CHAPTER 17

Amperometric Titrations

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17.1 INTRODUCTION

An extension of quantitative polarography is made use of in amperometric titrations of a large number of substances. The term "amperometric"

originated with Kolthoff and Pan,[1] but the term "limiting current" is preferred by others[2] when the limiting current is obtained using one polarizable electrode. The current due to diffusion (dropping mercury electrode, DME) or the limiting current in stirred solutions (rotating platinum electrode, RPE) is proportional to the concentration of an electroactive substance (Ox or Red). The change in concentration of an electroactive analyte, product, or titrant can be followed during the course of the titration by observing the change in current, at a constant applied potential, after each increment of titrant. Since the chapter on polarography deals with theory which is, in part, common to that required for an understanding of amperometric titrations, the reader is referred to that chapter before proceeding further.

A. CLASSIFICATION OF VOLTAMMETRIC TITRATIONS

An amperometric titration can be classified as a titrimetric (volumetric) method as well as a voltammetric method.

Voltammetric titrations may be divided into two groups:

1. Potentiometric titrations (at constant current which is either finite or essentially zero) employing one or two polarized electrodes.
2. Amperometric titrations (at a constant applied potential) employing one or two polarized electrodes.

a. One-polarized electrode amperometric titrations are believed to have been employed first for the titration of barium ions with sulfate by Heyrovský and Berezicky.[3]

b. Two-polarized electrode amperometric titrations were originally reported by Salomon.[4] This type was later referred to as a titration with a "dead-stop end point."[5]

The precision of amperometric titrations is generally better than 1% and is superior to that of polarographic measurements. The amperometric titration method can be employed to follow several types of chemical reactions such as precipitations, oxidation-reduction, and a few neutralization reactions. The concentration range of the electroactive substance(s) covered by this method is 10^{-2} to 10^{-6} *M*.

B. GENERAL APPARATUS

Any polarograph may be utilized to obtain the few current readings (at a constant applied potential) required before and after the end point in an amperometric titration. A simpler instrument such as the "Ampot"[6] or one similar to that illustrated in Fig. 17.1 is adequate for this purpose. Neither a precise potentiometer nor a calibrated galvanometer is required since the applied potential need only be adjusted to within ± 0.1 V and only the relative current is used.

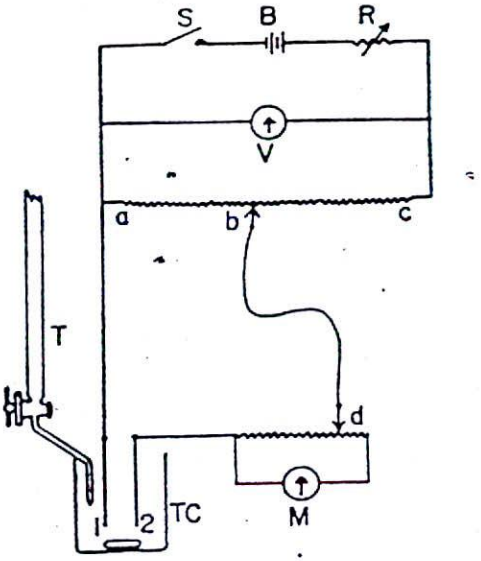

FIGURE 17.1: A simple schematic of the apparatus used in amperometric titrations: B, EMF source (battery etc.); a–c, device for selecting potential, voltage divider, etc; R, variable resistance for adjusting the potential span a–c; V, voltmeter; S, switch; M, microammeter for reading relative current; T, microburette (5–10 ml) with capillary tip; TC, titration cell; b, sliding contact for selecting voltage; d, sliding contact for selecting sensitivity of current reading device; 1, polarized indicator electrode, e.g., DME, RPE, (vibrating platinum electrode) (VPE), Pt wire, etc.; 2, nonpolarized reference electrode e.g., SCE, Hg/HgI, Ag/AgCl, Hg-Pool, etc., *or* second-polarized electrode e.g., Pt wire, in biamperometric titrations.

Volumetric flasks and transfer pipettes are required for the accurate preparation of solutions. A microburette (5 or 10 ml) is recommended. An oxygen-free nitrogen supply is essential to deoxygenate the titrate and titrant if a negative applied potential (vs. SCE) is required. Graph paper should be $8\frac{1}{2} \times 11$ in. with millimeter (or 20 lines/in.) ruling, unless otherwise specified.

17.2 AMPEROMETRIC TITRATIONS WITH ONE POLARIZED ELECTRODE

A. APPARATUS

1. Instrument

Any polarograph or device such as that shown in Fig. 17.1 can be used to impress a constant potential across the titration cell and measure the relative

current flow as a result of the reduction (or oxidation) occurring at the polarized electrode. Since there are numerous commercial instruments available, the reader is referred to the manufacturer's instructions for the details required in the operation of specific instruments.

2. Titration Cells

Any of several types of titration cells can be used. Many cells are commercially available or can be constructed in the laboratory. Several literature reviews include references concerning cells.

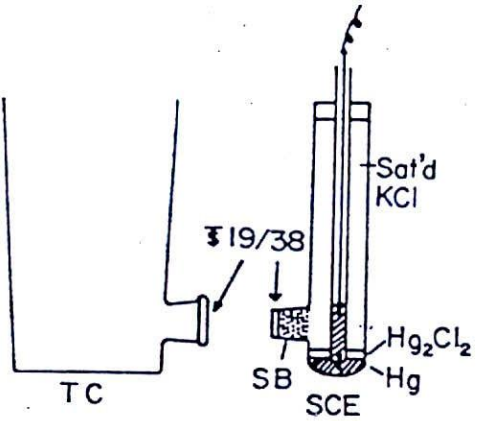

FIGURE 17.2: Modified amperometric titration cell; *TC*, titration cell (a 100-ml beaker with a ground-glass joint); *SB*, salt bridge consisting of a sintered-glass disk and agar gel plug saturated with KCl; SCE, saturated calomel electrode.

A simple beaker-type cell employing the Hg-pool as a reference electrode is frequently used. However, an H-type polarographic cell,[6] or a modification of this such as that used in the author's laboratory Fig. 17.2, is frequently preferred since the choice of the supporting electrolyte is not restricted. The SCE shown in Fig. 17.2 is easily constructed or the Sargent reference electrode section (S-29393) of the two-piece, H-form, polarographic electrolysis vessel (S-29392) can be used.[6] This titration cell (Fig. 17.2) is large enough to hold the titrate plus added titrant.

3. Indicator Electrodes

The most frequently used polarized indicator electrodes are the dropping mercury electrode (DME) and the rotating platinum electrode (RPE). Others include the rotating DME, graphite, and the vibrating platinum electrode (VPE). These and other electrodes are described in the literature (see review papers).

Advantages and Disadvantages of DME

a. A constantly renewed surface which is especially useful for precipitation titrations and yields reproducible currents.

b. The large hydrogen overvoltage of mercury permits the reduction of many substances having lower overvoltages.

c. Oxygen must be removed initially from the titrate and following each addition of titrant when the potential of this electrode is made more negative than about −0.1 V (vs. SCE). Time is required to deoxygenate these solutions with oxygen-free nitrogen to prevent the formation of the interfering oxygen wave(s).

d. A certain amount of "noise" may result from the charging current (required to charge the double layer of ions around the DME) being superimposed upon the diffusion current.

e. Applied potentials are limited to those which are less positive than about +0.1 V (vs. SCE) due to the dissolution of the mercury drop at more positive potentials ($Hg \rightarrow Hg(II) + 2e^-$).

Advantages and Disadvantages of RPE

a. This electrode actually compliments the DME since it is usable over a different range of potentials, e.g., +1.0 to −0.5 V, compared to +0.1 to −1.1 V (vs. SCE) for the DME when used in a supporting electrolyte of 0.5 *M* HCl. Above +1.0 V (vs. SCE) water in many supporting electrolytes is oxidized to O_2 at the RPE. These useful potential ranges are somewhat dependent upon the nature of the supporting electrolyte. Certain substances having oxidation and reduction potentials which lie in the range of the Pt electrode do not give rise to limiting currents with an RPE. The RPE also has a very low hydrogen overpotential and therefore has a very limited negative potential range (vs. SCE).

b. A larger diffusion current results from stirring due to a reduced diffusion layer. This accounts for the greater sensitivity when the RPE is used. A quiescent solution is mandatory for the regular DME.

c. A greatly reduced residual current results when the RPE is used, due to the lack of the repetitive charging current observed for the renewed mercury drops (see DME).

d. Only relative current values are required in amperometric titrations, thus the inherent disadvantages of solid microelectrodes in unstirred voltammetric measurements, such as the uncertainty of absolute potentials and less reproducible diffusion currents, are of no importance here.

e. The rotation of the RPE must be kept constant during the titration and this necessitates the use of a constant-speed stirring device.

Other solid polarizable electrodes can also be employed in solutions which are stirred by constant-speed stirrers.

4. Reference Electrodes

The most frequently used reference electrodes are the SCE, the Hg-pool, and the $Ag/AgCl_{(s)}$, all of which must be nonpolarizable. When these electrodes are incompatible with a particular system, others may be used.

In certain instances, one or more of the analyte, titrate, product, or indicator substance may be reduced or oxidized within the potential range of a selected reference electrode. When this occurs, it is only necessary to short circuit the two electrodes, i.e., connect the indicator and reference electrodes externally so that the indicator electrode assumes the same potential as the reference electrode. No external potential is required. Ewing[7] lists a number of selected reference electrodes and their potentials relative to the NHE (normal hydrogen electrode) and SCE. These may be employed in the manner just mentioned.

B. METHODOLOGY

Preparation for amperometric titration is similar to that for polarographic analysis, therefore the reader should be acquainted with the principles of polarography before reading this chapter.

If the half-wave potentials ($E_{1/2}$) of the possible electroactive (depolarizer) substances in a titration reaction are unknown, a separate polarogram of each substance should be obtained under the titration conditions. The possible depolarizers are indicated later [Eq. (17.1)] in Section 17.2C. From a knowledge of the $E_{1/2}$ values of each substance in the selected titration medium, it is possible to predict whether one or more depolarizer substances will give rise to a current at any selected applied potential. It will be shown later (under Section 17.2C) that the resulting curve shape may be dependent on the potential chosen for a particular amperometric titration. For example, if the selected applied potential is such that it produces a wave for both the analyte and titrant, a V-shaped titration curve is obtained. The location of the end point can be achieved with greater certainty in this instance than for an L-shaped curve. The applied potential is normally that which corresponds to the beginning portion of the limiting current plateau of the i vs. E_{appl} curve for an electroactive substance.

The titration media are the same as those employed for voltammetry (or polarography) of the same depolarizers. Solvents may be aqueous, nonaqueous or mixtures of these types. Added "inert" electrolytes are usually required to lower the resistance of the media to current flow and to minimize migration currents. The practical limits of concentration for a depolarizer are normally 10^{-2} to 10^{-5} M, but under favorable conditions this may be extended to 10^{-6} M. The titrant is usually 50- to 100-fold more concentrated than the analyte. This avoids significant dilution of the latter and circumvents the need for current corrections, except in very accurate work.

If the analyte is significantly diluted by a relatively large titrant volume,

the observed current readings must be multiplied by the factor $(V + v)/V$, where V is the initial volume of the analyte solution and v is the total volume of titrant added prior to the reading that is to be corrected.

Similarly with conductometric or photometric titrations, the data obtained in the vicinity of the end point is the least reliable. Therefore only 3 to 5 points on both sides of, and well removed from, the end point are required for a graphic location of the latter. An extrapolation of these linear portions of the plot of current vs. milliliters of titrant to a point of intersection is performed to locate the end point. The point of intersection corresponds to the end-point titrant volume read from the abscissa (Fig. 17.3).

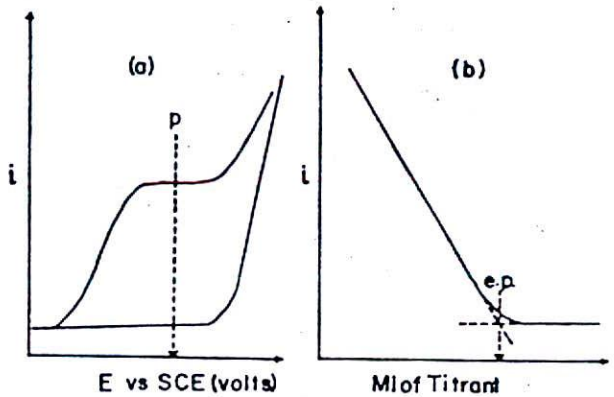

FIGURE 17.3: (a) Polarogram of an electroactive substance titrated in (b): P, selected applied potential to be used in titration (b); (b) amperometric titration curve of an electroactive analyte: e.p., end point located by extrapolation method.

If current values were read for constant increments of titrant throughout the entire titration, a marked curvature might be observed in the plot near the end point region. This curvature is a result of such factors as the solubility of precipitates, unstable complexes, hydrolysis of formed salts, incomplete or slow reactions, etc.

Both cathodic (reduction) and anodic (oxidation) currents are possible in amperometric titrations and these should be plotted in conformity with the conventions discussed in the chapter dealing with polarography.

C. TITRATION CURVE SHAPES

The titration curve is a plot of current vs. volume of titrant, at a constant applied potential (Fig. 17.3). The shape of this curve depends upon which substances in the following general equation are electroactive at the selected potential.

$$\underset{\text{sample}}{S} + \underset{\text{titrant}}{T} \rightarrow \underset{\text{product(s)}}{P} \qquad (17.1)$$

A number of possibilities exist in the general titration [Eq. (17.1)] for electroactive substances which determine the shape of a titration curve. Any one or more of the reactants and/or the products may give rise to an anodic or cathodic current at the selected potential. In addition to these, an indicator substance may either be added or generated in the reaction.

If the electroactive species in an amperometric titration are represented by T^* (titrant); A^* (analyte); P^* (a product); I^* (added indicator); I_g^* (generated indicator) and the inactive species by the same symbol less the asterisk, then curve shapes in Fig. 17.4 are representative of the following situations:

Curve shape (Fig. 17.4)	Electroactive species
a	T^*
b	I^* or I_g^*
c	A^* and T^*
d	A_a^* and T_c^*
e	A^*
f	A_a^* and T_c^*

where subscripts a and c refer to anodic oxidation and cathodic reduction, respectively.

Note: For additional possibilities see Ref. 8.

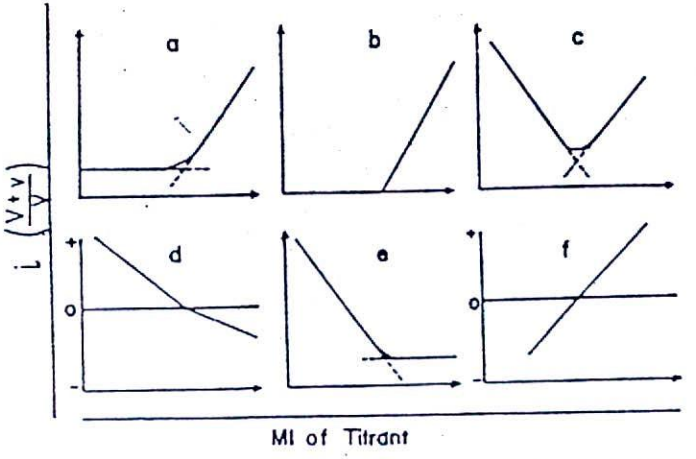

FIGURE 17.4: Typical amperometric titration curve shapes: $i(V+v)/V$ is the observed current corrected for dilution by the titrant volume. The various curves are described in the text.

D. GENERAL AMPEROMETRIC TITRATION PROCEDURE

Assuming a manual polarograph will be employed with an H-type titration cell, external SCE (Fig. 17.2), DME (or RPE), and a microburette, a general procedure is given here.

Obtain an i vs. E_{appl} curve (polarogram) of each possible electroactive substance entering or resulting from the titration reaction [Eq. (17.1)]. If the $E_{1/2}$ values of these depolarizers in the selected medium are known from experience, or obtained from the literature, this portion of the analysis need not be done.

The polarized electrode may be the DME if the applied potential is negative, or at least not greater than about +0.1 V (vs. SCE). The RPE is used in the range 0.0 to +1.0 V (vs. SCE). The unpolarizable reference electrode is usually an SCE having a large diameter salt bridge.

Dissolve the analyte (substance to be assayed) in 50 ml (or other appropriate volume) of a suitable solvent containing a large excess of unreactive electrolyte such as a halide salt, buffer, etc. Add a few drops of 0.2% gelatin solution (or other maximum suppressor) if the DME is used. Transfer all (or a large known portion) of this prepared solution to the titration cell and deoxygenate it with oxygen-free nitrogen gas for 15 min if the applied potential is to be more negative than about 0.0 V (vs. SCE). Approximately a 1 min deoxygenation is required in such instances after each addition of titrant. Adjust the applied potential to the selected voltage and record the current corresponding to 0 ml of titrant. The sensitivity must be set so that the galvanometer index remains on scale during the entire titration. This setting is made through trial and error or previous experience.

Add 1 ml of titrant from a microburette, mix the solution by means of a stream of nitrogen or a magnetic stirring device. Cease this auxiliary stirring and read the current when it assumes a steady value for the RPE or a repetitive value in a quiescent solution for the DME. A stream of nitrogen is directed over the solution to exclude oxygen when the DME is used. Repeat this procedure for 3 to 5 increments of titrant which are well removed from the end-point region. Repeat this sequence again well past the end point. The size and spacing of these increments will become obvious with experience, but they do depend on the amount of titrant required to reach the equivalence point of the reaction. If a significant change in the concentration of the analyte does not occur with dilution by the titrant, it should be possible to extrapolate to the point of intersection of the two straight lines which can be drawn through the points of the plot of i vs. milliliters of titrant (abscissa) Fig. 17.3. Determine the volume of titrant required by dropping a vertical line from the point of intersection to the volume axis. If curvature appears in the extrapolated current vs. titrant volume plot, each current reading must be replotted after correction for the dilution effect (see

text). This current correction is required only in those regions of the plot where the slope $\neq 0$.

In titrations which call for the RPE, a stationary platinum electrode and magnetic stirrer can be used, but the current values are less reproducible. If time permits, repeat the titrations two or three times to ascertain the precision attainable.

Examples of amperometric titrations with one polarized electrode are given in Table 17.1.

E. EXPERIMENTS

Experiment 17.1. Amperometric Titrations Employing the DME as the Polarized Electrode

Apparatus. A manual polarograph, *H*-type polarographic cell or modified version (Fig. 17.2), DME assembly; external SCE (part of H-type cell), deoxygenation apparatus including oxygen-free nitrogen, 5- or 10-ml microburette, volumetric flasks and pipettes of appropriate capacity.

Solutions. a. 0.05 *M* potassium dichromate ($K_2Cr_2O_7$) stock solution; use analytical reagent grade $K_2Cr_2O_7$ if primary standard grade not available

b. 0.005 *M* $K_2Cr_2O_7$ solution, prepared by an accurate 1 in 10 dilution of solution a

c. 0.02 *M* lead nitrate stock solution

Any one of the following supporting electrolytes:

i. 0.2 *M* potassium nitrate

ii. Acetate buffer (acetic acid and sodium acetate, 0.3 *M* in each).

iii. Equal volumes of i and ii.

0.2% gelatin solution (freshly prepared) or other maximum suppressor such as 0.2% Triton X-100 Solution.

Procedure

Part A. Selection of Applied Potential. Prepare 200 ml of 0.001 *M* $Pb(NO_3)_2$ in one of the supporting electrolytes (SE) just described, adding 1.0 ml of 0.2% gelatin before adding the SE to the 100-ml mark. Prepare 50 ml of 0.001 *M* $K_2Cr_2O_7$ as previously, except add 0.25 ml of the gelatin solution instead of 1.0 ml.

Transfer 50 ml of this dichromate solution (or an appropriate volume) to a titration cell, deoxygenate it with nitrogen for at least 15 min, then direct a small stream of nitrogen over the surface of the solution.

Using a DME assembly, start the mercury flow, then immerse the

capillary into the solution. Adjust the drop time to about 3 or 4 sec, and the sensitivity of the galvanometer to give about an 80% deflection at an applied potential of −1.0 V (vs. SCE).

Obtain a polarogram over the applied potential (E_{appl}) range of 0 to −1.1 V (vs. SCE), using small changes in potential in regions of greatest current change. Plot the i vs. E_{appl} curve and observe the voltage range corresponding to the limiting current plateau. Obtain another polarogram under the same conditions, except use 50 ml of the 0.001 M $Pb(NO_3)_2$ in place of the dichromate solution. Leave this solution in the titration cell for Part B. Plot the polarograms on the same graph paper. From the two polarograms select applied potentials which may be used to: (a) give a reduction current due to one species only, or (b) give reduction currents due to both Pb(II) and dichromate.

Part B. Amperometric Titrations

1. Using a potential selected in part A, titrate the deoxygenated lead solution prepared in part A with 0.005 M $K_2Cr_2O_7$ using a 10-ml microburette. Stop the stirring and/or nitrogen bubbling when reading the current after each 0.5-ml addition of titrant (after each 0.25-ml in regions of rapid current change). Continue the titration until the titrant volume approximates twice that required for the equivalence point. Plot current readings vs. milliliters of titrant (along abscissa). Observe the nature of the plot in the vicinity of the end point. Extrapolate the linear portions of the curve using about four current values on each side of, and well removed from, the equivalence point. The point of intersection corresponds to the end point.

Upon completion of the experiment clean the DME, while mercury is dropping by immersion in 1 M HNO_3, then rinse with water and dry with a tissue. Store the DME in air, inside a test tube. Also clean the titration cell with 1 M HNO_3 and rinse well with distilled or deionized water.

2. Repeat the titration using an applied potential at which both reactants are reduced.

Assuming the 0.005 M $K_2Cr_2O_7$ solution has been accurately standardized, what is the concentration of the nominally 0.001 M $Pb(NO_3)_2$?

Which titration (step 1 or 2) permits the most precise end point location? Explain.

3. If time does not permit the reader to perform both parts A and B, use applied potentials of 0.0 and −1.0 V (vs. SCE) for the potentials sought in part A, and carry out part B.

4. As an additional experiment titrate a solution which is 10^{-4} M in lead salt with a correspondingly less concentrated standard dichromate solution.

Are current corrections necessary, due to dilution caused by the titrant, in the titrations performed?

Check this for one or two situations. Ascertain the error, if any, if such corrections are not made.

TABLE 17.1: Amperometric Titrations Involving One Polarized Electrode

Substance	Electrodes[a] Ind.	Ref.	E volts (vs. SCE)	Titrant	Titration medium	References
Inorganic ions						
Al^{3+}	DME	SCE	0	0.6 *M* NaF	NaCl + 1 mM Fe^{3+} in (1:1) H_2O-EtOH	4
Br^-, I^- or Cl^-	RPE	SCE	0.05	0.001–0.05 *M* $AgNO_3$	0.8 *M* HNO_3 in H_2O-Me_2CO (1:1)	4
I^-	RPE	SCE	0.65	0.002 *M* KIO_3	1 *M* H_2SO_4	5
NH_3	RPE	SCE	0.2	0.01–0.001 *M* $Ca(OCl)_2$ or NaOBr	0.00125 *M* KBr + 0.15 *M* $NaHCO_3$	5
SCN^-	RPE	SCE	0.2	0.005–0.05 *M* $Ca(OCl)_2$	0.00125–0.24 *M* KBr + 0.15–0.17 *M* $NaHCO_3$	5
SO_4^{2-}	DME	SCE	−1.2	0.01–0.1 *M* $Pb(NO_3)_2$	20–30% aqueous alcohol	4
Organic compounds						
p-Aminophenol	RPE	SCE	0.0	0.05 *M* $K_2Cr_2O_7$	0.25–1 *M* H_2SO_4	4
Aminophenol, p-amino-salicyclic acid	RPE	SCE	−0.2	0.02 *M* $KBrO_3$	0.05 *M* KBr + 0.08 HOAc + 100 *M* HCl	3,4,6
Cysteine (R—SH)	RPE	Hg/HgI	−0.4	0.005–0.05 *M* CU^{2+}	0.05 *M* NH_3 + 0.15 *M* $Na_2S_2O_3$	4,7
Cysteine	RPE	Hg/HgI	−0.3	0.001 *M* $AgNO_3$		4
Phenobarbital elixir	DME	SCE	0.0	0.1 *M* Hg^{2+} acetate in 0.1 *M* HOAc	0.20 *M* NaOAc in EtOH-H_2O (4:1)	7
Amines, 4 N compounds	graphite	SCE (NaCl)	+0.55	XS of 0.1 *M* Na TPB, 0.1 *M* KCl	Acetate buffer	8
Thiols (−SH)	RPE	SCE	0.0 or −0.2	0.01 *N* $AgNO_3$	Ammoniacal or neutral	4,5,6
Thiourea	RPE	SCE	+1. to +1.1	0.01 *N* $AgNO_3$	H_2SO_4	4
Aldehydes and ketones	DME	SCE	−0.76	(2,4-dinitrophenyl) hydrazine	0.005 *M* H_2SO_4 and 50% EtOH	4

Nicotine	DME	SCE	−0.38	Silicotungstic acid	2–10 mg/50 ml in dilute HCl + KCl
Salts of N-containing bases (alkaloids): codeine, cocaine, atropine, cinchonine, quinine, papaverine, procaine, aminopyrine	DME	SCE	−0.65	Silicotungstic acid (1 mole per 2 or 4 moles of N-base); reacts rapidly, simple stoichiometric ratios, current read after 15–30 sec	0.05–0.2 *M* HCl
Strychnine, atropine, brucine, papaverine, cocaine, codeine, ethylmorphine	DME	SCE		As above	1. to 3 *M* HCl
Caffeine, theobromine, theophylline	DME	SCE		Silicotungstic acid (1 mole per 3 moles of N-base)	0.5 *M* HCl
Ascorbic acid	DME	SCE	0.0	Fe(III)	Acidic medium
			−0.1	$KMnO_4$ (in presence of I)	H_2SO_4 medium
	RPE	SCE		ICl	Acid medium
	RPE	SCE	+0.3	Chloramine-T	Acid medium
	DME	SCE	−0.85	2,6-dichlorophenolindo-phenol	Acetate-phosphate buffer (pH 2.0)
	RPE	SCE		$KBrO_3$	2 *M* HCl and KBr
	RPE	SCE	0.0	KIO_3	0.3 *M* HCl
Aniline and phenols	RPE	SCE	0.0	0.02 *M* $KBrO_3$	1 mg/ml, 25 ml MeOH and 65 ml H_2O and 5 ml HCl and 5 ml 2 *M* KBr
Phenols	RPE	SCE	+0.1 to 0.3	0.1 *N* $KBrO_3$ and 0.1 *N* KBr	HCl-MeOH-DMF
Dodecylpyridinium bromide	DME	SCE	−1.32	Sodium dodecylsulfate	0.1 *M* NaOH
Thiols (—SH)	DME	SCE	0 to −0.2	Hg(II)	Slightly acidic or neutral media
Cysteine	RPE	SCE	−0.2	Cu(II)	Ammoniacal medium

TABLE 17.1 (continued)

Substance	Electrodes* Ind.	Ref.	E volts (vs. SCE)	Titrant	Titration medium	References
Methylene blue, methyl violet	DME	SCE	−0.4 to −0.8	Silicotungstic acid	0.05–5 mg in 1 *M* HCl	4
Phenothiazines, and various antihistaminics			−0.65	Silicotungstic acid	3.5% HCl	4
Salts of: codeine, atropine, strychnine, quinine, papaverine, procaine, antipyrine, aminopyrine.	DME	Hg-pool	−0.4	Phosphotungstic acid	0.2 *M* HCl	4
Quinine chloride, papaverine HCl, strychnine HNO_3	DME	SCE	−0.45	Picric acid	Acidic media (pH 4.7)	4
Acridines	DME	SCE	0.0	0.05 *M* $K_2Cr_2O_7$	Acetate buffer (pH 4.8)	4
Alkalated barbiturates (also in dosage forms)	DME	SCE	0.0	0.05 *M* $Hg(NO_3)_2$	0.05 to 0.2 g in EtOH, or Me_2CO and 0.5 *M* KOH	4
Antipyrine	RPE	SCE	−0.25	0.05 *M* $Hg(NO_3)_2$	0.05 to 0.2 g in EtOH, or Me_2CO and 0.5 *M* KOH	4

Salicylates, and *p*-aminosalicylic acid	DME	SCE	0.0	0.05 *M* $Hg(ClO_4)_2$	0.02 to 0.2 g in alkaline media, obtain a 1:2 (Hg:salicylate ppt)	*, †
p-Aminosalicylic acid	RPE	SCE		0.02 *M* $KBrO_3$	1–2 mg in 100 ml solution containing (0.05 *M* KBr, 0.08 *M* HOAc and 100 *M* HCl)	†
Aromatic phenols and amines with free $-OH$ and $-NH_2$ groups, e.g., sulfas, alkaloids etc.	DME	SCE	−0.4	0.025 *M* *p*-diazobenzenesulfonic acid	25 ml Clark-Lubs buffer (pH 9.3) and 0.5 ml 0.5% gelatin cooled to 10°C	†

* Key: SCE, saturated calomel; DME, dropping mercury; RPE, rotating platinum; Hg/HgI, mercury-mercurous iodide; Hg-pool, mercury pool.

† I. M. Kolthoff and J. J. Lingane, *Polarography*, Vol. 2, 2nd. ed. 1952

‡ H. A. Laitenen, *Anal. Chem.*, 28, 666 (1956).

§ A. Berka, J. Dolezal, and J. Zyka, *Chemist-Analyst*, 54, 24 (1965).

¶ A. Berka, J. Dolezal, and J. Zyka, *ibid.*; 53, 122 (1964).

** M. Brezina and P. Zuman, *Polarography in Medicine, Biochemistry, and Pharmacy*, Interscience, New York, 1958.

†† E. M. Cohen and N. G. Lordi, *J. Pharm. Sci.*, 50, 661 (1961).

‡‡ J. E. Sinsheimer and D. Hong, *ibid.*, 54, 805 (1965).

§§ H. C. Börresen, *Anal. Chem.*, 35, 1096 (1963).

¶¶ I. M. Kolthoff, and W. E. Harris, *Ind. Eng. Chem., Anal. Ed.* 18, 471 (1946).

*** M. A. Medina and C. Cummiskey, *Chemist-Analyst*, 53, 17 (1964).

Experiment 17.2. Amperometric Titrations Employing the Rotating Platinum Electrode (RPE) as the Polarized Electrode

Apparatus. Manual polarograph, magnetic stirring device, RPE and constant rate motor (e.g., 600 rpm; E. H. Sargent & Co. Chicago). Titration cell and external SCE (Fig. 17.2), 10-ml microburette, pipettes, and volumetric flasks of appropriate number and capacity.

Solutions. 1×10^{-3} *M* As(III) solution (dissolve the As_2O_3 in a minimum of 3 *M* NaOH, and add sufficient concentrated HCl (ca. 12 *M*) and water to make the final solution 1 *M* in HCl); 1 *M* KBr; and 0.05 *N* $KBrO_3$ (0.140 g in 100 ml).

Note: If the galvanometer index goes off scale in a negative direction and the galvanometer leads cannot be readily switched, begin the titration with the zero current setting at midscale.

Procedure. Accurately pipette the following solutions into the titration cell: 25.0 ml 0.001 *M* As(III) solution, 15.0 ml of 1 *M* HCl, and 10.0 ml of 1 *M* KBr solution. Immerse the RPE (previously cleaned in hot HNO_3 and rinsed with water) in the titrate, add a stirring bar to the titration cell, and place a magnetic stirrer under it. Connect the electrodes to the appropriate terminals of the polarograph. Insert the tip of the burette (or capillary extension of same) below the surface of the titrate. Make certain the RPE is clear of any obstacle, then turn on the motor. Adjust the applied potential of the RPE to 0.2 V (vs. SCE). It is not necessary to remove dissolved oxygen from these solutions. Why? Titrate the As(III) solution with the standard 0.05 *N* bromate solution. Read the current after each 0.05-ml addition of titrant until a definite deflection of the galvanometer is produced, then after each 0.10-ml increment until several readings beyond the equivalence point have been recorded. Keep this solution if required later. The magnetic stirrer is used to hasten mixing, but should be turned off during current readings. Note that the current does not increase until the equivalence point is reached. Plot i vs. milliliters of titrant and determine the end point graphically. When are current corrections required in this titration, if at all? It may be necessary to repeat this titration if the correct sensitivity was not selected initially. How could this sensitivity have been determined prior to the titration? If time permits, obtain a voltammogram over a voltage range of +0.2 to +1.0 V (vs. SCE) for the solution just titrated, in which excess titrant is present. What is the active species undergoing reduction at the indicator electrode? Could you obtain this curve using the DME in place of the RPE? Give reasons for your answer.

This amperometric titration can be repeated with lower concentrations of As(III) and correspondingly lower concentrations of the titrant.

$$AsO_3^{3-} + BrO_3^- \rightarrow AsO_4^{3-} + Br^-$$

The first drop of excess $KBrO_3$ reacts with excess KBr in the acidic medium to produce free Br_2, which gives rise to the reduction current:

$$BrO_3^- + 5Br^- + 6H^+ \rightarrow 3Br_2 + 3H_2O$$

What possible pharmaceutical applications could be made with this titration? A few references should be consulted.

Experiment 17.3

For additional amperometric titrations employing either the DME or RPE as the polarized electrode, consult Table 17.1.

17.3 AMPEROMETRIC TITRATIONS USING TWO POLARIZED ELECTRODES

Two methods of voltammetry are very similar in that both give rise to similar titration curves and both employ two identical polarizable indicator electrodes (usually two platinum wires or pieces of foil). In potentiometric titrations using two polarizable electrodes (bipotentiometric method), a small constant current is applied and changes in voltage during the titration are recorded. Whereas, in amperometric titrations with two polarizable electrodes (biamperometric method) a small constant potential difference is applied and changes in current are followed during the titration.

A. TITRATION CURVE SHAPES

The titration curve shape depends on the reversibility or irreversibility of the redox couples (or systems) involved in the titration reaction, which determines the reaction at each electrode during the titration.

1. Titration Involving Two Reversible Redox Couples

The most widely cited example is that of the titration of ferrous iron with ceric ions,[9,10]

$$Fe(II) + Ce(IV) \xrightarrow{(H^+)} Fe(III) + Ce(III) \qquad (17.2)$$

In this instance, both redox couples, i.e., Fe(III)/Fe(II) and Ce(IV)/Ce(III), are reversible. In this example, ferrous iron is titrated with a standard ceric sulfate solution in an acidic medium and yields a curve similar to Fig. 17.5a. Before any titrant has been added, the anode can oxidize Fe(II), while only H^+ ions can be reduced at the cathode. Since the applied potential is much smaller than the potential difference between the E° (or $E^{\circ\prime}$, formal potential) values of the involved redox couples, Fe(III)/Fe(II) and Ce(IV)/Ce(III), little or no current flows and electrolysis is very small. However, following

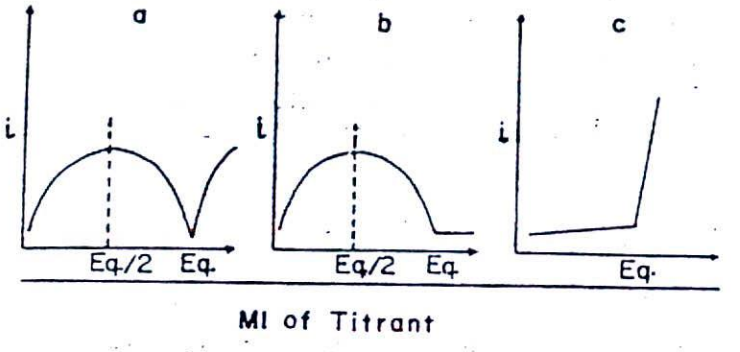

FIGURE 17.5: Typical biamperometric titration curves. (a) Involving two reversible redox couples, (b) involving one reversible redox couple (dead-stop end point), (c) involving one reversible redox couple (kick-off end point). Eq. = equivalence point.

the addition of Ce(IV) titrant, an equivalent amount of Fe(II) is oxidized to Fe(III), which can be reduced at the cathode. This is observed by an increased current flow due to the establishment of a reversible couple, Fe(III)/Fe(II), in the system. This current increases with addition of titrant until one-half of the original Fe(II) has been oxidized and [Fe(III)] = [Fe(II)]. At this point the concentration of Fe(II) being oxidized at the anode equals the concentration of Fe(III) being reduced at the cathode.

$$\text{Cathodic reduction: } Fe(III) + e^- \rightarrow Fe(II) \tag{17.3}$$

$$\text{Anodic oxidation: } Fe(II) \rightarrow Fe(III) + e^- \tag{17.4}$$

This maximum in the plot of i vs. milliliters of titrant represents the one-half equivalence point, where [Fe(III)] = [Fe(II)]. As the titration proceeds past this point, the [Fe(III)] increases and the [Fe(II)] decreases, resulting in a decreased total current flow due to the [Fe(II)] limitation imposed at the anode (anodic and cathodic currents are equal at all times). A minimum current occurs at the equivalence point, since all the Fe(II) ions have been oxidized to the Fe(III) state, and the applied potential is not sufficient to oxidize the Ce(III) ions which are present. Once past the equivalence point, the excess of Ce(IV) remains in solution establishing a new reversible redox couple, Ce(IV)/Ce(III). Immediately after the equivalence point the limiting factor controlling current flow is the [Ce(IV)], since a relatively larger concentration of Ce(III) is present. As the [Ce(IV)] builds up, the overall electrode reactions increase, i.e., Ce(IV) reduction at the cathode and Ce(III) oxidation at the anode, resulting in a rising current in the plot.

It is important to realize that the current does not reach 0 due to the presence of minute quantities of ions (of the redox couples) which are assumed to be absent. It is usually necessary to establish the exact location

of the equivalence point graphically, since some distortion of the ideal curve occurs in practice. Exceptions are made for those situations in which a very abrupt change in current occurs at the end point.

2. Titration Involving Only One Reversible Couple

Among the most familiar biamperometric titrations in which one couple is irreversible are those involving the titration of arsenite with iodine (or vice versa) and iodine with thiosulfate (or vice versa).

If identical polarizable platinum electrodes have a small constant potential (e.g., 0.01 to 0.1 V) impressed across them, the curve shape that results from the titration of iodine with thiosulfate (or arsenite) is similar to Fig. 17.5b. If thiosulfate (or arsenite) is titrated with iodine, the shape of the titration curve corresponds to Fig. 17.5c.

Iodine/Iodide is an example of a reversible couple in the examples illustrated in Fig. 17.5

$$\text{Anodic oxidation: } 2I^- \rightarrow I_2 + 2e^- \tag{17.5}$$

$$\text{Cathodic reduction: } I_2 + 2e^- \rightarrow 2I^- \tag{17.6}$$

In the titration of iodine with thiosulfate, the curve shape (Fig. 17.5b) may be explained as follows:

At the beginning, no current flows between the electrodes unless there is present in the solution a substance which can be oxidized at the anode and another substance which can be reduced at the cathode. Initially, only iodine exists in solution and therefore oxidation cannot occur at the anode. After a small addition of thiosulfate, iodide appears in solution as shown in

$$I_2 + 2Na_2S_2O_3 \rightarrow 2NaI + Na_2S_4O_6 \tag{17.7}$$

Since the anodic and cathodic currents are equal for a reversible redox couple, the magnitude of the current is established by the member of the couple present in the lowest concentration, i.e., $[I^-]$ early in the titration. As more thiosulfate is added, the iodide concentration increases, as does the current flow through the cell. This continues to the midpoint of the titration. At the one-half equivalence point, $[I] = [I^-]$, and the current reading reaches a maximum. After the midpoint in the titration, the remaining iodine concentration is less than that of the iodide formed, and the cathodic reduction becomes the current limiting factor. The total current flow continues to decrease until it reaches a value near zero at the end point, hence the name "dead-stop" end point. The current does not increase again after the end point due to the irreversibility of the tetrathionate/thiosulfate couple ($S_4O_6^{2-}/S_2O_3^{2-}$) and the small applied potential which is insufficient to oxidize iodide at the anode and reduce H^+ ions at the cathode.

Note: In the titration of 0.1 *N* Iodine USP with sodium thiosulfate solution, the actual titration curve looks like the last half of the curve shown in Fig. 17.5b due to the presence of KI in this iodine solution.

If a solution of thiosulfate (irreversible couple) is titrated with iodine (reversible couple), the current remains near zero prior to the equivalence point and increases abruptly thereafter (Fig. 17.5c) giving rise to the designation "kick-off" end point.

B. METHODOLOGY

The dual polarizable electrodes are usually two platinum wires each sealed in a glass tube, or two platinum foil or button-type electrodes. Larger electrode surfaces increase the current sensitivity. In certain instances, two mercury-plated platinum electrodes or two dropping mercury electrodes or two copper electrodes, etc., can be employed.

Frequently the sensitivity of this method depends upon the magnitude of the applied potential, it is therefore important that the resistance of the current indicating device be as low as possible to avoid a significant iR drop across it.

To minimize any change in the solution composition due to electrolysis, the surface area of the electrodes should be small (0.1 to 3 cm^2) and the applied potential kept to a low value (e.g., usually 10 to 500 mV). This is essential when an irreversible couple is involved in the titration.

When stationary solid electrodes are employed the solution must be stirred. Since the rate of stirring does affect the observed current, a constant-rate stirrer is preferred, however a magnetic stirrer is usually adequate. An increased rate of stirring can be used to increase the current sensitivity. Although a simple device may frequently be employed, as illustrated in Fig. 17.1, a polarograph is convenient and desirable for accurate work.

A major advantage of dual-polarized electrode amperometry is the simplicity of use and maintenance of the electrodes, especially in nonaqueous media, where reference electrodes are more difficult to make.

Note: If the applied potential in the dual-polarized electrode method is made sufficiently large, a diffusion-controlled current will be established early in the titration and the method will be identical to the one polarizable electrode method.

C. ADVANTAGES OF AMPEROMETRIC TITRATIONS

In the amperometric titration method there are fewer variables than with polarography, thus simpler, more rugged equipment can be employed. Also greater accuracy and sensitivity is possible than in polarography. Concentrations of certain substances can be determined between 10^{-1} and 10^{-5} M and in a few instances to 10^{-6} M. The method has a wider range of application than either potentiometric or polarographic methods.

D. APPARATUS

A manual polarograph is satisfactory. In addition, one requires a titration cell consisting of a 100-ml beaker, magnetic stirrer (or stirrer with a glass propeller), two identical platinum electrodes (usually two platinum wire or foil electrodes sealed in glass tubes), a 10-ml microburette, appropriate pipettes, and volumetric flasks for solution preparation.

E. GENERAL PROCEDURE

A polarizing potential is applied across the identical electrodes so that one becomes the anode and the other the cathode. The magnitude of this potential may be indicated or may have to be found experimently, however it usually lies between 10–500 mV. The titrant is added in 0.5-ml increments until a detectable change in current is observed, then in reduced increments of 0.1 ml. Allow time for mixing after each addition of titrant, then read the current when it becomes steady, plot the observed current on the ordinate vs. volume of titrant in milliliters along the abscissa.

The sensitivity setting should remain unchanged throughout the titration. If the "dead-stop" method is employed, the sensitivity should be adjusted to about 80% of full-scale deflection (FSD) during a trial run when the current flow is maximal. For the "kick-off" method, the sensitivity should be adjusted to about 80% FSD after four or five small increments of titrant have been added beyond the end point in a trial run.

F. TYPICAL AMPEROMETRIC TITRATIONS USING TWO POLARIZED ELECTRODES

A few common examples of biamperometric titrations to the "dead-stop" end point include the titration of iodine with thiosulfate, bromometric titrations, and various titrations with oxidizers such as ceric or permanganate ions, or reducing agents such as the ferrous or titanous ions.

Additional examples are found in Table 17.2.

G. EXPERIMENTS

Solutions

Ferrous ammonium sulfate (0.1 N)*

Ceric sulfate (0.1 N)*

Iodine (0.1 N)*

Sodium thiosulfate (0.1 N)*

0.025 M As_2O_3 (in 1 M $NaHCO_3$); prepare in a manner comparable to that for a standard solution of $KAsO_2$.*

* USP XVII, "Volumetric solutions."

TABLE 17.2: Amperometric Titrations Involving Two Polarized Electrodes*

Substance	E volts	Titrant	Titration medium	Reference
Inorganic examples				
Water (content)	0.025	Karl Fischer reagent	Ethylene glycol-pyridine (4:1)	
Sb(III)	0.200	Br_2†	(Excess) NaBr (0.2 *M*) + 1 *M* H_2SO_4	
As(III)	0.200	$KBrO_3$ (Br_2†)	(Excess) NaBr + 0.1 *M* H_2SO_4	
I^-	0.130	$KBrO_3$ (Br_2†)	(Excess) NaBr + 2 *M* HCl	
Ce(IV)	0.100	Fe(II)	3 *M* H_2SO_4	
$S_2O_3^{2-}$	0.135	I_2	0.1 *M* HCl (air-free)	
NH_3	0.150	BrO^-	Borate buffer (pH 8.5) containing 0.1 *M* NaBr	
Zn(II)	0.100	$K_4Fe(CN)_6$	(Slight excess EDTA), pH 2.1, and 10 drops $K_4Fe(CN)_6$ (10%) solution	
Organic examples				
Barbiturates (e.g., Phandorn, Evipan, Thiopentol)		Br_2*($KBrO_3$)	Try (excess) KBr + 2 *M* HCl (bromatometric method)	
Sulfanilamide and other sulfas		Br_2†	Bromatometric	
Phenothiazine and various derivatives		Br_2†	Bromatometric	
Phenothiazine and derivatives		Ce(IV)	H_2SO_4 solution	
Carbutamide		Br_2†	Bromatometric	
Phenol		Br_2†	Bromatometric	
Aromatic primary amines, e.g., various sulfonamides, amino-salicylic acid, etc.		$NaNO_2$	Diazatization in HCl solution with bromide as a catalyst	
Isonicotinic hydrazide		$NaNO_2$	In HCl solution	
Alkaloids (certain)		$AgNO_3$	Precipitate with tetraphenylboron, separate, and dissolve ppt in acetone, titrate TPB ion with $AgNO_3$	
Urea, thiourea, substituted quanidines		NaOMe, or $HClO_4$	In DMF and ethylene diamine or in F_3C-COOH, respectively	

Various olefins	$KBrO_3$	Bromatometric titration with $HgCl_2$ catalyst, to determine the bromine number	[4, 5, 6]
Unsaturated compounds		Determination of iodine numbers	[4, 7]
Ascorbic acid	$KBrO_3$		[4]
	ICl		[4]
	2,6-dichloroindophenol		[4, 8]
	$K_3Fe(CN)_6$		[4]
Oxalic acid	Ce(IV)	Glacial HOAc	[4, 9]
Cysteine	$K_3Fe(CN)_6$		[4, 10]
Glucose	Ce(III)	Add (excess)$K_3Fe(CN)_6$ and back titrate with Ce(III)	[11]
2,3-dimercaptopropanol	Br_2†		[12]

* Consult original references for details.

† Electrogenerated, may work with added titrant ($KBrO_3$ in presence of excess KBr and HCl). Bromatometric method.

[1] E. L. Bastin, H. Siegel, and A. B. Bullock, *Anal. Chem.* **31**, 468 (1959).
[2] R. A. Brown and E. H. Swift, *J. Am. Chem. Soc.*, **71**, 2717 (1949).
[3] L. Meites (ed.), *Handbook of Analytical Chemistry*, McGraw-Hill, New York, 1963, Sec. 5.
[4] K. Stulik and F. Vydra, *Chemist-Analyst*, **55**, 24 (1966).
[5] K. R. Srinivasan, *Analyst*, **75**, 76 (1950).
[6] H. G. Scholten and K. G. Stone, *Anal. Chem.*, **24**, 749 (1952).
[7] J. E. DeVries, S. Schiff, and E. S. C. Gantz, *Anal. Chem.*, **27**, 1814 (1955).
[8] H. D. DuBois and D. A. Skoog, *Anal. Chem.*, **28**, 624 (1948).
[9] ASTM, *1964 Book of ASTM Standards*, ASTM, Philadelphia, Part 17, 1964, p. 399, D 1158-59T.
[10] J. A. Duke and J. A. Maselli, *J. Am. Oil Chemists' Soc.*, **29**, 126 (1952).
[11] H. Liebmann and A. D. Ayres, *Analyst*, **70**, 411 (1945).
[12] O. N. Hinsvark and K. G. Stone, *Anal. Chem.*, **28**, 334 (1956).
[13] H. G. Waddil and G. Gorin, *Anal. Chem.*, **30**, 1069 (1958).
[14] N. H. Furman and A. J. Jr. Fenton, *Anal. Chem.*, **32**, 745 (1960).
[15] J. W. Sease, C. Niemann, and E. H. Swift, *Anal. Chem.*, **19**, 197 (1947).

Experiment 17.4. Biamperometric Titration Involving Two Reversible Couples, i.e., Fe(III)/Fe(II) and Ce(IV)/Ce(III)

Pipette 5.0 ml of 0.1 *N* ferrous ammonium sulfate into a 100-ml beaker, followed by 5 ml of sulfuric acid and about 10 ml of water. Immerse the platinum electrodes to a depth of 1/2 in. or more. Apply a potential of 400 mV, start the stirrer, attempting to keep the rate fairly constant during the titration. Titrate with standardized ceric sulfate solution, adding 0.5 ml increments at the beginning, decreasing these to 0.1 ml in the vicinity of the end point. Add about six small increments beyond the end point. Read the current after each addition of titrant and record the values. Plot the observed current *i* vs. milliliters of Ce(IV) as the titration is being performed. Explain the shape of this plot.

Experiment 17.5. Biamperometric Titration Involving One Reversible and One Irreversible Redox Couple (using the same apparatus employed in Experiment 17.4)

Pipette 5.0 ml of 0.1 *N* iodine solution into a 100-ml beaker. Add about 20 ml of water sufficient to immerse the dual platinum wire (or foil) electrodes. Apply a potential of between 25 to 100 mV, and adjust the sensitivity of the polarograph to obtain current reading of about 80% FSD. Titrate with 0.1 *N* sodium thiosulfate solution, recording the current reading after each 0.5-ml increment at the beginning and 0.1-ml additions near the end point. To facilitate the exact location of the end point, plot current vs. volume of titrant as indicated in Experiment 17.4. Continue the titration until five or six small (0.1-ml) increments have been added beyond the end point, where there is no appreciable change in current. Explain the shape of this plot.

H. ALTERNATE EXPERIMENTS

Use the same equipment and conditions, unless otherwise stated.

a. Titrate 5.0 ml of 0.1 *N* $Na_2S_2O_3$ solution with 0.1 *N* iodine solution. Explain the shape of the *i* vs. milliliters of titrant plot.

b. Titrate 5.0 ml of 0.05 *N* iodine (diluted with 20 ml of water) with 0.025 *M* As_2O_3 (in 1 *M* $NaHCO_3$), or the reverse of this.

$$As_2O_3^{2-} + I_2 + 2HCO_3^- \rightarrow As_2O_4^{2-} + 2I^- + H_2O + 2CO_2$$

Experiment 17.6. Consult Table 17.2 for Additional or Alternate Biamperometric Titrations, Preferably Those Involving an Organic Compound

QUESTIONS

Q17.1. State the advantages and disadvantages of the rotating platinum electrode (RPE) and the dropping mercury electrode (DME) for amperometric titrations.

Q17.2. Discuss the relative merits of dc polarographic analysis and amperometric titrations (keeping in mind the restrictive definition of polarography).

Q17.3. Contrast potentiometric and amperometric titration methods.

Q17.4. What other titrimetric methods employ a graphic means of end-point detection similar to that used in amperometric titrations? What are the values plotted against the volume of titrant in each case?

Q17.5. Briefly survey the applications of interest to a pharmaceutical analyst for "dead-stop" end-point titrations. Consult review articles given in the References.

Q17.6. Outline a procedure which might be employed in adapting the analysis of a suitable pharmaceutical preparation by the Volhard method to the amperometric titration technique. Use the same indicator substance, if desired. Is any advantage gained by this adaption for the usual routine analysis? Comment.

READING LIST FOR AMPEROMETRIC TITRATIONS

Articles and reviews

Anastasi, A., U. Gallo, E. Mecarelli, and L. Novacic, *J. Pharm. Pharmac.*, **8**, 241 (1956).

Berka, A., J. Doležal, and J. Zýka, *Chemist-Analyst*, **53**, 122 (1964); **54**, 24 (1965).

Charlot, G., and B. Trémillon, *J. Electroanal. Chem.*, **3**, 1 (1962).

Charlot, G., Badoz-Lambling, and B. Trémillon, *The Electrochemical Methods of Analysis*, Elsevier, Amsterdam, 1962.

Delahay, P., *New Instrumental Methods in Electrochemistry*, Wiley (Interscience), New York, 1954.

Delahay, P., *Instrumental Analysis*, Macmillan, New York, 1957, pp. 106–117.

Elving, P. J., I. Fried, and W. R. Turner, *U.S. At. Energy Comm.*, *COO-1148-84* (1964).

Ewing, G. W., *Instrumental Methods of Chemical Analysis*, McGraw-Hill, New York, 1954, Chap. 4.

Ewing, G. W., *Instrumental Methods of Chemical Analysis*, McGraw-Hill, New York, 2nd ed., 1960, pp. 215–220.

Furman, N. H. *Anal. Chem.*, **26**, 84 (1954).

Ishibashi, M., and T. Fujinaga, *Polarographic Methods of Chemical Analysis*, Maruzen, Tokyo, 1956, pp. 317–340.

Jolliffe, G. O., in *Practical Pharmaceutical Chemistry* (A. H. Beckett and J. B. Stenlake, eds.), Athlone Press, London, 1962, pp. 352–357.

Kalvoda, R., and J. Zýka, *Pharmazie*, **7**, 535 (1952).

Kolthoff, I. M., *Anal. Chem.*, **26**, 1685 (1954).

Kolthoff, I. M., and J. J. Lingane, *Polarography*, Wiley (Interscience), New York, 2nd ed., 1952, pp. 887–953.

Laitinen, H. A., *Anal. Chem.*, **21**, 66 (1949); **24**, 46 (1952); **28**, 666 (1956); **30**, 657 (1958); **32**, 1SOR (1960); **34**, 307R (1962).

Litaneau, C., and D. Cörmös, *Talanta*, **7**, 18 (1960).

Meites, L., *Polarographic Techniques*, Wiley (Interscience), New York, 1955, pp. 185–204.

Milner, G. W. C., *The Principles and Applications of Polarography and Other Electroanalytical Processes*, Longmans, Green, London, 1957, pp. 633–713.

Mitchell, J., and D. M. Smith, *Aquametry*, Wiley (Interscience), New York, 1948, pp. 86–93.

Müller, O. H., *The Polarographic Method of Analysis*, Chemical Education Publishing Co., Easton, Pa., 1951, pp. 118–128.

Reilley, C. N., *Anal. Chem.*, **28**, 671 (1956).

Stock, J. T., *Anal. Chem.*, 36, 355R (1964); 38, 452R (1966).
Stock, J. T., *Amperometric Titration*, Wiley (Interscience), New York, 1965.
Strobel, H. A., *Chemical Instrumentation*, Addison-Wesley, Reading, Mass., 1960, pp. 530–534.
Willard, H. H., L. L. Merritt, Jr., and J. A. Dean, *Instrumental Methods of Analysis*, Van Nostrand, Princeton, N.J., 3rd ed., 1958, Chap. 21.
Willard, H. H., L. L. Merritt, Jr., and J. A. Dean, *Instrumental Methods of Analysis*, Van Nostrand, Princeton, N.J., 4th ed., 1965, Chap. 26.
Zuman, P., *Organic Polarographic Analysis*, Pergamon Press, New York, 1964, pp. 145–165.
Zýka, J., in *Progress in Polarography* (P. Zuman and I. M. Kolthoff, eds.), Wiley (Interscience), New York, 1962, pp. 649–660.

Also see References and those in Chapter 16.

REFERENCES

1. I. M. Kolthoff and Y. D. Pan, *J. Am. Chem. Soc.*, 61, 3402 (1939).
2. J. Heyrovský and J. Kůta, *Principles of Polarography*, Academic Press, New York, 1966, pp. 267–272.
3. J. Heyrovský and S. Berezicky, *Collection Czech. Chem. Commun.*, 1, 19 (1929).
4. E. Salomon, *Z. Physik. Chem.*, 24, 55 (1897); 25, 365 (1898); *Z. Electrochem.*, 4, 71 (1897).
5. C. W. Foulk and A. T. Bawden, *J. Am. Chem. Soc.*, 48, 2045 (1926).
6. E. H. Sargent Co., *Bulletin P-5, Sargent Polarographs and Accessories*, Chicago.
7. G. W. Ewing, *Instrumental Methods of Chemical Analysis*, McGraw-Hill, New York, 1954, p. 77.
8. J. Jordan and J. H. Clausen, in *Handbook of Analytical Chemistry* (L. Meites, ed.), McGraw-Hill, New York, 1963, pp. 5-155–5-158.
9. D. G. Davis, in *Handbook of Analytical Chemistry* (L. Meites, ed.), McGraw-Hill, New York, 1963, pp. 5-164–5-165.
10. L. L. Leveson, *Introduction to Electroanalysis*, Butterworth, London, 1964, Chap. 4.
11. *United States Pharmacopeia*, Mack Printing, Easton, Pa., 17th rev. ed., pp. 1081–1088.