Catalytic Thermometric Titrimetry

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Contents

I. Introduction

Titrimetry is generally understood to be an analytical procedure in which a reagent (the titrant) is added to the sample (the titrand) until the reaction between the two has proceeded to completion. The end point of the reaction is located instrumentally or visually, and the concentration of the sample is calculated from the amount of reagent consumed. Jordan[1] points out that determination of the end point is a distinguishing feature of titrimetry and, indeed, ". . . is the very essence of titrimetric analysis".

End points may become evident in two fundamentally different ways: (1) as a change in a characteristic property of the titrant–titrand combination when the former reagent appears in stoichiometric excess, e.g., as a change in electrical conductivity (conductometric titrimetry), dielectric properties (high-frequency titrimetry), potential between two electrodes immersed in the sample solution (potentiometric titrimetry), or the heat evolved or absorbed (thermometric titrimetry); and (2) from the response of an indicator added to the titrand. It is desirable that this indicator response, which is normally the result of a reaction between the indicator and the titrant, should be detectable immediately after the determinative reaction is virtually complete.

Until comparatively recently, the only titrimetric indicators used were those that undergo a change in color or fluorescence in the region of the end point. There is no reason, of course, why indicators should be restricted to those of the visual type. In the last few years new indicator systems have been developed for use with instrumental methods of end-point detection. These methods measure some quality of the products of the indicator reaction and include spectrophotometry,[2–5] potentiometry,[2,4,5] thermometry (enthalpimetry),[2–4,5] biamperometry,[2–6] and the measurement of chemiluminescence.[6]

The use of a thermometric method for measuring the response of an end-point indicator has several attractive features: (1) the apparatus is simple, since all that is required is a temperature-measuring probe such as a thermometer or a thermistor connected through a bridge circuit to a chart recorder; (2) the measuring probes are inert to most solutions, and temperature changes in highly colored or viscous solutions can be measured without difficulty; (3) unlike the electrodes used in potentiometric or biamperometric titrimetry, the response of the measuring probes is virtually unaffected by voluminous or gelatinous precipitates, provided that stirring is effective; (4) the range of indicator reactions is virtually unlimited because all reactions are accompanied by a change in temperature, the magnitude of which can be adjusted by changing the concentrations of the reagents.

When a thermometric method is used to measure an indicator response, it is important that the temperature change occurs as soon as possible after the titrant appears in excess in the titration mixture. This requirement can be realized more effectively when the titrant functions as a catalyst, rather than as a simple reagent, in the indicator reaction. The technique in which the titrant functions as a catalyst for an exothermic reaction marking the end point of a titration has been given the name "Catalytic Thermometric Titrimetry" by Vajgand and Gaál.[7] The present review is intended to be a critical evaluation of the published work on catalytic thermometric titrimetry, commencing with the original paper on the subject, published by Vaughan and Swithenbank in 1965.[8]

Conventional and catalytic thermometric titrimetry differ fundamentally. The former is a procedure in which the heat of reaction between the titrant and titrand is monitored, and in which the heat changes depend on the sample size, while the latter relies on an indicator to locate the end point and the heat changes depend on the amount of added indicator. An important difference between visual and thermometric end-point indication is the amount of indicator required in a titration. It is generally advisable to use the minimal amount of a visual indicator, but the thermometric indicator should be a major constituent of the sample solution if a substantial rise in temperature at the end point is desired.

Several textbooks[9–12] and reviews[2,13–18] on thermometric titrimetry have appeared in recent years. These are concerned mainly with the conventional method and treat the subject of catalytic thermometric titrimetry only briefly. Probably the most detailed account to date of the latter, in a textbook, is the one by Vaughan[11] in "Thermometric and Enthalpimetric Titrimetry".

II. Historical Background

In the first account of the use of thermometric indicators in titrimetry, appearing in 1965, Vaughan and Swithenbank[8] showed that when acetone is used as a sample solvent in the titration of weak acids with alcoholic potassium hydroxide a
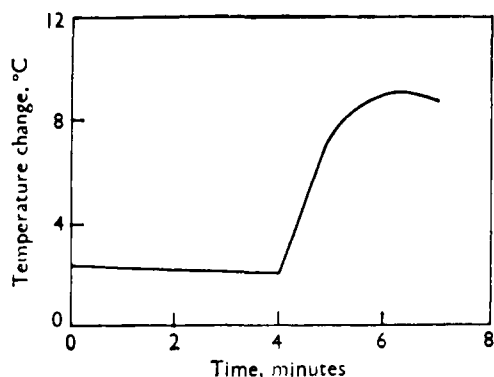
Figure 1. Titration of an acidic substance with acetone as solvent and thermometric indicator. From Vaughan and Swithenbank,[8] with permission of the Chemical Society.

TABLE I. Effect of the Rate of Addition of Titrant in the Catalytic Thermometric Titration of Silver with 0.01 M Potassium Iodide (Ce(IV)-As(III) Indicator System) [a]

Titration rate, μL min^{-1}	Rel std dev, %
5	-1.00
55.68	+0.95
556	+1.7
5568	+3.7

[a] From Weisz et al.[21] with permission of Springer-Verlag.

temperature rise occurs in the vicinity of the expected end point. The temperature rise resulted from the exothermic, alkali-catalyzed, dimerization of the acetone, and was of the order of 5 °C, with 1 M potassium hydroxide as the titrant (Figure 1).

In the following year, Vajgand and Gaál[7] reported on the use of the heat of reaction of the perchloric acid catalyzed hydration of acetic anhydride to indicate the end point in the titration of tertiary amines and salts of organic acids with perchloric acid.

The application of acid- and base-catalyzed vinyl polymerizations as means of end-point indication in catalytic thermometric titrations of organic bases and acids, respectively, was described by Greenhow in 1972.[19,20]

While the catalytic thermometric technique was being developed in the field of organic analysis, Weisz, Kiss, and their co-workers were investigating its use for the determination of inorganic substances. In 1969, Weisz, Kiss, and Klockow[21] reported that the heat evolved in the iodide-catalyzed oxidation of arsenic(III) with cerium(IV) could be used to locate the end point in titrations of silver, mercury(II), and palladium(II) solutions with iodide. Later, Weisz and Kiss[22] determined chelating agents and inorganic cations by titrimetric procedures in which the catalytic action of manganese(II) on either the decomposition of hydrogen peroxide or the oxidation of resorcinol with hydrogen peroxide forms the basis of thermal methods of end-point indication.

III. Chemistry of the Titration Process

A catalytic thermometric titration comprises two sequential processes: (a) the determinative reaction (eq 1) in which the titrand and titrant undergo stoichiometric combination, and (b) the indicator reaction (eq 2), in which a small excess of titrant catalyzes a reaction involving the indicator constituents. In the ideal titration (Figure 2a)[23] the sample, until it is neutralized by the titrant, would inhibit the indicator reaction completely, and the titrant would initiate the indicator reaction immediately on appearing in the solution in excess. If such a situation were possible, a sharp rise in temperature would occur to mark the end point of the titration. In practice, reactions 1 and 2 overlap, and a more typical titration curve is the one shown in Figure 2b; the overlap corresponds to the rounded portion of the curve. Although no distinct inflection occurs, satisfactory end points can
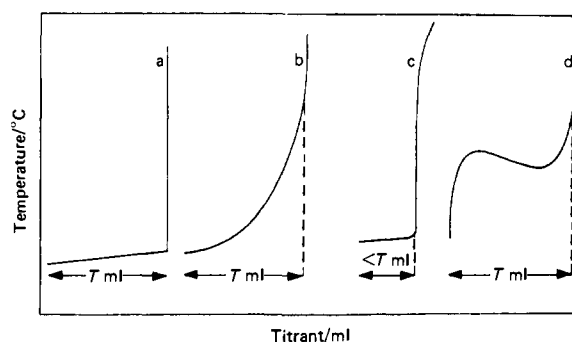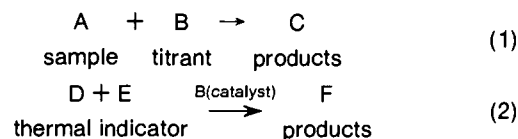

Figure 2. Catalytic thermometric titration curves: (a) ideal titration curve, (b) polymerization retardation without complete inhibition, (c) limited inhibition of polymerization, and (d) delayed inhibition of polymerization. T is the expected stoichiometric titer. From ref 23 with permission of the Chemical Society.

sometimes be located by drawing tangents to one "arm", or to both arms, of the titration curve (see section IV.C). Another form of the titration curve is seen when the indicator reaction (2) commences prematurely, but as the temperature rises the titrand consumes the titrant more rapidly, thus inhibiting the indicator reaction which recommences only after the determinative reaction is virtually completed (Figure 2d).[23,24]

$$A + B \rightarrow C \qquad (1)$$
$$\text{sample} \quad \text{titrant} \quad \text{products}$$

$$D + E \xrightarrow{\text{B(catalyst)}} F \qquad (2)$$
$$\text{thermal indicator} \quad \text{products}$$

The typical titration curve, Figure 2b, illustrates the competitive nature of the two steps in the catalytic thermometric titration and the need to select indicator reagents and titrants with the appropriate catalytic and kinetic characteristics. The overlap of the determinative and indicator reactions can be attributed to the mildly catalytic properties of the products of the determinative reaction and/or the titrant concentration in the solution exceeding the threshold limit of its catalytic activity before the determinative reaction has proceeded essentially to completion. It is possible, for example, for the phenate ion produced in the titration of phenols with strong alkali to be sufficiently basic to initiate an alkali-catalyzed reaction, while in the titration of very weak bases with strong acids, the protonated base may be an effective catalyst for an acid-catalyzed reaction.[25] Weisz, Kiss, and Klockow[21] have shown that the titration error can be related to the rate of addition of titrant in the determination of silver with 0.01 M potassium iodide. Thus, when titrant is added at 5 μL min^{-1} the error is -1.00%, while it becomes +0.95% when the addition rate is 55.68 μL min^{-1} (Table I).

The determinations possible by the catalytic thermometric method are limited by the availability of suitable indicator reactions, since it is necessary that the sample to be determined should be an efficient inhibitor of, and the titrant should be an effective catalyst for, the indicator reaction.

The available indicator reactions, the effect of their chemistry on the determinative reaction and titrimetric efficiency, the influence of solvents on the titration process, and the possibility of selective determinations by the use of appropriate indicator systems are discussed below.

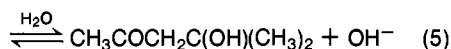## A. Mechanisms of Indicator Reactions

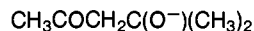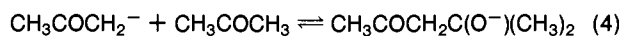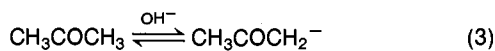Reactions that have proved to be suitable for end-point indication fall broadly into three groups: (i) polymerizations catalyzed by strong alkalis, strong acids, and iodine (these include ketone and aldehyde condensations, anionic polymerization, and cationic polymerization); (ii) esterifications and hydrolysis catalyzed by strong acids; (iii) oxidation-reduction processes catalyzed by iodide ion and transition metal ions.
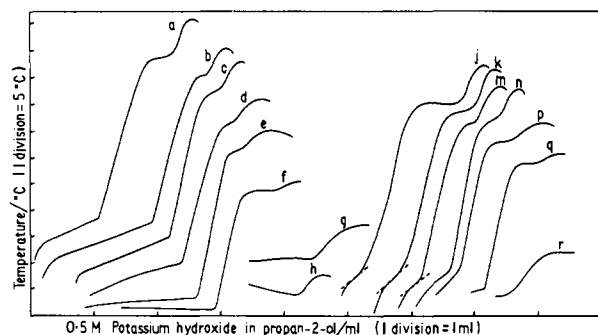
Figure 3. The titration of benzoic acid in aquueous and nonaqueous acetaldehyde, with 0.5 M potassium hydroxide in propan-2-ol as titrant and acetaldehyde as thermometric indicator; benzoic acid (mg)–acetaldehyde (mL)–water (mL): (a) 34.1:4:0; (b) 67.0:4:0.1; (c) 63.5:4:0.5; (d) 60.0:4:1; (e) 80.4:4:2; (f) 64.6:3:3; (g) 42.8:1:5; (h) 44.1:4 (acetone solvent):0. (j) to (r) are as (a) to (g), respectively, with the benzoic acid omitted. From ref 28, with permission of Pergamon Press.

1. Ketone and Aldehyde Condensations

The acetone indicator reaction employed by Vaughan and Swithenbank[8] in the nonaqueous titration of weak acids can be represented by the three equations:

$$CH_3COCH_3 \underset{}{\overset{OH^-}{\rightleftharpoons}} CH_3COCH_2^- \qquad (3)$$

$$CH_3COCH_2^- + CH_3COCH_3 \rightleftharpoons CH_3COCH_2C(O^-)(CH_3)_2 \qquad (4)$$

$$CH_3COCH_2C(O^-)(CH_3)_2$$
$$\overset{H_2O}{\rightleftharpoons} CH_3COCH_2C(OH)(CH_3)_2 + OH^- \qquad (5)$$

At equilibrium the acetone–diacetone alcohol system contains a high proportion of acetone; consequently, the heat generated is much less than would have been obtained by the complete conversion of the acetone.

Acetaldehyde was examined briefly by Vaughan and Swithenbank as a possible thermometric indicator.[8] They found that an exothermic reaction was initiated almost immediately on adding alkali titrant to acetaldehyde containing a weak acid, i.e., before the acid sample could be titrated, and suggested that the different reactivities of acetone and acetaldehyde could be explained in terms of the kinetics of the two condensation processes. Pointing out that, according to Sykes,[26] reaction 4 is slow while the corresponding step in the condensation of acetaldehyde is fast, they conclude that when acetone is used as an indicator the acid sample can be neutralized before the dimerization commences, but with acetaldehyde this is not possible.

The kinetics of the aldol reaction are more complex than is assumed in the above explanation, and are dependent on the concentration of the acetaldehyde.[27] A reevaluation of acetaldehyde as a thermometric indicator[28] has shown that, while the exothermic reaction observed by Vaughan and Swithenbank does precede the neutralization of the acid sample by the titrant, a second temperature rise occurs at the theoretical end point, and this is of the order of 25 °C (Figure 3). The initial exotherm is believed to be caused by the hydration of acetaldehyde when an aqueous titrant is used or by hemiacetal formation if the titrant solvent is an alcohol. Unlike the acetone reaction, acetaldehyde self-condensation occurs readily in the presence of water, and sharp end-point inflections are obtained when acids in aqueous acetaldehyde are titrated with aqueous titrant.

Although simple aliphatic ketones other than acetone appear to be insufficiently reactive to be useful as thermometric end-point indicators for the nonaqueous titration of acids, cyclopentanone, cyclohexanone, and 1-phenyl-1-propanone are effective indicators.[29] When they are used as solvents for the acid sample, rises in temperature of about 11, 7 and 0.7 °C, re-
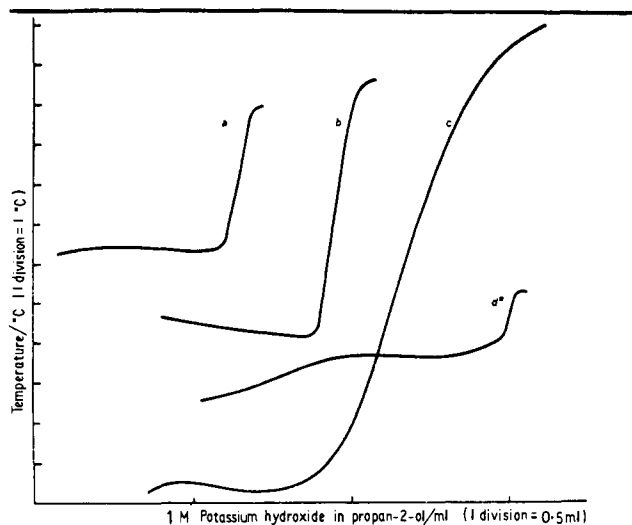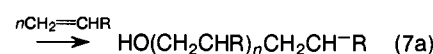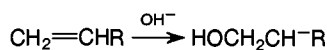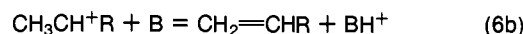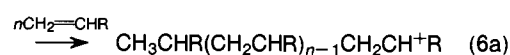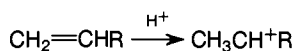

Figure 4. Titrations with ketones as solvents (5 mL) and thermometric indicators, benzoic acid (mg): (a) acetone, 68.3; (b) cyclohexanone, 51.3; (c) cyclopentanone, 54.5; (d) propiophenone, 108.7 (1 division = 0.5 °C). From ref 29, with permission of the Society of Chemical Industry.

spectively, are obtained at the end point with 1.0 M potassium hydroxide in propan-2-ol as the titrant (Figure 4). The greater temperature change experienced with the cyclic ketones, as compared to acetone, is probably due to differences in the self-condensation reactions. Thus cyclopentanone undergoes an irreversible self-condensation to yield 2-cyclopentylidene-cyclopentanone,[30] while cyclohexanone yields a trimer, dihydroxytricyclohexyl.[31] The much smaller temperature rise achieved when 1-phenyl-1-propanone is treated with alkali suggests that an equilibrium mixture is formed containing a high proportion of the original ketone.

2. Vinyl Polymerization

Vinyl monomers that undergo rapid ionic polymerization initiated by strong acids or strong bases are potentially useful as thermometric end-point indicators for the nonaqueous titration of bases and acids, respectively, because bases either neutralize the acid catalyst directly or inhibit cationic polymerization initiated by the acid, while acids similarly prevent or inhibit anionic polymerization initiated by the bases. The polymerizations should be initiated as soon as the inhibitor, i.e., the titrand, has been neutralized by reaction with the strong acid or strong base, if the conditions for an ideal catalytic thermometric titration are to be met.[23]

Acrylonitrile, alkyl acrylates, and dialkyl itaconates have been shown to be suitable thermometric indicators for the titration of organic acids,[32] while 2-phenylpropene and alkyl vinyl ethers can be used as indicators for the titration of organic bases.[33] The polymerization and inhibition reactions for base (B), and acid (HA) titrands are summarized by eq 6a and 6b, and 7a and 7b, respectively:

$$CH_2{=}CHR \overset{H^+}{\longrightarrow} CH_3CH^+R$$

$$\overset{nCH_2{=}CHR}{\longrightarrow} CH_3CHR(CH_2CHR)_{n-1}CH_2CH^+R \qquad (6a)$$

$$CH_3CH^+R + B = CH_2{=}CHR + BH^+ \qquad (6b)$$

$$CH_2{=}CHR \overset{OH^-}{\longrightarrow} HOCH_2CH^-R$$

$$\overset{nCH_2{=}CHR}{\longrightarrow} HO(CH_2CHR)_nCH_2CH^-R \qquad (7a)$$

$$HOCH_2CH^-R + HA = HOCH_2CH_2R + A^- \qquad (7b)$$

Titrants that are also suitable as polymerization catalysts are perchloric acid, used with 2-phenylpropene as the indicator, boron trifluoride etherate, used with alkyl vinyl ethers as indicators,[20,33] and n-butyllithium, potassium hydroxide, potassium ethoxide, potassium methoxide, and tetra-n-butylammonium hydroxide, all of which are effective polymerization catalysts for acrylonitrile, alkyl acrylates, and alkyl itaconates.[32]

Perchloric acid is unsuitable as a titrant catalyst for use with the alkyl vinyl ether indicator because the polymerization is initiated before the base analyte is neutralized, while boron trifluoride is insufficiently active to serve as a catalyst for the polymerization of 2-phenylpropene for the purpose of end-point indication.[33]

In nonaqueous solution, iodine can function as an initiator for the cationic polymerization of certain vinyl monomers.[34] The initiating species is either I^+ or I_3^+ and the counterion is probably I_3^- (eq 8a). Only the alkyl vinyl ethers have been found to be suitable monomers for use as end-point indicators for thermometric nonaqueous iodometric titration.[35,36] Other monomers, including styrene and 2-methyl-1,3-butadiene, respond too slowly to the initiator to show a detectable end point in the titrations. The polymerization (eq 8b) and inhibition (eq 8c) reactions are similar to those shown in eq 6a and 6b, with I^+ or I^{3+} replacing H^+ in eq 6a:

$$2I_2 \rightleftharpoons I^+I_3^-; \quad 3I_2 \rightleftharpoons I_3^+I_3^- \qquad (8a)$$

$$CH_2{=}CH(OR) \xrightarrow{I^+(or\ I_3^+)} ICH_2CH^+(OR)$$

$$\xrightarrow{nCH_2{=}CH(OR)} I[CH_2CH(OR)]_nCH_2CH^+(OR) \quad (8b)$$

$$ICH_2CH^+(OR) + B \rightarrow CH_2{=}CH(OR) + BI^+ \qquad (8c)$$
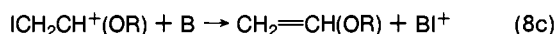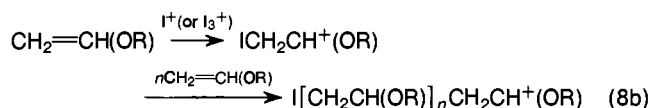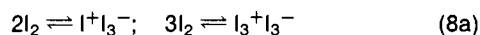
The catalyst ion pair initially forms a π complex with the vinyl ether, which then rearranges to the cation shown in eq 8b.[34]

3. Reactions of Anhydrides with Water, Alcohols, and Phenols

Powerful proton donors, such as solutions of mineral acids in acetic acid, catalyze the highly exothermic hydrolysis of aliphatic acid anhydrides and the acylation of alcohols and phenols.[37] The mechanism of these reactions is not definitely known, but presumably protonation of the anhydride by the catalyst occurs in the first instance.[38,39] If strong or weak bases are present in the reaction mixture they will, in the ideal situation, remove the catalyst and prevent the initiation of hydrolysis or acylation until the catalyst appears in sufficient excess. The hydrolysis and acylation reactions can, therefore, be used as a means of end-point indication in the titration of bases with an acid that can function as a catalyst for these reactions.

Vajgand and Gaál[7] first applied the hydrolysis reaction to the determination of tertiary amines and salts of organic acids. They used perchloric acid in acetic acid as the titrant and a solution of 2% of water and 8% of acetic anhydride in acetic acid as the sample solvent and thermometric indicator. Later,[40] Vajgand, Gaál, and Brusin generated the acid titrant coulometrically. Primary and secondary amines could not be determined satisfactorily by this method because they are acetylated and the amides formed are insufficiently basic to be titrated. The difficulty in determining very weak bases, including caffeine and 2-methyl-5-nitroimidazole, was attributed to the presence of water, itself a weak base, in the reaction mixture. To overcome this difficulty, the authors used quinol, both as a reagent to replace water in the indicator reaction and for the generation of protons at a platinum electrode. They suggested that the indicator reaction was the addition of acetic anhydride to the quinoid (quinonoid) system, but later in their paper they referred to the "acetic anhydride–hydroquinone indicator reaction". Acetic anhydride undergoes addition to quinones in strongly acid media


$$(9)$$
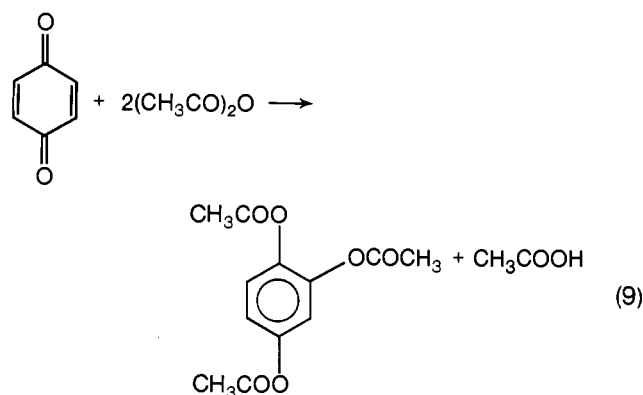
by the Thiele–Winter reaction (eq 9),[41] but the temperature changes associated with it would be small in the titration of small samples by the coulometric method, unless additional quinone was included in the sample solution. In the procedure described by Vajgand, Gaál, and Brusin, the acetylation of unoxidized quinol would be the more likely indicator reaction.

Goizman[42] has reported on the use of normal alcohols, ethylene glycol, and phenol instead of water as indicator reagents, in conjunction with acetic anhydride, for the titration of potassium hydrogen phthalate and some tertiary amines with 0.1 M perchloric acid in acetic acid. The temperature rise obtained with phenol as the hydroxyl component was considerably greater than that achieved with ethylene glycol and the 1-alkanols. Apparently some difficulty was encountered with temperature changes occurring before the end point is reached, because it is suggested that (a) the amount of acetylatable component in the sample mixture should be a minimum, and (b) most of the titrant should be added to the sample solution containing the acetic anhydride but not the hydroxyl component, and then the hydroxyl component be added and the titration completed. Temperature changes at the end point are shown to exceed 5 °C.

The use of acetylation and the Thiele–Winter reaction for end-point indication has been investigated by Greenhow,[25] who found that the latter reaction does not proceed readily when trace amounts of perchloric acid in acetic acid are added to mixtures of acetic anhydride and 1,4-benzoquinone. Quinol, on the other hand, undergoes rapid acetylation in the presence of perchloric acid and can be used for end-point indication. However, it is not entirely suitable because some acetylation occurs before the expected end point in the titration of weak bases such as pyridine and quinoline (Figure 5). Some other aliphatic and aromatic hydroxyl compounds, 4-hydroxy-4-methylpentan-2-one (diacetone alcohol) and quinhydrone, for example, are more suitable reagents in terms of the end-point sharpness achieved. The quinhydrone was found to be superior to other hydroxylic compounds examined as an indicator reagent for the determination of the very weak bases, caffeine, theophylline, and urea (Figure 6). It is proposed that end-point sharpness in acetylation end-point indication reactions can be related to hydrogen bonding in the hydroxylic reagent. Thus, quinhydrone is a strongly hydrogen-bonded molecular complex, and it is probable that the hydrogen bonding remains unchanged until the end point of the reaction, when the presence of free perchloric acid brings about its fission. This is confirmed by the sharp change in color occurring at the end point of titrations in which quinhydrone is the hydroxylic indicator reagent, when the dark green, almost opaque, solution of quinhydrone changes in color to pale yellow, the color of uncomplexed 1,4-benzoquinone in solution. Acetylation of the quinhydrone cannot take place, of course, until fission of the hydrogen bonds is brought about. Intramolecular hydrogen bonding can occur in diacetone alcohol, but the shape of the titration curves indicates that it is not as strong as the bonding in quinhydrone. A transient pink color develops at the end point when diacetone alcohol is an indicator component,
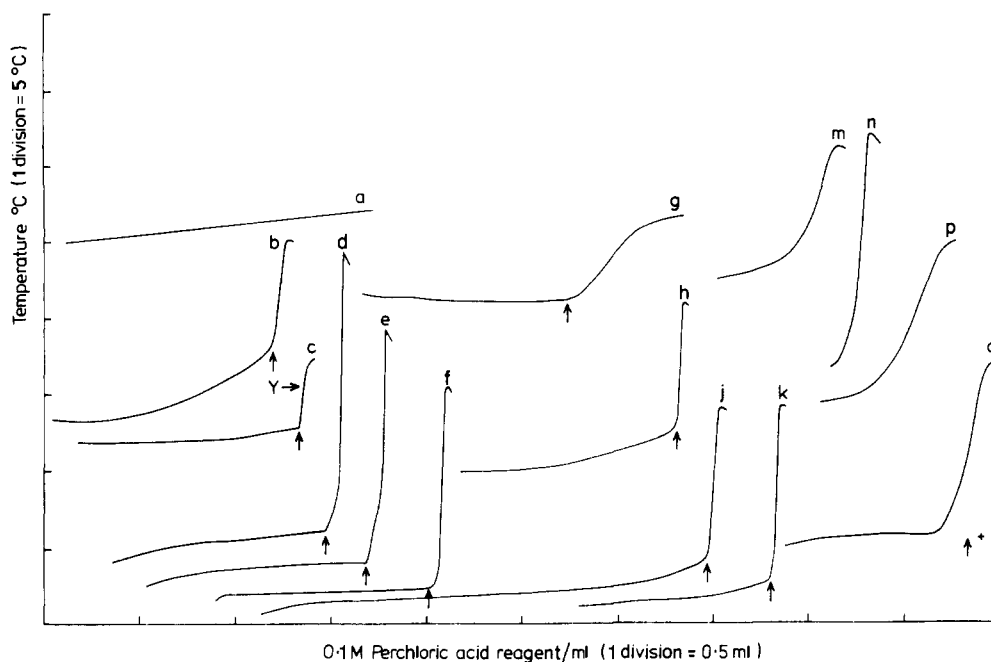
Figure 5. Titrations of aliphatic amines, 2-methylpyridine, and quinoline with 0.1 M perchloric acid in acetic acid (acetic anhydride–hydroxyl compound indicator system). Amine/mg: (a–h) quinoline, 15.2; (j) 2-methylpyridine, 23.5; (k) tripropylamine, 15.2; (m) butylamine, 13.1; (n) tris(hydroxy-methyl)methylamine, 12.6; (p) morpholine, 20.0; (q) benzylamine, 24.7. Hydroxyl indicator reagent (4 mequiv): (a) 1,4-benzoquinone (included for comparison); (b) hydroquinone; (c) quinhydrone; (d) butan-1-ol; (e) 2-methylpropan-2-ol; (f, j–q) 4-hydroxy-4-methylpentan-2-one; (g) salicyclic acid: (h) 3,5-dimethylphenol. Acetic anhydride indicator reagent, 5 mL; † end point (inflection); Y, color change, opaque to clear yellow; + theoretical end point. From ref 25, with permission of the Chemical Society.
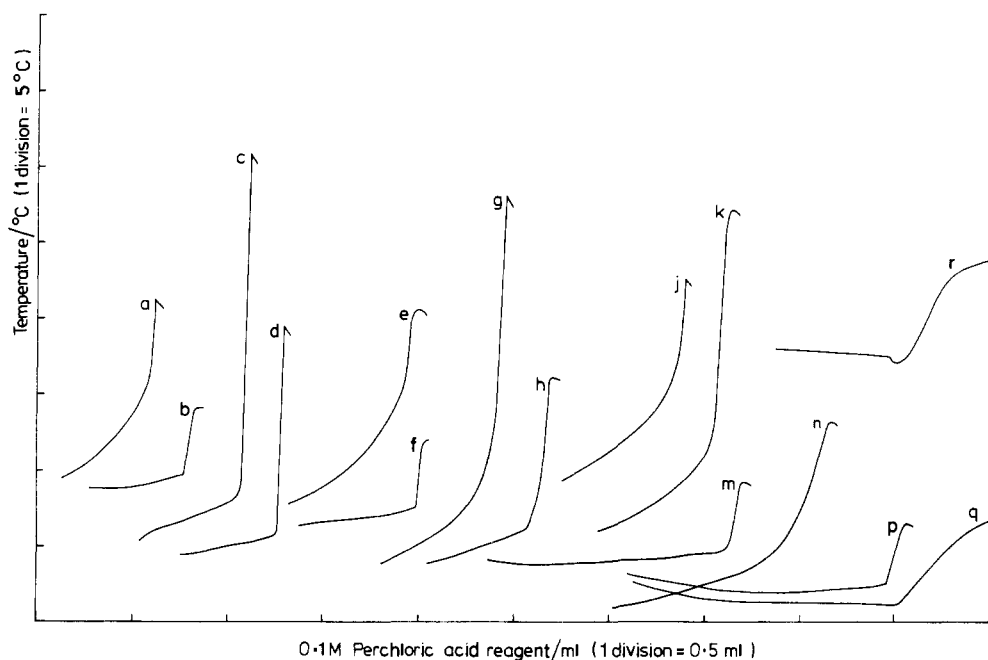
Figure 6. Titrations of antipyrine, caffeine, theophylline, and urea with 0.1 M perchloric acid in acetic acid (acetic anhydride–hydroxyl compound indicator system). Amine/mg: (a–d) antipyrine, 9.4; (e–k, r) caffeine, 12.0; (m) theophylline, 25.0; (n) theophylline, 22.5; (p) urea, 9.0; (q) urea, 8.5. Hydroxyl indicator reagent (4 mequiv): (a, e) hydroquinone; (b, f, m, p) quinhydrone; (c, g) butan-1-ol; (d, h, n) 4-hydroxy-4-methylpentan-2-one; (j) 3,5-dimethylphenol; (k) pyrocatechol (8 mequiv) (q, r) salicylic acid. Acetic anhydride indicator reagent, 5 ml. From ref 25, with permission of the Chemical Society.

but the structural significance of this has not yet been elucidated.

4. Oxidation of Arsenic(III) by Cerium(IV)

In 1928, Willard and Young[43] reported on the use of potassium iodide and some other compounds, as catalysts for the cerium(IV)–arsenic(III) reaction:

$$2Ce(IV) + As(III) \overset{I^-}{\rightleftharpoons} 2Ce(III) + As(V) \qquad (10)$$
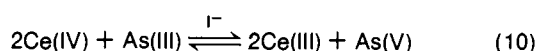
Some years later, Sandell and Kolthoff[44] showed that the rate of the reaction was proportional to the concentration of the iodide ions, and they determined trace amounts of iodide by measuring the progress of the reaction by a chronometric method involving a visual measurement of the completion of the oxidation. In recognition of the analytical importance of the iodide catalysis the reaction is often referred to as the "Sandell–Kolthoff reaction".

In a review of catalytic titrants and the catalytic indication of end points, Mottola[45] suggested that Yatsimirskii and Fedorova[46]

had carried out what might be regarded as the first application of catalytic end-point detection when they measured the rate of this iodide-catalyzed reaction photometrically in the presence of silver ions. They added increasing amounts of iodide to identical solutions containing silver ions and the cerium(IV)–arsenic(III) reagents. Until sufficient iodide had been added to precipitate virtually all of the silver as the iodide, the slope of the log absorbance vs. time graph remained constant, but immediately a sufficient amount of iodide was present in the solution to catalyze the reaction; the slope of the first-order plot changed dramatically with increasing iodide concentration, thus enabling the "end point" to be located and the silver content to be calculated.

Later, in 1966, Weisz and Muschelknautz[47] described a more conventional titrimetric method in which the iodide-catalyzed reaction served to indicate a visual end point in the titration of silver ions with iodide solution. The color change is from intensive golden yellow (cerium(IV) ions) to milky yellow (silver iodide precipitate). They also determined chloride, bromide, and thiocyanate by a similar procedure, in which a known amount of silver nitrate was first added to precipitate these anions, and the excess of silver ions was titrated with the iodide solution, as above. In addition to visual observation of the end point, spectrophotometric,[4,5,48] potentiometric,[4,5,48–50] biamperometric,[4,5] and thermometric methods have been used to detect the onset of the iodide-catalyzed indicator reaction. The thermometric method was first reported by Weisz, Kiss, and Klockow,[21] who determined mercury(II), palladium(II), iodide, cyanide, ferrocyanide, and sulfide, in addition to silver and the anions mentioned above.

5. Transition-Metal Catalysis of the Decomposition of Hydrogen Peroxide and Oxidations with Hydrogen Peroxide

Several liquid-phase oxidation reactions that are catalyzed by transition metal ions have been investigated as potential reactions for use as a means of end-point indication in titrimetric procedures.[3,4,6,47,51,52] In most of those reported in the literature, hydrogen peroxide is used as the oxidizing reagent, but perborate,[47] periodate,[52] and persulfate[4] have also been considered. Some transition metals catalyze the exothermic decomposition of hydrogen perioxide, and this reaction too has been used for end-point indication.[22]

In their original investigation of the application of catalyzed oxidation reactions as a means of end-point indication in titrations, Weisz and Muschelknautz[47] made use of the earlier findings by Bognár[53] that cobalt catalyzes the oxidation of polyhydric phenols by hydrogen peroxide or sodium perborate in alkaline media. They pointed out that the catalytic activity of the cobalt was removed by chelating it with EDTA or CDTA (trans-1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid), and they demonstrated that when a mixture of EDTA or CDTA with hydrogen peroxide or sodium perborate and a polyhydric phenol was titrated with a cobalt(II) solution, the oxidation reaction was not initiated until all the ligand had undergone reaction and free cobalt ions appeared in the solution. The end point was marked by a color change caused by the formation of a deeply colored oxidation product. They determined EDTA and CDTA by direct titration, and cobalt(II) in solution by using the "unknown" cobalt solution as the titrant and a known amount of EDTA as the titrand, a procedure known as inverse titration.

Weisz and Janjic[51] carried out a more detailed evaluation of these oxidation reactions for end-point indication. They used other metal salt catalysts, including those of manganese(II), and other oxidizable compounds, including N,N-dimethyl-p-phenylenediamine, together with hydrogen peroxide and sodium perborate as the indicator reagents.

Like the cerium(IV)–arsenic(III) reaction, these oxidations can

be detected instrumentally as well as visually. Spectrophotometric,[3,4,50] potentiometric,[2,54] biamperometric,[3–6] chemiluminescence,[6] and thermometric[22,55] methods have been described.

In 1970, Weisz and Kiss[22] showed that the initiation of the oxidation indicator reaction could be detected thermometrically. They evaluated two indicator reactions, the oxidation of resorcinol with hydrogen peroxide and the decomposition of hydrogen peroxide, and used manganese(II) salts as catalyst for both reactions and as the titrant. Shiokawa and Suzuki[56] had reported earlier that the decomposition of hydrogen peroxide is catalyzed by manganese(II), copper(II), and palladium(II). Weisz and Kiss found that similar thermometric end points were obtained with both indicator systems. Kiss[55] later carried out thermometric titrations using the same indicator systems, but with samples dissolved in dimethyl sulfoxide. The end-point inflection was claimed to be sharper than that obtained by using aqueous solutions.

More recently,[3,4] Weisz and Pantel have reported on the use of the copper(II)-catalyzed oxidation of hydrazine with hydrogen peroxide as an indicator system for end-point detection (eq 11). The catalyst is more active as an amine complex than as the free ion, and the temperature rise at the end point is much larger than that achieved in the catalyzed oxidations and hydrogen peroxide decomposition used in the earlier work, so much so that the elaborate precautions needed to prevent heat loss and to provide a measurable temperature change at the end point, when the latter indicator reactions are used, are unnecessary.

$$2H_2O_2 + NH_2NH_2 \xrightarrow{Cu^{2+}} N_2 + 4H_2O \qquad (11)$$
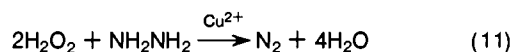
B. Influence of the Thermometric Indicator on the Determinative Reaction

When the indicator reagents are major constituents of the sample solution, as they usually are in catalytic thermometric titrimetry, the possibility arises of significant effects caused by their solvent properties and by interaction of the reagents with the sample. Some effects that may be attributable to the indicator reagents are discussed below.

1. Acetone and Acetaldehyde

When acetone[8] was used as the solvent and thermometric indicator in the nonaqueous titration of succinic acid with potassium hydroxide in propan-2-ol, only one of the carboxyl groups was determined, under the conditions described, although both groups can be titrated in aqueous solution by conventional methods, e.g., by using a visual indicator. Similarly, only one carboxyl group in succinic and oxalic acids is determined when anhydrous acetaldehyde is used as the solvent and thermometric indicator, provided that the sample solution is sufficiently dilute.[58] However, when these acids are titrated in aqueous acetaldehyde the end-point inflection corresponds to the titration of both carboxyl groups.

A systematic study of the influence of acetone and acetaldehyde on the measured reaction stoichiometries in the catalytic thermometric titration of dicarboxylic acids[58] has shown that the results obtained in the determination of oxalic and succinic acids are dependent on the solvent properties of the sample solution when the end point is indicated. The measured reaction stoichiometries increase with increasing concentration of the sample, and this effect is apparently due to the increase in the water content of the sample solution with increase in sample size. Water is formed during neutralization of the acid, and similar increases in measured reaction stoichiometry are obtained by adding small amounts of water to the sample solution instead of increasing the sample size. Methanol in the sample solution

has an effect on the measured reaction stoichiometry similar to that of water.

It is concluded that intramolecular hydrogen bonding in the oxalate and succinate monoanions is so strong that the second carboxylic acid group cannot be determined in solution in the relatively poorly solvating solvents acetone, acetaldehyde, and propan-2-ol (the titrant solvent), but that water and methanol solvate the carboxylate ions and release the acid function for titration. The superior solvating power of water and methanol for intramolecular hydrogen bonded monoanions of dicarboxylic acids has been discussed recently by Chantooni and Kolthoff.[59]

2. Acrylonitrile and Alkyl Vinyl Ether

In the presence of strong alkali, acrylonitrile cyanoethylates compounds containing replaceable ("active") hydrogen:

$$CH_2{=}CHCN + RH \xrightarrow{OH^-} RCH_2CH_2CN \qquad (12)$$
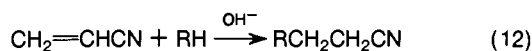
Consequently, when acrylonitrile is used as an indicator in the catalytic thermometric titration of acids, with strong alkali, cyanoethylation of the sample compound is possible. If the cyanoethylated function is acidic, cyanoethylation will interfere with the thermometric titration, and low titration values will result. The magnitude of this interference will clearly depend on the relative rates of the determinative (neutralization) and cyanoethylation reactions. Phenols can be titrated with no evidence of cyanoethylation,[19,32] but several thiols have been found to be almost completely cyanoethylated before they can be neutralized.[60] The same thiols can be determined by using acetone as the thermometric indicator. Titration values considerably lower than those expected were obtained when acrylonitrile was used as the indicator in the titration of sulfanilamide,[61] and the low results have been attributed to cyanoethylation during the course of the titration.

The addition of alkyl vinyl ethers to thiols, by a reaction similar to cyanoethylation, has been proposed to explain the low titration values obtained in attempts to determine thiols by catalytic thermometric titration with iodide, using alkyl vinyl ethers as thermometric indicators.[35] This explanation is supported by the earlier work by Kipnis, Solonay, and Ornfelt,[62] who showed that some thiols undergo addition to alkyl vinyl ethers.

3. Acetic Anhydride

Publications reporting on the use of mixtures of acetic anhydride and water or acetic anhydride and acetylatable coreagents as indicators for the thermometric titration of bases with perchloric acid have claimed only that the method is suitable for the determination of tertiary amines and metal carboxylates.[7,40,63,64]

Acetic anhydride will acetylate primary and secondary amines during the course of their titration with perchloric acid, the latter functioning as a catalyst, and the basic properties of the amines are thereby reduced. An attempt to determine acetylatable amines by catalytic thermometric titration[25] showed the reaction stoichiometries to be lower than would be expected if the amines had been completely neutralized. It was suggested[25] that the magnitude of the titration values would depend on the time during which the amine and acetic anhydride had been in contact when the end point was indicated.

C. Solvent and Titrant Effects

In most of the reported applications of catalytic thermometric titrimetry, inorganic samples have been determined as their aqueous solutions with aqueous titrants, while organic samples have been titrated in nonaqueous solution with reagents dissolved in organic solvents. Exceptions to this generalization are the use of dimethyl sulfoxide by Kiss[55] as a solvent in titrations of metals and chelating agents (section III.A.5) and the titration of organic acids in aqueous acrylonitrile[65] and aqueous acetaldehyde[28] with both aqueous and nonaqueous solutions of potassium hydroxide.

In the present review, it is convenient to consider effects resulting from the use of different solvent and titrant systems under the headings "Organic Solvents" and "Water and Methanol". Methanol is considered together with water because effects resulting from its inclusion in titration solvent systems are due mainly to its highly reactive hydroxyl group.

1. Organic Solvents

Apart from the work by Kiss on dimethyl sulfoxide, investigations of the effects of organic solvents in catalytic thermometric titrimetry appear to have been confined to acid–base titrations.

Attempts have been made to explain the effects of different solvents, or combinations of solvents, in the titration of acids[66] and bases[25,63] in nonaqueous solution, and acids in mixtures of organic solvents and water.[28,65] Vajgand, Kiss, Gaàl, and Zsigrai[63] reported that when a mixture of acetic anhydride and water is used as a thermometric indicator in the titration of organic bases, weak bases such as antipyrine ($pK_b = 12.4$) cannot be determined satisfactorily as a solution in acetic acid containing 8% of acetic anhydride and 2% of water. However, when the acetic acid content is reduced by increasing the ratio of acetic anhydride to acetic acid, or by replacing acetic acid by nitromethane, greater temperature changes occur at the end point, and results with higher precision are obtained. They suggest that the improvements achieved by using different solvents confirm the dominant role of the dielectric constant of the solvent. However, some recent studies,[25] in which a mixture of acetic anhydride and 4-hydroxy-4-methylpentan-2-one is used as the indicator reagent, have shown that sharper end points can be obtained in the determination of the very weak base caffeine ($pK_b = 13.4$) when some of the acetic anhydride ($\epsilon = 20.7$) is replaced by nitromethane ($\epsilon = 36.0$), dichloromethane ($\epsilon = 9.1$), or 1,2-propanediol carbonate ($\epsilon = 69.0$). In this instance, therefore, there appears to be no simple relationship between the end-point sharpness and the dielectric constant of the solvent.

Similar solvent effects have been observed when cationic polymerization is used as a means of end-point indication in the determination of organic bases.[33] Thus, improved end-point inflections are obtained in determinations in which 0.01 and 0.001 M perchloric acid and boron trifluoride titrants are used, when these are prepared by diluting the 0.1 M titrants, in acetic acid and 1,4-dioxane, respectively, with 1,2-dichloroethane or nitroethane instead of with the original solvents. Acrylonitrile, also, is an effective dilution solvent for the boron trifluoride reagent. When different solvents are used for the sample and titrant, temperature changes, caused by the heat of mixing, occur during the titration. There is, for example, a significant endotherm when titrants containing nitroethane are added to bases dissolved in acetic acid. These titrant effects are summarized in Figures 7 and 8.[33]

In cationic polymerization, the dielectric constant of the solvent system might be expected to influence the kinetics of the initiation of the polymerization reaction. In a solvent with a high dielectric constant the ionic catalyst would tend to form free ions rather than ion pairs, and the former would normally be the more active species catalytically. However, Ledwith and Sherrington[67] point out that solvents of high polarity can destabilize the transition state and cause a reduction in the rate of initiation. In the above titrimetric studies,[33] 1,2-dichloroethane, a solvent with a low dielectric constant, was found to be rather more effective in terms of the sharpness of the temperature rise at the end point
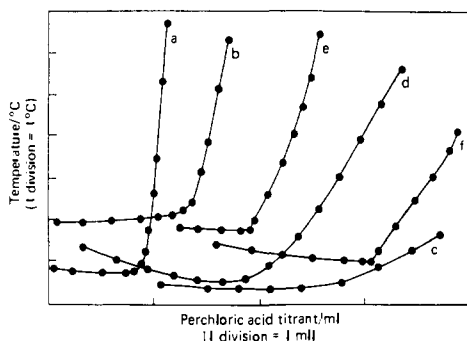
Figure 7. Effect of titrant molarity and titrant solvent on the shape of the thermometric titration curve: perchloric acid titrants (morpholine sample; 2-phenylpropene indicator). Data given in the order: molarity, diluent for 0.1 M HClO$_4$ in CH$_3$COOH, mg of morpholine, mL of 2-Phenylpropene, where A = acetic acid, N = nitroethane, and X = 1,2-dichloroethane: (a) 0.1, -, 10, 10; (b) 0.01, A, 2, 10; (c) 0.002, A, 0.2, 2; (d) 0.002, N, 0.2, 2; (e) 0.002, X, 0.2, 2; (f) 0.001, X, 0.1, 2. From ref 33, with permission of the Chemical Society.
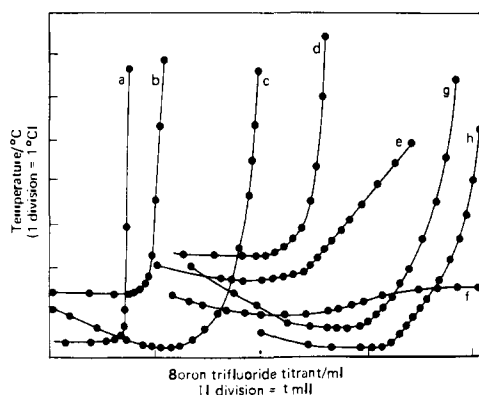

Figure 8. Effect of titrant molarity and titrant solvent on the shape of the thermometric titration curve: boron trifluoride titrants (morpholine sample; 2-methylpropyl vinyl ether indicator). Data given in the order molarity, diluent for 0.1 M BF$_3$·(C$_2$H$_5$)$_2$O in dioxan, mg of morpholine, mL of 2-methylpropyl vinyl ether, where D = dioxan, N = nitroethane, X = 1,2-dichloroethane, and C = acrylonitrile: (a) 0.1, -, 10, 10; (b) 0.01, D, 2, 10; (c) 0.002, N, 0.2, 2; (d) 0.002, X, 0.2, 2; (e) 0.002, C, 0.2, 2; (f) 0.001, D, 0.1, 2; (g) 0.001, N, 0.1, 2; (h) 0.001, X, 0.1, 2. From ref 33, with permission of the Chemical Society.

than nitroethane, a solvent with a much higher dielectric constant. This could be partly explained by the occurrence of the endotherm preceding the end-point inflection when nitroethane is a constituent of the titrant (Figure 7d).

Vaughan and Swithenbank[8] have examined the effects of solvents on the efficiency of the acetone indicator method for the titration of weak acids (Figure 9). The addition of 59% of pyridine or 25% of benzene reduces the temperature rise at the end point by about 50%, but the end-point inflection remains sharp; on addition of 50% of benzene or nitrobenzene the temperature rise is further reduced and the end point becomes less apparent, because the rate of temperature rise falls off sharply with the further reduction in the acetone concentration of the solution.

When acrylonitrile is used as a thermometric indicator in the titration of weak acids (section III.A), the composition of the solvent has an important influence on the shape of the titration curve. Systematic studies have shown that the incorporation of an appropriate solvent in the sample solution can improve the end-point sharpness[23,68] while by the use of solvent mixtures it is possible to control the reaction stoichiometry in the determination of some polyfunctional acids.[23,66,68] In a preliminary investigation,[66] Greenhow and Hargitt found that when potassium hydroxide in propan-2-ol is used as the titrant, the measured reaction stoichiometries in the titrations of succinimide,
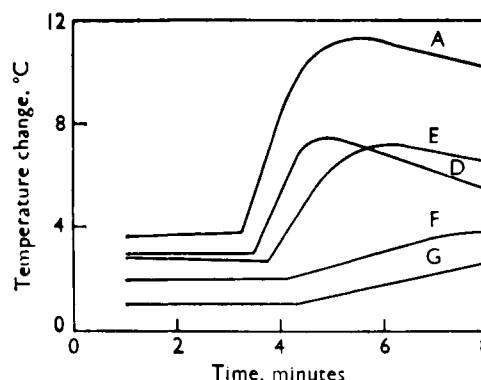
Figure 9. Effect of solvents on catalytic thermometric titrations with acetone as the indicator: (A) acetone only; (D) 59% pyridine; (E) 25% benzene; (F) 50% benzene; (G) 50% nitrobenzene. From Vaughan and Swithenbank,[8] with permission of the Chemical Society.

TABLE II. Catalytic Thermometric Titration of Succinimide (1), Phthalimide (2), and 2,6-Di-tert-butyl-4-methylphenol (3) Using Acetone and Acrylonitrile as End-Point Indicators[a]

Stoichiometry of the neutralization reaction[b]					
1	2	3	Titrant[c]	Solvent[d]	Indicator[d]
0.27	0.51	0.31	K	D	AN
0.28	0.46	0.31	B	D	AN
0.65	0.82	0.26	N	D	AN
1.0	1.0	0.97	K	AN	AN
0.58	0.67	0.27	B	AN	AN
1.0	1.0	1.0	K	A	A

[a] From ref 66, with permission of the Chemical Society. [b] Equivalents of titrant per molecule of sample. [c] Titrants: K, 0.5 M potassium hydroxide in propan-2-ol; B, 0.1 M tetra-n-butylammonium hydroxide in toluene-methanol; N, 0.1 M sodium methoxide in methanol. [d] Solvents and indicators: A, acetone; AN, acrylonitrile; D, dimethylformamide.

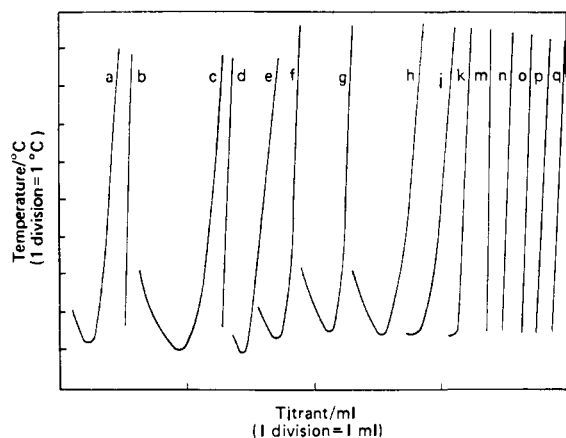**TABLE III. Catalytic Thermometric Titration of Resorcinol Using Acetone and Acrylonitrile as End-Point Indicators[a]**

Indicator	Titrant[b]	Solvent	Stoichiometry[c]
Acetone	K	Acetone	2.0
Acetone (50%)	K	Acrylonitrile (50%)	2.0
Acrylonitrile	K	Acrylonitrile	2.0
Acrylonitrile	B	Acrylonitrile	1.3
Acrylonitrile (50%)	B	Dimethylformamide (50%)	1.0
Acrylonitrile (30%)	B	Dimethylformamide (70%)	1.0
Acrylonitrile (50%)	K	Dimethylformamide (50%)	1.5

[a] From ref 66 with permission of the Chemical Society. [b] Titrants: K, 0.5 M potassium hydroxide in propan-2-ol; B, 0.1 M tetra-n-butylammonium hydroxide in toluene-methanol. [c] Of the neutralization reaction.

phthalimide, 2,6-di-tert-butyl-4-methylphenol and resorcinol are influenced significantly by changing the sample solvent from acrylonitrile to a mixture of acrylonitrile and dimethylformamide (Table II). Resorcinol can be determined as either a monofunctional or a difunctional acid by using an appropriate solvent system and titrant (Table III). Low titration values are obtained, irrespective of the solvent system, when tetra-n-butylammonium hydroxide in toluene–methanol is used as the titrant. Tables II and III include, for comparison, results obtained when acetone is the solvent. It can be seen that with acetone alone or a mixture of acetone and acrylonitrile as the solvent, high titration values are obtained.

In a more systematic investigation[23,68] of these solvent and titrant effects, it was observed that when potassium hydroxide in propan-2-ol is used as the titrant, the sharpness of the end

Titrant/ml
(1 division=1 ml)

Figure 10. Effect of solvent composition on the shape of catalytic thermometric titration curves (acrylonitrile indicator). Solvent/mL and titrant/M: (a) A 4 and K 0.1; (b) A 4 + D 1 and K 0.1; (c) A 2 + B 2 and K 0.1; (d) A 2 + B 2 + D 1 and K 0.1; (e) A 4 and K 0.5; (f) A 3 + B 1 and K 0.5; (g) A 2 + B 2 and K 0.5; (h) A 1 + B 3 and K 0.5; (j) A 3 + P 1 and K 0.1; (k) A 3 + P 1 and K 0.5; (m) A 2 + P 2 and K 0.5; (n) A 3 + P 1 + D 0.5 and K 0.1; (o) A 4 and Q 0.1; (p) A 2 + B 2 and Q 0.1; (q) A 3 + P 1 and Q 0.1 (A, acrylonitrile; D, dimethylformamide; B, benzene; P, pyridine; K, potassium hydroxide; Q, tetrabutylammonium hydroxide). From ref 23, with permission of the Chemical Society.

point can be improved markedly by including a small amount of dimethylformamide or dimethyl sulfoxide in the sample solvent. In Figure 10, this effect is shown for blank titrations, when the solution at the end point contains the minimum amount of the titrant solvent. The increased end-point sharpness can be attributed to the effect of the dipolar aprotic solvents on the catalytic activity of the titrant. Both dimethylformamide and dimethyl sulfoxide have high dielectric constants, which favors ionization of the titrant, and both solvate the potassium ion only, which favors the separation of unsolvated hydroxide ions.[69] Potassium hydroxide in organic solvents normally exists as a mixture of ion pairs, K^+OH^-, solvent-separated ion pairs, and free ions. The free anion is much more effective than the ion pair as a catalyst for anionic polymerization,[70] and this explains the effect on end-point sharpness of adding the dipolar solvents. In Figure 10, it can be seen that even when acrylonitrile, which has a high dielectric constant ($\epsilon = 33$), is used as the solvent, the end point of the blank titration is not sharply defined. It is proposed[23] that the solvating power of the dipolar aprotic solvent, as measured by the electron-pair donicity,[71] is more important than the dielectric constant in controlling the anion activity and, therefore, the rate of polymerization.

As might be expected, benzene, which has a low dielectric constant and a low donicity, has an adverse effect on the end-point sharpness (Figure 10c,h), while pyridine, which has a low dielectric constant but a high donicity, is more effective than acrylonitrile but not as effective as dimethylformamide, in terms of the end-point sharpness achieved (Figure 10j,k).

Tetra-n-butylammonium hydroxide, in contrast to potassium hydroxide, has a bulky cation and tends to ionize completely to yield hydroxyl ions. As a result, rapid ionic polymerization occurs, even in the absence of the dipolar aprotic solvents, when this titrant is used (Figure 10o,p,q).

The content of the titrant solvent in the sample solution at the end point will depend on the amount of titrant added. A study of the effect of increasing the content of the titrant solvent, propan-2-ol, in the solvent mixture has shown[23] that the blank titration value is reduced and the end-point inflection is sharpened (Figure 11). The heat of mixing, prior to the end point, was found to be endothermic when titrant is added to either acrylonitrile or a mixture of acrylonitrile and dimethylformamide, and exothermic when titrant is added to a mixture of acrylonitrile and propan-2-ol. Thus it was possible to obtain a zero heat of mixing by a judicious selection of solvent mixtures (Figure 11n,s).

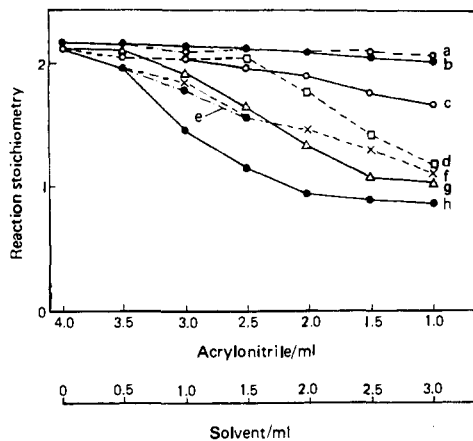
0.1 M potassium hydroxide reagent/ml
(1 division=1 ml)
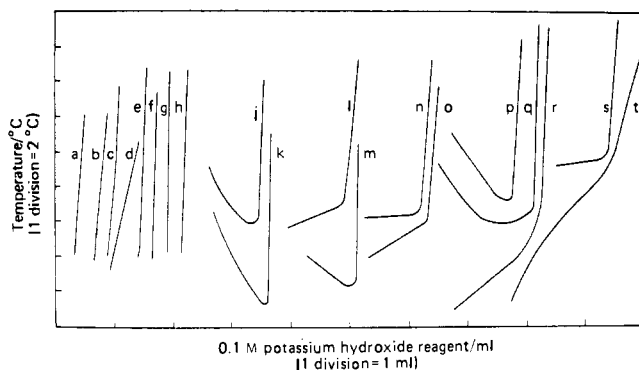
Figure 11. Effect of propan-2-ol on the shape of catalytic thermometric titration curves (0.1 M potassium hydroxide reagent; acrylonitrile indicator). Solvents/mL: (a) A 3 + Pr 1; (b) A 1 + Pr 3; (c) A 2 + Pr 1 + B 1; (d) A 1 + Pr 1 + B 2; (e) A 2 + Pr 2 + P 1; (f) A 2 + Pr 1 + P 2; (g) A 3 + Pr 2 + D 1; (h) A 1 + Pr 3 + D 1. Benzoic acid titrations (0.1 mequiv): (j) A 5; (k) A 4 + D 1; (l) A 4 + Pr 1; (m) A 1 + D 4; (n) A 1 + Pr 1 + D 3; (o) A 1 + Pr 2 + D 2. Resorcinol titrations (0.1 mequiv): (p) A 1 + D 4; (q) A 5; (r) A 4 + Pr 1; (s) A 1 + Pr 1 + D 3; (t) A 1 + Pr 4. (A, acrylonitrile; Pr, propan-2-ol; B, benzene; P, pyridine; D, dimethylformamide). From ref 23, with permission of the Chemical Society.

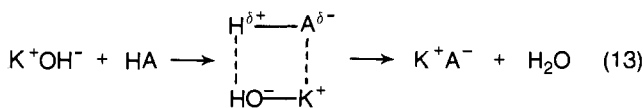
Acrylonitrile/ml

Dimethyl sulphoxide/ml
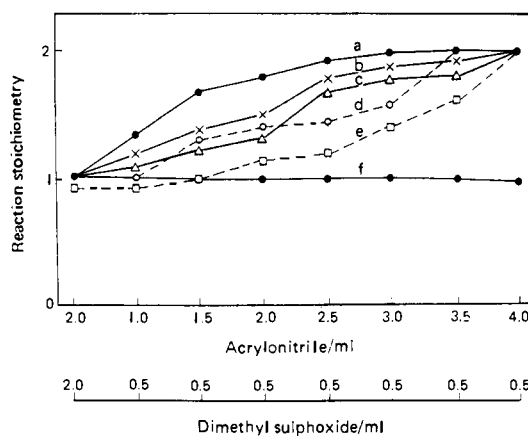
Figure 12. Solvent effects in the catalytic thermometric titration of (a) salicylic acid, (b) pyrocatechol, (c) 2,2'-dihydroxydiphenylmethane, (d) hydroquinone and (e) 2,2'-dihydroxybiphenyl (0.5 M potassium hydroxide reagent); (f) compounds a-e titrated with 0.1 M tetrabutylammonium hydroxide (0.05 mmol samples. acrylonitrile indicator). From ref 23, with permission of the Chemical Society.

An examination[23,68] of the effect of the sample solvent in titrations of some polyfunctional acids has shown that increasing the amount of dipolar aprotic solvent in the titration solution decreases the measured reaction stoichiometry. Thus, in titrations of resorcinol, pyrocatechol, quinol, salicyclic acid, 2,2'-dihydroxybiphenyl, and 2,2'-dihydroxydiphenylmethane with potassium hydroxide reagent (Figure 12), both acid functions are determined when acrylonitrile alone is used as the solvent, while only one acid function is determined when the sample is dissolved in a 1:1 mixture of acrylonitrile and dimethyl sulfoxide. Similar results are obtained when dimethylformamide, N,N-dimethylacetamide, 1-methyl-2-pyrrolidone, and hexamethylphosphoramide are used instead of dimethyl sulfoxide (Figure 13). Intermediate reaction stoichiometries are observed when the above determinations are carried out with solvent mixtures containing intermediate amounts of the dipolar aprotic solvents. It is deduced[23] that neutralization of the second acidic function and initiation of the polymerization reaction are competing processes, and the dipolar aprotic solvents have the greater influence on the latter. It is proposed that when the solvent mixture contains only a small amount of these solvents the titrant will exist mainly as ion pairs, and, in this form, it will undergo reaction with the weaker function of the difunctional acid through a four-center intermediate:

Figure 13. Solvent effects in the catalytic thermometric titration of 0.1 mmol of resorcinol (0.5 M potassium hydroxide reagent). Solvents: (a) acetone, (b) pyridine, (c) sulfolane, (d) hexamethylphosphoramide, (e) 1-methyl-2-pyrrolidone, (f) N,N-dimethylacetamide, (g) dimethylformamide, (h) dimethyl sulfoxide (acrylonitrile indicator). From ref 23, with permission of the Chemical Society.

$$K^+OH^- + HA \longrightarrow \begin{array}{c} H^{\delta+}\!\!-\!\!A^{\delta-} \\ | \qquad | \\ | \qquad | \\ HO\!\!=\!\!K^+ \end{array} \longrightarrow K^+A^- + H_2O \quad (13)$$

When tetra-*n*-butylammonium hydroxide was used instead of potassium hydroxide as the titrant in the determination of the above difunctional acids, only one of the two acid groups had been titrated when the end point was indicated (Figure 12). As noted already, this catalytic action of the quaternary ammonium hydroxide might be due to its being fully ionized in the organic media and initiating the polymerization in preference to neutralizing the second, weaker, acidic function. The virtual absence of the second neutralization stage could be explained by prevention of the formation of the proposed four-center intermediate by the difficulty in accommodating the bulky tetrabutylammonium cation.

Primary and secondary amines are unsuitable as solvents when acrylonitrile is used as a thermometric indicator because they readily undergo alkali-catalyzed cyanoethylation, and the resulting exothermic reaction either masks the end-point inflection or reduces its sharpness.[32]

Four titrants (tetra-*n*-butylammonium hydroxide, sodium methoxide, potassium methoxide, and potassium hydroxide, in nonaqueous solution) and five sample solvents (pyridine, dimethylformamide, dimethyl sulfoxide, 1,1,3,3-tetramethylurea, and N,N,N',N'-tetramethyl-1,2-diaminoethane) have been evaluated in the determination of the acidic functions of sulfanilamide derivatives of pharmaceutical importance by catalytic thermometric titrimetry.[61] Acrylonitrile was used as the indicator reagent. Most of the sulfanilamide derivatives could be titrated satisfactorily with all the titrant–solvent combinations, but sulfanilamide itself could be determined only with 1.0 M potassium hydroxide in propan-2-ol as the titrant and acrylonitrile alone as the solvent. The very weak base sulfaguanidine gave very rounded titration curves with most of the titrant–solvent combinations, showing considerable overlap of the determinative and indicator reactions. However, acceptably sharp end-point inflections were achieved by using 0.1 M potassium hydroxide in propan-2-ol as the titrant and either dimethyl sulfoxide or 1,1,3,3-tetramethylurea as the solvent.

2. Water and Methanol

Titrations are often carried out with nonaqueous solutions when unsatisfactory results are obtained under aqueous conditions, for example, in the determination of weak acids and bases. It might be expected, therefore, that the addition of water
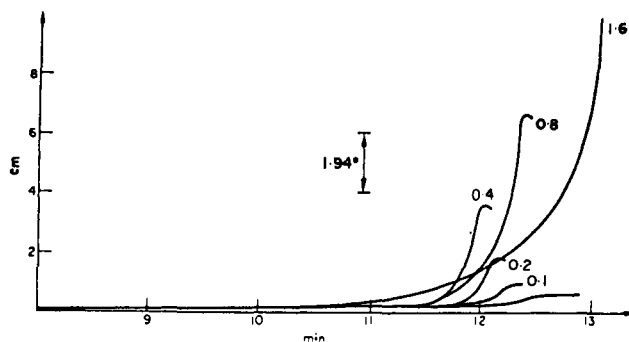
Figure 14. The effect of water in the indicator reaction on the shape of curves in catalytic thermometric titrations. The numbers on the curves represent the percentage of water added in the analysis (acetic anhydride–water indicator system). From Vajgand et al.,[40] with permission of Pergamon Press.
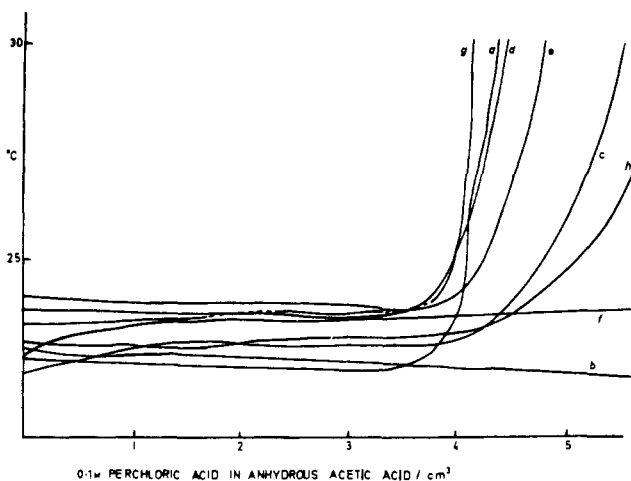

Figure 15. Effect of water and methanol on thermometric titrations (2-phenylpropene indicator). Sample, 27 mg of pyridine in 5 mL of toluene; solvent, 15 mL of 2-phenylpropene: (a) no addition, (b) +35.0 mg of water, (c) +16.1 mg of water, (d) +36.4 mg of water +0.5 g of molecular sieve 3A, (e) +105.2 mg of water +0.5 mg of molecular sieve 3A, (f) +402.1 mg of methanol, (g) +80.2 mg of methanol, (h) +160.2 mg of methanol. From ref 20, with permission of the Society of Chemical Industry.

to the sample solution in nonaqueous catalytic thermometric titrations would have an adverse effect, even if the water did not interfere with the thermometric indicator reaction.

In their study of the application of coulometric methods of titrant generation to the catalytic thermometric titration of tertiary amines and metal carboxylates, Vajgand, Gaál, and Brusin[40] found the water content of the sample solution to be of decisive importance when the reaction between acetic anhydride and water was used to indicate the end point. The temperature increase after the end point was lower, the lower the water content, but the slope of the titration curve was sharpest when the water content was under 0.4% (Figure 14). Only by reducing the water content to a very low value, or by eliminating it completely and using the reaction between acetic anhydride and a mixture of quinol and 1,4-benzoquinone for end-point indication, was it possible for them to determine very weak bases such as caffeine.

When cationic polymerization is used as a means of end-point detection, the presence of water is undesirable because it inhibits the polymerization. Thus, 0.2% of water in a 3 + 1 mixture of 2-phenylpropene and toluene completely prevents the initiation of the polymerization by 0.1 M perchloric acid, while 0.1% of water in the same mixture gives rise to a titrimetric end-point inflection much inferior to that obtained under the corresponding anhydrous conditions (Figure 15).[20] Water also reduces the efficiency of the boron trifluoride catalyst used in combination with
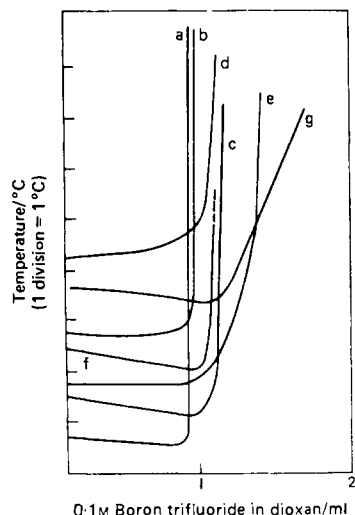
Figure 16. Effect of water on the catalytic thermometric titration of morpholine (10 mg in 1 mL of toluene plus 10 mL of 2-methylpropyl vinyl ether indicator) with 0.1 M boron trifluoride in dioxan: (a) no water added; (b) +10 mg of water; (c) +22 mg of water, (d) +95 mg of water; (e) +120 mg of water; (f) +104 mg of water +0.5 g of molecular sieve 4A; and (g) +73 mg of water (only 2 mL of 2-methylpropyl vinyl ether). From ref 33, with permission of the Chemical Society.

the 2-methylpropyl vinyl ether indicator (Figure 16), but the effect on the sharpness of the end-point inflection is not as marked as it is with perchloric acid.[33] With both these catalyst–monomer systems it was found possible to reduce the inhibiting action of the water substantially by adding molecular sieve 3A or 4A to the sample solution.[33]

Small amounts of water do not inhibit the cationic polymerization in iodometric catalytic thermometric titrations in which ethyl vinyl ether is used as the indicator reagent.[36] Instead, the water is consumed in a reaction with the titrant and the vinyl monomer and is thereby determined.

Siggia[72] has shown that vinyl ethers can be determined iodometrically by their reaction with iodine and an alcohol:

$$ROCH{=}CH_2 + I_2 + R'OH \rightarrow ROCH(OR')CH_2I + HI \quad (14)$$
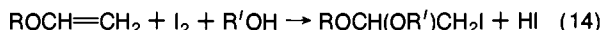
and it seems likely that water would undergo a similar reaction to yield the substituted alcohol $ROCH(OH)CH_2I$, which could combine further with iodine and vinyl ether. However, in the iodometric titration, the reaction stoichiometry in the determination of water is dependent on the rate of addition of the titrant and is much lower, in terms of atoms of iodine combining with molecules of water, than the value predicted from the above equation.[36] Thus, when 0.05 M iodine reagent is added to the sample solution at a rate of 0.06 ml min⁻¹, about 1 atom of iodine is consumed by 13 molecules of water when the end point is indicated.

The effect of water in the nonaqueous catalytic thermometric titration of weak acids has been found to depend on the thermometric indicator employed. The best results are obtained with the acetone indicator method when the system is water free,[8] and it is generally recommended that the water content of the acetone be less than 0.2%. The change in the shape of the titration curve as the water content of the acetone is increased is shown in Figure 17. Apparently, the rate of conversion of acetone to diacetone alcohol decreases sharply with the increase in water content. In contrast, the alkali-catalyzed aldol condensation of acetaldehyde is not prevented by the addition of water, even in substantial amounts, and the water has the effect of improving the sharpness of the end-point inflection (Figure 3).[28] The reactive species in the alkali-catalyzed polymerization are probably the hydrate and hemiacetal, formed by the reaction of water and propan-2-ol, respectively, with the acetaldehyde. An increase in the sharpness of the end-point
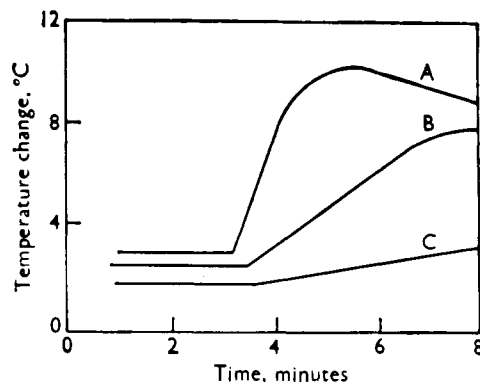
Figure 17. The effect of water on catalytic thermometric titrations with acetone as the indicator: (A) dry acetone; (B) acetone containing 0.2% water; (C) acetone containing 2.0% water. From Vaughan and Swithenbank,[8] with permission of the Chemical Society.
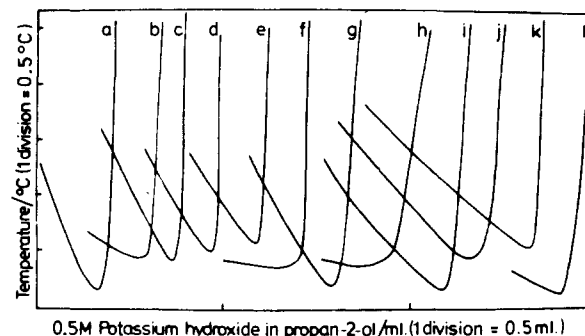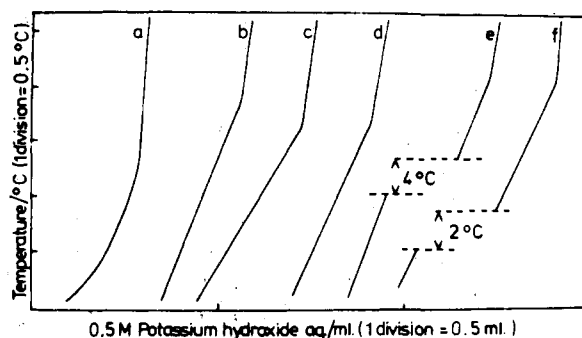

Figure 18. The catalytic thermometric titration of acids in aqueous solution with 0.5 M potassium hydroxide in propan-2-ol (acrylonitrile indicator): (a) glycine (1.5%) concentration in aqueous solution; (b) cysteine (2%); (c) valine (2%); (d) benzoic acid (2%); (e) phenol (2%); (f) phenol (10%); (g) resorcinol (2%); (h) resorcinol (10%); (i) oxalic acid (2%); (j) phosphoric acid (1%); (k) phosphorous acid (1.1%); (l) boric acid (1%). Conditions: titrant is added at 0.2 mL/min to a mixture of the aqueous sample containing 0.1 mmol of the acid, 4 mL of dimethyl sulfoxide, and 2 mL of acrylonitrile. From ref 65, with permission of the Pergamon Press.

inflection in catalytic thermometric titrimetry can usually be attributed to a reduction in the extent to which the determinative and indicator reactions overlap. The effect of added water on acetaldehyde-indicated reactions may be due to the water reducing the rate of the indicator reaction or increasing the rate of the determinative reaction, or both.

Although it is known that protogenic solvents inhibit or reduce the rate of anionic polymerizations,[73] water contents of at least 1% can be tolerated without the sharpness of the end-point inflection showing a significant decrease when acrylonitrile is used as a thermometric indicator.[19] In a recent investigation of the effect of water on the acrylonitrile indicator system[65] it has been shown that by using dimethyl sulfoxide as a cosolvent and 0.5 M potassium hydroxide in propan-2-ol as the titrant, 0.1-mmol amounts of strong and weak acids can be determined as their 1 to 10% aqueous solutions (Figure 18). It was also possible to obtain acceptably sharp end points when 2% aqueous solutions of acids were titrated with 0.5 M aqueous potassium hydroxide (Figure 19). The success of these titrations has been attributed partly to the strong hydrogen-bond acceptor properties of dimethyl sulfoxide which cause the water molecules in the solution to be immobilized.[74] It is suggested, further,[65] that chain transfer and cyanoethylation reactions, involving water and/or propan-2-ol, are mainly responsible for the rise in temperature occurring at the end point in the titrations.

The effect of methanol on indicator reactions in catalytic thermometric titrations is similar to that of water, but generally is less marked. Addition of methanol to the acetone indicator has

Figure 19. The catalytic thermometric titration of acids in aqueous solution with 0.5 M aqueous potassium hydroxide (acrylonitrile indicator). Conditions: as in Figure 18, apart from the titrant. The acid samples are 2% aqueous solutions: (a) arginine; (b) phenol; (c) resorcinol; (d) benzoic acid; (e) phosphoric acid; (f) phosphorous acid. From ref 65, with permission of the Pergamon Press.

an adverse effect, and acetone solutions containing about 5% methanol were found to be almost ineffective as indicators.[58] Surprisingly, methanol is unsuitable also as a solvent for use with the acetaldehyde-indicator system, although the higher alkanols are satisfactory.[58]

As might be expected, the acrylonitrile-indicated titrations are affected little by the presence of methanol and propan-2-ol in considerable proportions, since both alcohols are introduced into the sample solution as titrant solvents. However, a high proportion of methanol, namely 5–25 ml of acrylonitrile, has been found to inhibit the polymerization at the end point almost completely.[19]

Methanol, like water, inhibits cationic polymerization, but the 0.1 M perchloric acid–2-phenylpropene catalytic thermometric titration system will tolerate about 1% of methanol in the sample solution before the end-point inflection becomes difficult to detect[20] (Figure 15). The boron trifluoride–2-methylpropyl vinyl ether system is less affected by hydroxylic solvents, and 1% solutions of morpholine in methanol have been titrated successfully.[33]

Methanol is determined by the Siggia reaction[72] (eq 14) when it is present in solvent systems used in nonaqueous iodometric titrations in which the cationic polymerization of ethyl vinyl ether is used for end-point indication. However, higher alkanols, such as butan-1-ol and pentan-1-ol, and phenol are not titrated.[75]

D. Selectivity

The basic principle of catalytic thermometric titrimetry is the catalytic initiation of an exothermic reaction by an excess of titrant and, as a consequence, only one end point is usually indicated, however complex the sample. In contrast, techniques that monitor some property of the titrand during the course of the titration can be used to determine the composition of mixtures, because inflections occur in the titration curves corresponding to the separate components. Although the catalytic thermometric method is unselective in principle, the fact that different combinations of solvents, indicator reagents and titrants can give rise to different results in determinations of the same compound or mixtures of compounds may be used in some instances as a basis for selective determinations. As noted in section III.B, many thiols are not determined when the acrylonitrile indicator is used; however, they are titrated when either acetone or cyclohexanone is the indicator reagent,[60] and it is possible, therefore, to determine thiols and carboxylic acids selectively in mixtures by carrying out two titrations, one with each of the "selective" indicators.

A similar approach has been used for the separate determination of resorcinol and phenol,[66] and resorcinol and phenol moities in novolacs[76] and resoles[77] in their respective mixtures. The selectivity in this instance is achieved by using solvent
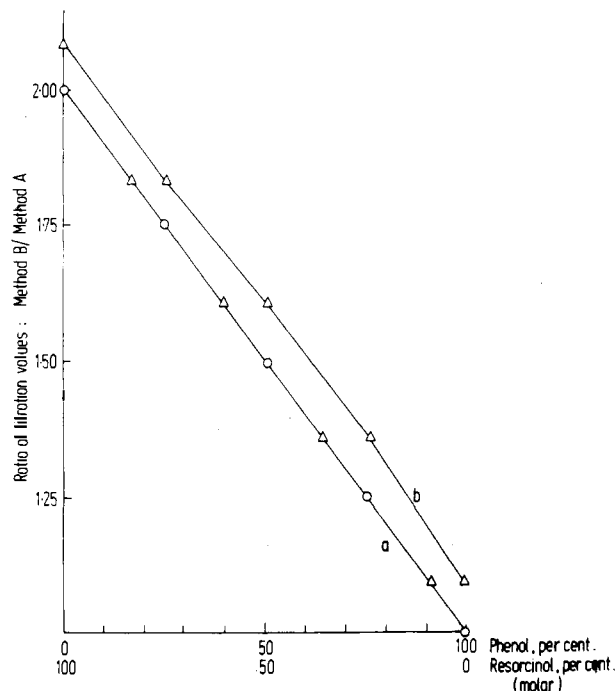
Figure 20. Calibration graphs for the determination of phenol; resorcinol ratios by catalytic thermometric titration. (a) Mixtures of phenol and resorcinol. The points marked O refer to the mixtures and those marked △ refer to data from curve b. (b) Phenol–resorcinol–formaldehyde cocondensates (novolac resins). Method A: 5 mg of resin in 3 ml of dimethyl sulfoxide + 1 mL of acrylonitrile titrated with 0.0961 M KOH in propan-2-ol. Method B: 5 mg of resin in 0.5 mL of dimethyl sulfoxide + 4 mL of acrylonitrile, titrated with 0.4545 M KOH in propan-2-ol. From ref 76.

mixtures in which the resorcinol can be titrated as either a mono- or dibasic acid, dependent on the solvent composition. The solvent systems are discussed in section III.C. Phenol and the phenol moieties in the resins are titrated only as monofunctional acids, and the composition of the mixtures can be calculated from the results obtained by using two appropriate solvent systems with the aid of a simple calibration graph (Figure 20).

In titrations of some polyfunctional organic acids,[23] intermediate inflections occurred in the titration curves. These were found to correspond to the neutralization of stronger acid groups, and they have been attributed to the ineffectiveness of the weaker acid groups in inhibiting the polymerization reaction completely. As a result, the titration curve shows two or more inflections bounding the regions within which the polymerization reaction is retarded to different degrees. Titration curves illustrating this phenomenon are shown in Figures 21 to 23.
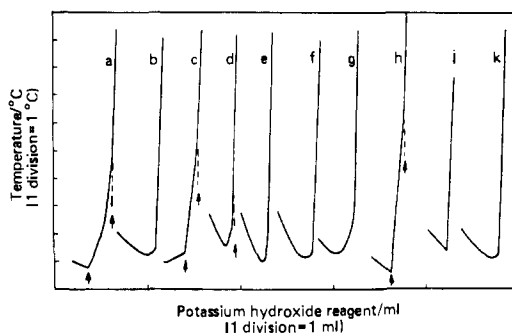
IV. Experimental Techniques

A. Apparatus

The temperature changes measured in catalytic thermometric titrimetry are usually several orders greater than those occurring in conventional thermometric titrimetry. As a consequence of this, The elaborate precautions required in the latter technique to prevent the loss of heat are not normally required in the former one.

The apparatus used by Vaughan and Swithenbank,[8] the originators of the technique, is shown in Figure 24. The temperature is measured with a thermistor connected through a simple bridge circuit to a recorder and titrant is added continuously from a motor-driven syringe buret. The titration vessel is a 20-mL beaker fitted with a cap through which passes the syringe needle, thermistor, inert gas inlet, and stirrer. A similar apparatus, but with an operational amplifier to amplify the signal

0.5 M potassium hydroxide reagent/ml
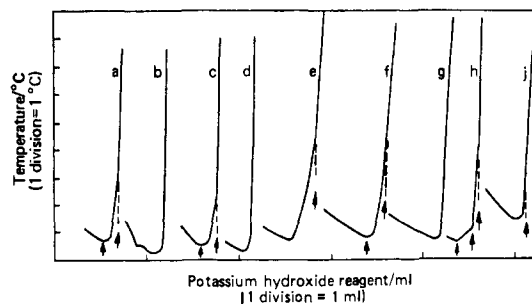(1 division = 1 ml)
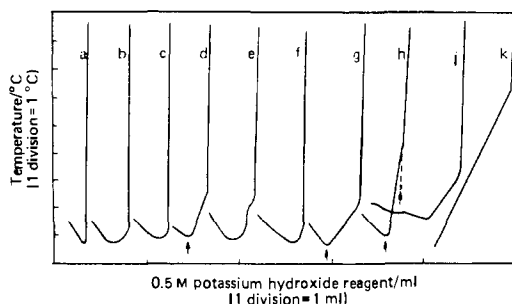
Figure 21. Titration curves for benzenecarboxylic acids (0.5 M potassium hydroxide reagent; acrylonitrile indicator). Acids and reaction stoichiometry: (a) benzoic 1.0; (b) phthalic 2.0; (c) isophthalic 2.0; (d) terephthalic 2.0(1); (e) 1,2,3-tricarboxylic 2.8; (f) 1,2,4-tricarboxylic 3.0; (g) 1,3,5-tricarboxylic 3.0 (1); (h) 1,2,4,5-tetracarboxylic 4.0 (3); (j) pentacarboxylic 5.0; (k) hexacarboxylic 5.6. The end points are denoted by arrows; 0.1-mmol samples except for (h) (0.05 mmol). Values in parentheses are reaction stoichiometries indicated by the inflections preceding the final end point. Solvents: (a–e, g and j) 4 mL of acrylonitrile + 1 mL of dimethylformamide; (f) 4 mL of acrylonitrile + 1 mL of 1-methyl-2-pyrrolidone; (k) 5 mL of acrylonitrile + 0.7 mL of dimethyl sulfoxide + 1 mL of methanol; (h) 8 mL of acrylonitrile + 1.7 mL of sulfolane + 0.25 mL of dimethylformamide. From ref 23, with permission of the Chemical Society.

Potassium hydroxide reagent/ml
(1 division = 1 ml)

Figure 23. Titration curves for hydroxy benzoic acids (0.5 M potassium hydroxide reagent; acrylonitrile indicator). Benzoic acids and solvents/ml (with reaction stoichiometry in parentheses): (a) 2-hydroxy and A 4 + S 0.5 (2.0; 1); (b) 3-hydroxy and A 4 + D 1 (2.0); (c) 4-hydroxy and A 4 + D 1 (2.0; 1); (d) 2,4-dihydroxy and A 4 + D 1 (3.0); (e) 2,6-dihydroxy and A 11 + S 4 + D 1 + H₂O 0.2 (3.0); (f) 3,4-dihydroxy and A 10 + D 1 (3.0; 2); (g) 3,5-dihydroxy and A 4 + D 1 (3.0); (h) 2,3,4-trihydroxy and A 11 + S 4 + D 1 + H₂O 0.2 (3.9; 3; 1); (j) 3,4,5-trihydroxy and A 5 + D 1 (4.0). The end points are denoted by arrows. (a–c) and (e–g), 0.1 mmol; (d, h, and j) 0.05 mmol. A = acrylonitrile; S = dimethyl sulfoxide; D = dimethylformamide. The second and third values in parentheses are the stoichiometries indicated by the inflections preceding the final end points. From ref 23, with permission of the Chemical Society.

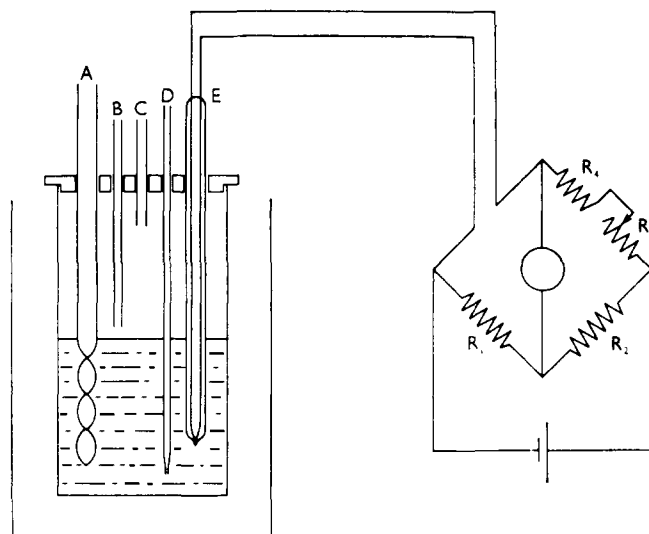
Potassium hydroxide reagent/ml
(1 division = 1 ml)

Figure 22. Titration curves for polyhydric phenols (0.5 and 1.0 M potassium hydroxide reagent; acrylonitrile indicator). Compounds/mmol and solvents/mL (with reaction stoichiometry in parentheses): (a) pyrocatechol 0.2 and A 16 + S 2 (2.0; 1); (b) resorcinol 0.1 and A 3.5 + S 0.5 (2.0); (c) hydroquinone 0.2 and A 20 + S 2 (2.0; 1); (d) phloroglucinol 0.05 and A 4 + D 0.5 (3.0); (e) pyrogallol 0.05 and A 10 + D 1 (3.0); (f) tetrachloropyrocatechol 0,1 and A 4 + D 1 (2.0); (g) tetrabromopyrocatechol 0.1 and A 4 + S 1 (2.0); (h) 2,2′-dihydroxybiphenyl 0.1 and A 12 + S 1.5 (2.0; 1.2); (j) 3,5,6,3′,5′,6′-hexachloro-2,2′-dihydroxydiphenylmethane 0.05 and A 3 + D 1 (2.0); (k) 2,2-bis(4-hydroxyphenyl)propane 0.1 and A 4 + D 1 (2.0). The end points are denoted by arrows; (a) and c) 1.0 M reagent. A = acrylonitrile; S = dimethyl sulfoxide; D = dimethylformamide. The second values in parentheses are the stoichiometries indicated by the inflections preceding the final end points. From ref 23, with permission of the Chemical Society.

Figure 24. Apparatus for catalytic thermometric titration (acetone indicator): (A) glass stirrer; (B) acetone inlet; (C) air inlet; (D) titrant tubing; (E) thermistor. Resistors: R₁ and R₂, 1000 Ω; R₃, 1000-Ω variable; R₄, 1500 Ω. From Vaughan and Swithenbank,[8] with permission of the Chemical Society.

from the thermistor bridge and a more effectively insulated reaction vessel, was used by Weisz, Kiss, and Klockow[21] for the catalytic thermometric titration of inorganic ions (Figure 25). The elaborations were required, apparently, because the temperature changes marking the end point were considerably less than those obtained with the acetone indicator.
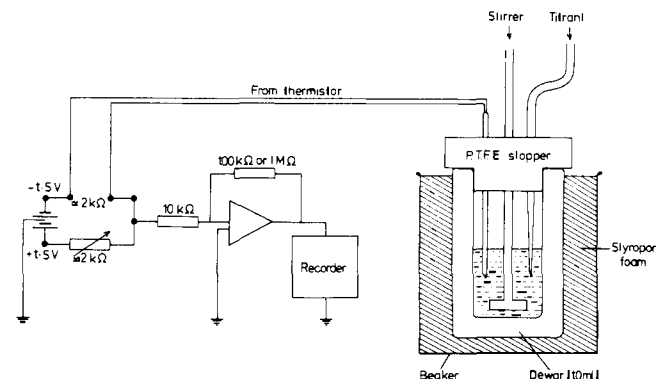
Efficient stirring is essential in the catalytic thermometric method to prevent local titration concentration, which could cause premature initiation of the indicator reaction. Both conventional glass stirrers and magnetic stirrers are widely used, but the former are more effective with sticky viscous solutions. When acetone and the vinyl monomers are used as indicator reagents, the temperature changes are such that a simple manual titration apparatus is adequate. Thus, the phenols content of coal tar fractions has been determined in acetone solution by adding titrant dropwise from a buret to the stirred solution and measuring the temperature with a 5–45 °C thermometer.[78] A similar apparatus (Figure 26) has been used for the titration of

Figure 25. Apparatus for catalytic thermometric titration (cerium(IV)–arsenic(III) indicator reaction). From Weisz et al.,[21] with permission of Springer-Verlag.

a wide range of acids[32] and bases[33] with vinyl monomers as the thermometric indicators. In determinations with the latter indi-
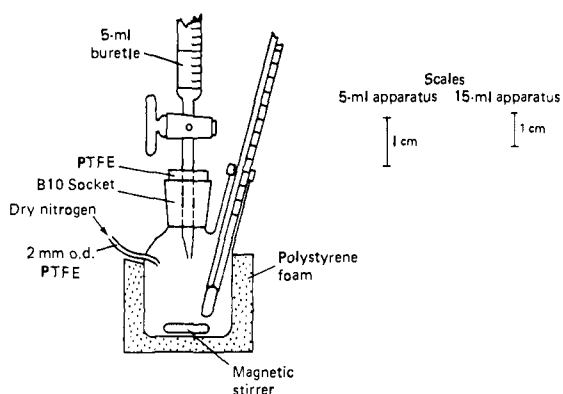
Figure 26. Manual apparatus for catalytic thermometric titration (acetone and acrylonitrile indicators). From ref 32, with permission of the Chemical Society.

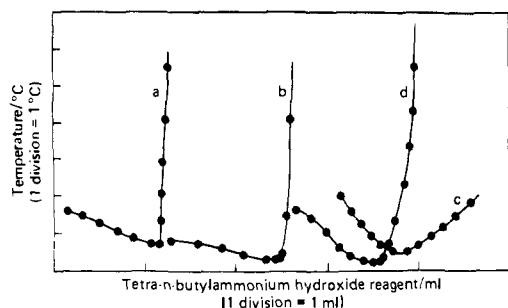**Figure 27.** Thermometric titration of benzoic acid with 0.1 to 0.001 M tetra-n-butylammonium hydroxide reagent (acrylonitrile indicator). Data are given in the order: molarity, mg of benzoic acid, mL of acrylonitrile, apparatus, where A = 50-mL beaker, B = 12-mL beaker, and C = 5-mL closed apparatus (Figure 26): (a) 0.1, 12.2, 10, A; (b) 0.01, 1.22, 2, B; (c) 0.001, 0.036, 1, B; (d) 0.001, 0.036, 1, C. From ref 32, with permission of the Chemical Society.

cators it was found possible to obtain satisfactory results in the titration of 0.0002 mequiv of benzoic acid with 0.001 M tetra-n-butylammonium hydroxide (Figure 27) and 0.001 mequiv of morpholine with 0.001 M perchloric acid (Figure 7) or 0.001 M boron trifluoride (Figure 8). The manual apparatus has been advocated by Parry-Jones[79] for use in educational projects.

Vajgand, Gaál, and Brusin[40] have developed a coulometric apparatus for catalytic thermometric titration (Figure 28). With it, they have determined tertiary amines and metal carboxylates, by titration with acid generated at a mercury or platinum anode, and weak acids by titration with alkali generated at the cathode. Sodium perchlorate in a mixture of acetic anhydride and acetic acid was the supporting electrolyte when a mixture of acetic anhydride and water was used as the indicator reagent, while quinol was used to generate the acid titrant when the reaction of acetic anhydride with quinol and, possibly 1,4-benzoquinone formed by the electrolytic oxidation, served to indicate the end point in the determination of the bases. In the titration of acids, sodium perchlorate in acetone was the supporting electrolyte for the generation of alkali, and acetone was the end-point indicator.

B. Titration Procedures

Direct-, reverse-, back-, and substitution procedures have been employed in catalytic thermometric titrimetry. Only the direct method appears to have been used in determinations involving acetone, acetaldehyde, vinyl monomers, and mixtures of acetic anhydride with water or organic hydroxyl compounds as the thermometric indicators, but there is no reason why reverse- and back-titration should not be carried out, if so desired.

All four titration procedures have been employed by Weisz,
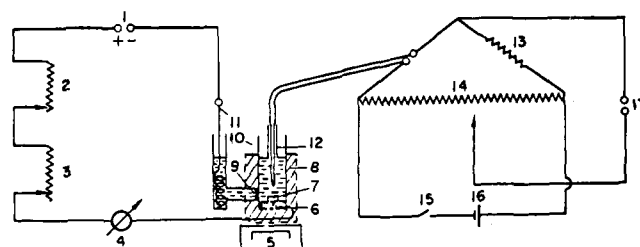
Figure 28. Schematic diagram of coulometric catalytic thermometric titration: (1) source of dc (voltage stabilizer ST-12, RR Zavodi Niš); (2) 10-kΩ semivariable resistor; (3) 100-kΩ semivariable resistor; (4) milliammeter BL 2 with scale in 0.01-mA divisions; (5) magnetic stirrer; (6) mercury anode; (7) magnet; (8) insulator; (9) sintered-glass disk, porosity 4; (10) coulometric titration cell; (11) platinum cathode; (12) thermistor (5 kΩ); (13) 5-kΩ resistor; (14) 10-kΩ rheostat; (15) switch; (16) 2.6-V battery; (17) recorder. From Vajgand et al.,[40] with permission of the Pergamon Press.

Kiss, and their co-workers[21,22,55] in the analysis of cations, anions, and chelating agents in aqueous solutions, while Kiss[55] has carried out direct- and back-titrations of solutions of chelating agents and cations, respectively, in dimethyl sulfoxide. In substitution titrations described by Kiss,[55] the titrant is not the catalyst for the indicator reaction, but liberates the catalyst from an inactive compound or complex as soon as it appears in the solution in excess, i.e., at the conclusion of the determinative reaction. For example, in the determination of silver, mercury(II), and palladium(II), a small amount of silver, mercury(II), or palladium(II) iodide is included, together with cerium(IV) and arsenic(III) indicator reagents, in the sample solution. The sample is titrated with potassium thiocyanate and a small excess of thiocyanate liberates iodide from the "inert" metal iodide, and the indicator reaction is initiated. In a similar manner, manganese(II) can be liberated from its complex with EDTA by titration with a solution of a zinc, cadmium, copper(II), nickel, indium, mercury(II), or lead(II), salt, and it will then initiate the decomposition of hydrogen peroxide or the oxidation of resorcinol by hydrogen peroxide. This substitution reaction can be used for the direct titration of chelating agents or the reverse titration of the above metal salts.

Aqueous and nonaqueous titrants ranging in molarity from 0.00001[55,80] to 1[8] have been used to determine sample sizes in the range 0.2 μg[80] to about 1 g. The preferred rates of titrant addition from motor-driven piston burets or syringes lie in the range 0.03 to 0.2 mL min^{-1}. Weisz, Kiss, and Klockow[21] found that the rate of addition giving rise to the minimum error in the determination of silver, by titration with 0.01 M potassium iodide, lies between 0.005 and 0.056 mL min^{-1} (see Table I).

The choice of titrant and sample solvent is important when determinations are carried out in nonaqueous solution (section III.C) and, as Kiss[55] has shown, it can be advantageous to use dimethyl sulfoxide instead of water in the determination of some inorganic substances.

The rise in temperature at the end point will be related not only to the amount of indicator reagents in the sample solution, as already noted, but also to the enthalpy and rate of the indicator reaction. When indicator reagents such as acetone, cyclohexanone, acetaldehyde, vinyl monomers, and mixtures of acetic anhydride with organic hydroxyl compounds are major components of the sample solution, rises in temperature from 4 to 25 °C can be achieved, depending on the reagent used and the molarity of the titrant.

In many other catalytic thermometric titrations much lower temperatures changes at the end point have been reported. For example, in their determination of silver at the 0.1 ppm level, using the cerium(IV)–arsenic(III) indicator reaction, Burton and Irving[80] measured the temperature changes with the chart recorder setting at 0.05 °C full scale. The temperature changes measured by Vajgand, Gaál, and Brusin[40] in the determination
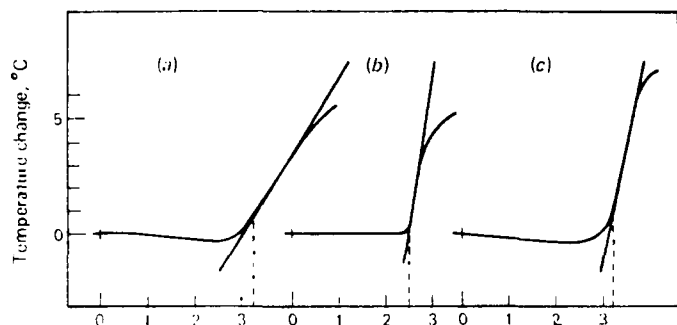
Figure 29. Titration curves for (a) coal; (b) phenol; (c) 2,6-di-*tert*-butyl-4-methylphenol showing the location of the end point (acetone indicator method; 1 M potassium hydroxide in propan-2-ol titrant). From Vaughan and Swithenbank,[81] with permission of the Chemical Society.

of caffeine in nonaqueous solution were in the range 0.06 to 0.19 °C.

C. End-Point Location

The location of the point on the titration curve corresponding to a stoichiometric determinative reaction has been the subject of considerable investigation. When the temperature rise marking the virtual completion of the determinative reaction does not give rise to a sharp inflection in the titration curve, it is necessary to locate the exact end point by using an appropriate geometric procedure. Vaughan and Swithenbank[81] found that the temperature rise is curved prior to the end point when sterically hindered phenols and coal samples are determined by the acetone indicator method. Tests with the sterically hindered phenols showed that the stoichiometric end point coincided with the point where a tangent drawn to the main temperature rise leaves the titration curve at its lower temperature end (Figure 29). The same procedure has been used in determinations of acids in which the anionic polymerization of vinyl monomers serves as the indicator reaction.[32]

The point of intersection of tangents drawn to the two "arms" of the titration curve has been taken as the end point by Vajgand and his co-workers in the determination of bases[7,40] and by Burton and Irving in the determination of mercury(II) and silver by the cerium(IV)–arsenic(III) indicator method.[80]

When the cationic polymerization of vinyl monomers was used to indicate the end point in the titration of bases,[33] it was found that the titration volume required by the stoichiometry of the reaction was the volume corresponding to the "upturn" temperature, where the titration curve leaves a tangent drawn to its horizontal part (Figure 30).

In nonaqueous iodometric titrations, in which the iodine-catalyzed polymerization of alkyl ethers is used for end-point indication,[35,36,75,82] the inflection in the titration curve has been taken as the end point (Figure 31). It does not necessarily correspond to the titrant volume for the stoichiometric reaction, but this is not important in the iodometric titrations because the blank titration value is significant; consequently the sample titration volume is measured as the difference between two measured volumes and errors in end-point location tend to cancel out.

V. Applications

The range of compounds that can be determined by catalytic thermometric titrimetry is limited by the indicator reagent–titrant combinations available. However, many acid–base, precipitation, complexometric, and nonaqueous iodimetric reactions have been shown to be amenable to study by the technique. In general, each of these four types of reaction is suitable for the determination of particular groups of compounds, and it is convenient to consider the applications of the thermometric method
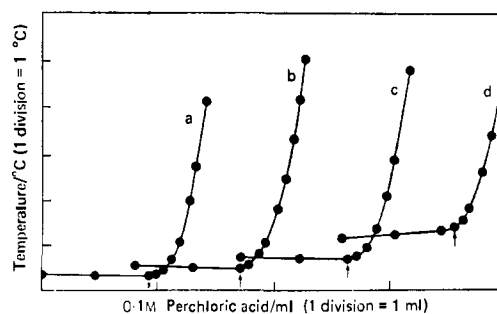
Figure 30. Titration curves obtained in determinations of bases by a manual method, showing the location of the end point (2-phenylpropene indicator): (a) L-Dopa (19.8 mg); (b) (−)-adrenaline (18.0 mg); (c) L-noradrenaline (16.9 mg); (d) dopamine hydrochloride (19.1 mg). From ref 24, with permission of the Chemical Society.
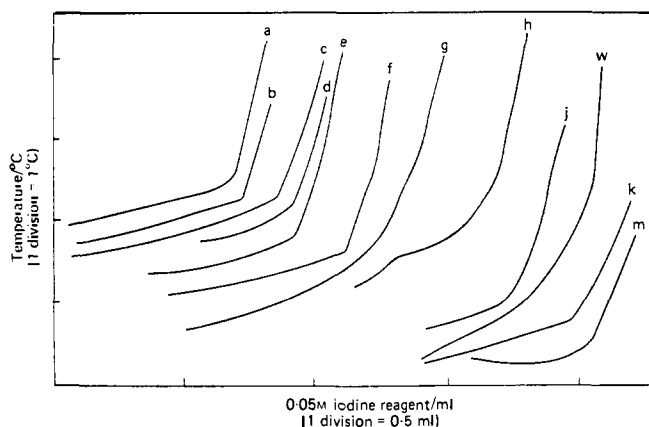
Figure 31. Catalytic thermometric titration of organic bases, water, and quaternary ammonium halides with 0.05 M iodine reagent (ethyl vinyl ether indicator). Compounds/mg: (a) *n*-butylamine, 0.84; (b) tris(hydroxymethyl)methylamine, 1.2; (c) pyridine, 1.3; (d) hexamethylenetetramine, 1.6; (e) morpholine, 1.89; (f) 8-hydroxyquinoline, 2.9; (g) pyridine *N*-oxide, 2.3; (h) triphenylphosphine, 7.4; (j) cetyltrimethylammonium bromide, 4.0; (k) tetra-*n*-butylammonium iodide, 9.3; (m) benzyldimethylmyristylammonium chloride, 5.0, and (w) water, 10.0. From ref 36, with permission of the Chemical Society.

according to the reaction involved. The analytical procedures used for the determination of the different classes of compounds and ions are summarized in Tables IV to VII.

A. Acid–Base Reactions

1. Determinations of Acids and Acidic Substances (Table IV)

Both the acetone and acrylonitrile indicators have been used extensively for the nonaqueous titration of mono- and polycarboxylic acids, mono- and polyhydric phenols, and other weak acids including imides, sulfonamides, thioamides, keto-enols, and thiols.[8,32,60,61] The acrylonitrile indicator has the advantage of being the more responsive to small amounts of the catalyst titrant, and the limit of determination with this indicator is about 0.0001 mequiv of acid when a 0.001 M titrant is used.[32] Details of the solvent systems used in determinations of benzene carboxylic acids, phenols, and hydroxybenzoic acids are given in Figures 21, 22, and 23, respectively.

Drugs with acidic functional groups, including sulfanilamide derivatives,[61] catecholamines,[24] and barbiturates[83] have been determined in the pure form and in formulations. Acrylonitrile was used as the indicator for the sulfanilamide and catecholamine determinations, and both acetone and acrylonitrile were evaluated as indicators for the determination of the barbiturates. The usual excipients in drug formulations, i.e., starch, lactose, talc, and magnesium stearate, do not interfere in the assay of the acidic function of the active constituent.

TABLE IV. Titration of Acids and Acidic Substances

Acids and acidic substances	Indicator reagents (mL)	Titrant, molarity	Sample size, mequiv	Sample solvent (mL)	Rel std dev of results, %	ΔT,[a] °C	Ref
Mono- and polycarboxylic acid; mono- and polyhydric phenols; imides, keto-enols; aromatic nitro compounds; alkyl and aryl thiols; thiol functions on heterocyclic compounds; thioamides; cyanuric and thiocyanuric acids; coal tar oils; creosote; bituminous coal; barbiturates	Acetone[b] (3–10)	KOH,[c] 1.0 (and alkali-generated coulometrically)	0.05–1.0	Benzene, pyridine (0–2)	0.57–1.4	~5	8 11 60 32 8, 78 81, 84, 85 83
Boric acid; phosphoric acid; carboxylic acids; amino acids; keto-enols (in aqueous and nonaqueous solution)	Acetaldehyde, (3)	KOH,[d] 0.5	0.03–0.5	Water (2)		~25	28
Mono- and polycarboxylic acid; mono- and polyhydric phenols; imides, keto-enols; cyanuric and thiocyanuric acids; some thiols; sulfanilamides; catecholamines; vegetable tannins; phenol- and resorcinol–formaldehyde resins; barbiturates	Acrylonitrile[e] (2–10)	KOH,[c] 0.001–1.0 Bu₄NOH,[f] 0.001–0.1	0.001–1.0	Dipolar aprotic solvents (0.5–5)	0.41–1.78	10–15	32 60, 61 24, 68 76, 77 83
Aqueous solutions of: benzoic, oxalic, phosphoric, phosphorous, and boric acids; phenol; resorcinol; amino acids	Acrylonitrile (2)	KOH,[d] 0.5	0.1–0.2	Dimethyl sulfoxide, (5), water (0.2–1.0)		2–3	65

[a] Temperature rise at end point under optimum conditions. [b] Similar results are obtained with cyclohexanone. [c] In propan-2-ol. [d] In propan-2-ol or water. [e] Similar results are obtained with methyl acrylate and dimethyl itaconate. [f] In methanol–toluene, 1:3.

The acetone- or acrylonitrile-indicator methods have been found suitable for the determination of the acidic constituents of complex substances such as coal,[81] coal-tar oils,[78] coal-tar creosote extracted from treated timber,[84] tar-oil preservatives extracted from textiles,[85] polystyrene resins with carboxyl end groups,[86] mineral insulating oils,[87] bitumens,[88] vegetable tannins,[68,74] and phenolic resins.[76,77] An acetone-indicator method employing a simple manual apparatus has been adopted as a standard procedure for the determination of phenols in coal-tar oils[78] and tar-oil preservatives.[85]

Coal samples were dispersed by grinding in pyridine before titration, and the phenolic hydroxyl values so determined were higher than those obtained by nonaqueous potentiometric titration and acetylation methods.

Premature polymerization occurred when the acrylonitrile indicator was added to some of the mineral insulating oils; this may have been initiated by free radicals arising from the decomposition of peroxidized oils, since it was effectively prevented by the addition of a nonacidic antioxidant, tetraethylthiuram disulfide. The acid numbers measured by catalytic thermometric titration were considerably higher than those obtained for the same oils by using an established procedure with visual indication of the end point. It is probable that the latter method does not determine very weak acids such as phenols.

The phenolic resins examined were of two types: novolacs and resoles. The former are obtained as anhydrous solids and were titrated in nonaqueous solutions; the latter were prepared as aqueous solutions and were titrated as such, after adding dimethyl sulfoxide to the sample solution.

Inorganic and organic acids can be determined in aqueous solution by catalytic thermometric titrimetry by using acetaldehyde[28] or acrylonitrile[65] as the indicator reagents and aqueous or alcoholic potassium hydroxide as the titrant. Although acetaldehyde is a satisfactory indicator for use in the determination

of carboxylic and stronger acids, it gives rise to poorly defined end points in the titrations of phenols. The acrylonitrile indicator cannot tolerate as much water as the acetaldehyde one is able to, probably because the polymerization does not proceed effectively unless most of the water is immobilized by the added dimethyl sulfoxide. However, this indicator is more satisfactory than acetaldehyde for the determination of phenols. Details of some determinations of aqueous acids using acrylonitrile as the indicator are given in Figures 18 and 19.

2. Determinations of Bases (Table V)

The application of acid-catalyzed hydration and esterification of acetic anhydride or propionic anhydride as indicator reactions appears to be limited at present to the determination of tertiary amines, urea, and metal carboxylates in nonaqueous solution.[7,25,40] In contrast, cationic polymerization initiated by perchloric acid or boron trifluoride etherate has been used as an indicator reaction for the determination of primary, secondary, and tertiary amines, amides, metal carboxylates, and some other basic compounds including dimethyl sulfoxide and hexamethylphosphoramide. In the determination of some amides, aniline derivatives, and heterocyclic nitrogen compounds the reaction stoichiometries measured by using the boron trifluoride titrant catalyst were significantly lower than those obtained with perchloric acid as the reagent.[33] The basic function in tris(hydroxymethyl)methylamine, 4-nitroaniline, 4-hydroxyaniline, hydrazobenzene, acetamide, and dimethylformamide was determined only when the perchloric acid reagent was employed, and in the determination of 1,2-diaminobenzene, although both amine groups were titrated with the latter reagent, only one group was titrated with boron trifluoride, when the end point was indicated.[33]

Both the esterification and cationic polymerization reactions are suitable for the determination of bases down to the

TABLE V. Titration of Bases

Bases	Indicator reagents (mL)	Titrant, molarity	Sample size, mequiv	Sample solvent (mL)	Rel std dev of results, %	ΔT,[a] °C	Ref
Alkyl, aralkyl, and hetero-cyclic tertiary amines, including antipyrine, cinchonine, pyridoxine and caffeine; sodium and potassium carboxylates	Acetic anhydride[b] (0.5–2) + water (0.12–0.5)	HClO₄,[c] 0.25 (and acid generated coulometrically)	0.008–1.4	Acetic acid, acetic anhydride, nitromethane (7–25)	0.07–0.8	0.06 to 2	7, 40, 63, 64
Alkyl, aralkyl, and hetero-cyclic tertiary amines, including antipyrine, caffeine, and theophylline; urea, sodium, potassium, calcium, and cobalt carboxy-lates	Acetic anhydride[b] (1–5) + organic hydroxyl compounds (4 mequiv)	HClO₄,[c] 0.001– 0.1	0.0001–0.1	Acetic anhydride, dichloromethane, nitromethane		5 to 15	25, 40, 42
Primary, secondary, and tertiary alkyl, aralkyl, and aryl amines; heterocyclic amines; amides, including hexamethylphosphoramide; dimethyl sulfoxide; amino acids; catecholamines; alkaloids	2-Phenylpropene (2–10)	HClO₄,[d] 0.001– 0.1	0.0001–0.1	Toluene, acetone, acetic acid, nitroethane, 1,2-dichloro-ethane	0.77–1.58	5 to 15	20, 33 24 89
Primary, secondary, and tertiary alkyl, aralkyl, and aryl amines; heterocylic amines; dimethyl sulfoxide; hexamethylphosphoramide	2-Methylpropyl vinyl ether (2–10)	BF₃·Et₂O[e]	0.0001–0.1	Toluene, acetone, acetic acid, nitroethane, 1,2-dichloro-ethane	0.58–1.39	5 to 20	33
Primary, secondary, and tertiary alkyl, aralkyl, and aryl amines; heterocyclic amines, including hexamethyl-enetetramine; triphenyl-phosphine	Ethyl vinyl ether (2–5)	I₂[f] 0.005– 0.05	0.0001–0.1	Dimethyl formamide, acrylonitrile (1–2)	0.51–1.82	2 to 10	35, 36

[a] Temperature rise at end point under optimum conditions. [b] Propionic anhydride may also be used. [c] In acetic acid and mixtures of acetic acid with acetic anhydride or 1,2-dichloroethane or nitromethane. [d] In acetic acid and mixtures of acetic acid with 1,2-dichloroethane or nitroethane. [e] In dioxan and mixtures of dioxan with 1,2-dichloroethane, acrylonitrile, or nitroethane. [f] In dimethylformamide.

0.0001-mequiv level, but the method using the acid-catalyzed hydration of acetic or propionic anhydride as the indicator reaction appears to be an order lower in sensitivity.

An advantage of catalytic thermometric titration over the more conventional potentiometric and visual-indicator methods for the nonaqueous titration of amine hydrochlorides is that, when cationic polymerization is used for end-point indication, it is not necessary to reduce the acidity of the hydrogen chloride by adding mercury(II) acetate to the sample solution.[89]

Nonaqueous catalytic thermometric iodimetry can be used for the determination of some organic bases. The determinative reaction is not a normal acid–base titration, and is considered below in section V.D.

B. Precipitation Reactions (Table VI)

At present, the only catalytic thermometric titration procedure based on a precipitation reaction in the determinative stage is the one employing the iodide catalysis of the cerium(IV)–arsenic(III) reaction for end-point indication. Cations that remove iodide from the sample solution by the formation of an insoluble iodide can be determined directly. Anions that can be removed from the sample solution by precipitation with one of these cations can be determined by back titration. Silver, mercury(II), and palladium(II) have been determined by titration with potassium thiocyanate by means of substitution titration. A small amount of silver, mercury(II), or palladium(II) iodide is included in the sample solution and, when all the sample has been titrated, a small excess of titrant displaces iodide ions from the metal

iodide and the indicator reaction is initiated. Table VI lists the ions that have been determined. This indicator reaction is extremely sensitive; thus, 1.32 μg of Pd^{2+} and 0.200 μg of Hg^{2+} have been determined by titration with 10^{-4} M[22] and 10^{-5} M[80] solutions of potassium iodide, respectively.

C. Complexometric Reactions (Tables VI and VII)

Complex formation is a possible alternative to precipitation as a determinative reaction, i.e., as a means of "neutralizing" the catalyst, in inorganic catalytic thermometric titration. Indeed, because the mercury(II) iodide, formed in the direct determination of Hg^{2+} by the cerium(IV)–arsenic(III) indicator method, is slightly soluble in water, premature initiation of the indicator reaction would have occurred in the determinative stage if the soluble iodide had been a simple salt and not a complex.

Complex formation with EDTA, and similar chelating reagents, is an effective way of eliminating the catalytic power of transition metal cations in solution. It is the basis of the determinative reaction in catalytic thermometric methods in which mangan-ese(II)[22] and copper(II)[3,4] salts are used both as titrants, and as catalysts for indicator reactions involving oxidations with hy-drogen peroxide or the decomposition of hydrogen peroxide. EDTA and some other chelating reagents can be determined directly by these methods (Table VII), but the indirect determi-nation of cations is probably more important (Table VI). The concentration of the manganese(II) and copper(II) solutions have been determined by the inverse titration procedure, in which the unknown solution is the titrant and EDTA in known concentration

TABLE VI. Titration of Inorganic Cations and Anions

Cations	Titration procedure[a]	Indicator reagents	Other reagents	Titrant, molarity	Sample size, mequiv	Rel std dev of results, %	ΔT,[b] °C	Ref
Ag^+, Hg^{2+}, Pd^{2+}	D	Ce(IV)[c] + As(III)[d]		KI, aq, 10^{-2}–10^{-5}	2×10^{-6} to 10^{-2}	0.1 to 1.9	0.03–0.2	21, 80
Ag^+, Hg^{2+}, Pd^{2+}	S	Ce(IV)[c] + As(III)[d]	AgI, HgI$_2$, PdI$_2$	KSCN, aq, 10^{-2}	0.05– 3 mg	<1		55
Zn^{2+}, Cd^{2+}, Cu^{2+}, Ni^{2+}, Mn^{2+}, Pd^{2+}, Hg^{2+}, Sn^{2+}, Al^{3+}, In^{3+}, Ga^{3+}, Th^{4+}	B	H_2O_2[e] + resorcinol[f] or H_2O_2[g]	EDTA, 10^{-2} M	MnCl$_2$, aq, 10^{-4}– 2×10^{-2}	10^{-3} to 10^{-2}	0.1 to 1.1		22
Zn^{2+}, Cu^{2+}, Ni^{2+}, Pb^{2+}, Hg^{2+}, Sn^{2+}, In^{3+}, Ga^{3+}, Th^{4+}, Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}, Co^{2+}, Bi^{3+}, Pd^{2+}	B[h]	H_2O_2[i] + resorcinol[i] H_2O_2[g]	EDTA or CDTA, 2×10^{-2} M	Mn(NO$_3$)$_2$,[h] 2×10^{-2}	1.5 µg to 3.5 mg	<1	h	55
Cu^{2+}	R	H_2O_2[k] + N_2H_4[l]	EDTA, 10^{-2} M	Cu(II), aq	~0.1		m	3, 4

Anions								
Cl^-, Br^-, I^-, SCN^-, $[Fe(CN)_6]^{4-}$, S^{2-}	B	Ce(IV)[c] + As(III)[d]	AgNO$_3$, Hg(OAc)$_2$, PdCl$_2$	KI, aq, 10^{-2}	5×10^{-4} to 5×10^{-3}		~0.03	21

[a] D = direct, S = substitution, B = back, R = reverse titrations. [b] Temperature rise at end point. [c] 0.4 N cerium(IV) sulfate, 0.1 mL. [d] 1.3 N sodium arsenite, 0.1 mL. [e] 5% H_2O_2, 1 mL. [f] 5% resorcinol, 1 mL. [g] 30% H_2O_2, 0.3 mL. [h] Sample, reagents, and titrant in dimethyl sulfoxide solution. Temperature changes greater than in aqueous systems. [i] 10% H_2O_2, 0.1 mL. [j] 10% resorcinol, 0.1 mL. [k] 30% H_2O_2, 0 5 mL. [l] 5% N_2H_4, 1 mL. [m] Much greater ΔT than with H_2O_2 or H_2O_2–resorcinol.

TABLE VII. Miscellaneous Titrations

Compounds	Indicator reagents	Titrant molarity	Sample size	solvent (mL)	Rel std dev of results, %	ΔT,[a] °C	Ref
EDA; CDTA	H_2O_2[b] + resorcinol[c] or H_2O_2[b]	MnCl$_2$, 10^{-4} to 2×10^{-2}	5×10^{-6} to 10^{-2} mequiv	H_2O	0.4–1.3		22
EDTA[d]	H_2O_2[e] + resorcinol[f] or H_2O_2[e]	Zn(II), Cd(II), Cu(II), Ni(II), In(III), Hg(II) or Pd(II), 2×10^{-2}	50 µg to 2 mg	H_2O	<1		55
EDTA; CDTA; NTA	H_2O_2[b] + resorcinol[c] or H_2O_2[g]	Mn(NO$_3$)$_2$[h] 10^{-4} to 2×10^{-2} (10^{-5})	1.5 µg to 3.5 mg	DMSO (1.5)	<1	i	55
NaI; KI; ZnI$_2$; NiI$_2$; PbI$_2$	Ethyl vinyl ether (2 to 3 mL)	I$_2$,[j] 5×10^{-3} to 5×10^{-2}	5×10^{-4} to 1.0 mmol	DMF, acrylonitrile, chloroform (2–5)	0.2–1.43	2–10	82
Quaternary ammonium halides							36
Organic hydrazines and hydrazides							35, 36
Water							36
Metal O-alkyl dithiocarbonates							35, 82
Metal dithiocarbamates and phosphorodithioates							75

[a] Temperature rise at end point. [b] 5% H_2O_2, 0.1 mL. [c] 5% resorcinol, 0.1 mL. [d] Substitution titration, with Mn(II)–EDTA complex in the sample solution. The titrants can be determined by reverse titration. [e] 30% H_2O_2, 0.5 mL. [f] 30% resorcinol, 0.1 mL. [g] 30% H_2O_2, 0.3 mL. [h] In dimethyl sulfoxide (DMSO). [i] Temperature changes greater than in aqueous systems. [j] In dimethylformamide (DMF).

is the titrand. Zinc, cadmium, copper(II), nickel(II), manganese(II), lead(II), mercury(II), tin(II), aluminum(III), indium(III), gallium(III), and thorium(IV) can be determined by adding a known amount of EDTA, in excess, to the sample, and back-titrating the excess with manganese(II).

Back titration is unsuitable for the determination of cations that are displaced from their complexes by manganese(II) unless, of course, the displaced cation is itself a catalyst for the indicator reaction. This last situation obtains in substitution titrations. In these a small amount of manganese(II)–EDTA complex is in-

cluded in a sample solution containing a chelating agent as the titrand, and the latter is titrated with solutions of zinc, cadmium, copper(II), nickel(II), indium(III), mercury(II), or lead(II), all of which displace manganese(II) from its complex. The concentrations of these titrant solutions can be determined by the inverse titration of a known concentration of chelating agent.

Kiss,[55] in his evaluation of dimethyl sulfoxide as a solvent for these complexometric titrations, showed that nitrilotriacetic acid (NTA), which could not be determined by the aqueous method, can be determined satisfactorily in dimethyl sulfoxide by direct

titration. Zinc, copper(II), nickel(II), lead(II), mercury(II), tin(II), indium(III), gallium(III), thorium(IV), magnesium, calcium, strontium, barium, cobalt(II), bismuth(III), and palladium(II) were also determined in the nonaqueous solvent by back titration with 2×10^{-2} M manganese(II) after adding an excess of EDTA; the alkaline earth metals, and cobalt(II), bismuth(III), and palladium(II), could not be determined by the corresponding aqueous procedure. It was found possible to mask aluminum with triethanolamine to prevent it from interfering in the nonaqueous determination of the alkaline earths and, similarly, to mask aluminum with sodium fluoride in determinations of copper(II), nickel(II), zinc, and cadmium, and to mask copper(II), nickel(II), cobalt(II), zinc, and cadmium with potassium cyanide in determinations of the alkaline earths.

The sensitivity of the complexometric method is about the same as that of the precipitation method and can be used for determinations down to about the 1.4-μg level by using 10^{-4} M titrants. Kiss claims that when the determinations are carried out in dimethyl sulfoxide solution, satisfactory results can be obtained in the titration of chelating agents with 10^{-5} M reagent.

D. Nonaqueous Iodometric Titrations (Tables V and VII)

The nonaqueous iodometric titration method, in which the cationic polymerization of ethyl vinyl ether is the indicator reaction, has been used to determine amines, triphenylphosphine, quaternary ammonium halides, hydrazines, hydrazides, metal iodides, metal O-alkyl dithiocarbonates, metal dithiocarbamates, sodium trithiocarbonate, metal phosphorodithioates, and water.

In the determination of amines a complex is formed by reaction of iodine with the basic nitrogen atom. Four atoms of iodine combine with one molecule of pyridine as follows:

$$C_6H_5N + 2I_2 \rightleftharpoons C_6H_5N \cdot 2I_2 \rightleftharpoons C_6H_5N \cdot I^+I_3^- \qquad (15)$$
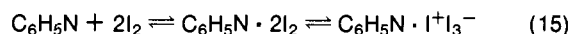
and the reaction, in terms of the consumption of reagent, is therefore four times as sensitive as acid–base titration. However, the measured reaction stoichiometries in the iodometric titrations are not as predictable as in acid–base titrimetry, and for aliphatic amines and pyridine derivatives they have been shown to range from about 3.6 to about 4.6, depending on the structure of the base.[36] The weakly basic aniline derivatives form iodine complexes less readily than do aliphatic amines and pyridine bases, and the measured reaction stoichiometries are much lower, e.g., 1.8 for 4-methylaniline, and in some instances, 0, e.g., for 4-nitroaniline and diphenylamine.

When quaternary ammonium halides and metal iodides are titrated with iodine under nonaqueous conditions, polyhalide anions are formed, and the stoichiometry of the reaction corresponding to the indicated end point is dependent on the stability of these ions. In the titration of tetra-n-butylammonium bromide and cetylpyridinium bromide, the end-point indication corresponds approximately to the formation of BrI_2^- ions, and in the titration of potassium and nickel iodides the titration values correspond closely to those required for the formation of I_3^- and $2 \times I_3^-$, respectively, but in some other halide titrations the measured reaction stoichiometries diverge widely from integral values, and calibration graphs are then required for quantitative work.

The reaction of the iodine titrant with hydrazines and hydrazides is an oxidation process.[36] Gasometric studies of the reactions between iodine and benzoylhydrazine and iodine and isonicotinoylhydrazine, under the conditions used in the nonaqueous titrations but with the ethyl vinyl ether omitted, confirm that nitrogen is evolved, and in amount approximating to that required by the following reaction:

$$RCONHNH_2 + 2I_2 \rightarrow RCOI + 3HI + N_2\uparrow \qquad (16)$$

As in the other iodometric titrations, the measured reaction stoichiometries are dependent on the structure of the analyte, and in most instances are not integral values.

The determinative reactions in the iodometric titration of O-alkyl dithiocarbonates, dithiocarbamates, trithiocarbonate, and phosphorodithioates are also oxidation processes, and they result in the formation of disulfides from the acid radicals and polyiodides of the metals. Because a polyiodide is formed when the end point is indicated, the nonaqueous iodometric titration is more sensitive than the corresponding aqueous iodometric titration, in which only sufficient iodine is consumed to yield the disulfide and the normal metal iodide.[75,82] Solutions of dithiocarbamates and phosphorodithioates in hydrocarbon oils, which are used as oil additives, can be determined directly in concentrations down to about 0.05% m/v.[75]

The rate of titrant addition affects the titration value in the determination of water by the iodometric method, and it is necessary to construct a calibration graph and to use a constant rate of titrant addition in the analysis for trace amounts of water. The calibration graph for the range 0 to 8 mg is linear when 0.05 M iodine in dimethylformamide is added at 0.06 mL^{-1} to 1 mL solutions, to which has been added 2 mL of the indicator reagent.[36]

VI. Scope and Limitations

The scope of catalytic thermometric titrimetry is limited by the availability of suitable combinations of indicator and determinative reactions, and the intrinsic lack of selectivity of the method of end-point indication.

The chemistry of the indicator reaction determines the nature of the titrant, and therefore the choice of determinative reaction, and the suitability of a particular determinative reaction will be influenced by the concentration of catalytically active species attained in the titrand solution before the theoretical end point is reached.

In practice it has been found that a wide range of strong, weak, and very weak acids and bases can be determined in nonaqueous solution. In general, the sharpness of the end-point inflection is dependent on the strength of the acid or base titrated, and on its concentration. The precision of the measured titration values decreases with the deterioration in end-point sharpness, and the limit of determination when the acetylation or polymerization methods of end-point indication are used is usually about 0.0001 mequiv of the acid or base.

Acids, but not bases, can be determined in aqueous solution with the indicator systems at present available.

There is some evidence from the titration of bituminous coal samples[81] and 2,2'-dihydroxydiphenylmethane[76] that the catalytic thermometric method is capable of determining very weak acids that cannot be titrated potentiometrically. One of the phenolic hydroxyl groups in the latter compound is so strongly intramolecular hydrogen bonded that it is not determined by the potentiometric methods that are usually successful for the titration of very weak acids.[90] However, using the catalytic thermometric procedure with an appropriate titrant–solvent–indicator system, an end point is obtained corresponding to the neutralization of both hydroxyl groups.

A major application of the thermometric method could be as an alternative to nonaqueous potentiometric and visual-indicator titrimetry recommended for the assay of acidic and basic active constituents in pharmaceutical formulations. Since it is not necessary to add mercuric acetate to reduce the acidity when basic groups in amine hydrochlorides are determined, provided that the 2-phenylpropene indicator is used, thermometric methods might be preferable to existing ones for the assay of pharmaceutical products of this type.

Nonaqueous iodometric catalytic thermometric titrimetry in its present state of development is not selective, and it suffers from the disadvantage that the reaction stoichiometries are often

unpredictable. The method is, however, applicable to the determination of many compounds that are oxidized by, or form complexes with, iodine in nonaqueous solution, and its use in structural investigations is yet to be evaluated.

The selective determination of certain acid species (thiols, carboxylic acids, polyhydric phenols) in mixtures has been achieved by comparing the titration values obtained when different combinations of titrant, solvent, and thermometric indicator are used. This comparison technique should prove useful in structural studies. Thus, the different results obtained with perchloric acid and boron trifluoride as titrants for bases, and potassium hydroxide and tetrabutylammonium hydroxide as titrants for acids, could be related to structural characteristics of the titrand molecules.

At present, the catalytic thermometric procedures developed for the determination of inorganic anions and cations are applicable to a wide range of transition metal cations but to relatively few anions.

In the cerium(IV)–arsenic(III) indicator method, the cations and anions must be removed from the liquid phase virtually completely by precipitation, but the scope of the method for cation determination involving complexation is limited only by limitations on the chelating power of broad spectrum reagents such as EDTA and CDTA.

Both procedures for the titration of cations are extremely sensitive and might be considered for trace analysis down to the 0.1-ppm level.

VII. References

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