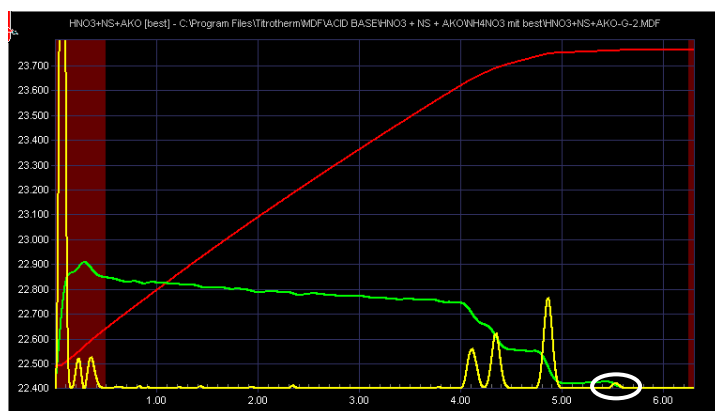


Figure 7 : 0.89 [g] solution and addition of 0.033 [g] NH_4NO_3 Filter factor 50

The calculation of 2.3.1 is used to determinate the % of masse of different product. The formula for HNO_3 is done because a part of nitric acid is used to protonise EMP and NS. EMP and NS are, as seen previously, soluble in water only in protonised form.

$$\% \text{ mass Nitric acid } (\text{HNO}_3) = (\text{EP4 [ml]} - \text{EP3 [ml]} + \text{EP1 [ml]} - \text{Blanc}) \cdot \text{titer of NaOH} \cdot 6.3 / \text{Committed masse}$$

For the first determination we have make a mix with a known composition and see if the potentiometric and thermometric analyses are the same or not. For the result you can look at Table 6

Table 6 : Results of solution test

Type *	HNO ₃ [%]		EMP [%]		NS [%]		NH ₄ NO ₃ [%]	
	Average	Standard deviation	Average	Standard deviation	Average	Standard deviation	Average	Standard deviation
Potentiometric (3)	33.24	0.04	7.14	0.06	3.43	0.13	0.52	0.10
Thermometric (6)	32.54	0.24	7.13	0.12	3.31	0.16	0.37	0.04
Calculated	32.69	-	7.16	-	3.39	-	0.43	-

* In brackets is the number of analyses.

The T test and F test are applied to the potentiometric and thermometric answer In Table 7, given the result of the tests, the average and the distribution are the same for 99% and 95% of signification.

Then we have tested the “Ansatz Lösung” solution with every compound in it, the detection of NH₄NO₃ is not as easy as in the solution self made. Results are shown in Table 7.

Table 7 : Composition of “Ansatz Lösung” determined by both methods.

Type*	NH ₄ NO ₃ add	HNO ₃ [%]		EMP [%]		NS [%]		NH ₄ NO ₃ [%]	
		Average	Standard deviation	Average	Standard deviation	Average	Standard deviation	Average	Standard deviation
Potentiometric (3)	without	37.72	0.03	8.65	0.23	3.72	0.04	-	-
Thermometric (6)	without	37.72	0.16	8.68	0.08	3.89	0.27	-	-
Thermometric (6)	with	37.26	0.21	8.81	0.34	3.53	0.24	0.42	-

* in brackets is the number of analyses.

In Table 7 the first column of NH₄NO₃ said if we have added NH₄NO₃ to see it or not. As we can see, the addition of a part of NH₄NO₃ influences the response of the other compounds but only visually not a significant difference on the [ml] of titrant used. To determine the % of mass on NH₄NO₃ we have made a graph with in X axis additional mass [g] and in Y axis mass found [g]. This analysis is made for filter factor 60 and gives this response: $Y = 1.0289X + 0.0042$ for 3 points $\sum(y-\hat{y})^2 = 3.72 \cdot 10^{-8}$. The slope is near one, factor has a big influence of the response of the system. For example, for this experiment a filter factor of 70 give a response of 0.9 % NH₄NO₃ for a slope of 0.85 and a filter factor of 50 give a response of 0.2 % NH₄NO₃ for a slope of 1.14. Figure 8 shows a titrograme of potentiometric for the “Ansatz lösung” with method 2.3.1.B. The Figure 9 is a thermogramme of thermometric titration for the “Ansatz Lösung” without addition of NH₄NO₃ and on Figure 10 we can see the influence of an addition of NH₄NO₃ to the stabilization of the system.

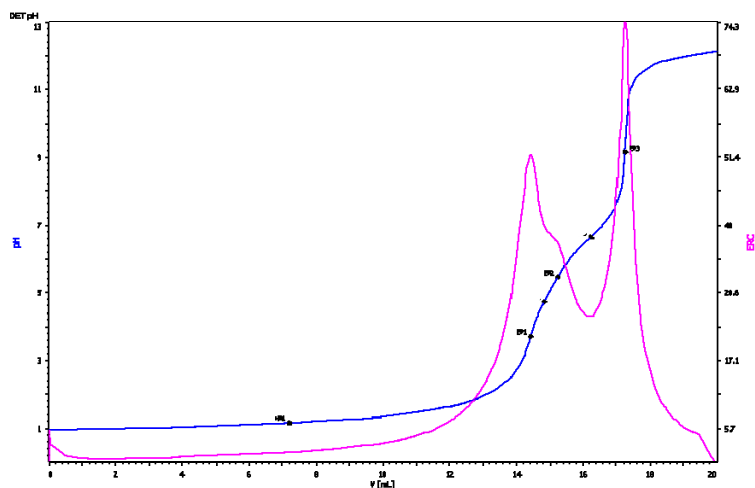


Figure 8 : titrograme of potentiometric titration with "Ansatz Lösung"

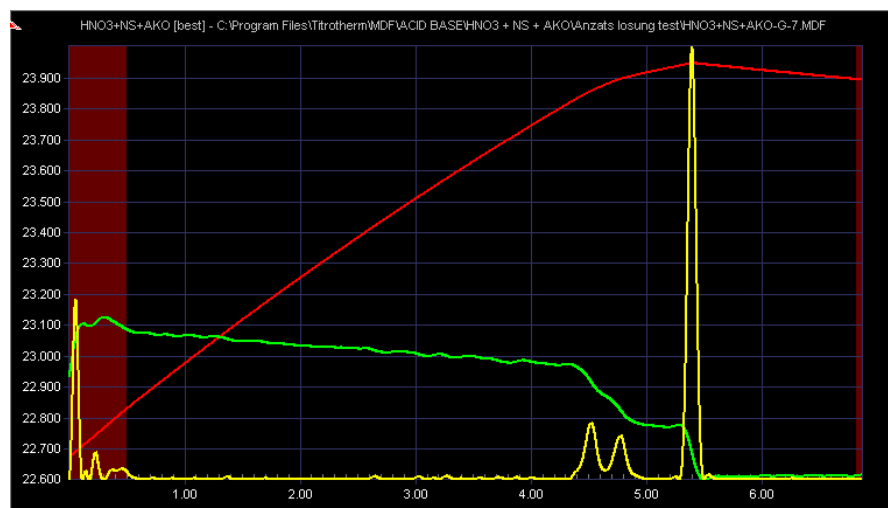


Figure 9 : thermogramme of thermometric titration with 0.86 [g] "Ansatz Lösung" Filter factor 60

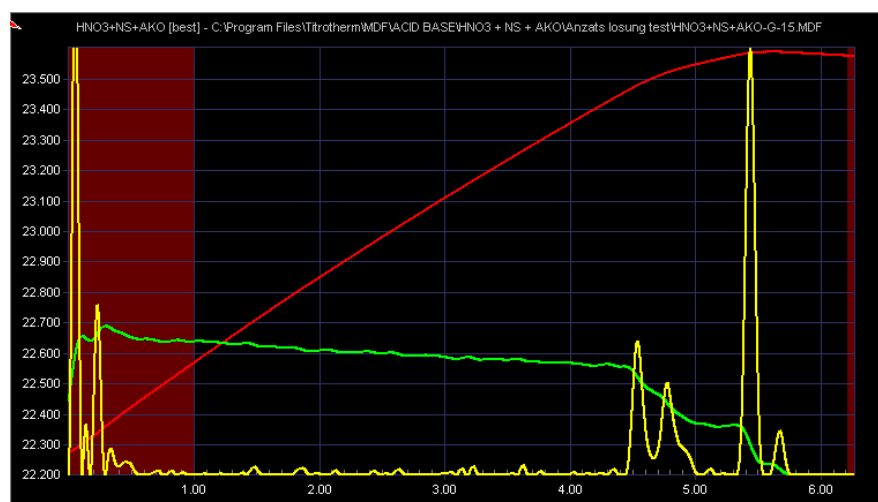


Figure 10 : thermogramme of thermometric titration with 0.87 [g] "Ansatz Lösung" + 15 [mg] NH_4NO_3 Filter factor 60

The Figure 10 can be seen with different filter factor in annex [A4].

Also with these results we can understand which is the biggest problem of the thermometric analyses on acid base complex titration, and also what is the biggest strength of this titration.

In this part a thermotitration have results that we can compare with potentiometric titration. The thermometric titration absolutely demands an optimization and a blank. Time for an analysis is somewhat similar. The filter factor is a very important factor as well as the agitation and the delivery rate that must be optimized in order to have good result. The quantity of titred solution must be bigger than reagent solution and the quantity of analyte must be optimized. When all optimizations are made we can split and have some beautiful peaks. That will give an easier identification of the substance search. But it is not possible to dissociate two acid or base with the same enthalpy of reaction and the same constant of dissociation.

Table 8 : Thermometric titration VS Potentiometric titration for acid base analyses.

Important Things	Thermometric Titration	Potentiometric titration
LOD and LOQ	Depend on the temperature of titrant and sample solution Obtained with curve	Depend very slightly on the temperature
Precision See Table 6 and 7	Equal to a potentiometric analysis	Equal to a thermometric analysis
Minimal number of titration	2 (for have the curve for the bank)	1
Theory VS Practice	Assessment of Heat and of Material Hard to have all parameters	See Theoretical part 1.1 Relatively easy to have all parameters

3.3 Titration of Aldehyde, Ketone and Alcohol

A lot important molecules, especially the ones of pharmaceutical interest, possess a keto, aldehyde or alcohol group. The goal was to have a simple method for quantification of these compounds.

3.3.1 Aldehyde and Ketone

For the titration of aldehyde and ketone we have a big challenge and for this problem we have searched method that can be used without sample preparation. Also for that we were careful to use a fast and quantitative reaction that reacts with the aldehyde and ketone.

3.3.1.1 Precipitation

Many aldehydes and ketone form precipitates with 2,4 dinitrophenylhydrazone. This reaction was largely used for the identification of the aldehyde and ketone.

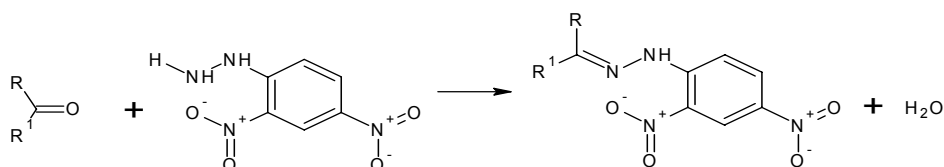


Figure 11 : Reaction of 2, 4 dinitrophenylhydrazone.

First tests are made with 2,4 dinitrophenylhydrazone, and rapidly we have problem because this product have bad solving in water, ethanol and ethyl acetate, so testing it with ethyl acetate and acetic acid is not better. Then this experiment was done with sulfuric acid ~50% and it gets better. But for thermometric analysis the titrant must not have a too high energy of solubility in the analysed solution, because when it is the case the enthalpy of reaction can be masked by the enthalpy of solubility of the titrant. So this method was abandoned.

3.3.1.2 Reduction of aldehyde and ketone

LiAlH_4 and NaBH_4 are common reducing agent for aldehyde and ketone. The first is very reactif and shows some safety risk because it reacts with water and is not too specific for this titration.

The second has better selectivity and have a good solubility in methanol. But when we make the titrant, also about 1 [mol/l] is sufficient because 1 NaBH_4 reacts with 4 carbonyls groups, MeOH and NaBH_4 react by creating H_2 and this H_2 can make explosions. It is possible that it doesn't react with ether or tetrahydrofuran, but time to exploit this method is up.

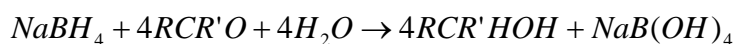


Figure 12 : Reaction of NaBH_4 on aldehyde.

On Figure 12 the R' and R can be H or a alcyle rest and we can see that 1 mol of NaBH₄ reacts with 4 mol aldehyde or ketone then the water is added only at the end of the reaction between the two other compounds.

3.3.1.3 Oxydation of aldehyde

A method was found, it is the reaction of aldehyde with freshly prepared silver-ammonium complex. But this compound can explode during the storage. Also this safety risk won't be taken.[12-13]

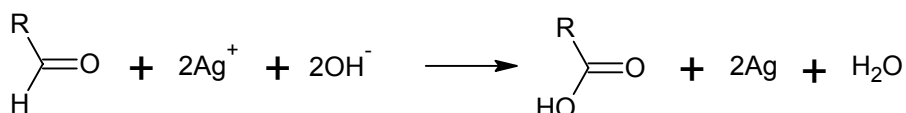


Figure 13 : Reaction of Ag⁺ on aldehyde.

3.3.1.4 Formation of bisulfite with formaldehyde

In [7] the method is for the determination of formaldehyde but this method is not a direct method to determine the formaldehyde. It needs a sodium sulfite solution and after that the titration is made with a standard acid.

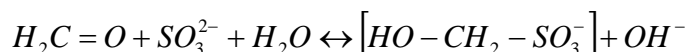


Figure 14 : Reaction of Formation of bisulfite with formaldehyde

As seen this problem is very difficult to resolve and haven't a solution for the moment.

3.3.2 Alcohol

This class of compounds is not mentioned in the goals of the Diploma work, but we thought since aldehyde and ketone have not worked another important functional groups to experiment in the organic chemistry is the alcohol group. And alcohol is a result of an oxydo-reduction reaction of aldehyde or ketone too. To see this function we have taken a polar substance with a good solubility in water (1.48 [g]) the N-Bromosuccinimide [15]. This product is a source of bromonium (Br⁺), an oxidant of secondary alcohols, primary and secondary amines, and thiol; with thirdly amine the C-N band is cut and formed secondary amine and aldehyde. [15].

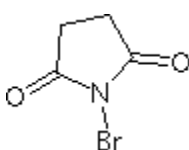


Figure 15 : N-Bromosuccinimide (NBS) [24]

To work with this substance, we must determine a standard to found its titer.

This standard is the $\text{Na}_2\text{S}_2\text{O}_3$ himself standardized by KIO_3 .

The determination of the titer of $\text{Na}_2\text{S}_2\text{O}_3$ 0.1M by potentiometric and by thermometric titration gave 1.005. The method used for thermometric titration is method 2.3.2 A and for potentiometric titration it is given on annex [A6].

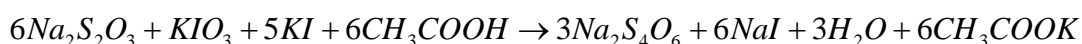


Figure 16 : Reaction of $\text{Na}_2\text{S}_2\text{O}_3$ and KIO_3 in presence of KI and Acetic acid

The determinations of the test of the solid NBS powder by thermometric titration gave $96.3\% \pm 1.7\%$, the value specified by the supplier is $\geq 95\%$. The method used for this thermometric titration is method 2.3.2 B.

The determination of the titer of NBS solution with thermometric titration gives the result you can see on Table 9.

Table 9 : Results of determination of titer solution NBS after 3 day stored at 4.5 °C protected from light.

Calculated*	Found	S Found	Loss in 3 Days
0.0099	0.0096	0.0000	-3.5%

* with the factor found with the NBS powder

The solution is really not stable for long time storage, 4 day max if it is kept on fridge and without light. But to keep it in a fridge creates some problems for the titration if the titrant is too cold the titration is very bad.

With all this titred solutions of NBS 0.0096M we can begin to work.

Ascorbic acid is tested by this method, but at first the NBS solution is too diluted to take direct weighing. To make the analysis we made a solution about 0.02 M of ascorbic acid and then the titration is made with volume samples.

This method gives good results that are given in Table 10 and a thermogramme is visible in Figure 18.

In Table 10 the result given is in the certificate of analysis and the number of analyses is 6.

Table 10 : Results of concentration determination of ascorbic acid in the ascorbic acid bottle in % (w/w)

% Given	% Found	S Found
99.8%	99.5%	0.3%

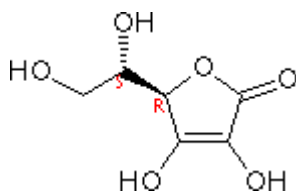


Figure 17 : L(+)-Ascorbic acid (Vitamin C) [24]

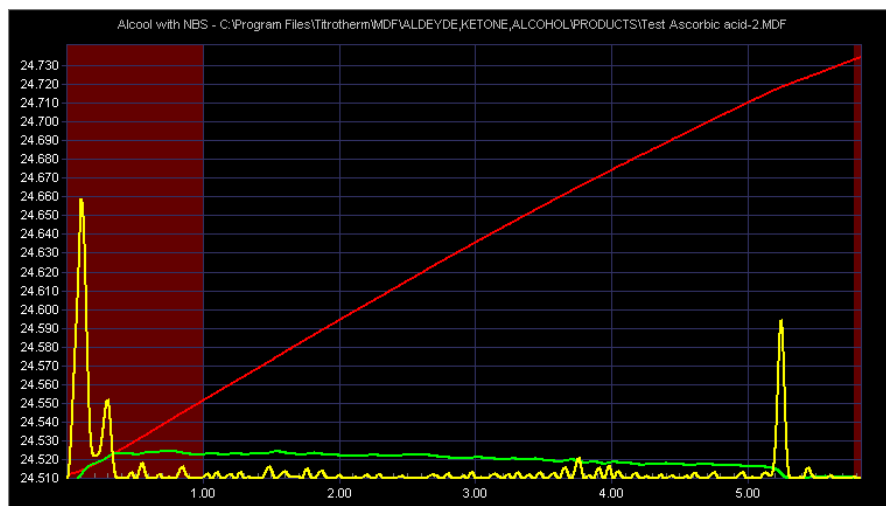


Figure 18 : Thermogram of ascorbic acid titred with NBS 0.01M filter factor 40

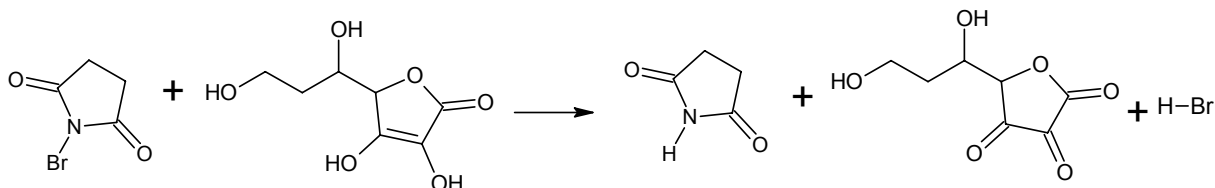


Figure 19 : L(+)-Ascorbic acid Reaction with NBS

As shown in Figure 17 the ascorbic acid is a compound with an en-diol function and it is oxidized with NBS or Iodine to form a compound with two ketones. It is possible to improve this analysis with a more concentrate titrant and a bigger sample or even better with a weighted sample.

After that we try with H_3PO_2 a substance that is not completely oxidized also it can react with NBS. But in this concentration with this titrant and with an addition of CH_3COOH and KI solution we can not see a reaction or at least the enthalpies are too little to see them.

The same situations are observed with L-Carnitine and with the Tylosin derivate modified on the aldehydhe function.

It is possible to see a reaction for these tree products if the titrant is more concentrated and the sample bigger.

This part requests more work and time to optimize all setting and see all possibilities

3.4 Titration of Water

The thermometric determination of water is based on the acid catalyzed hydrolysis of orthoesters or ketals. Triethyl orthoformate (TEOF) Figure 20 and Aceton-dimethylacetal (DMP) Figure 21 are suggested by [7]. The enthalpy of reaction of TEOF is negative (exothermic) on the contrary the enthalpy of reaction of DMP is positive (endothermic).

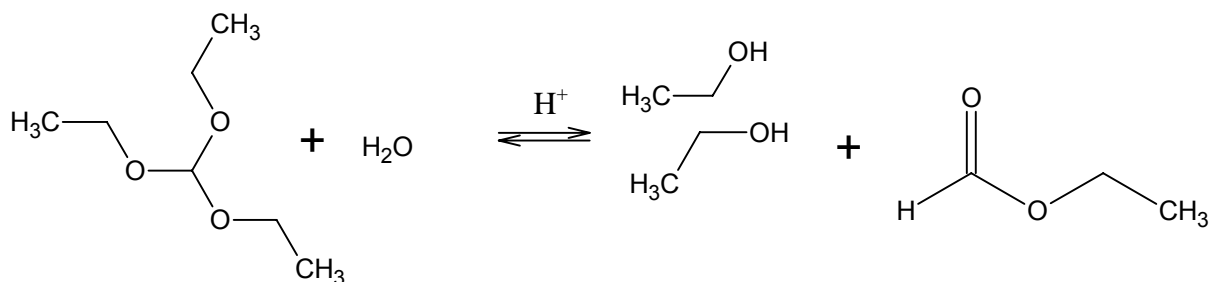


Figure 20 : Reaction of TEOF with water

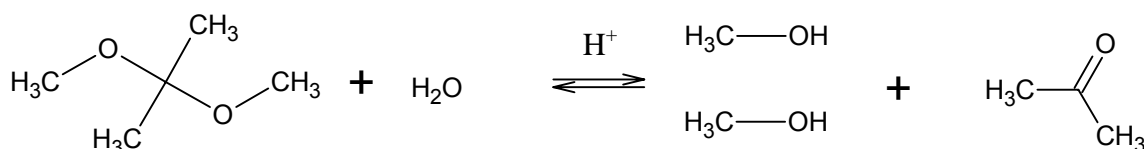


Figure 21 : Reaction of DMP with water

The description of thermometric titration is as follow:

- Titrant ~2M TEOF or DMP in Iso propanol water free
- Solution for dilute Sample: ~1%v/v Methanesulfonic acid in Iso propanol water free

Commercial iso propanol contains water, resulting in an unacceptable high Blank. Stirring the alcohol over night with a molecular sieve reduce the blank from 1.60 [ml] to 0.19 [ml] also about 90% less, see Figure 22 to look at the difference of the two blanks.

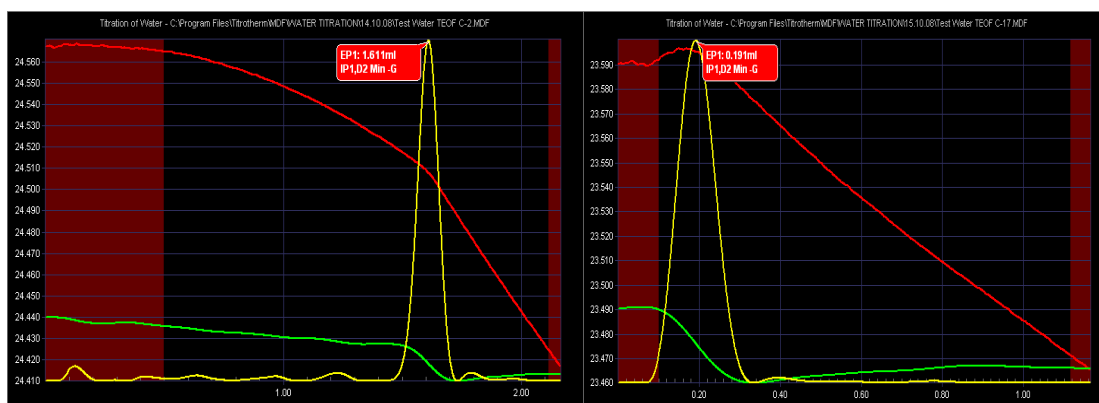


Figure 22 : Influence on blank by drying iso propanol: left iso propanol as obtained, right after stirring over molecular sieve over one night titred with TEOF

Now here is the problem, the titrant and the tested solution can contain water due to the water in the solvents, which is determined in addition to the water contained in the sample.

We have tried to simplify the method by combining titrant and acid catalyst solution. Unfortunately these solutions of TEOF and DMP in isopropanol are not stable in the presence of methanesulfonic acid.

A solution of DMP immediately turns black after the addition of methansulfonic acid. A hypothetical reaction sequence propose that the catalyze by acid form a highly stable carbonium ion(1). This can eliminate a proton and form a reactive vinglether (2). Then both intermediates start a cationic polymerization (3). see Figure 23

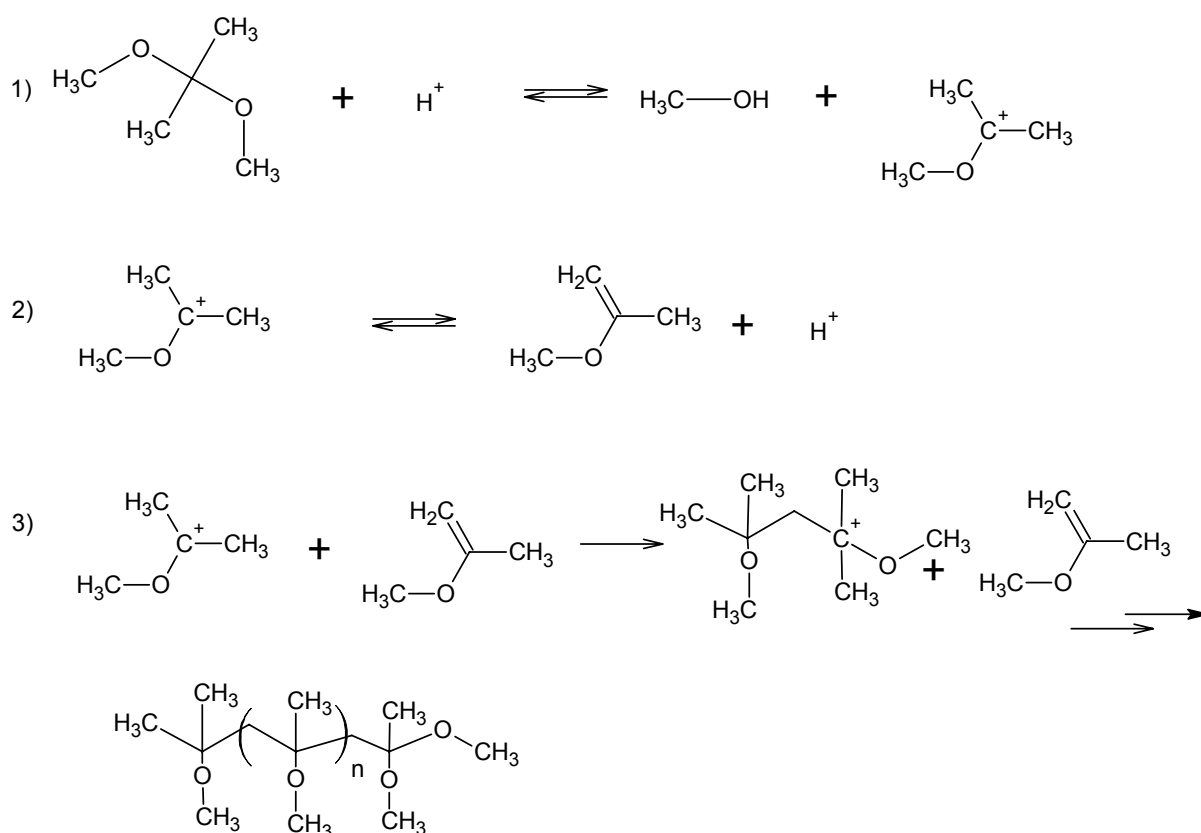


Figure 23 : Reaction postulated for the color obtained in mixing DMP and Methanesulfonic acid

3.4.1 Determination of water equivalent of titrant

For the determination of the titer of Triethyl ortoformate or Aceton-dimetylacetal the commercial water standard Hydranal 5.00 was used. The optimal mass of the standard is between 5.0 and 8.0 [g], with a smaller mass less titrant is consumed, but the influence of the variance of the blank is bigger.

3.4.1 Water content of conc. Sulfuric acid

Sulfuric acid is a strong acid and disturbs the Karl Fischer reaction. Only after addition of bases like pyridine it is possible to determine the quantity of water. This means that the determination of water quantity by Karl Fischer is quite complicated.

Experiments are made with sulfuric acid 96.30% to determine the quantity of water contained in it.

Table 11 : Water content of conc. Sulfuric acid, obtained with different methods

Analysis	Average	Standard Deviation	Number of analyses
Certificate Value	3.70%	-	-
Karl Fischer Value	3.82%	0.01%	2
Thermometric DMP Value	4.06%	0.24%	5
Thermometric TEOF all Value ^{A)}	4.62%	0.43%	6
Thermometric TEOF Value ^{B)}	4.48%	0.60%	5

^{A)} contained only TEOF in iso propanol as titrant.

^{B)} contained TEOF and ~1% volume Methansulfonic acid in iso propanol as titrant

In the Table 11 the analysis column give the information of which analysis and titrant are used in this experiment. For the Karl Fischer volumetric experiment made in methanol the titrant is Hydrannal complex 5. This titration gives this result after a special preparation of the sample $3.82\% \pm 0.01\%$. The sample preparation is given in [14] and was modified as follows: 5 [ml] acid are added to a mixture of 25 [ml] pyridine and 20 [ml] methanol, (the quantity of water in this two last reagents must be known). This result is compared with a sample of 5 [ml] pure water to replace acid, water = 100% so acid = x% previously the value of water contained in all solvents has to be subtracted.

The test t and F are made for all the results one by one, it gives this responses: for t test all analyses are ok as $\mu_1 = \mu_2$ and for the F test with 99% all are ok as $\sigma_1 = \sigma_2$ but with 95% the Karl Fischer analysis is not in the same distribution than the other analyses.

It is possible to make a device with combined thermometric and Karl Fischer titration. This combined device can also made a preparation of the solvent water free with Karl Fischer titration and then make a normally thermometric titration. This preparation can remove the problem of the big blank. But the problem of water in titrant is enjoy present.

3.4.1 Water content of Ascorbic acid

Ascorbic acid is a strong reacting agent. It reacts with iodine in the Karl Fischer reagent, see Figure 24, and this is why it is not possible to determine the water contained according to Karl Fischer.

The same experiments are made in thermometric with ascorbic acid. Ascorbic acid contained too less water, therefore we had to add water. With this method we can see a good answer, although the powder is not dissolved in iso propanol. The quantity found is $93.5\% \pm 4.8\%$ of the quantity added. It is possible that a part of this water is kept by ascorbic acid.

The Karl Fischer volumetric titrations consumed too much iodine, for that reason it has not functioned because the iodine reacts with the vitamin C, as it is shown in Figure 24.

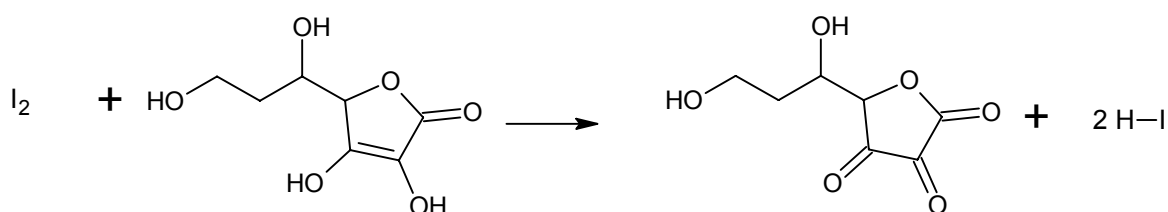


Figure 24 : Reaction of Ascorbic acid with I_2

L-Carnitine and K_3PO_4 is only tested once to see, but these two compounds as ascorbic acid are not dissolved in iso propanol and the quantity of water found is then equal as the blank.

So no other tests are made on this two products.

Determination of water caused many problems:

- Solvent cannot be dried in situ before titration as it is the case by Karl Fischer titration solvent that has to be dried before use and has to be stored protected from moisture.
- Large samples weights are needed to compensate the high blanks.
- Poor solubility of many samples in iso propanol, resulting in large delay time before titration

Table 12 : Thermometric titration VS Karl Fischer titration for water analyses.

Important Things	Thermometric Titration	Karl Fischer Titration
LOD and LOQ	Same as acid base titration but with biggest blank and the standard deviation of it. Obtained with curve	Depends not on the temperature and can be conditioned before analysis. More than 0.1 ml titrant used and the tolerance of dosino is 20 µl.
Precision See Table 11	Worse than Potentiometric titration	Better than Thermometric titration
Minimal number of titration	2 (to have the curve for the blank)	1
Theory VS Practice	Assessment of Heat and Material Difficult to have all parameters	See Theoretical part 1.2 Relatively easy to have all parameters
Reagent	Stable when no H^+ in solution	React with Water
Strong acid	Cause no problems	pH has been adjusted (sample preparation)
Reducing agent	Cause no problems	Titration not possible
Aldehyde and ketone	Cause no problems	Special reagent necessary

In the end the titration are made with, as titrant, a solution of $\sim 1.3\text{M}$ iso propanol in MTBE dry. The vessel and the installation are prepared before analysis to be water free and in an amorphous atmosphere. Then 40 ml of MTBE dry is added in the vessel rinsed with N_2 . The sample is prepared in syringe and directly injected in the vessel before the start.

The result obtained for Methyl magnesium bromide in diethyl ether $\sim 3\text{M}$ is with thermometric method 2.815 ± 0.055 [mol/l] with 5 analyses and the same Grignard treated with the colorimetric method in [A8] give the result 2.845 ± 0.000 [mol/l] with 3 analyses. So test T gives that the average of these two results are the same. But the test F gives that the two distributions are not the same.

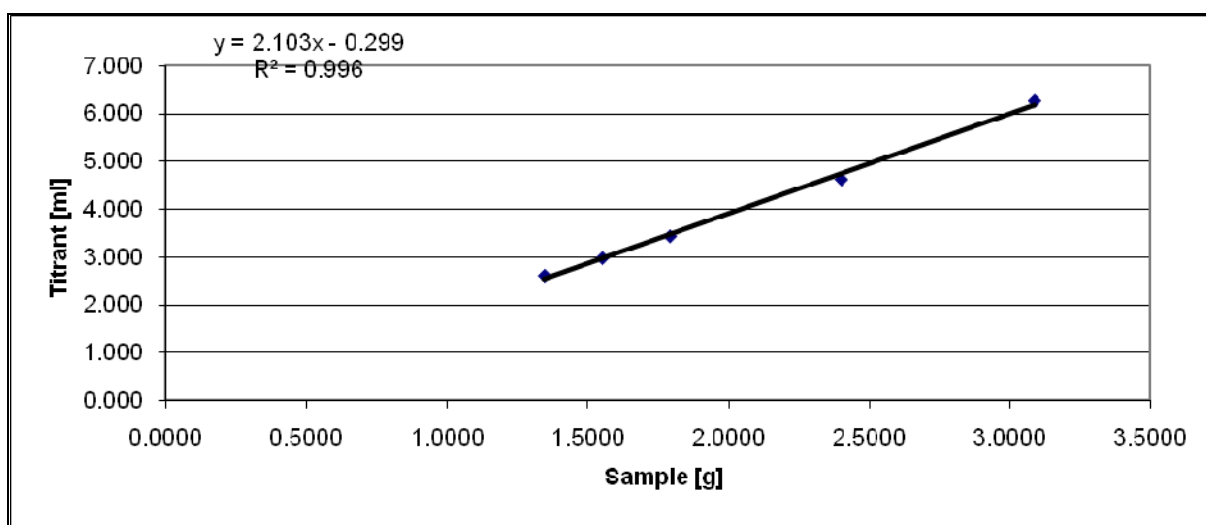


Figure 26 : Visualization of the results found in thermometric titration for Methyl magnesium bromide in diethyl ether $\sim 3\text{M}$

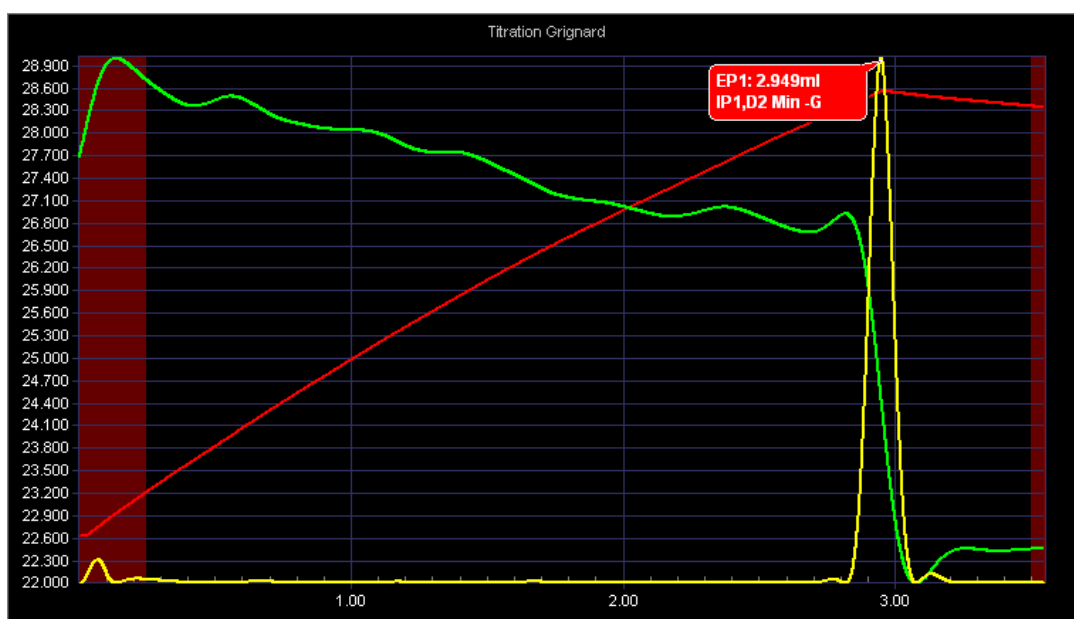


Figure 27 : Thermogram of titration of Grignard reagent.

Determination of Grignard cause many problems:

- Solvent THF and other organic solvents cannot be used because the silicone of the thermoprobe reacts with it.
- The N_2 cannot be added during analysis but only used for preparation of the vessel.
- Grignard reacts very strongly with air
- Boiling and evaporation of the solvent in the titrant.

Table 13 : Thermometric titration VS Colorimetric analysis.

Important Things	Thermometric Titration	Colorimetric Titration
Precision See above	Worse than Colorimetric titration	Better than Thermometric titration
Minimal number of titration	2 (to have the curve for the blank)	1
Analysis preparation	Titrant must be freshly made (evaporation of MTBE or iso propanol) Automation possible	Vial drying Grignard stays much time in syringe than in thermometric titration Automation not possible

Tests are made to see if adding ion Ag^+ as catalysis is better or not than MnSO_4 . The addition of AgNO_3 reduces the effect of the two first peaks but it gives no much better answer and it can react with other product titred by manganometric titration.

The effects of quantity of Mn^{2+} added are tested and the result gives for potentiometric titration a curve style polynomial order 2 and in thermometric too. See Figure 29. and Figure 30.

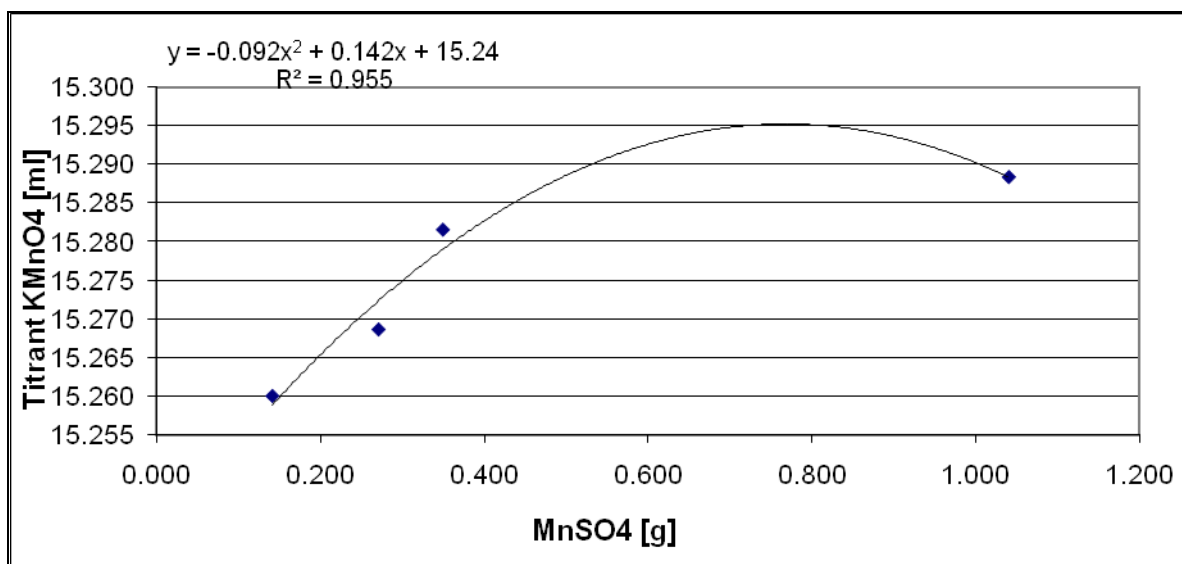


Figure 29 : Result of the effect of MnSO_4 addition on the potentiometric titration.

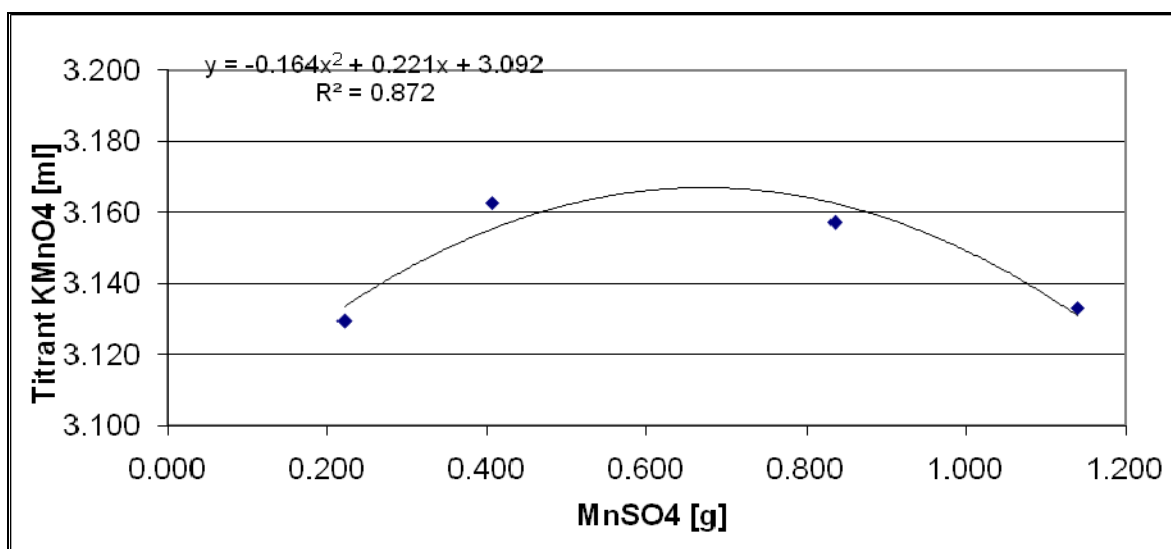
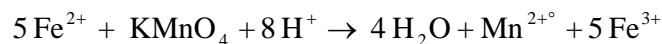


Figure 30 : Result of the effect of MnSO_4 addition on the thermometric titration.

Also as shown the oxalic acid sodium is a bad standard for the thermometric titration so three other reagents are tested as standard. And with them no addition of Mn^{2+} are made because the reaction past much faster than with oxalate acid sodium.

3.6.2 Titration of Fe^{2+}

The result obtained by taking Fe^{2+} as standard is good but the problem is that we don't have a certified substance of it. The product taken for this thermometric analysis is the ammonium iron sulfate hexahydrat.



Test is made to see if the Ag^+ works as catalysis agent but it reacts with the ammonium iron sulfate hexahydrat.

See the response of this analysis without addition of MnSO_4 in Figure 31.

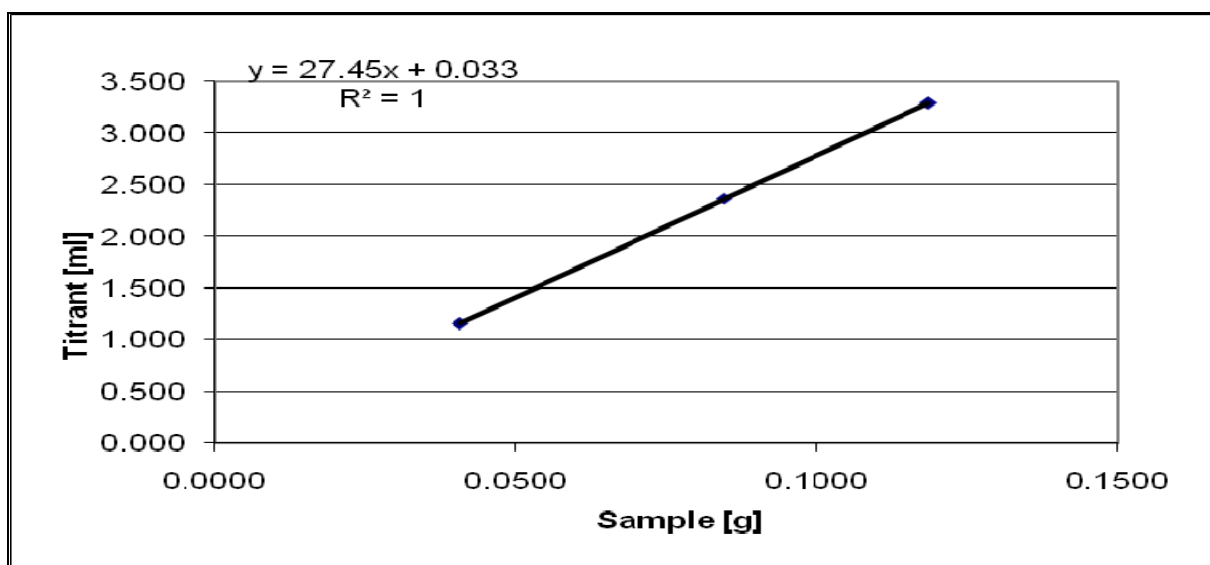


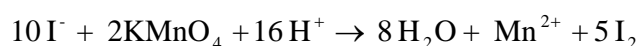
Figure 31 : Result of the analysis of Fe^{2+} without MnSO_4 addition on the thermometric titration.

The addition of MnSO_4 is not necessary because the reaction takes place without the two first peaks.

The result obtained for the titer of KMnO_4 calculated with the purity value of the bottle is 0.955 ± 0.001 .

3.6.3 Titration of KI

The result obtained by taking KI as standard is good but the problem is at end of this titration iodine in vessel are hard to wash.



Test is made to see if the Ag^+ works as catalysis agent but it reacts with Iodine ion.

See the response of this analysis without addition of MnSO_4 in Figure 32.

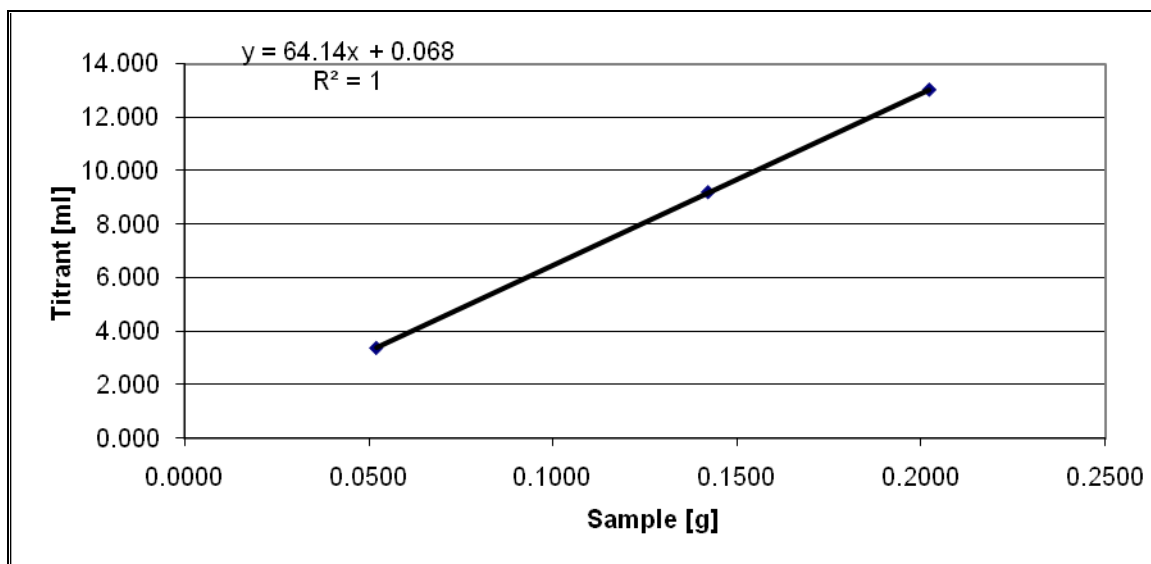
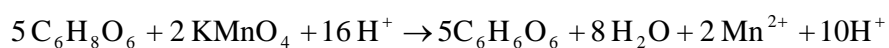


Figure 32 : Result of the analysis of KI without MnSO_4 addition on the thermometric titration.

The addition of MnSO_4 is not necessary because the reaction takes place without the two first peaks. The result obtained for the titer of KMnO_4 calculated with the purity value of the certificate found in [25] is 0.935 ± 0.002 .

3.6.4 Titration of Ascorbic acid

The result obtained with ascorbic acid as standard gives bad answer. The problem is the fact that after the titration the solution returns to a colorless solution.



Test is made to see if the Ag^+ works as catalysis agent but it have no detectable influence on the titration. See the response of this analysis without addition of MnSO_4 in Figure 33.

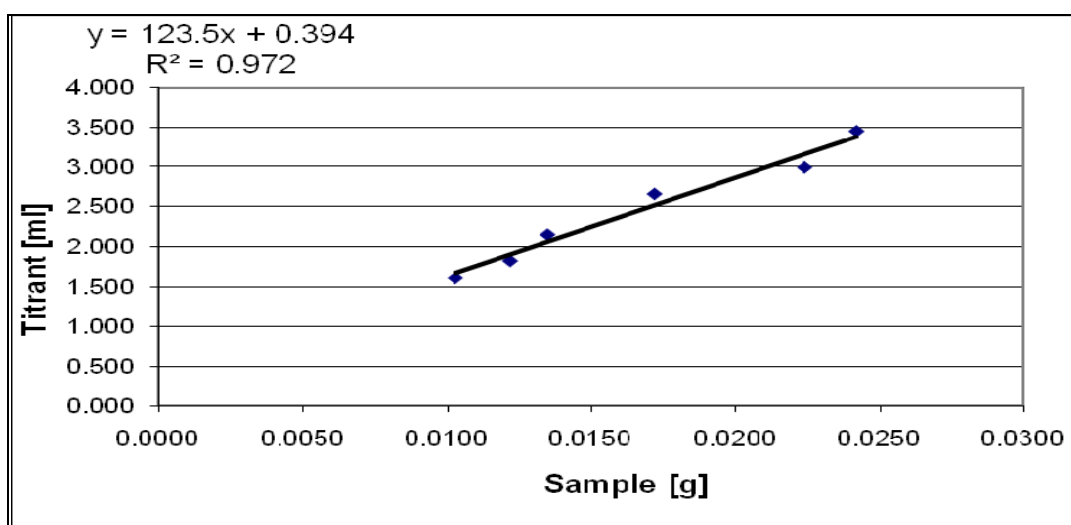


Figure 33 : Result of the analysis of Ascorbic acid without MnSO_4 addition on the thermometric titration.

The addition of MnSO_4 is not necessary because the reaction takes place without the two first peaks. The result obtained for the titer of KMnO_4 calculated with the purity value of the certificate is 0.842 ± 0.044 .

Test is to see if the result of titer is the same when the titration of the standard oxalic acid sodium added to ascorbic acid as catalysis has the same response. To see the thermotitration of these two compounds look at Figure 34.

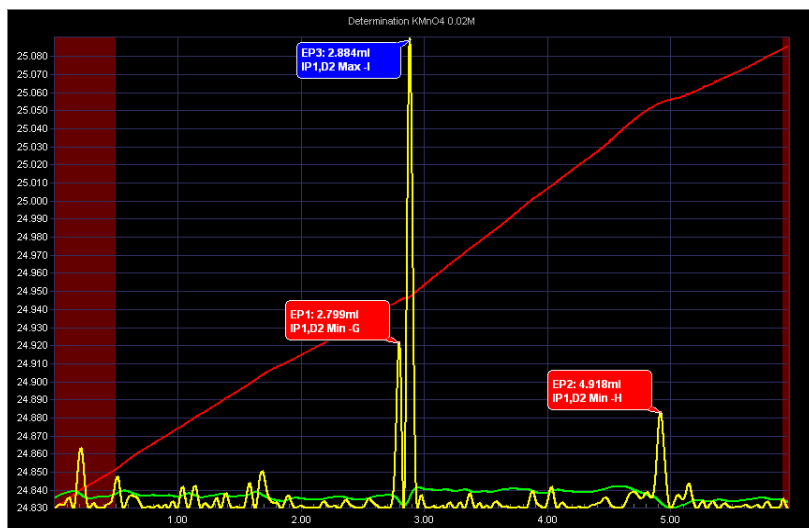


Figure 34 : Thermogram of a mix of Ascorbic acid and oxalic acid sodium titred by KMnO_4

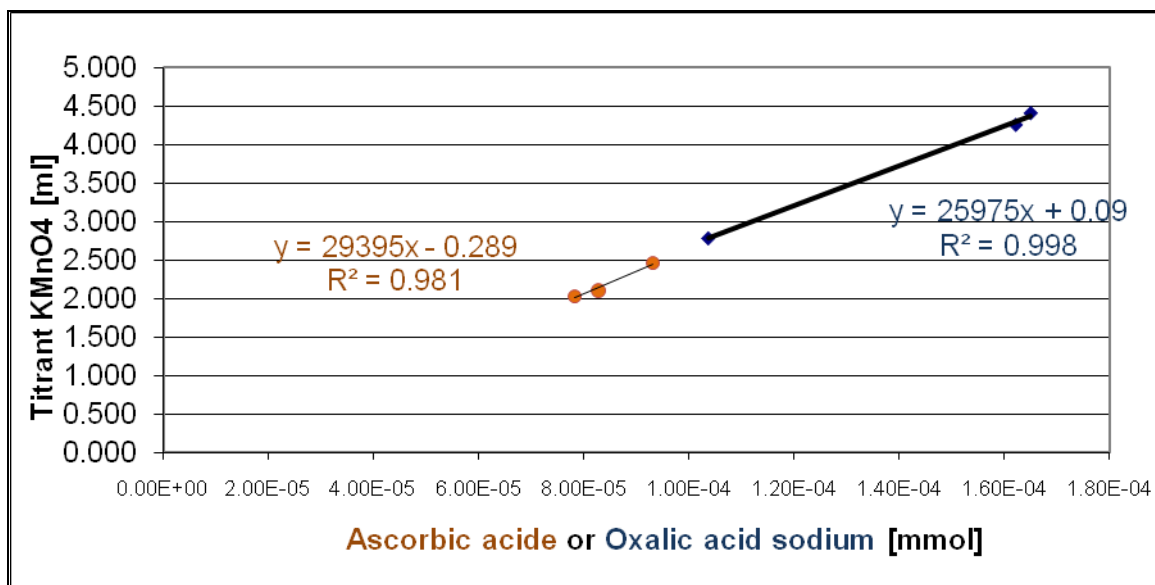


Figure 35 : Result of the analysis of Ascorbic acid and Oxalic acid sodium without MnSO_4 addition on the thermometric titration.

Also the two compounds give the same response for the titer of this solution, so for Ascorbic acid 0.735 ± 0.011 and for oxalic acid sodium 0.737 ± 0.011 .

Determination of KMnO_4 cause many problems:

- The standard used in potentiometric titration doesn't work in thermometric titration because it produces gas.
- The standard that could get in thermometric titration have no certificate of values
- Ag^+ as catalysis does not work for many titration

Table 14 : Thermometric titration VS potentiometric titration.

Important Things	Thermometric Titration	Potentiometric Titration
Precision See above	Worse than potentiometric titration	Better than Thermometric titration
Minimal number of titration	2 (to have the curve for the blank)	1
Standard	It is better when no gas is produced because it disturbed the analysis with a loss of heat.	Can produce gas

4 Conclusions

The important factors for a thermometric titration are all the following: the stirring, the addition [ml/min], the position of the burette, the filter factor of analysis, the quantity of titrant used and the temperature of the titrant and temperature of the sample solution. All these factors have an effect on the response of the titration. The minimal titration to have a result is two for thermometric titration because the blank of the analysis must be found. The thermometric acid-base titration is as precise as potentiometric dynamic acid-base titration and does not take more time.

For thermometric titration of the aldehyde and ketone the investigation must be pushed forward because the good titrant is not very easy to find in order to make a titration with no sample preparation.

The titration with NBS of ascorbic acid gives good results and it is interesting to make more experimentation with this titrant more concentrated.

The thermotitration of water has two big advantages over the Karl Fischer titration. There is the possibility to analyse a solution of concentrated acid without preparation of sample and the possibility to titer compounds which react with Iodine. But the big disadvantages are the conditioning of the sample solvent and the presence of a not negligible quantity of water in the titrant. All these parameters give also a big blank and in the same time a big error. The TEOF product is preferred as DMP because it makes an exothermic reaction more visible and it can be prepared with methansulfonic acid for a time of 8 hours. And as seen above to remove the blank problem, a device combined Karl Fischer and thermometric can be realized.

The Grignard titration by thermometric is a very good answer for the problem of determination of how many [mol/l] contain the concentrated solution. This method can be improved in an adapted inert area. The precision is a little better than colorimetric titration but it demands much preparation and can be automated.

The thermometric titration for manganometric gives result but the problem is caused by the standard, it is not a good standard for thermometric titration. So for example the Fe^{2+} gives some better answer and no Mn^{2+} is requested as catalyst for this analysis.

To conclude the Titrotherm 859 is a device with a big potential but not as replacement for all existing analyses but to complete the existing methods of titration for specific problems. This software can be improved with for example the possibility to stack two graphics or the possibility to have a cursor to follow the curve and detect manually the end point. The hardware is good but a temperature control in the titrant and the possibility to adjust it would be a great improvement, and in the same time the possibility to adjust the temperature of the vessel.

5 Bibliography

Polycopy- Course :

- [1] R. Ciccirelli, Cours de chimie analytique / Volumétrie / Filière chimie, HES-SO Valais Sion, (2007-2008)
- [2] F. Zonnevillle, Cours chimie générale / Filière chimie, HEVs Haute Ecole Valaisanne Sion, (2005-2006)
- [3] J. Besse, Thermodynamique Chimique / Filière chimie, HEVs Haute Ecole Valaisanne Sion, (2005-2006)
- [4] G. Boureau, Thermodynamique Chimique, Correspondance geb@ccr.jussieu.fr, (2004)

Book :

- [5] D. R. Lide, Handbook of chemistry and physics, 85^{ème} édition, CRC press, (2004-2005)
- [6] -, Guide labo/ le guide pratique du laboratoire de chimie / 4 chimie analytique, 3^{ème} édition, ELAR-FR école d'ingénieurs et d'architectes de Fribourg, (2001)
- [7] Tomas S., Monograph / Practical thermometric titrimetry, Metrohm Ltd., (2006)
- [8] -, Titrotherm 859 / Thermometrischer titrator- die ideale Ergänzung zur potentiometrischen Titration, Metrohm Ltd., (2007)
- [9] -, Titrotherm 859 / Installation instruction, Metrohm Ltd., (2006)
- [10] L. Gros, Practical titration / Training Manual for titrimetric volumetric analysis, Metrohm Ltd. (2005)
- [11] -, AQUASTAR / Karl Fischer titration basics, EMD Chemikals Inc., (-)
- [12] R. Kaiser, Quantitative Bestimmung Organischer Funktioneller Gruppen / Methoden der analyse in der chemie band 4, Akademische Verlagsgesellschaft Frankfurt am Main, (1966)
- [13] S. Veibel, Analytik Organischer Verbindungen, Akademie-Verlag-Merlin, (1960)
- [14] E. Scholz, Karl Fischer Titration / Determination of water, Springer-Verlag Berlin, (1984)
- [15] N.K. Mathur and C.K. Narang, The determination of organic compounds with N-Bromosuccinimide and allied reagents, Academic press London, (1975)

Publications :

- [16] Fadhil M.Najib & Sadir Z. & Ahmad M. Abdulla, Talanta Vol. 71, A new sensor for thermometric titrations, p. 141-148, (2007)
- [17] G. Burgot & J.-L. Burgot, Journal of pharmaceutical and biomedical analysis Vol. 30, Protometric thermometric titration of sparingly soluble compounds in water in the presence of *n*-octanol, p. 625-634, (2002)
- [18] J.-L. Burgot & al., Thermochimica acta Vol. 424, Thermodynamic investigation of the water/*n*-octanol partition coefficient value of a 5-formyl-1,2-dithiole-3-thione, p. 143-147, (2004)
- [19] B. F. Abramovic & al., Journal of AOAC International Vol. 81, Expert system for catalytic titrimetry – part 2 determinations of monobasic carboxylic acids, p. 1077-1087, (1998)
- [20] T. K. Smith, Journal of the American oil chemists' society Vol. 80, analysis of FFA in edible oils by catalyzed end-point thermometric titrimetry (CETT), p.21-24, (2003)
- [21] K.Basavaiah, B.C. Somashekar and V.Ramakrishna, Acta pharm. Vol. 57, Rapid titrimetric and spectrophotometric methods for salbutamol sulfat in pharmaceuticals using N-Bromosuccinimide, p. 87-98 (2007)

Internet :

- [22] Encyclopédie anglaise et française, <http://en.wikipedia.org> & <http://fr.wikipedia.org> (01.04.2008)
- [23] Site de l'entreprise Metrohm, <http://www.metrohm.com/> (01.04.2008)
- [24] Site de recherche de réactif, <http://chemexper.com> (13.05.2008)
- [25] Site de recherche de certificat d'analyse, <http://www.sigmaaldrich.com> (10.11.2008) & <http://fr.vwr.com> (10.11.2008)

6 Annexes

- [A1]** Technical data on the device provided by Metrohm [5]
- [A2]** Method “start” obtained on [23].
- [A3]** Factorial designs result.
- [A4]** Thermogram effect of filter factor
- [A5]** Sheet of determination of titer NaOH
- [A6]** Method of potentiometric determination of $\text{Na}_2\text{S}_2\text{O}_3$ 0.1M titer
- [A7]** Method of Karle Fischer titration.
- [A8]** Method to determine the molarities of a Grignard reagent.
- [A9]** Method of potentiometric determination of KMnO_4 0.02M titer
- [A10]** Presentation of thermometric reaction
- [A11]** Effect of Volume on the thermogram
- [A12]** Software explanations

Signature:

Julien Fardel

[A1] Technical data on the device provided by Metrohm [5]

In this section you will find the most important technical datas of the Ti-trotherm Interface, a list of standard and optional accessories and the warranty and conformity declarations.

3.1 Technical data

Provided that nothing to the contrary is mentioned, the published values are typical technical data.

3.1.1 Interfaces

Measuring Interface NTC 10 kOhm

<i>Measuring range</i>	-10 ... +50 °C
<i>Resolution</i>	0.00001 °C
<i>Measuring cycle</i>	20 ms at 50Hz mains frequency 16.67 ms at 60Hz mains frequency
<i>Measuring uncertainty</i>	± 0.1 °C

USB connections

<i>USB ports</i>	2 USB downstream ports (type A sockets), 500 mA each, for connection of other Titrotherm Interfaces or peripheral devices such as printer
------------------	---

Controller connection

<i>Controller port</i>	USB upstream port with additional signals (mini DIN socket) for the connection of computer to control the instrument.
<i>Computer connection</i>	With 6.2151.000 Cable

MSB connections (MSB = Metrohm Serial Bus)

<i>Dosing device</i>	Connection of max. 4 external dosing drives (Dosino, MSB 1 to MSB 4)
<i>Stirrer</i>	Connection of max. 4 stirrers Stirrer control: on/off; manual or coordinated with the method run. 15 steps for speed and direction of rotation selectable.

3.1.2 Mains connection

<i>Voltage</i>	100...240 V (± 10%)
<i>Frequency</i>	50...60 Hz
<i>Power consumption</i>	45 W
<i>Fuses</i>	electronic overload protection

3.1.3 Safety specifications

<i>Construction and testing</i>	According to EN/IEC/UL 61010-1, CSA 22.2 No. 61010-1 protection class 1
<i>Safety information</i>	The Installation Instructions contain safety information that must be observed by the user in order to ensure the safe operation of the instrument.

3.1.4 Electromagnetic compatibility (EMC)

<i>Emission</i>	Standards complied with : - EN/IEC 61326 - EN 55022 / CISPR 22
<i>Immunity</i>	Standards complied with : - EN/IEC 61326 - EN/IEC 61000-4-2 - EN/IEC 61000-4-3 - EN/IEC 61000-4-4 - EN/IEC 61000-4-5 - EN/IEC 61000-4-6 - EN/IEC 61000-4-11 - EN/IEC 61000-4-14

3.1.5 Ambient temperature

<i>Nominal working range</i>	+5 °C...+45 °C (at max. 85% rel. humidity)
<i>Storage</i>	-20 °C...+60 °C
<i>Transport</i>	-40 °C...+60 °C

3.1.6 Reference conditions

<i>Ambient temperature</i>	+25 °C (± 3 °C)
<i>Rel. humidity</i>	$\leq 60\%$
<i>Warmed-up condition</i>	Instrument in operation for at least 30 min
<i>Validity of data</i>	After adjustment

3.1.7 Dimensions

<i>Housing material</i>	Metal housing, surface-treated
<i>Width</i>	142 mm
<i>Height</i>	64 mm
<i>Depth</i>	231 mm

[A2] Method "start" obtained on [23].



Thermo. Titr. Application Note No. H-016

Title: Determination of Acetic, Phosphoric and Nitric Acid Mixtures

Scope: Determination of mixtures of phosphoric, nitric and acetic acids used in etching of aluminium in the manufacture of semi-conductor devices.

Principle: Titration with standard NaOH to obtain three endpoints

Endpoint 1	Endpoint 2	Endpoint 3
HNO ₃ (fully dissociated)	HOAc (pKa = 4.75)	
H ₃ PO ₄ (pKa ₁ = 2.12)	H ₃ PO ₄ (pKa ₂ = 7.21)	H ₃ PO ₄ (pKa ₃ = 12.36)

Reagents: 2 mol/L NaOH (standardized)
NaCl solution, saturated (approximately 35% w/v)

Method: Basic Experimental Parameters:

Data rate (per second)	10
Titration delivery rate (mL/min.)	2
No. of exothermic endpoints	3
Data smoothing factor	60

Procedure: Approximately 10mL deionized water and 15mL saturated NaCl solution is dispensed into a titration vessel. The vessel is then tared or weighed on a balance reading to 0.1mg. Approximately 0.5mL of concentrated acid is then rapidly dispensed into the vessel, and then re-weighed. The mass of dispensed acid is entered into the software. For assays of dilute solutions, an aliquot up to 10mL can replace all or part of the deionized water content of the beaker. Alternatively, approximately 4mL of concentrated acid mixture is weighed into a beaker, and transferred with deionized water to a 200mL volumetric flask containing 120mL saturated NaCl solution. The flask is made to volume with deionized water. 25mL aliquots are taken for titration. The solution is titrated with standardized 2M NaOH to obtain 3 exothermic endpoints.

Results:**1. Titres (sample mass \equiv 0.7444g each titration)**

Endpoint 1	Endpoint 2	Endpoint 3
2.559 \pm 0.006 mL	5.720 \pm 0.004 mL	8.115 \pm 0.004 mL

2. Acidic Components

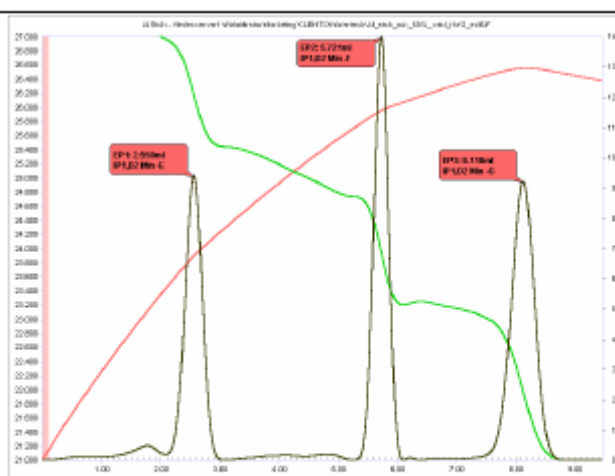
%w/w H_3PO_4	%w/w HNO_3	%w/w CH_3COOH
63.07 \pm 0.10	2.44 \pm 0.14	12.34 \pm 0.08

Calculation:

$$H_3PO_4 \%w/w = \frac{((EP3 - EP2) \times M NaOH \times FW H_3PO_4 \times 100)}{(\text{sample mass, g} \times 1000)}$$

$$HNO_3 \%w/w = \frac{(((EP1 - \text{Blank}) - (EP3 - EP2)) \times M NaOH \times FW HNO_3 \times 100)}{(\text{sample mass, g} \times 1000)}$$

$$HOAc \%w/w = \frac{(((EP2 - EP1) - (EP3 - EP2)) \times M NaOH \times FW HOAc \times 100)}{(\text{sample mass, g} \times 1000)}$$

Thermometric Titration Plot:**Legend:**

Red = solution temperature curve

Green = first derivative curve

Black = second derivative curve

[A3] Factorial designs result.

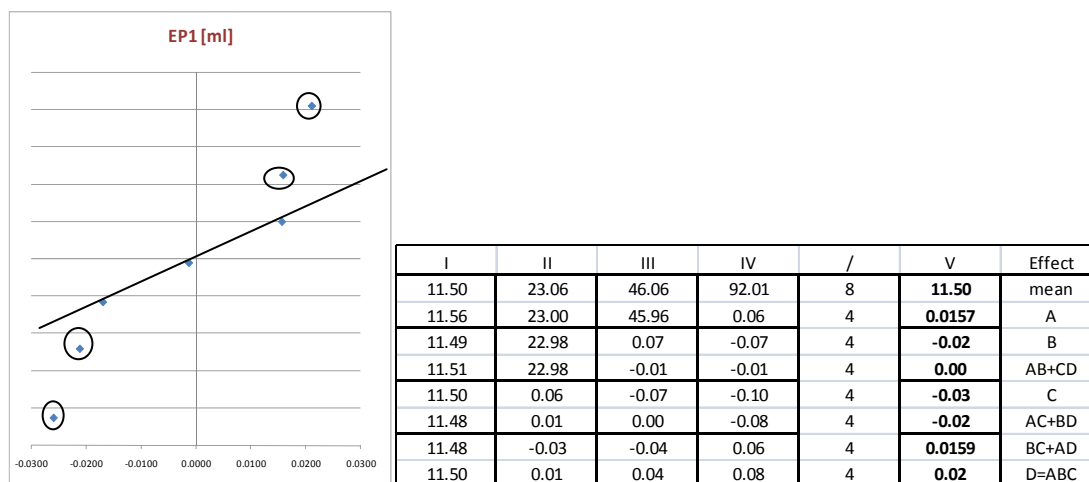


Figure 36 : Visualisation of the result of factorial designs with as response the titrant [ml] for EP1

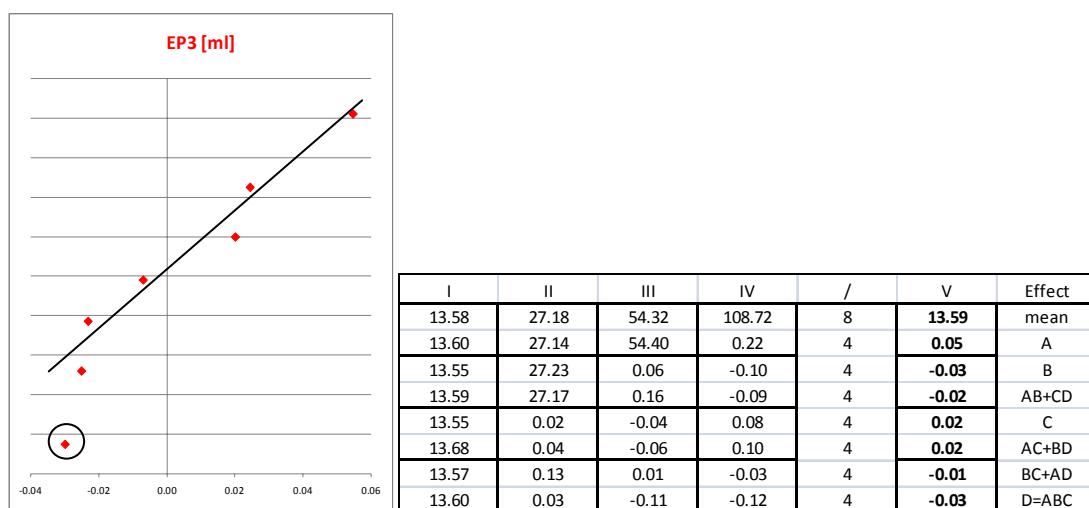


Figure 37 : Visualisation of the result of factorial designs with as response the titrant [ml] for EP3

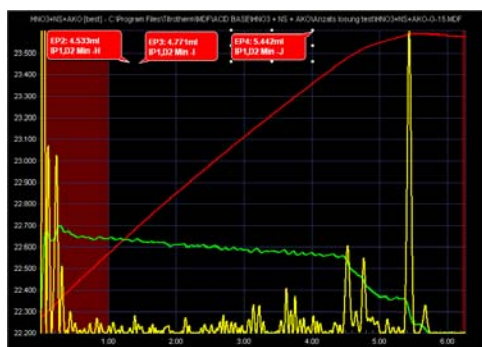
[A4] Thermogram effect of filter factorAnalysis of 0.8679[g] solutions "Ansatz Lösung" + 0.0149[g] NH_4NO_3 

Figure 38 : thermogram Filter factor 30



Figure 41 : thermogram Filter factor 60

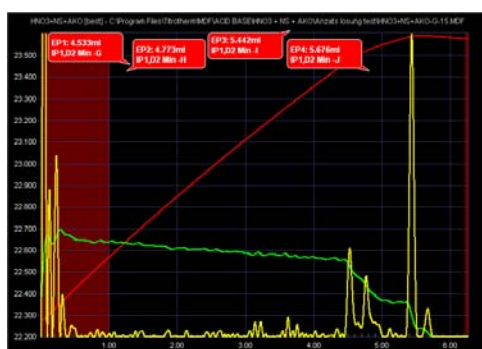


Figure 39 : thermogram Filter factor 40

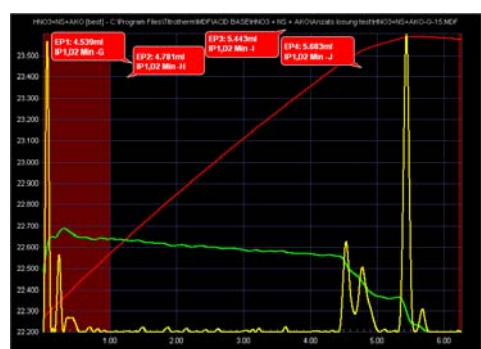


Figure 42 : thermogram Filter factor 70



Figure 40 : thermogram Filter factor 50

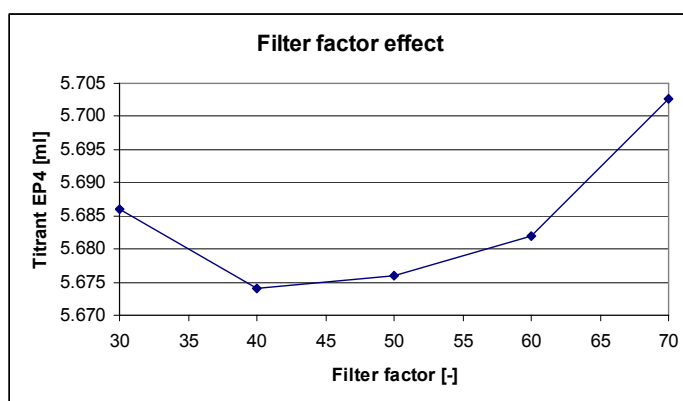


Figure 43 : Effect of filter factor on volume for titrated EP4

The best filter factor is found as seen above in the chapter 1.4.1

[A5] Sheet of determination of titer NaOH

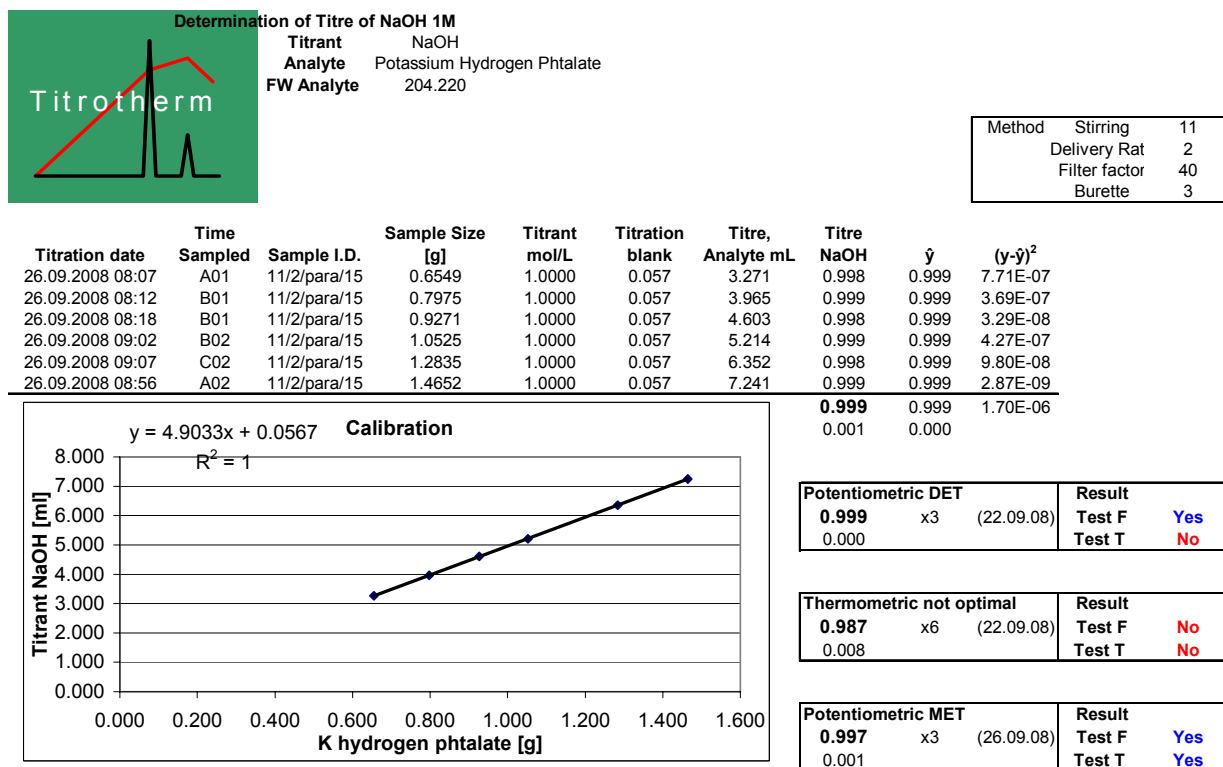


Figure 44 : Results of determination of NaOH 1M titer with optimization method

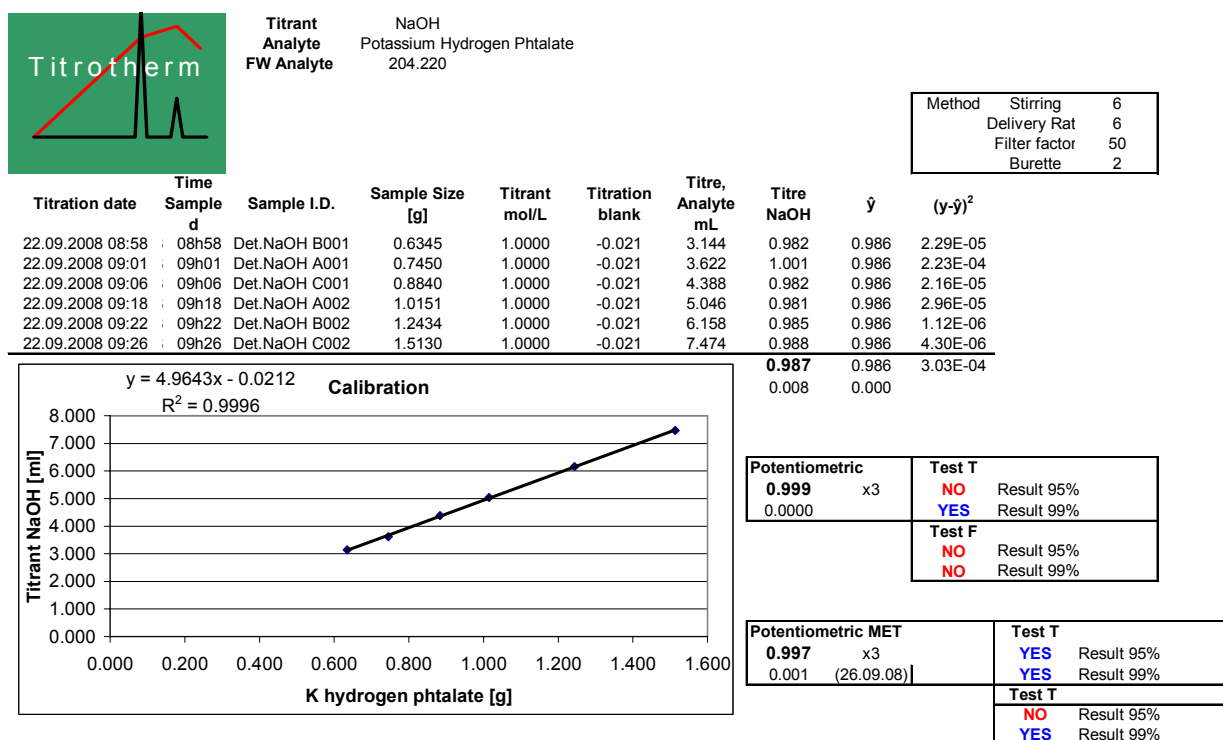


Figure 45 : Results of determination of NaOH 1M titer with method found in Annex [A3]

[A6] Method of potentiometric determination of $\text{Na}_2\text{S}_2\text{O}_3$ 0.1M titer

Titrant: $\text{Na}_2\text{S}_2\text{O}_3$ 0.1M

Sample weight precisely 80-105 [mg] of KIO_3 / Add 5 [ml] of HCl ~32% / Add 1 [g] KI

DET U Parameters:

- | | |
|-------------------------------------|------------------------------|
| - Electrode of platinum | - Pause 35 [s] |
| - Reference Ag/AgCl | - Input 1 |
| - EP Potentiometric determination | - Temperature 25.0 [°C] |
| - Density measure 4 | - Stop Volume 30 [ml] |
| - Min. Increment 10.0 [μl] | - Stop pH Off |
| - Delivery rate max [ml/min] | - Stop EP 9 |
| - Measurement Drift 30 [mV/min] | - Filling speed max [ml/min] |
| - Waiting 32[s] | - Statistic On |
| - Start Volume Off | - EP-Criteria 5 |
| - Dose speed max [ml/min] | - EP-Anchored all |

Calculation:

Titer $\text{Na}_2\text{S}_2\text{O}_3 = (60 * \text{Purity of } \text{KIO}_3 [\%] * \text{weight sample [g]}) / (\text{EP[ml]} * \text{Titer solution } \text{Na}_2\text{S}_2\text{O}_3[\text{mol/l}] * 214.00[\text{g/mol}])$

[A7] Method of Karle Fischer titration.

Titrant: Hydranal composite 5.00

Sample: with weight precisely a volume of ~2 ml of sample in a syringe.

Parameters:

- | | |
|----------------------------------|-------------------------------------|
| - Electrode Karle Fischer | - Temperature 25.0 [°C] |
| - Pause 0 [s] | - Time interval measurement 2.0 [s] |
| - Start Volume 0 [ml] | - Stop Volume 100.00 [ml] |
| - EP up to 250.0 [mV] | - Filling speed max [ml/min] |
| - Delivery rate optimal [ml/min] | - Condition On |
| - Stop criteria Drift | - Drift correction automatic |
| - Stop drift 30 [μl/min] | |
| - Extraction time 60 [s] | |

Calculation:

Water [%] = 0.1 * Titer titrant / 10 / Sample weight

[A8] Method to determine the molarities of a Grignard reagent.

Reagents:

- Nitrogen
- Xylol water free
- 2-Butanol Water free
- Molecular sieve
- 2,2'Biquinoline

Solution:

Prepare a solution 1 M of 2-Butanol in Xylol then 12 h to molecular sieve.

Preparation of sample:

Free the vial for headspace GC chromatography from water and rinse it to Nitrogen during 5 [min].

Weighting 5-10 [mg] of 2,2'Biquinoline in the vial add a magnets stirrer and close it

Pierce the septum with two syringe needles and rinse with Nitrogen during 5 [min] too.

Add precisely in vial 0.700 [ml] of the solution 1 M of 2-Butanol in Xylol

Complete a 1.00 [ml] syringe of Grignard reagents, previously rinsed with Nitrogen.

Then titer with agitation until the color change for white milk to brown.

Calculate:

$$C_{\text{Titrant}} = \frac{10 * m}{FW}$$

C_{Titrant} = Concentration of titrant 2-Butanol in Xylol [mol/l]

10 = Factor

m = masse weigh of 2- Butanol [g]

FW = Molare masse of 2-Butanol, 74.12 [g/mol]

$$C_{\text{Grignard}} = \frac{C_{\text{Titrant}} * V_{\text{Titrant}}}{V_{\text{Grignard}}}$$

C_{Grignard} = concentration of Grignard solution [mol/l]

V_{Titrant} = volume of solution in vial [ml]

V_{Grignard} = volume of Grignard used to color change [ml]

[A9] Method of potentiometric determination of KMnO_4 0.02M titer

Titrant: KMnO_4 0.02M

Sample: weight precisely 95-110 [mg] of Oxalic acid Sodium / Add 10 [ml] of H_2SO_4 ~20% / Add 0.5 [g] $\text{MnSO}_4 \cdot \text{H}_2\text{O}$ / Add to 60 [ml] with H_2O dest.

DET U Parameters:

- | | |
|-----------------------------------|------------------------------|
| - Electrode of platinum | - Pause 60 [s] |
| - Reference Ag/AgCl | - Input 1 |
| - EP determination Potentiometric | - Temperature 25.0 [°C] |
| - Density measure 4 | - Stop Volume 20 [ml] |
| - Min. Increment 10.0 [μl] | - Stop pH Off |
| - Delivery rate max [ml/min] | - Stop EP 9 |
| - Measurement Drift 30 [mV/min] | - Filling speed max [ml/min] |
| - Waiting 32[s] | - Statistic On |
| - Start Volume 14.00 [ml] | - EP-Criteria 5 |
| - Dose speed max [ml/min] | - EP-Anchored Greatest |

Calculation:

Titer $\text{KMnO}_4 = (2 * \text{Purity of Oxalic acid Sodium } [\%] * \text{weight sample } [\text{g}] * 1000) / (\text{EP}[\text{ml}] * \text{Titer solution } \text{KMnO}_4[\text{mol/l}] * 134.00[\text{g/mol}] * 5)$

[A10] Presentation of thermometric reaction (the ΔH is in absolute value)

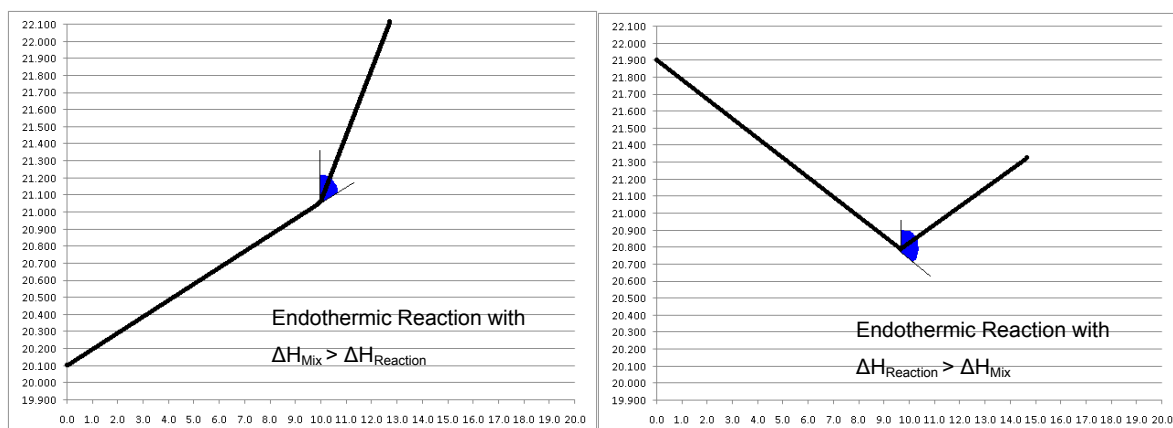


Figure 46 : Thermogram of endothermic reactions, in X axis Titrant [ml] and in Y axis Temperature [°C]

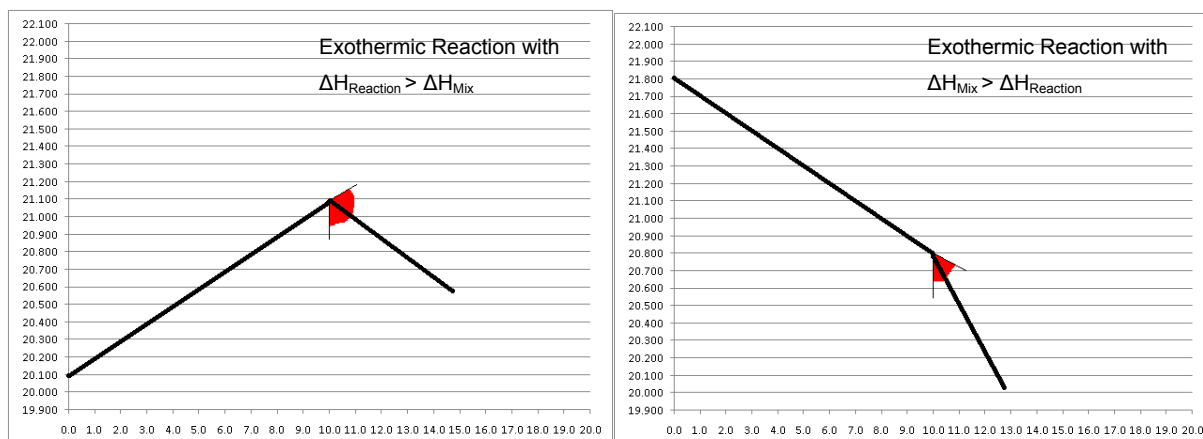


Figure 47 : Thermogram of exothermic reactions, in X axis Titrant [ml] and in Y axis Temperature [°C]

In Figure 46 and Figure 47 the parts of Circle colored are the other possibility to have the same type of reaction.

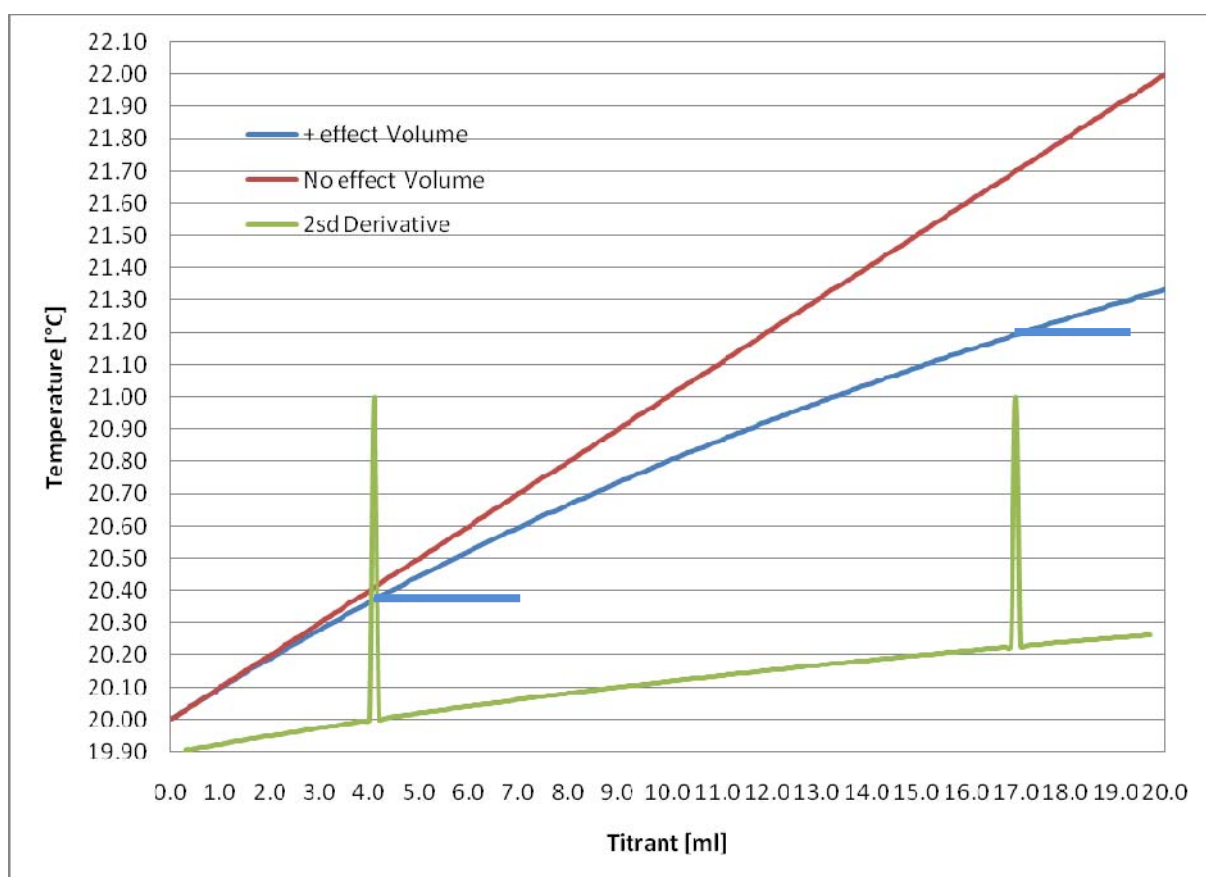
[A11] Effect of Volume on the thermogram

Figure 48 : Thermogram With or Without effect of volume increase. With two examples of endpoint with their second derivative.

Conditions to make this curve in Table 15

Table 15 : Value exploited for make the Figure 48.

Parameters	Value
Sample start [g]	40
Solution H ₂ O Cp [J/(g·K)]	4.184
Density of all solutions [kg/l]	1.00
Q [Eq. 14] [J]	16.736
Titrant Temperature [°C]	20.000
Slope Temp./Volume [°C/ml]	0.1
Start Temperature [°C]	20.000

[A12] Software explanations

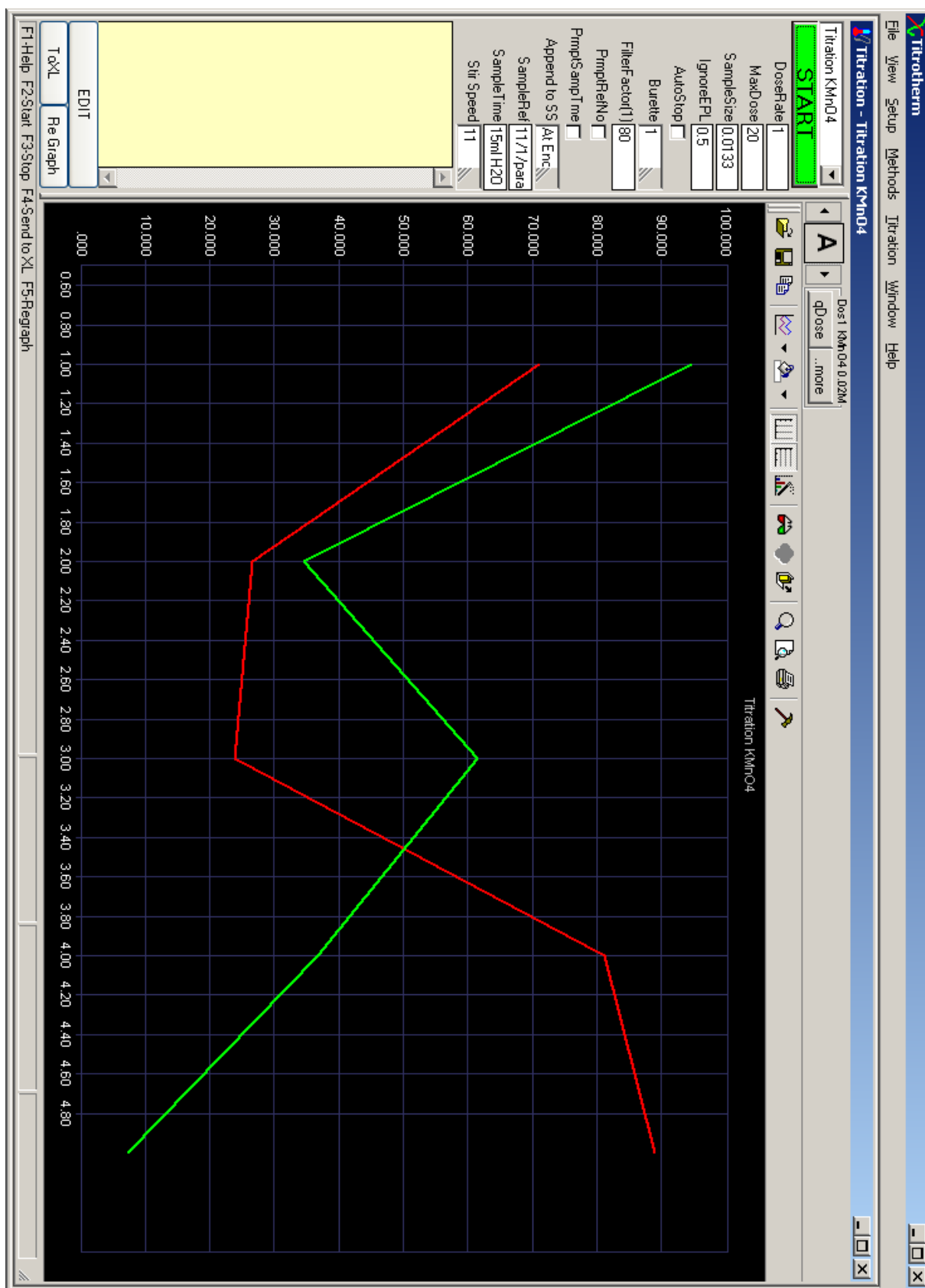


Figure 49: First page of software Titrotherm.

The figure displays four screenshots of the 'Edit Method 230, Titration KMnO4' dialog box in the Titrotherm software, showing different tabs: Setup, Inputs, End Points, and Results.

Setup Tab: Method name: Titration KMnO4. Titrant: KMnO4 0.02M (0.1N). Mol/L: 0.02. XCol: E. Blank (mL): 0. F. Quick List: ☒ Stir Speed, ☒ Dose rate, ☒ Sample size, ☒ Maximum dose, ☒ Burette number. Chained method: No Chained Method. Start Sequence: START (green button), Pre-Dose + Back-Titration Setup, Delay(s): 30, RUN (green button). Pre-Dose + Back-Titration Setup: Add PreDose, Remove PreDose.

End Points Tab: Quick List: ☒ Ignore endpoints left 0.5. Stop When: Direct > 0.5, 1stD <, 2ndD. Run On For: 0.5 ml. Quick List: ☒ QuickList AutoStop, ☐ Enable. Sort EP's in order of appearance: ☐. Buttons: Delete, New End Point. Table:

EP1	Input	EP On	Peak type	%Height	XL column	Output
1		Second Derivative	Min	10	G	mL

Inputs Tab: Select Input: 1. Add Input, Remove Input. Plot Data: ☒ Min Deriv for Full Scale, ☒ Deriv 1, ☒ Deriv 2. Quick List: ☒ Graph raw data, ☒ Graph 1st deriv, ☒ Graph 2nd deriv, ☒ Peak accent. Filter factor: 80. Real time filter: ☐. Damping left: 0.1. Filter Raw Data: ☐.

Results Tab: Template: C:\Program Files\Titrotherm\Templates\w-KMnO4_EP_Single_. Worksheet: TitrationKMnO4-D. MDF: TitrationKMnO4-D. ☒ Auto Save MDF when titration stops. User field: ☐. Analyst name: Julien Fardel. Job ref. #: ☐. Quick List: ☒ Sample ref. # 11/1/para/3, ☒ Prompt for ref no., ☒ Sample time 15ml H2O et, ☒ Prompt for sample time, ☒ Append to worksheet. Start row: 11. Titration date: A. Sample ref. #: C. Time sampled: B. Total titre: ☐. Last data point: ☐. Spreadsheet: No Locking. Max Workbooks Open: 10. Password Protect: ☐.

Figure 50 : Method creator of the Software Titrotherm.

All results are given in an excel file and this excel file must be created before beginning of the method.