Non Aqueous Titration

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NONAQUEOUS ACID–BASE TITRATION.

Titration in water solutions is limited by factors:

- **It is impossible** to titrate for a mix of acids or the bases
- **It is impossible** to titrate for a mix of strong and weak acids (bases)
- **It is impossible** to titrate separately for a mix of acids (bases) with near constants of dissociation
- **It is impossible** to define substances which are insoluble in water.

Non- aqueous titrations have the following advantages

- Organic acids and bases that are insoluble in water are soluble in non- aqueous solvent.
- A non-aqueous solvent may help two are more acids in mixture. The individual acid can give separate end point in different solvent.
- Enlargement of solubility range: many substances that are not soluble in water can be easily titrated in water-free media (e.g. fats and oils) Enlargement of application range: weak bases and acids can be easily
- titrated
- Substance compositions that cannot be separately determined in aqueous media can often be titrated in non-aqueous media
- Non-aqueous solvents are useful for the titration of very weak acids or bases that cannot be titrated in water
- Non aqueous titrations are simple and accurate, examples of non aqueous titration are :
- Ephedrine preparations, codeine phosphate in APC, tetracycline, teramycin, Anti- histamines and various piprazine preparations.

Non- aqueous solvents and its types:

Solvent which are used in non aqueous titration are called non aqueous solvent.

They are following types:-

1. Aprotic Solvent
2. Protogenic Solvent
3. Protophillic Solvent
4. Amphiprotic Solvent

1. Aprotic Solvent :

   Aprotic solvent are most important solvent in this titration. This solvent are chemically inert and they work as a catalyst. Like this solvent are increase the rate of speed in reaction and also decrease the rate of speed in reaction during the chemical process or reaction it will depend on condition. Neither acidic nor basic (inert solvent),

   The most important examples of aprotic solvent are chloroform and benzene.
2. Protogenic Solvent

   Protogenic solvent are acidic in nature. And they can donate the proton, and they enhance the strength of weak bases. Examples of Protogenic solvent are hydrochloric acid and sulphuric acid.
3. Protophillic Solvent

   Protophillic solvent are basic in nature. Which possess a high affinity for proton.

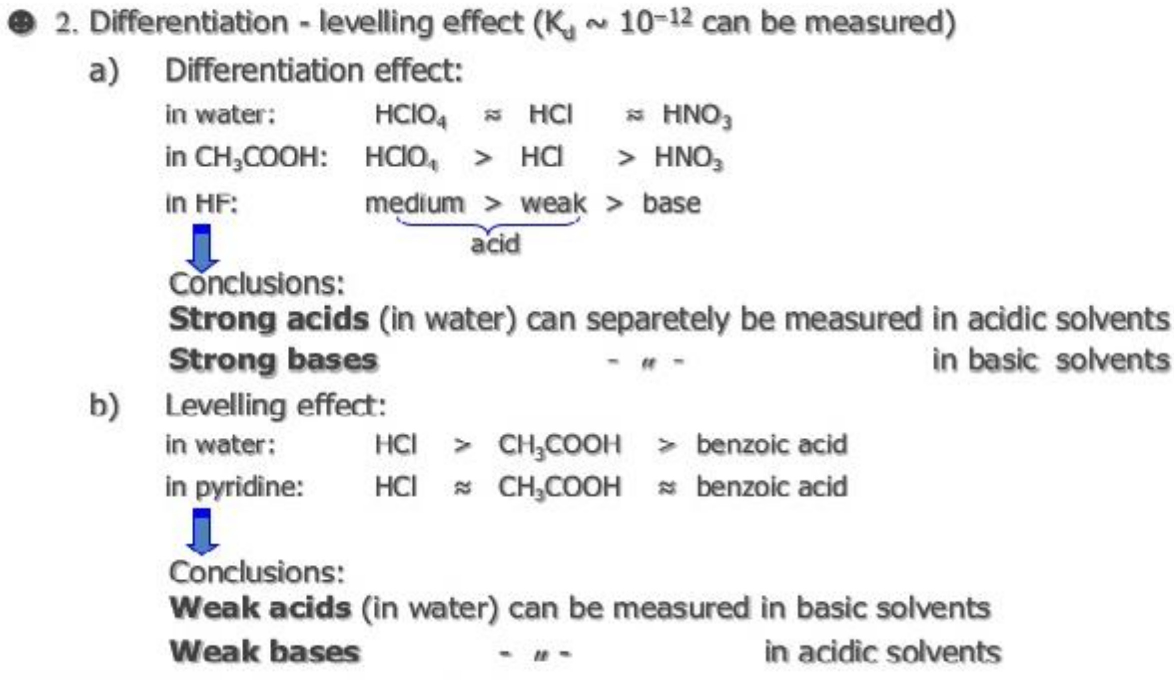
   Examples:-Liquid ammonia, amines and ketone.
4. Amphiprotic Solvent

   Amphiprotic solvent are those solvent they work as a both mean Protogenic or Protophillic. It means Amphiprotic solvent are acidic and basic in nature. And they are accept the proton and donate For examples:- Water, Alcohols and weak organic acids

Levelling effect, levelling & differentiating solvents

- The apparent strength of a protonic acid is dependent on the solvent in which the acid is dissolved.
- When all the acids in the acid chart which are stronger than H_3O^+ ion (i.e., the acids above H_3O+ acids) are added to H_2O, they donate as proton to H_2O to H_3O+ ion and appear to have equal strength, since all these acids are levelled to the strength of H3O+ ion which is left in solution and is common to all such solutions.
- This phenomenon viz. The strength of all the acids becomes equal to that of H_3O^+ ion is called leveling effect of the solvent, water, and here water is called a leveling solvent for all these acids.
- In aqueous solution all very strong bases like Na^+H^-, $Na^+NH_2^-$, $Na^+OC_2H_5^-$ are levelled to the strength of OH^- ion, for they react completely with H_2O to produce OH^- ions.
- The solvent in which complete proton-transfer occurs are called levelling solvents.
- In other words, the solvent in which the solute is ~100% ionised, are called levelling solvents.

- Since HF and HCl both are ~ 100% ionised in liquid NH_3 to give ~100% NH_4^+ ions, these appear to be of equal strength and liq. NH_3 acts as a levelling solvent for HF and HCl. In H_2O, HF is only partially ionised, whereas HCl and HBr are ~ 100% ionised.
- Thus H_2O is a differentiating solvent for HF, but for HCl and HBr it is a leveling solvent. Several mineral acids are partially ionised in glacial CH_3COOH medium because CH_3COOH is a poor proton-acceptor but rather a better proton donor. CH_3COOH, therefore, acts as a differentiating solvent towards the mineral acids. But, for bases, CH_3COOH act as a leveling solvent.



● 2. Differentiation - levelling effect (K_d ~ 10^{-12} can be measured)

a) Differentiation effect:

in water: $HClO_4 \approx HCl \approx HNO_3$

in CH_3COOH: $HClO_4 > HCl > HNO_3$

in HF: $\underbrace{\text{medium} > \text{weak}}_{\text{acid}} > \text{base}$

Conclusions:

Strong acids (in water) can separetely be measured in acidic solvents

Strong bases - " - in basic solvents

b) Levelling effect:

in water: $HCl > CH_3COOH >$ benzoic acid

in pyridine: $HCl \approx CH_3COOH \approx$ benzoic acid

Conclusions:

Weak acids (in water) can be measured in basic solvents

Weak bases - " - in acidic solvents

Detection of end point:

Visual indicator are formed to the most suitable for the detection of end point in non-aqueous titration.

The important indicator used for non-aqueous titration is follow:-

Crystal violet:- It is used as 0.5% solution in glacial acetic acid, it gives voilet colour in basic medium and yellowish green in acidic medium. It is most widely use for the titration of pyridine with prechloride acid.

Oracet Blue B Indicator:- It is prepared o.5% glacial acetic acid. It gives blue colour in basic medium while pink colour in acidic medium.

Selection of solvents for NAT:

Acetic acid used for titration of weak bases, Nitrogen containing compounds

Acetonitrile / with ACOH: Metal ethanoates Alcohols (IPA, nBA) : Soaps and salts of organic acids, DMF: Benzoic acid, amides etc

Titrants used for NAT:

Perchloric acid in acetic acid, Amines, amine salts, amino acids, salts of acids

Potassium Methoxide in Toluene-Methanol

Quan ammonium hydroxide in Acetonitrile, pyridine, Acids, enols, imides & sulphonamides

Assay by NAT:

Acidimetry in Non-aqueous Titrations— It can be further sub-divided into *two* heads, namely:

(i) Titration of primary, secondary and tertiary amines, and

(ii) Titration of halogen acid salts of bases.

Acidimetry in Non-aqueous Titrations

Example : Primary amines

METHODOLOGY: Four steps

(i) Preparation of 0.1 N Perchloric acid

(ii) Standardization of 0.1 N Perchloric Acid

(iii) Choice of Indicators, and

(iv) Effect of Temperature on Assays

(i) Preparation of 0.1 N Perchloric acid

Materials Required: 8.5 ml of perchloric acid (70.0 to 72.0%) ; 1 Litre of glacial acetic acid ; 30ml of acetic anhydride.

Procedure: Gradually mix 8.5 ml of perchloric acid to 900 ml of glacial acetic acid with vigorous and continuous stirring. Now add 30 ml acetic anhydride and make up the volume to 1 litre with glacialacetic acid and allow to stand for 24 hours before use.

The acetic anhydride reacts with the water (approx. 30%) in perchloric acid and some traces in glacialacetic acid thereby making the resulting mixture practically anhydrous. Thus, we have :

$H_2O + (CH_3CO)_2O \rightarrow 2CH_3COOH$

Acetic acid acetic anhydride

Standardization of 0.1 N Perchloric Acid

- Add 25 ml of glacial acetic acid and attach a reflux condenser fitted with a silica-gel drying tube. Warm until the salt gets dissolved completely. Cool and titrate with
- 0.1 N perchloric acid by making use of either of
- the following *two* indicators :

(*a*) acetous crystal violet-2 drops, end point Blue to Blue-Green (0.5% w/v)

(*b*) acetous oracet blue B-2 drops, end point Blue to Pink.

Sr.No.	Name of Indicator	Colour change		
		Acidic	Neutral	Basic
1	Crystal violet (0.5% w/v in glacial acetic acid)	Violet	Bluish Green	Yellowish Green
2	Oracet Blue B(0.5% in glacial acetic acid)	Blue	Purple	Pink
3	α-Naphtholbenzein (0.2% in glacial acetic acid)	Blue	Magenta	Dark green
4	Quinalidine Red (0.1% in methanol)	Magenta	-	Colourless

Precautions:

(*a*) Perchloric acid is usually available as a 70 to 72% mixture with water .It usually undergoes a spontaneous explosive decomposition and, therefore, it is available always in the form of a solution.

(*b*) Conversion of acetic anhydride to acetic acid requires 40-45 minutes for its completion. It being an exothermic reaction, the solution must be allowed to cool to room temperature before adding glacial acetic acid to volume.

(*c*) Avoid adding an excess of acetic anhydride especially when primary and secondary amines are to be assayed, because these may be converted rapidly to their corresponding acetylated non-basic products:

$R—NH2 + (CH3CO)_2O \rightarrow R.NH.(CH3CO) + CH3COOH$

Primary amine Acetylated product

(*d*) Perchloric acid is not only a powerful oxidising agent but also a strong acid. Hence, it must be handled very carefully.

Other Examples:

Sr. No.	Name of Substance	Indicator
1	Amantadine hydrochloride	Crystal Violet
2	Chlorpromazine hydrochloride	Methyl orange
3	Clonidine hydrochloride	α -Naphthol benzein
4	Cyproheptadiene.HCl	Crystal Violet
5	Ephedrinehydrochloride	Crystal Violet

Preparation of 0.1 N Potassium Methoxide in Toluene-Methanol

Materials Required: Absolute methanol : 40 ml ; dry toluene : 50 ml ; potassium metal : 4 g.

Procedure: Add into a dry flask, a mixture of methanol (40 ml) and dry toluene (50 ml) and cover it loosely. Carefully add freshly cut pieces of potassium metal to the above mixture gradually with constant shaking. After complete dissolution of potassium metal, add enough absolute methanol to yield a clear solution. Toluene 50 ml is added with constant shaking until the mixture turns hazy in appearance. The process is repeated by the alternate addition of methanol and benzene until 1 litre of solution is obtained, taking care to add a minimum volume of methanol to give a visible clear solution.

Preparation of 0.1 N Sodiun Methoxide

It is prepared exactly in a similar manner as for 0.1 N Potassium Methoxide, using 2.3 g of freshly-cut sodium in place of potassium.

Preparation of 0.1 N Lithium Methoxide

It is prepared as for 0.1 N Potassium Methoxide, but using 0.7 g of lithium in place of potassium.

Standardization of 0.1 N Methoxide Solution

Materials Required: Dimethylformamide (DMF) : 10 ml ; Thymol blue (0.3% in MeOH) ; 0.1 N lithium methoxide in toluene methanol ; benzoic acid : 0.6 g.

Procedure : Transfer 10 ml of DMF in a conical flask and add to it 3 to 4 drops of thymol blue and first neutralize the acidic impurities present in DMF by titrating with 0.1 N lithium Methoxide in toluene-methanol. Quickly introduce 0.06 g of benzoic acid and titrate immediately with Methoxide in toluene methanol.

Caution: Care must be taken to avoid contamination of neutralized liquid with atmospheric carbon dioxide.

$Na + CH_3OH \rightarrow CH_3ONa + H\uparrow$

Interaction between sodium metal and methanol is an exothermic reaction and hence, special care must be taken while adding the metal into the dry solvent in small lots at intervals with adequate cooling so as to keep the reaction well under control.

$H_2O + CH_3ONa \rightarrow CH_3OH + NaoH$ $H_2CO_3 + 2CH_3ONa \rightarrow 2CH_3OH + Na_2CO_3$

Preparation of 0.1 N Tetrabutyl ammonium Hydroxide in Toluene-Methanol

Materials Required: Tetrabutyl ammonium iodide : 40 g ; absolute methanol : 90 ml ; silver oxide : 25 g ; dry toluene : 150 ml.

Procedure: Carefully dissolve 40 g of tetrabutylammonium iodide (Bu4NI) in 90 ml of absolute methanol, add to it 20 g of finely powdered purified silver oxide and finally shake the mixture thoroughly for 1 hour. Centrifuge about 2-3 ml of the resultant mixture and test for iodide in the supernatant liquid. In case, it gives a positive test, add about 2 g more of silver oxide and shake for an additional period of 30 minutes. The said method may be repeated until the supernatant liquid obtained is completely free from iodide. The mixture thus obtained is filtered through a fine sintered glass filter and finally rinse the container with 3 portions, each of 50 ml of dry toluene. These washings may be added to the filtrate and the final volume is made up to 1 litre with dry toluene. The clear solution may be flushed with CO2-free nitrogen for at least five minutes and duly protected from both CO2 and moisture during storage.

$2Bu_4NI + Ag_2O + H_2O \rightarrow 2Bu_4NOH + 2AgI$

Tetrabutyl- ammonium bromide

Standardization of 0.1 N Tetrabutylammonium Hydroxide

Materials Required : Benzoic acid : 60 mg ; dimethylbromide : 10 ml ; thymol blue solution (0.3% w/v in methanol) ; 0.1 N tetrabutylammonium hydroxide.

Procedure: Accurately weigh about 60 mg of benzoic acid into 10 ml of previously neutralized Dimethyl formamide to the blue colour of thymol blue (3 drops) by titration against 0.1 N tetrabutylammonium hydroxide. Allow the benzoic acid to dissolve gradually and completely and titrate with 0.1 N tetrabutylammonium hydroxide.

$0.01221\ g\ C7H6O2 \equiv 1\ ml\ of\ 0.1\ N$