2.6. Non-aqueous titration

2017-01

Acids and bases have long been defined as substances that, when dissolved in water, furnish hydrogen and hydroxyl ions, respectively. This definition, introduced by Arrhenius, fails to recognize the fact that properties characteristic of acids or bases may also be developed in other solvents. A more generalized definition is that of Brönsted, who defined an acid as a proton donor, and a base as a proton acceptor. Even broader is the definition of Lewis, who defined an acid as any material that will accept an electron pair, a base as any material that will donate an electron pair, and neutralization as the formation of a coordination bond between an acid and a base.

The apparent strength of an acid or base is determined by the extent of its reaction with a solvent. In aqueous solutions all strong acids appear equally strong because they react with the solvent to undergo complete conversion to hydronium ion (H_3O^+) and the corresponding anion. In a weakly protophilic solvent such as acetic acid, the extent of formation of the acetonium ion ($CH_3COOH_2^+$) due to the addition of a proton provides a more sensitive differentiation of the strength of acids and shows that the order of decreasing strength for acids is perchloric, hydrobromic, sulfuric, hydrochloric and nitric.

Acetic acid reacts incompletely with water to form a hydronium ion and is therefore a weak acid. In contrast, it dissolves in a base such as ethylenediamine and reacts so completely with the solvent that it behaves as a strong acid.

This so-called levelling effect is also observed for bases. In sulfuric acid almost all bases appear to be of the same strength. As the acid properties of the solvent decrease in the series sulfuric acid, acetic acid, phenol, water, pyridine and butylamine bases dissolved in them become progressively weaker and the differences between bases are accentuated. In order of decreasing strength strong bases of value for non-aqueous titrations are potassium methoxide, sodium methoxide, lithium methoxide and tetrabutylammonium hydroxide.

Many water-insoluble compounds acquire enhanced acidic or basic properties when dissolved in organic solvents. Thus the choice of the appropriate medium and titrant permits the determination of a variety of such materials by non-aqueous titration. Further, depending upon which part of a compound is physiologically active, it is often possible to titrate that part by proper selection of solvent and titrant. The types of compounds, in a non-aqueous medium, that may be titrated as acids, usually by lithium methoxide or tetrabutyl ammonium hydroxide, include acid halides, acid anhydrides, carboxylic acids, amino acids, enols such as barbiturates and xanthines, imides, phenols, pyrroles and sulfonamides. The types of compounds, in a non-aqueous medium, that may be titrated as bases by perchloric acid, include amines, nitrogen-containing heterocyclic compounds, quarternary ammonium compounds, alkali salts of organic acids, alkali salts of inorganic acids and some salts of amines. Many halide salts of weak bases and some quaternary ammonium compounds may be directly titrated in acetic anhydride using, preferably, potentiometric end-point detection or an indicator such as malachite green or crystal violet.

In the titration of a basic compound, amphiprotic solvents which have both protophilic and protogenic properties (e.g. acetic acid and the alcohols), which dissociate to a slight extent, are used as the medium. When acetic anhydride (halide salts of weak bases and quaternary ammonium compounds) is the medium, a volumetric solution of perchloric acid in glacial acetic acid may be used as the titrant. When ethanol is used as the medium for halide salts of weak bases the titrant is a volumetric solution of sodium hydroxide. In the titration of an acidic compound a volumetric solution of lithium methoxide in a methanol-toluene solvent is often used. For many applications it is convenient to use a solution of tetrabutylammonium hydroxide in toluene; sodium methoxide, formerly in wide use, may often give rise to troublesome gelatinous precipitates.

Because of interference by carbon dioxide, solvents for acidic compounds must be protected from excessive exposure to the atmosphere by a suitable cover or by an inert atmosphere during the titration. A blank determination should be carried out and the volume generally should not exceed 0.01 mL of a 0.1 mol/L titrant for each mL of solvent.

The end-point may be determined visually by colour change or preferentially by potentiometry. It should be recognized that certain indicators in common use (crystal violet, for example) undergo a series of colour changes and, in establishing a non-aqueous titration method for a particular use, care should be taken to ensure that the colour change specified as the end-point of the titration corresponds to the maximum value of dE/dV (where E is the electromotive force and V the volume of titrant) in a potentiometric titration of the substance under consideration.

When using titrants prepared with solvents that may have a relatively high coefficient of expansion, for example, glacial acetic acid, toluene, etc., care should be taken to compensate for differences in temperature that may exist between the time the titrant is used and that at which it was standardized. When the temperature (t_2) at which the titration is carried out differs from the temperature (t_1) at which the titrant was standardized, multiply the volume of the titrant required by $[1 + 0.001(t_1 - t_2)]$ and calculate the result of the assay from the corrected volume.

Recommended procedures

Method A (i) – for halide salts of organic bases

Dissolve a quantity of the substance being examined to give an expected titration volume of between 70–90% of the burette volume, in 50 mL of dehydrated ethanol R and 5.0 mL of hydrochloric acid (0.01 mol/L) VS. Carry out a potentiometric titration

using sodium hydroxide (0.1 mol/L) VS. Read the volume added between the two points of inflexion.

Method A (ii) – for bases, their salts and quaternary ammonium compounds

Prepare a solution as specified in the monograph or dissolve the substance being examined in a suitable volume of medium (acetic anhydride R with or without the addition of formic acid R or dioxan R. The titration blank for the medium is to be established in a separate determination. When the end-point is determined visually by colour change, add 2–3 drops of crystal violet/acetic acid TS and titrate with perchloric acid of the specified concentration (mol/L) to the appropriate colour change of the indicator. When a different indicator is specified in the monograph this indicator should also be used for the neutralization of the medium and the standardization of the titrant.

When the equivalence point is determined potentiometrically the indicator is omitted and neutralization of the medium and standardization of the titrant are also carried out potentiometrically with a suitable indicator electrode and a reference electrode (usually silver/silver chloride).

Method B (for acids)

The titrant, solvent and (in the case where the end-point is determined visually) the indicator to be used for each substance, are specified in the monograph.

Protect the solution and titrant from carbon dioxide of the atmosphere throughout the determination. This may conveniently be done by replacing the air above the titration liquid with nitrogen.

Dissolve the substance being examined in a suitable volume of the solvent previously neutralized to the indicator, warming and cooling if necessary, or prepare a solution as specified in the monograph. Titrate to the appropriate colour change of the indicator. Carry out a blank determination and make any necessary corrections. The titrant is standardized using the same solvent and indicator as specified for the substance.

When the equivalence point is established potentiometrically the indicator is omitted and neutralization of the solution and standardization of the titrant are also carried out potentiometrically.