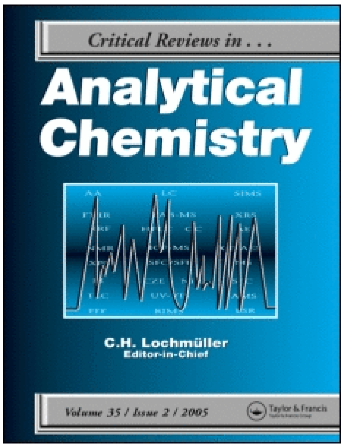

Critical Reviews in Analytical Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713400837

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To cite this Article Kratochvil, Byron and Coetzee, J. F.(1971) 'Analytical Oxidation-Reduction Reactions in Organic Solvents', Critical Reviews in Analytical Chemistry, 1: 4, 415 — 454

To link to this Article: DOI: 10.1080/1040834nu08542740

URL: http://dx.doi.org/10.1080/1040834nu08542740

ANALYTICAL OXIDATION–REDUCTION REACTIONS IN ORGANIC SOLVENTS

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I. INTRODUCTION

The use of nonaqueous solvents as media for chemical reactions has developed rapidly in the last 20 years. Prior to that time only scattered explorations of solvent-solute effects had been reported, and still fewer investigations of the effects of solvents on equilibria and reaction rates had been made. Classic pioneering studies include the conductance work in organic solvents of P. Walden, C. A. Kraus, and their co-workers early in the century (a single paper by Walden and Birr reported conductance data on 35 salts in acetonitrile), and the work in inorganic solvents by L. Audreith in the 1930's. These early studies of the physical properties of the solvents and their solutions did not trigger much response, perhaps in part because of difficulties associated with purification of the solvents, and also because there seemed to be no particular advantage to the replacement of water as solvent for most applications. Besides, much remained to be learned about aqueous solutions and water itself (this is still true today).

In the late 1940's, however, the use of organic solvents as media for the titrimetric determination of weak acids and bases became important. Nonaqueous solvents have two particular advantages over water for this purpose: one is the improved solubility of organic reactants and products, and the other is the increased acid or base strength available for the titrant through elimination of solvent leveling effects. Detailed understanding of the nature of the species present in these systems was lacking, however, and most developments came through intuition and trial and error. Titrants developed during this time included perchloric acid in glacial acetic acid for the titration of weak bases, and sodium and potassium methoxide, along with tetrabutylammonium hydroxide, in benzene-methanol for the determination of weak acids.

About this time interest in the fundamental properties of solvents developed and information on solvent purification, on solvation of ions and molecules, and on the thermodynamics and kinetics of solute processes in various media began to appear. However, in spite of the volume of data being gathered at the present time, our knowledge of the structure of most pure liquids (and this applies to water as much as, if not more than, it does to other solvents) is still discouragingly small. The tools available for probing liquid structure at the molecular level are for the most part few and indirect, and theories describing the liquid state are still inadequate to treat the multiple effects of hydrogen bonding, dipole interactions, and other short-range forces that are necessary to explain the bulk properties and solvating ability of most liquids.

Still, knowledge of nonaqueous solvent behavior is growing from several directions. Theoretical developments are evolving, along with a fund of experimental information on a range of solvents from fused salts to organic hydrocarbons to liquid metals.

This review covers one aspect of the overall field, that of analytical oxidation-reduction reactions. This area is still in early stages of development despite the existence of a large electrochemical literature dealing with nonaqueous solvents. A glance at reviews on the polarography of organic compounds, for example, reveals many references to polarographic studies in water-free media but few on quantitative determinations. The analytical possibilities of nonaqueous electron-transfer systems have considerable promise, however; points that will be considered here include solvents, solvent effects on rates and mechanisms of electron transfer, representative analytical applications, and some problems and possible directions of future work.

II. GENERAL CONSIDERATIONS IN SOLVENT SELECTION

Introduction

In this section some general aspects of solvents, solvent-solute interactions, and solvent effects on solute-solute interactions will be considered from the point of view of their effects on oxidation-reduction reactions.

For a solvent to be useful in electron-transfer reactions it should be resistant to oxidation or reduction, so that reagents covering a wide potential span may be employed. It also should be capable of dissolving a wide range of ionic and molecular solutes, and it should be convenient to purify and handle. No one solvent satisfies all these criteria, and compromises are always necessary. Thus, water does not have the potential range available in many other solvents, Lewis bases such as acetonitrile and dimethylformamide dissolve many inorganic salts to only a limited extent, and sulfolane and ethylene carbonate are viscous and freeze near room temperature. Often, too, impurities may be present that interfere even at trace levels with analytical systems and that are difficult to remove. All these factors enter into the selection of a solvent for a particular reaction or investigation, so a judicious balancing of advantages and disadvantages of various solvents is required before a final choice can be made.

A. Classification of Solvents

A classification of solvents helps to clarify patterns and identify properties useful in solvent selection for individual applications. Unfortunately a single classification satisfying all areas of nonaqueous solvent study has not yet been devised; in fact, criteria necessary in one area may not be appropriate in another. Thus, a classification useful for acid-base work may not be applicable for investigations of solvation.

Bates[1] has discussed the scheme proposed by Bronsted,[2] who divided solvents into four classes: protogenic (proton donating), protophylic (proton accepting), amphiprotic (both proton donating and accepting), and aprotic (neither proton donating or accepting). Bronsted then further divided each of these classes into two subdivisions on the basis of dielectric constant, above and below about 30. This value was chosen because at lower levels many ionic solutes begin to show appreciable association.

Bronsted's classification, however, takes into account only interactions between the solvent and hydrogen ion. It can be made more widely applicable by replacing the proton with a Lewis acid (an electron acceptor) and the Bronsted base with a Lewis base (an electron donor). Specific solvation effects now can be included because many reactions of metal cations with solvents can be considered as Lewis acid-base systems. This approach, though broad in scope, still has several disadvantages. An obvious one is that a particular solvent may function as a Lewis base toward one substance but not toward another; for example, acetonitrile is a good Lewis base toward silver(I), but poor toward hydrogen ion. Another drawback to a general classification based only on dielectric constant and Lewis acid-base properties is that it does not specifically take into account hydrogen-bonding effects in hydroxylic and other solvents, which affect both the properties of the pure solvent and those of solutes dissolved in it. (Hydrogen-bonding will, of course, affect both the dielectric constant and the Lewis acid-base properties of a solvent.) Thus, some nonionic solutes such as sugars are soluble in water (dielectric constant 78) because of solvent-solute hydrogen bonding; by contrast, the solubility of sugars in propylene carbonate (dielectric constant 69) is slight.

The solvents in group 5 of Table 1 are currently the most promising for analytical redox reactions, as those in the other classes generally have drawbacks either in performance or in handling properties. Acetic acid (group 4) has been popular for electron-transfer reactions but has the disadvantages of extensive ion-association and slow rates of reaction between solutes. A Lewis acid of high dielectric constant (group 3) would be very useful; unfortunately, the only one in this category is hydrogen cyanide (dielectric constant 107), which is too toxic and has too low a boiling point (25.7°C) to be suitable for routine use.

A solvent classification of some utility for oxidation-reduction systems, based on an extension of the basic scheme of Bronsted, is given in Table 1, along with representative solvents of each class. In this table an arbitrary value of 25 for the dielectric constant is used as the dividing line between dipolar and nonpolar solvents.* Values from 15 to 30 have been suggested in the literature; the choice is arbitrary because there is a smooth gradation throughout this region. A tabulation of selected solvents together with physical properties and solvent classification by the above scheme is given in Table 2.

Metals in various oxidation states are useful for analytical oxidation-reduction applications in nonaqueous solvents just as they are in water. Metal salts are often quite soluble in dipolar organic solvents because of specific solvation of the metal cation, a Lewis acid, by the Lewis base solvent. Specific solvation may also stabilize certain oxidation states, thereby making some couples stronger oxidants or reductants than they are in water. In such instances studies of the coordination chemistry of metal ions in Lewis base solvents provide useful information on the nature of the species present. Meek and Drago[3] have proposed a coordination model that interprets some of the results observed in systems of this type, and Gutmann[4] has made studies of the Lewis basicity of many solvents toward the Lewis acid antimony chloride by calorimetric measurement of the enthalpy of reaction between $SbCl_5$ and dipolar Lewis bases in dichloroethane. With these techniques systematic correlations are feasible, and future refinements should make such approaches even more useful.

TABLE 1
A Solvent Classification for Nonaqueous Electron Transfer Reactions

Solvent Class	Examples
Solvents of dielectric constant:	
1. greater than 25 that have both Lewis acid and base properties	water, methanol, ethylene glycol
2. less than 25 that have both Lewis acid and base properties	ethanol, isopropanol
3. greater than 25 that have Lewis acid properties	hydrogen cyanide
4. less than 25 that have Lewis acid properties	acetic acid
5. greater than 25 that have Lewis base properties	acetonitrile, dimethylsulfoxide, dimethylformamide, dimethylacetamide, propyo propylene carbonate, ethylene carbonate, formamide, sulfolane, γ-butyrolactone
6. less than 25 that have Lewis base properties	pyridine, triethylamine, ethylenediamine, acetone, tetramethylurea, acetic anhydride, morpholine
7. greater than 25 that have negligible Lewis acid or base character	nitromethane, nitrobenzene
8. less than 25 that have negligible Lewis acid or base character	n-hexane, toluene, cyclohexane

B. Solute-Solvent Interactions

The analytical utility of a nonaqueous solvent is determined in part by the range of materials it is able to dissolve. Organic solvents, of course, generally provide increased solubility of organic solutes, but this gain is frequently offset in part by a corresponding decrease in the solubility of electrolytes. Therefore, it is worth considering here some of the factors that determine the solubility of molecules and ions in a solvent.

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* The use of dielectric constant as an index of polarity is in itself rather arbitrary as was pointed out by the referee. Other indices, such as Kosower's Z-values or Gutmann's donor numbers, may also be used as estimates of solvent polarity. In any system specific solute effects make classifications limited in application.

TABLE 2
Physical Properties of Some Selected Nonaqueous Solvents[a]

Solvent	Dielectric Constant	Boiling Point	Melting Point	Density[b]	Viscosity[c]	Dipole Moment[c]	Coeff. of Cubic Exp.[c]	Solvent Classification
n-Hexane	1.91	69	−94	0.659_{20}	0.33_{20}	0		8
Cyclohexane	2.10	81	6.5	0.778_{20}	0.80	0	0.0011_{20}	8
p-Dioxane	2.21	101	12	1.036_{20}	1.2 0.59	0.45	0.0010	8
Toluene	2.38	111	−95	$0.868_{20/20}$	0.55	0.37_{25}	0.0011	8
Triethylamine	2.42	90	−115	$0.729_{20/20}$	0.36_{25}	0.75_{25}		6
iso-Propylether	3.88	69	−60	$0.725_{20\cdot 8/0}$		1.26_{25}		6
Ethyl acetate	6.02	77	−84	$0.902_{20/}$	0.45_{20}	1.83_{25}	0.0014_{20}	6
Acetic acid	6.4	118	16.5	$1.050_{20/}$	1.22_{20} 2.23	0.83	0.0011_{20}	4
Morpholine	7.33	128	−5	$0.999_{20/4}$	2.37	1.75_{25}	0.009	6
Ethyl formate	7.1	54	−80	$0.924_{25/}$	0.40_{20}	1.96_{25}		6
Tetrahydrofuran	7.6	66	−108	$0.888_{20/4}$	0.55_{20}	1.75_{25}		6
Methyl formate	8.5	32	−99	$0.974_{20/4}$	0.35_{20}	1.77g		6
Pyridine	12.3	115	−42	$0.987_{20/4}$	0.97_{20}	2.20		6
iso-Propyl alcohol	13.8_{20}	82	−86	$0.786_{20/20}$	2.08_{24}	1.80_{25}	0.0011_{20}	2
Ethlenediamine	14.2_{20}	117	8.5	$0.900_{20/20}$	1.6_{20}	1.90		6
Trimethylphosphate	20.6	197	−4b	1.214_{20}		3.02_{20}		6
Acetic anhydride	20.7	140	−73	$1.082_{20/4}$	0.91_{20}	3.15_{20}		6
Acetone	20.7	56	−95	$0.791_{20/}$	0.32	2.74	0.0014_{20}	6
Tetramethylurea	23.1	178	1	$0.972_{15/}$		3.49		6
Benzonitrile	25.2	191	−14	$1.001_{25/4}$	1.24_{25}	3.16_{20}		5
2,4-Pentane-dione (acetylacetone)	25.7	133	−23	$0.972_{25/4}$		2.81_{16}		5
Methanol	32.6	65	−98	0.792	0.55	1.66	0.0012	1
Nitrobenzene	34.8	211	6	1.203	1.98	3.99		1
Acetonitrile	36.0	82	−45	0.777	0.35	3.37	0.0014	5
Nitromethane	35.8_{30}	101	−29	$1.131_{25/4}$	0.62_{25}	3.54		7
Dimethylformamide	36.7	153	−61	$0.944_{25/4}$	0.80_{25}	3.82		5
Ethyleneglycol	37.7	197	−12	$1.113_{20/20}$	19.9_{20}	2.20_{15}	0.0006_{25}	X1
Dimethylacetamide	37.8	166	−20	$0.937_{25/4}$	0.92_{25}	3.5		5
γ-Butryolactone	39_{20}	204	−44	1.124_{25}	1.75_{25}	4.33		5
Sulfolane	43.3_{30}	285	28	$1.262_{30/4}$	10.30	4.81		5
Dimethylsulfoxide	46.7	189	18	$1.101_{20/}$	1.99_{25}	4.3	0.0009_{20}	X5
Propylene carbonate	69.0_{23}	242	−40	$1.206_{20/4}$	3.2_{20}	4.98_{25}		5
Ethylene carbonate	81	248	36	$1.322_{40/}$	2.55_{25}	4.87		5
Formamide	109_{20}	193	−5	$1.002_{20/20}$	3.30_{25}	3.2		5

[a] Data taken primarily from Marsden, C. and Mann, S., *Solvents Guide,* 2nd ed., John Wiley Sons, New York, 1963.

[b] Subscripts indicate temperature in deg. C at which density was measured. Where two numbers are given, the specific gravity is reported relative to water weighed at the second temperature.

[c] Where the temperature at which the property was measured is available it is indicated by a subscript.

1. Molecules in Solution

For an ideal solution of a solid in a liquid at some temperature T in degrees Kelvin, the solubility in terms of the mole fraction of solute present in solution, x, is given by

$$\ln a_s = \ln x = \frac{\Delta H_f}{R}\left[\frac{1}{T} - \frac{1}{T_m}\right] \quad (1)$$

where a_s is the activity of the solid solute at temperature, T, H_f is the heat of fusion of the solute, R is the gas constant, and T_m is the melting point temperature of the solute. This equation assumes that the difference between the heat capacities of the reactants and the products is small enough to render ΔH_f essentially constant over the temperature range from T to T_m.

For real solutions several complications arise. In the simplest case of a molecular solute in a solvent classified by Hildebrand as "regular", i.e., one in which thermal motion is sufficient to overcome any segregation due to unequal molecular attraction and in which no solvation is occurring, the solubility of a solid in a liquid can be expressed as

$$RT \ln \frac{a_s}{x} = V\phi^2(\delta_1 - \delta_2)^2 \quad (2)$$

where x again is the mole fraction of solute, V is the molar volume of the solute, ϕ is the volume fraction of solvent in the mixture, and δ_1 and δ_2 are solubility parameters for the solvent and solute.[5] These parameters are equal to the energy of vaporization of 1 cc of the pure component, generally as a liquid, and have been tabulated for a variety of substances.[6] An approximate value for a_s can be calculated from Equation 1. Calculated and experimental values agree well for systems such as iodine in hydrocarbons and halogenated hydrocarbons.

For less ideal systems a variety of specific solvation effects such as hydrogen bonding and covalent bonding (complexation), the presence of solvent dipoles, binding forces in crystalline solutes, and so on comes into play.

2. Ions in Solution

The formation and behavior of ionic species in nonaqueous solvents are especially important because in electron-transfer processes ions are likely to be present as reactants or products even in media of low dielectric constant.

The solubility of ionic solutes is a function of the structure of the solid and the activity of the ions in solution. Mathematically, this can be expressed for an electrolyte A_xB_y at equilibrium with a solvent by the relations

$$a_{A_xB_y(\text{solid})} = a_{A_xB_y(\text{in solution})} =$$
$$(a_A)^x{}_{(\text{in solution})}(a_B)^y{}_{(\text{in solution})}$$

In a solvent where considerable solvent-ion interaction is present a salt may be completely dissociated, while with lesser solvent interaction, association (ion pairing) may occur. Excluding specific interactions for the moment, the effect of the dipole moment of the solvent molecules on the change in free energy of solvation of a spherical ion of charge Z and radius r on transfer from solvent 1 to solvent 2 is given by the well-known Born equation

$$G_i^o = -\frac{NZ^2e^2}{2r}\left(\frac{1}{D_1} - \frac{1}{D_2}\right) \quad (3)$$

Here D_1 and D_2 are the bulk dielectric constants of solvents 1 and 2. This expression cannot be carried very far into the realm of practical application, however, because it imposes several stringent limitations on the system. The ions must be spherical and possesses no dipole, either permanent or induced, and it is also assumed that the solvent dielectric constant retains its bulk value even in the vicinity of the strong electrostatic field of an ion. Attempts to correct for dielectric saturation around ions have not been very satisfactory; therefore the Born equation can provide at present only a qualitative guide to the extent of solvent-ion interaction.

A solvent effect on ionic activity coefficients is predicted by the appearance of the solvent dielectric constant in the denominator of the extended Debye-Hückel expression. For an ion i at 25°C the activity coefficient is

$$\log \gamma_i = -\frac{353\, Z_i^2 \mu^{1/2}}{D^{3/2} + (2.91\ 10^8)\mu^{1/2}\, Da} \quad (4)$$

where γ_i is the activity coefficient of ion i, z_i the charge on the ion, μ the ionic strength, a the ion size parameter, and D the dielectric constant of the solvent. Using a value for a of 4 Å for a 1:1 electrolyte, values of $\gamma^{\pm}$ calculated from Equation 4 are shown in Figure 1 as a function of ionic strength for dielectric constants of 78 (water) and 36 (acetonitrile nitromethane). The difference in activity coefficients is large at low ionic strengths but becomes relatively constant at ionic strengths above about 0.05.

C. Solvent Effects on Electron-Transfer Equilibria

The effect of solvent on the equilibrium constant of an electron-transfer process cannot be predicted with any degree of confidence. Experimental thermodynamic data are lacking for most solvent-solute species, and approximations made from solvation-shell calculations require many assumptions. Accordingly, recourse must be had to tabulations of experimentally determined reduction potentials in the solvent under study, from which these equilibrium constants can be calculated for reversible couples. Most of the available electrochemical data are based on voltammetric measurements that have not provided standard potentials; however, they do give relative stabilities of couples in various solvents.

Many aqueous analytical reagents are not useful in nonaqueous solvents because of low solubility or decreased oxidizing or reducing power resulting from specific solvent effects. Thus, potassium permanganate and dichromate are insoluble in many solvents of low dielectric constant. Also, many redox reagents are effective only when protons are available. Sometimes solubility can be increased by selection of a different cation or anion for a reagent. For example, triphenylmethylarsonium permanganate is soluble in solvents such as chloroform and nitrobenzene, and iron(II) perchlorate is soluble in aprotic organic solvents and acetic acid. Selective solvation in turn may increase the oxidizing or reducing power of a substance; the oxidation ability of copper(II) in acetonitrile is an example (see section IV-B).

D. Solvent Effects on Electron-Transfer Rates

The role played by the solvent in determining

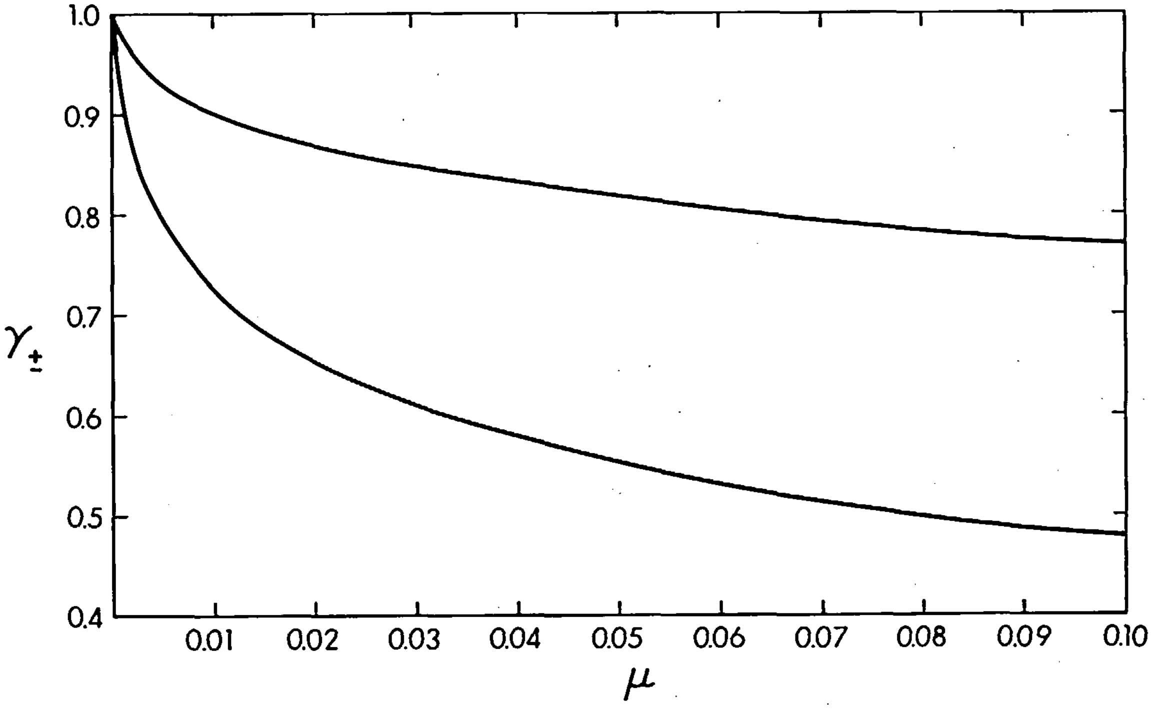

FIGURE 1. Effect of solvent dielectric constant on activity coefficients predicted by the Debye-Huckel Limiting Law (Equation 4) at various ionic strengths. Upper curve, dielectric constant 36; lower curve, dielectric constant 78.

the rate and pathway of an electron-transfer process is significant. Ionic or molecular reactants solvated by an aprotic organic solvent are likely to differ appreciably in size, shape, and charge distribution from the same reactant in water, and the resulting homogenous reaction rates can vary widely. The solvent dielectric constant again appears to be important. According to Scatchard,[6] for ion-ion reactions the effect of dielectric constant can be estimated by

$$\ln \frac{k_1}{k_2} = \frac{Z_A Z_B e^2}{rkT} \left(\frac{1}{D_2} - \frac{1}{D_1} \right) \tag{5}$$

where k_1 and k_2 are rate constants for a reaction in solvents of dielectric constant D_1 and D_2, Z_A and Z_B are the charges on the reactants A and B, r is the radius of the A-B species at the time of reaction (usually taken to be $r_A + r_B$), k is the Boltzmann constant, and T is the absolute temperature. This general dependence of the natural logarithm of the rate constant on the reciprocal of the solvent dielectric constant has also been obtained by an approach based on Coulombic energy considerations.[7]

Equation 5 predicts that a change in dielectric constant from 78 to 36 should cause a decrease in reaction rate by a factor of 10^7 if A and B are singly charged and r is 4 Å. This factor will become larger as the charge on the reactants is increased, as the dielectric constant is decreased, and as r is decreased. Experimental results indicate that the theoretical expressions are followed fairly well above dielectric constants of 50 to 60 but begin to deviate from the experimental results at lower values.[8]

Reactions between ions and dipolar solute molecules also are influenced by dielectric constant, and calculations of the extent of the effect have been made by Laidler[9,10] and by Amis.[11,12] If both reactants are dipolar molecules, the effect is reduced appreciably according to rough calculations incorporating electrostatic dipolar forces.[9] At this level van der Waals forces may have appreciable effects and should probably be taken into account.[13]

It has been pointed out by Kosower that the polarity of a solvent is significantly increased by the addition of salts that are appreciably dissociated.[14] He suggests that the polarity of such salt solutions can be measured empirically by measuring the wavelength of the charge-transfer band of 1-ethyl-4-carbomethoxypyridinium iodide in the solution; the lower the polarity of the pure solvent, the greater the increase in polarity produced by an ionic solute. An increase in the rate of an electron-transfer reaction by a factor of 25 may be possible for some reactions upon going from pure 1,2-dimethoxyethane to a 0.1 *M* solution of tetra-*n*-butylammonium perchlorate. The predicted corresponding increase in acetonitrile is a factor of about five. Thus high salt concentrations may be advantageous in accelerating reactions in some circumstances.

Solvent viscosity will also affect reaction rates if the electron-transfer step is sufficiently rapid that the rate depends upon the frequency with which the reactants come close enough to each other to interact. Rates which are diffusion-controlled usually have small activation energies and are relatively temperature-independent. Studies of diffusion-controlled rates in homogeneous electron transfer have been made by Wells, who found that in the oxidation of isopropanol by photo-excited anthraquinone-2-sulfonate ion, a temperature-independent reaction, the rate varied with the viscosity of the *tert*-butyl alcohol-water medium, as predicted by the collision frequency.[15] When the oxidant was manganese(III), the reaction became temperature-dependent, and the rate could be correlated with changes in dielectric constant. In another example, the iron(III)-(II) exchange rate has been studied by isotopic techniques in several solvents. The rate in 0.01 *M* aqueous perchloric acid is 10^8 times that observed in 0.01 *M* perchloric acid in isopropanol,[16] while days were required to achieve half-exchange in dry nitromethane.[17] Clearly, factors other than dielectric constant are involved, and solvent-solute interactions such as hydrogen bonding and Lewis acid-base interaction affect rates of transfer.

From a practical point of view these results indicate that reaction rates of many electron-transfer systems in solvents of dielectric constant below 25 to 30 are rather low. Although other effects may influence rates to varying degrees, it will generally be necessary when performing analytical titrations in these solvents to wait for reactions to come to equilibrium in the vicinity of the end point.

III. EXPERIMENTAL CONSIDERATIONS

The principal experimental problem associated with the use of nonaqueous solvents is that of solvent purification. Other factors that may need consideration are protection of purified solvent and solutions from water in the atmosphere and difficulties in electrochemical measurements owing to high resistances of solutions prepared from low dielectric constant solvents.

A. Solvent Purification

Obtaining organic solvents in highly pure form can be a time-consuming and difficult part of the research effort. For some solvents the nature and extent of the impurities present are well known and procedures for their removal well worked out, but for many information is lacking. Often a method of purification is used simply because it decreases polarographic residual currents or reduces an absorption band in the ultraviolet or infrared. Distillation, frequently under reduced pressure, is the most widely used technique for purifying solvents. Sometimes chemical pretreatment to remove acidic or basic impurities, or removal of large amounts of water by preliminary drying with molecular sieves, is helpful.

In some cases simple fractional distillation will not remove certain impurities. For example, ethylenediamine forms an azeotrope with water, and formamide and propylene carbonate undergo decomposition on heating. Special types of systems such as spinning band columns or Podbelniak stills may assist in the separation of contaminants with boiling points near that of the solvent. Techniques such as preparative gas chromatography or sublimation at low temperatures and pressures may provide a very pure product, but the amounts that can be processed are so small as to preclude widespread use. They are helpful, however, in obtaining small amounts of highly pure material for the measurement of physical constants.

Often the choice of a purification procedure is governed by the intended use of the solvent. For example, if small amounts of acrylonitrile can be tolerated in acetonitrile, simple fractional distillation from calcium hydride is generally satisfactory. Acrylonitrile interferes with ultraviolet and electrochemical measurements, however, so more extensive treatment is required if these techniques are to be used. Different commercial sources of a solvent may contain different impurities, depending on the methods used for synthesis or purification of the crude material. Thus, acetonitrile obtained as a by-product from the synthesis of acrylonitrile contains, in addition to acrylonitrile, hydrogen cyanide.

As will be mentioned later, formamide is a solvent worthy of more attention on the basis of its physical and chemical properties, but the difficulties in purification, along with decomposition of the purified material on storage, makes careful investigations a formidable undertaking.

In general, the identification and assessment of impurities in a solvent used for fundamental investigations is one of the first tasks of an investigator. As Popov has pointed out,[18] the validity of much early work on nonaqueous solvents is in doubt because trace impurities were either not recognized or ignored. Therefore, fundamental studies of a solvent should be done on material purified as carefully as possible. The effects of solvent contaminants on the reaction of interest can then be measured by deliberate addition; if they are negligible, care to ensure removal of these materials becomes unnecessary.

Several methods for the detection and identification of solvent impurities are now available. One of the most useful is gas chromatography for volatile molecular contaminants; another is conductivity for ionic impurities. In a pure solvent the specific conductance depends on the extent of self-ionization (autoprotolysis constant), and any conductance above this is caused by impurities. Some solvents undergo so little self-ionization, however, that trace impurities make determination of the autoprotolysis constant by conductance measurements impossible, and the minimum specific conductance is unknown. In such cases one can try various purification procedures, using the conductance as an indicator or purity.

The most ubiquitous contaminant in nonaqueous solvents, water, is still best measured by Karl Fischer titration, although a few other methods applicable to a specific solvent may be as accurate and more rapid. Among the alternative techniques available are quantitative measurements of absorption in the infrared region from 1 to 6 microns, and measurements in the visible or ultraviolet region of products of reaction or interaction between water and various reagents. In the infrared region, measurements at 1 micron have been used to determine water in acetone, acetic acid, acetic anhydride, methanol, ethanol, glycerol, and pyridine in the range from 0.1 to more than 1 weight percent. The method can also be used with acetonitrile, though the sensitivity is too low to be useful at the trace level.[20]

Spectrophotometric methods utilizing the spectral shift of a solvatochromic dye in a solvent of low polarity upon the addition of water have been proposed.[21] Using the most sensitive betaine-type dyes, the limit of detection in mg of water per ml of solvent is 0.06 for acetonitrile and dioxane, 0.09 for acetone, 0.13 for pyridine, 25 for isopropanol, and 40 for ethanol.[22]

Perhaps the most elegant technique yet devised for the determination of water consists of a probe in which the capacitance of a hygroscopic dielectric between two electrodes is measured.[23] The capacitance varies as a function of the water present in the dielectric and, after calibration, yields a sensitive and accurate measurement of the water in a solvent or gas.

Voltammetric methods for water have been developed in a number of solvents. The procedure usually involves reduction to hydrogen, and is generally quite sensitive. Care is needed to avoid water contamination from the atmosphere, supporting electrolyte, and apparatus.

Methods for purification of various solvents are scattered throughout the literature; Table 3 lists recommended procedures for a few of the more interesting solvents for oxidation-reduction work.

B. Reference Electrodes in Organic Solvents

A study of electron-transfer reactions in any solvent necessarily begins with electrochemical measurements involving some type of reference electrode. In water a variety of reference electrodes is available whose characteristics have been thoroughly and repeatedly studied, but this is not the case in other solvents. Therefore, beginning studies in a new solvent must include, besides identification and elimination of impurities in the solvent, the development of a satisfactory reference electrode. Information in this area is available in a chapter by Hills on reference electrodes in nonaqueous solutions,[24] and in a recent chapter by Butler on reference electrodes in aprotic organic solvents.[25] These reviews cover in detail the problems involved in the establishment of reliable references and list available electrodes.

The prime requirement of a reference electrode is stability. A second desirable property is that it not be readily polarized or, if it is, that the potential return to the initial value after polarization. The advent of high impedance electronic measuring instruments, however, has reduced current drain during measurement to the point where polarization effects are minimal. Finally, the electrode should be simple to prepare and maintain. The most suitable reference electrodes are prepared from couples where a well-defined, reversible reaction takes place at the electrode surface.

The most widely used reference in nonaqueous solvents is the aqueous saturated calomel electrode (SCE). Contact between the SCE and the solution under study is made by a bridge solution of an electrolyte in the nonaqueous solvent. This arrangement introduces a junction potential of unknown and varying magnitude that is not desirable in careful work. However, for routine analytical measurements where absolute potential values are not critical the aqueous calomel electrode may be the best choice. Attempts have been made to estimate the junction potential between water and other solvents; for example, a junction potential of 34 mV between water and acetonitrile has been reported.[26]

The silver-silver ion couple appears to be the most widely used nonaqueous reference system, and because of its stability, wide applicability, and ease of preparation, is recommended as the system of choice in most cases. The couple is reversible in a wide range of solvents; those of analytical interest in which it has been employed as a reference or as a reversible couple include acetamide,[27] acetic acid,[28] acetone,[29] acetonitrile,[30] γ-butyrolactone,[31] dichloromethane,[32] diethylether,[33] 1,2-dimethyloxyethane,[34] dimethylacetamide,[35] dimethylformamide,[36] dimethylsulfone,[37] dimethylsulfoxide,[38] formamide,[35] formic acid,[39] hexamethylphosphoramide,[35] N-methylacetamide,[40] N-methylformamide,[41] nitroethane,[38] nitromethane,[42] propylene carbonate,[43] pyridine,[44] sulfolane,[45] and tetrahydrofuran.[46] Silver nitrate or perchlorate is generally used. Sometimes silver chloride is employed with a tetraalkylammonium or alkali chloride salt in an electrode of the second kind, but this couple cannot be used in solvents where silver ion undergoes appreciable association with halide to give species of the type AgX, AgX_2, and so on. A tabulation of solubility-product and complex-formation constants for the silver halides in a

TABLE 3

Methods of Purification for Several Organic Solvents

Solvent	Common Impurities[a]	Suggested Procedures	References
Acetonitrile	Acrylonitrile, ammonia, acetic acid, hydrogen cyanide	Preliminary drying with molecular sieves; distillation from P_2O_5, then from CaH_2. To remove traces of unsaturated nitriles at the expense of adding a trace of NH_3, precede above procedure with refluxing and distillation from KOH. Traces of aromatic hydrocarbons can be removed by distillation from benzoylchloride, then from permanganate.	Coetzee, J. F., *Pure Appl. Chem.*, 13, 427 (1966).
Dimethylacetamide	Acetic acid, aromatic hydrocarbons (used industrially in isolation of product)	One or more distillations under vacuum.	Vaughn , J. W., in *Chemistry of Nonaqueous Solvents*, Vol. II, Lagowski, J. J., Ed., Academic Press, New York, 1967, 237.
Dimethylformamide	Dimethylsulfide	Preliminary drying with molecular sieves; distillation at 2.5 to 8mm (33 to 49° C) from P_2O_5 using a nitrogen bleed through the distillate.	Ritchie, C. D. and Megerle, G. H., *J. Amer. Chem. Soc.*, 89, 1447 (1967).
Dimethylsulfoxide	Dimethylsulfide	Preliminary drying with molecular sieves; vacuum distillation twice at about 40° C, the second time from sodium amide in a rotary evaporator.	Ritchie, C. D. Skinner, G. A. and Badding, V. G. *J. Amer. Chem. Soc.*, 89, 2063 (1967).
Formamide	Formic acid, ammonium formate, ammonia.	Distillation twice, the first time from CaO at 1 mm Hg, followed by several fractional crystallizations.	Dawson, L. R. Wilhoit, E. D. and Sears, P. G. *J. Am. Chem. Soc.*, 79, 5906 (1957).
Methyl formate	Methanol, formic acid	Preliminary drying with molecular sieves; distillation from lithium powder at atmospheric pressure.	Abens, S. G.,Nerz, W. C. and Walk, C. R. NASA Contractors' Report CR-72535 April 1968.
Propylene carbonate	1,2–and 1,3–Propylene glycol, propylene oxide, allyl alcohol	Preliminary drying with molecular sieves; distillation at 0.5–2 mm (72–85° C). Low boiling organic substances can be removed by passing N_2 through the solvent for several days.	Jasinski, R. J. and Kirkland, S.,*Anal. Chem.*, 39, 1663 (1967).
Sulfolane	3–Sulfolene	Vacuum distillation at 90 to 100° C from CaH_2. For removal of traces of sulfolene, heat with NaOH at 170 to 180° C for 24hr, removing gaseous products with an N_2 bleed through the Solvent; then pass through a mixed bed of cation and anion macroreticular resins before the distillation.	Coetzee, J. F., Simon, J. M., and Bertozzi, R. J.,*Anal. Chem.*, 41, 766 (1969).

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[a] Water is present in varying amounts in all solvents unless special precautions are taken to keep the purified material protected from the atmosphere.

number of solvents is included in the review by Butler referred to above.[25] Halide complexes are undesirable in a reference electrode because of the liquid-junction potential they introduce (because the mobilities of AgX_2^- and X^- differ), and because the anionic complexes of silver in some solvents, such as acetonitrile, form so slowly as to cause long term drift in the electrode potential.

Another class of reference electrodes that has received study in various solvents is that consisting of metal amalgams plus metal halides as electrodes of the second kind. Some metals and solvents in which they are reported to function reasonably satisfactorily as reference systems include mercury in formamide, dimethylformamide, and propylene carbonate; cadmium in formamide; and zinc in formamide.[25]

Alkali metal amalgam-alkali metal salt couples also have been found to be stable and reproducible in those solvents that are stable to reduction, including propylene carbonate, nitromethane, dimethylsulfoxide, dimethylformamide, and γ-butyrolactone, but problems associated with exclusion of oxygen and water during preparation, use, and storage make them inconvenient for most applications.

Finally, soluble oxidation-reduction couples at an inert surface, usually platinum, have been used to a limited extent. Some attention has been directed toward the hydrogen-hydrogen ion electrode, but the results have not been very successful. Unstable readings, attributed to reduction of the solvent by hydrogen at the platinum-black surface of the electrode, have been reported in acetonitrile, dimethylsulfoxide, and pyridine,[25] and solvents such as nitromethane and nitrobenzene are readily reduced by hydrogen. The hydrogen electrode can be used in acetic and formic acids,[24] and in formamide, N-methylformamide, and propylene carbonate.[25]

Complexes of the copper(II) - (I) and iron(III) - (II) couples with ferroin-type ligands (*o*-phenanthroline, bipyridine) can also be used as references. Copper(I) is stable in several solvents, including acetonitrile, dimethylformamide, and pyridine. The copper amalgam-copper(I) couple could probably also be used as a reference electrode in these solvents, as it has been shown to be stable and reversible in acetonitrile.[47]

The iodine-iodide couple is also reversible and stable in many solvents. The stability of the triiodide complex varies with the solvent, and it is actually the triiodide-iodide couple that is involved.

C. Electrochemical Methods

A comprehensive survey of the literature dealing with electrochemical studies in organic solvents is beyond the scope of this article, and the present discussion will be restricted to consideration of some experimental aspects of the measurements, with reference to specific solvents and systems only by way of illustration. As was pointed out previously, the number of analytical applications in this area is much smaller than the number of fundamental studies, although the latter have often shown, for example, that the height of a diffusion-controlled polarographic wave was proportional to the concentration of the electroactive species, and so have provided bases for possible analytical methods. We will first consider diffusion-controlled processes, and then processes involving total electrolysis of the compound or ion to be determined.

Polarography (voltammetry at the dropping mercury electrode (DME)) is convenient for rapid surveys of solutes in a given solvent. It provides information on general trends of solvent stabilization of metal ions and on oxidation and reduction of organic compounds, though mercury oxidation limits its electrochemical range in the anodic region. In most nonaqueous media the resistance is high, and a three-electrode system is necessary to compensate for *iR* drop in the solution. The effectiveness of the three-electrode system depends upon the specific resistance of the solution under study, the current passing between the DME and the counter electrode, and on the location of the DME, counter, and reference electrodes relative to each other in the solution. The optimum configuration is with the DME between the counter electrode and the reference electrode, and with the distance between the DME and the reference electrode held to a minimum.[48] This is accomplished by drawing the tip of the reference electrode out into a tube of very small diameter (Luggin capillary) and positioning it as close to the DME as possible. An arrangement of this kind can reduce the *iR* drop to a small value, though it cannot be completely eliminated in solutions of high resistance.

Voltammetry at solid electrodes such as platinum, gold, or carbon allows studies of oxidation reactions to the electrochemical limit of the supporting electrolyte or solvent. The primary disadvantage of these materials as electrodes is that the past history of the electrode surface, or the presence of traces of adsorbed impurities on the surface, tends to make current-voltage curves non-reproducible. For this reason they are not widely used in routine analytical applications.

Analytical techniques involving total electrolysis include coulometry and electrodeposition. Both constant-current and controlled-potential coulometry are well suited to use in nonaqueous solvents, and systems used in water can be applied to most nonaqueous media with little modification. The basic techniques are well outlined in the literature[49] and applications are reviewed biannually in the Reviews issue of *Analytical Chemistry.*

Electrodeposition has been little used as an analytical method in non-aqueous solvents, but could be more widely employed. A number of reversible metal-metal ion systems have been recently documented, particularly by U.S. government-sponsored studies on nonaqueous solvents as electrolytes for secondary high-energy-density batteries. Analyses can be completed either by weighing the electrode before and after depositing the substance to be determined, or by measuring the current required to strip the deposit from the electrode. The latter process, called stripping analysis, is especially effective in trace determinations. Metal ions in aqueous solutions at concentrations as low as 10^{-9} *M* can be electrodeposited into a mercury drop by slow electrolysis from a stirred solution, then stripped out of the drop rapidly and measured by reversing the potential and recording the current-time curve.

Combinations of electrochemistry with various techniques such as ESR and ultraviolet-visible spectroscopy are also used to elucidate reaction mechanisms and to study reaction rates. These hybrid systems will very likely find their way into direct analytical application in the future.

D. Titrations in Nonaqueous Solvents

C. Gravimetric Titrations

Conventional nonaqueous titrations are often hindered by the high coefficient of expansion of organic solvents, frequently on the order of five times that of water, and by handling problems that result from high viscosities, high vapor pressures, and solvent decomposition during storage. Many of these problems can be circumvented by the technique of gravimetric titration. In this method the weight of titrant delivered is measured rather than the volume. If the titrant is prepared on a moles of solute per weight of solution basis (note that this is not the same as molality), the calculations are simple and straightforward. Although weight titrations have been known for many years, they have been considered too slow and tedious to warrant widespread use. However, the method has several advantages. High precision can be attained when an analytical balance is used for the weighings, and buret and pipet calibration and drainage errors are eliminated. Also, temperature control to minimize solvent expansion and contraction errors becomes unnecessary.

To avoid the problems of fragility and awkwardness associated with conventional weight burets, plastic squeeze bottles of hypodermic syringes can be used. Because a squeeze bottle does not conveniently deliver single drops, a medicine dropper top can be incorporated into the bottle for use near the end point. A titration thief is an aid with this system. Hypodermic syringes of any capacity up to 50 ml may be employed. Best results are obtained if they are fitted with a glass capillary tip to provide more precise delivery of small drops and to minimize evaporation of volatile solvent during titration. Lubrication of the plunger with silicone grease so that it operates fairly stiffly gives positive control during delivery and prevents leakage during weighing. In most cases the accuracy of an analytical balance is not needed, and it can be replaced by a top-loading balance accurate to the nearest 10 mg or so. For routine work a commercial titration device is available in which the bottle of titrant remains on the balance pan and titrant is delivered to the titration vessel through thin tubing. If the balance is equipped with an inverted optical scale, the weight of titrant delivered can be read directly from the scale. This system is as fast and simple as conventional titrations.

Titrations in nonaqueous solvents need not be less precise than those in water. With a top-loading balance, precision equivalent to, or better than, that found in conventional aqueous titrations is easily obtainable in nonaqueous systems with little sacrifice in time. For example, weight titrations of ferrocene with copper(II) in acetonitrile, performed using hypodermic syringes as weight burets, weighing on an analytical balance, and employing a dilute solution of titrant near the equivalence point, gave standard deviations on the order of 0.3 parts per thousand.[50]

2. *End-Point Detection*

All of the methods of end-point detection used in aqueous solutions may be applied with varying degrees of effectiveness to nonaqueous oxidation-reduction titrations. These involve electrochemical and optical techniques, along with a few others not falling into these two classes. A partial list includes potentiometric (conventional and with polarized electrodes), conductometric, and oscillometric (high-frequency) electrochemical methods, photometric and visual indicator (conventional and fluorometric) optical methods, and enthalpimetric (thermometric) and cryoscopic methods.

Potentiometry is the technique most widely used for end-point detection in nonaqueous oxidation-reduction reactions because it provides maximum information during the investigation of new reactions, and is a relatively straightforward technique. Since for end-point detection the potential of the reference electrode need be stable only for the duration of the titration, systems other than those known to be thermodynamically well behaved may be used. For example, glass and antimony electrodes often make satisfactory references for titrations in acetic acid or acetonitrile. This greatly simplifies electrode preparation and maintenance.

If a reaction is to be applied to routine use but not automated, other more rapid or simpler ways of finding the end point may be sought. Visual indicators are the most convenient if available. A few have been used in glacial acetic acid(see Table 4). Work in other solvents is sparse, but Rao and Murthy found that ferroin and diphenylamine behave reversibly, and methyl red and Janus green irreversibly, as indicators for the titration of hydroquinone with cerium(IV) in acetonitrile,[51] and certain of the substituted ferroins are applicable to copper(II) titrations in acetonitrile.[52]

Amperometry and constant-current potentiometry are useful adjuncts to conventional potentiometry. The widest application of polarized electrodes in nonaqueous oxidation-reduction titrations has been in the Karl Fischer determination of water.

Other less common end point methods have been explored to varying degrees. Thermometric (enthalpimetric) methods, which have been used in nonaqueous acid-base systems, can also be applied to oxidation-reduction reactions. For example, end points in titrations of ferrocene, thiourea, and iodide with copper(II) in acetonitrile, and with cerium(IV) in propylene carbonate, can be located with precisions of about five parts per thousand.[53] The technique is particularly useful for titrations of mixtures where the free energies of the reactions are similar but the enthalpies differ appreciably (as with the calcium- and magnesium-EDTA complexes in water), though such systems are fairly rare.

Analyses based on hearts of reaction are also possible by a technique known as direct injection enthalpimetry (DIE). In this procedure an excess of reagent is added all at once to a solution containing the substance to be determined and the temperature rise is recorded. By calibration of the system with one or more known quantities of the substance to be determined, the relation between temperature rise and amount is established. Accuracies on the order of 1% are obtainable. An application of DIE to the Karl Fischer method for water has been described.[54] It is particularly useful in this case because the heat of reaction, −16.1 kcal per mole of water, is appreciable.

No applications of cryoscopic titration methods to nonaqueous oxidation-reduction reactions have appeared, though they have been used for titrations of bases in benzene. This technique, along with optical and enthalpimetric methods, has the advantage of being applicable to work in solvents of low dielectric constant, where electrochemical methods are frequently difficult to use.

Photometric end-point detection is also useful, especially for reactions that have moderate to low equilibrium constants. Data taken well before and after the equivalence point are extrapolated to give an end point that is typically precise to within a percent or so. With continuous flow titration systems the time and effort required are no greater than with conventional potentiometric end-point detection methods.

IV. OXIDATION-REDUCTION REACTIONS IN SOME SELECTED SOLVENTS

A. Acetic Acid

Acetic acid is not a typical solvent for analytical electron-transfer reactions in that it has a low

TABLE 4

Analytical Oxidation-Reduction Titrations in Acetic Acid

Reagent	Compounds Titrated	Method of Equivalence-Point Detection[a]	Remarks	Ref.
$Pb(OAc)_4$	Vicinal *cis*-diols	Pot.	Pb-Pt electrode pair.	70
	Hydroquinone, tetrachlorohydroquinone, benzylmercaptan, pyrocatechol, mandelic acid, ascorbic acid	Pot.	Last two slow.	71
	Hydrazine and substituted hydrazines, ascorbic acid	Pot.	Samples dissolved in buffered aqueous solution	72
	Ascorbic acid, 2-naphthol, hydroquinone	Visual indicator	N,N'-bis-4-(methoxyphenylamino)phenylthiourea as indicator; yellow to violet color change	73
	Cr(II), Sn(II), Fe(II), Ti(III), Sb(III), As(III)	Pot.	Samples dissolved in aqueous mineral acids	74
	SO_3^{2-}, SCN^-, Fe(II), $AsCl_3$	Pot. and Amp.	NaAc or $HClO_4$ required; SCN^- oxidized to SO_4^{2-} CN^-; $AsCl_3$ gives two breaks, As(III) → As(V) and $Cl^- \rightarrow Cl_2$	75
	Thioglycolic acid, mercaptans.	Pot.	Water generally present	76
	Tartaric acid	Pot.	80% HAc–20% H_2O solvent, back-titration of excess $PbAc_4$ with std. hydroquinone	77
	α-Hydroxy acids, mannitol	Pot.		78
$(NH_4)_2Ce(NO_3)_6$	Fe(II)	Biamp. and Pot.	In 0.6 *M* $HClO_4$	79
	$H_2C_2O_4$	Biamp.	In 1 *M* $HClO_4$	80
	α-Hydroxy and α-keto carboxylic acids	Biamp.	In 1 *M* $HClO_4$; oxidation rates vary widely	81
$(NH_4)_2Ce(NO_3)_6$	Thiourea	Pot.	Ce(IV) dissolved in tri-n-butylphosphate: CCl_4 (1:4), thiourea in HAc; added excess Ce(IV) back-titrated with hydroquinone.	83
Br_2	Fe(III), Tl(I), Sb(III), As(III), Hg(I), SeO_2, Ti(III), hydroquinone, resorcinol, catechol, tetrachlorohydroquinone	Pot.	Most reactions require NaOAc; As(III) oxidized at 50° C; SeO_2 slow; resorcinol and catechol involve bromination; hydroquinone bromination and oxidation.	82
	SCN^-, SO_3^{2-}, Fe(II), As(III), Sb(III)		NaOAc required in most cases.	84

TABLE 4 (Continued)

Analytical Oxidation-Reduction Titrations in Acetic Acid

Reagent	Compounds Titrated	Method of Equivalence-Point Detection[a]	Remarks	Ref.
	Aniline, dimethylaniline, ascorbic acid, hydroquinone, antipyrine, benzylmercaptan			71
	Ascorbic acid, hydroquinone, 2-naphthol	Visual indicator	N,N'-bis-4(4-methoxyphenylamino)phenylthiourea as indicator; yellow to violet color change.	73
	Phenols	Constant current pot.	Pyridine added as catalyst.	85
	Unsaturated organic compounds	Polarog.-pot.	Chloranil reference electrode.	86
	Phenol, α-naphthol, pyrocatechol, naphthalene, thymol, oleic acid, cholesterol, limonene, determination of iodine value of fixed and volatile oils	Pot.	Platinum-calomel electrodes.	87
	Sulfa drugs	Pot.	NaOAc added; platinum-calomel electrodes	88
	Resorcinol, thymol, salicylic acid, certain anaesthetics and alkaloids	Visual	Excess standard Br_2 back-titrated iodometrically.	89
	Guaiacol, potassium guaiacolsulfonate, phenacetin, phenazone		Water added in some cases	90
	Thymol, procaine HCl			91
	Phenols with free *o*- or *p*-positions		Pyridine added as catalyst	92
	Various drugs			93
	Olefins	Spectrophotometric	Solvent-85% HAc, 10% H_2O, 5% CCl_4	94
Co(III)	Various metal salts		Metals in aqueous HCl; Co(III) in HAc	95
	Fe(II), As(III)	Pot.		96
H_2O_2	Organic sulfides	Pot.	Sulfides oxidized to sulfoxides with H_2O_2, sulfoxide titrated with $HClO_4$ in acetic anhydride	97
$NaMnO_4$	Fe(II), Ti(III), resorcinol, hydroquinone	Pot.		82

TABLE 4 (Continued)

Analytical Oxidation-Reduction Titrations in Acetic Acid

Reagent	Compounds Titrated	Method of Equivalence-Point Detection[a]	Remarks	Ref.
CrO_3	Sb(III), Ti(III), Fe(II), Hg(I), hydroquinone, resorcinol, diphenylamine, *p*-aminophenol, metol	Pot.	H_2SO_4 required for Fe(II), Sb(III), and *p*-aminophenol oxidation; metol slow.	82
ICl	SO_3^{2-}, Hg(I), Fe(II), Sb(III), As(III)	Pot. and biamp.	NaOAc required in all cases but Hg(I); SO_3^{2-} and Fe(II) show two breaks, first to I_3^-, then to I_2; others show only one.	98
ICl	Hydroquinone, oleic acid, resorcinol	Pot.	Titrant stable only two to three days; NaOAc required.	71
ICl_3	SO_3^{2-}, Hg(I), Fe(II), Sb(III), As(III)	Pot.		99
tert-Butyl hypochorite	I^-, $C_2O_4^{2-}$, styrene	Pot. and biamp.	Titrant slowly decomposed by H_2O and light; styrene oxidation required presence of LiCl.	100
Dichloramine-T	I^-, Fe(II), Sn(II), ascorbic acid, thioglycolic acid			101
ClO_2	I^-, hydroquinone	Pot.	I^- determinable in the presence of Br^- and Cl^-; $I^- \rightarrow I_2$	102 103
$CrCl_2$	Fe(III)	Pot.	Titrant unstable	82
$Fe(ClO_4)_2$	CrO_3, $NaMnO_4$	Biamp.	Potentials unstable	104
	U(III)	Pot.	Excess Fe(II) backtitrated with $Pb(OAc)_4$	105
$TiCl_3$	Fe(III), quinone, tetrachloroquinone	Pot.		82
Ascorbic acid	Br_2, Au(III), Hg(II)	Pot.		106
Hydroquin-one	ClO_2	Pot.		103
$Na_2S_2O_4$	Br_2, CrO_3, $KMnO_4$, ICl, BrO_3 , IO_3^-, chloramine-T	Pot.		107
$VOAc_2$	CrO_3, BrO_3 , $KMnO_4$, $PbAc_4$			107
o-Hydroquinone	Br_2, $PbAc_4$, ICl	Pot.		107

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[a] Pot. = potentiometric; Amp. = amperometric; Biamp. = biamperometric (amperometry with two polarized indicator electrodes).

dielectric constant. It is also difficult to purify rigorously and is not convenient to handle. Despite these disadvantages, however, it has been more widely used as an analytical medium than any other solvent, probably because of its ready availability at low cost and its history of analytical use as a solvent for acid-base titrations. The most common oxidation-reduction titrants are ammonium hexanitratocerate and lead tetraacetate, although a variety of oxidants and reductants have been reported for a limited number of systems. Some of the reagents proposed are listed in Table 4.

Lead tetraacetate was first used as an oxidant by Dimroth in 1920 for the conversion of quinizarine to quinizarine quinone. It is a powerful oxidant, the formal reduction potential being about 1.6 V in perchloric acid.[55] The pure salt is indefinitely stable in a cold, dark, water-free environment, but readily turns brown through formation of lead dioxide when exposed to traces of moisture. A saturated solution in anhydrous acetic acid is 0.072 *M*, and is reported to be stable in the dark.

Many oxidations by lead tetraacetate are slow, as might be expected for an essentially undissociated compound in a low-dielectric-constant solvent. Drifting potentials near equivalence points are common. Rates of oxidation are increased by the presence of an acid or base such as water, acetate ion, or perchloric acid. The analytical utility of this reagent has been studied by Tomiček and by Berka and their co-workers, the latter especially in acetic acid-water mixtures where rates are appreciably faster. The kinds of substances that have been determined are summarized in Table 4.

The mechanism of oxidation by lead(IV) has been studied for a variety of organic and inorganic systems. With cerium(III) the mechanism proposed is

$$\mathrm{Pb(IV)} + \mathrm{Ce(III)} \xrightarrow{\text{slow}} \mathrm{Pb(III)} + \mathrm{Ce(IV)}$$

$$\mathrm{Pb(III)} + \mathrm{Ce(III)} \overset{\text{fast}}{\rightleftharpoons} \mathrm{Pb(II)} + \mathrm{Ce(IV)}$$

The first step is rate-determining, and the second is rapid and reversible.[56] Oxidation of cobalt(II) to cobalt(III) is considerably more complex, and a complicated mechanism involving a dimeric cobalt(II) species is necessary to explain the rate data.[57]

The oxidations of inorganic compounds by lead tetraacetate in acetic acid are likely to be true electron-transfer processes, but the reactions with organic compounds often may not be. In some cases, as in the reaction with *p*-methoxytoluene, oxidation seems to take place by acetoxy radicals, leading to products that are different from those formed on oxidation by known electron-acceptor reagents such as manganese(III) acetate under the same conditions.[58] Several ionic and radical mechanisms for organic oxidations by lead(IV) are considered possible by Criegee;[59] which occurs depends on the substrate present. For hydroquinones direct electron transfer is feasible, but for mercaptans the reaction is postulated to be:[60]

$$\mathrm{R-SH} + \mathrm{Pb(OAc)_4} \longrightarrow \mathrm{R-S-Pb(OAc)_3} + \mathrm{HOAc}$$

$$\mathrm{R-S-Pb(OAc)_3} \longrightarrow \mathrm{R-S^+} + \mathrm{Pb(OAc)_2} + \mathrm{OAc^-}$$

$$\mathrm{R-S^+} + \mathrm{RSH} \longrightarrow \mathrm{R-S-S-R} + \mathrm{H^+}$$

The reaction is quantitative and may be used as the basis of an analytical method.

Cerium(IV) is a strong oxidant in glacial acetic acid, just as it is in aqueous acids and in acetonitrile, but again its reactions tend to be slow. A variety of non-quantitative organic oxidations has been studied[61] but only a few have analytical use (Table 4).

The oxidation of oxalic acid by cerium(IV) in anhydrous acetic acid was at one time thought to proceed via a mechanism that involved solvent participation because carbon dioxide produced in the reaction was found by carbon-14 tracer experiments to come from the solvent and not from the oxalic acid.[62] However, a repetition of the original experiment has shown that oxidation of acetic acid by cerium(IV) can account for carbon-14 activity present in the carbon dioxide.[63] This possibility was suggested by the original workers to explain the slow decrease in concentration of cerium(IV) solutions in acetic acid with time; the rate of acetic acid oxidation can be increased by photochemical or thermal means.

Some reactions of bromine in acetic acid with organic compounds are clearly oxidation processes. Others involve bromination of aryl or olefinic functions, and still others, such as that with hydroquinone, involve both oxidation and bromination. Bromination is favored under anhydrous conditions, but if either water or sodium acetate is present oxidation often occurs as well.[65] Bromination has been carried out both by coulometric generation of bromine from bromide and by titration with solutions of bromine or tribromide in glacial acetic acid. In the presence of excess bromide, solutions of bromine in acetic acid are relatively stable, the concentration decrease averaging about 0.2% a day. A variety of olefins can be titrated directly in 85% acetic acid-10% water-5% carbon tetrachloride.[66] Water is added to increase the rate of reaction of bromine; carbon tetrachloride is used to dissolve the olefins prior to titration. A spectrophotometric end-point method is convenient, the absorbance of excess bromine being followed at 400 nm.

An interesting analytical determination of sulfides involves an initial oxidation to the corresponding sulfoxide by hydrogen peroxide in acetic acid.[67] The sulfoxide is then titrated with perchloric acid in acetic anhydride. Oxidation times vary with the organic sulfide, but 15 to 60 minutes is typical.

Mercaptans have also been titrated in glacial acetic acid with lead(IV) acetate.[68] Thioglycolic acid, alkyl mercaptans, and benzylmercaptan can be determined with accuracies on the order of 1% or better. Conditions for quantitative oxidation vary with the compound being oxidized. Thiosemicarbazide requires the presence of 15% perchloric acid in the reaction mixture and back-titration of excess lead(IV) with hydroquinone. Reactions with cysteine and thiourea are too slow to be analytically useful.

Si-H groups in organosilicon compounds can be coulometrically determined by reaction of the hydrogen with chlorine or bromine generated at a platinum anode in acetic acid.[69] The reaction is

$$\mathrm{Si-H + Br_2 \longrightarrow Si-Br + HBr}$$

End-points can be obtained amperometrically to within about 5% of the correct value.

B. Acetonitrile

Acetonitrile has been the aprotic organic solvent most studied from an electrochemical point of view. Reasons for its popularity include a convenient liquid range, ready availability as a by-product of acrylonitrile synthesis, wide electrochemical range, moderate dielectric constant, and low toxicity. It has the disadvantages of being difficult to purify and of tending to polymerize in the presence of acids or bases, but, on the whole, it is one of the most useful solvents available at the present time. Some of its physical properties are listed in Table 1. It is miscible with water and many organic solvents, including most organic acids, aldehydes, esters, ethers, and chlorinated hydrocarbons. It is a powerful solvent for a wide range of organic compounds and a number of inorganic salts, though it solvates anions of low polarizability relatively poorly, with the result that many ionic metal chlorides, for example, are only slightly soluble. On the other hand, salts with highly polarizable anions such as iodide and thiocyanate, and predominantly covalent chlorides such as $ZnCl_2$, typically are quite soluble.

The numerous reviews of acetonitrile as a medium for electrochemical reactions include one by Gedansky and Pribadi[108] surveying electrochemical cell potentials and polarographic data, and those of Danyluk[109] and Charlot and Tremillon[110] covering general solvent and acid-base properties in addition to electrochemistry.

Acetonitrile is not toxic, but it should be handled with the reasonable care accorded all relatively volatile organic compounds. Adequate ventilation should be provided to minimize prolonged inhalation of the vapors, and extensive contact with the skin should be avoided.

The purification of acetonitrile is difficult and time-consuming. Among the impurities present in the commercial material are acetic acid, ammonia, acrylonitrile, ammonium acetate, acetamide, hydrogen cyanide, and water. A variety of purification methods has been proposed and is reviewed by Coetzee.[111] The choice of methods depends upon the particular application since a procedure recommended for removal of one contaminant may introduce another. Thus, unsaturated nitriles such as acrylonitrile can be removed by refluxing with potassium hydroxide, but the operation introduces traces of ammonia. The best procedure for electrochemical use of the solvent is probably that in which treatment with calcium hydride followed by distillation from phosphorus pentoxide is carried out twice, the second distillation being done very slowly to minimize the acrylonitrile content.[112] For ultraviolet spectroscopy and conductance work the most satisfactory procedure appears to be that of O'Donnell, Ayres, and Mann,[113] modified by adding a small amount of calcium hydride to the final distillation flask after a forecut has been taken[114] to remove most of the water.

For routine work the aqueous SCE is probably the most convenient reference electrode if liquid-junction potentials are not important, and if the possibility of water contamination of the acetonitrile solution is not critical. The best reference electrode in acetonitrile for precision measurements is the silver–0.01 *M* silver nitrate electrode in acetonitrile, which was shown in 1928 to have Nernstian response,[115] and was first suggested as a reference by Pleskov in 1948.[116] The stability and reversibility of this electrode have recently been confirmed.[30] Its only drawback appears to be a tendency to polarize when currents of any magnitude are passed through it; in these cases either higher concentrations of silver nitrate can be used or a three-electrode system can be employed.

The available potential range in acetonitrile extends from about +2.2 V to −3.1 V versus the silver–0.01 *M* silver nitrate reference couple.[117] Both measurements were made at a polished platinum electrode in 0.1 *M* alkali metal or tetrabutylammonium perchlorate solutions. Within this wide potential range the number of metal ions and organic compounds that can be electrolyzed is extensive. The reviews mentioned above in conjunction with the comprehensive list of references included in the review on reference electrodes by Butler cover the field exhaustively. The electrochemical reactions discussed here will be those that either have been proposed as analytical methods or show promise of development into quantitative procedures.

1. Electrochemical Systems in Acetonitrile

In a number of cases polarography in acetonitrile may be used analytically. Europium, samarium, and ytterbium are reported to be determinable in mixtures of the lanthanides by polarography in acetonitrile.[118] In each case two waves are observed corresponding to reduction from the three to two and two to zero oxidation states; the first wave is used for the analytical measurement. The tris-bipyridine complex of nickel(II) is reported to give two waves also, both of which are diffusion-controlled.[119] The first wave corresponds to a two-electron reduction to a neutral species, and the second to a subsequent one-electron reduction to a univalent anion. Bipyridine is lost readily from the neutral and anionic forms, so analytical measurements would presumably have to be made in solutions containing an excess of bipyridine. Anionic complexes of other transition metals with bipyridine have been prepared by the same workers so that the method may be applicable to the analysis of other metals as well.

The electrochemistry of the halide ions has been studied extensively in acetonitrile. Iodide is reversibly oxidized in two steps, first to triiodide and then to iodine at −0.25 and +0.40 V. Cyclic voltammetry[120] at platinum electrodes indicates that oxidation to triiodide is a third-order electrode reaction corresponding to

$$3\ I^- \rightleftarrows I_3^- + 2\ e^-$$

and that oxidation of triiodide to iodine proceeds according to the equations

$$I_3^- \rightleftarrows I_3 + e^-$$

$$2\ I_3 \rightleftarrows 3\ I_2$$

Neither the oxidation of iodide nor that of triiodide is completely reversible, apparently because of adsorption of reaction products in the triiodide case. Cathodic scans on cyclic voltammograms of iodide also do not appear to be reversible, possibly due to regeneration of iodide ion through a chemical reaction, or to interaction between iodide and an adsorbed substance that inhibits the electrode reaction. Iodine is further oxidized electrochemically at graphite electrodes to iodine(I).[121] Bromide and chloride are also oxidized in two steps at platinum.[122] In each case the anodic waves correspond to oxidation first to X_3^- and then to X_2.

Thiocyanate is oxidized to thiocyanogen in acetonitrile either electrochemically or by homogeneous oxidation with iron(III) perchlorate.[123, 124] Thiocyanogen, $(SCN)_2$, is stable in acetonitrile solutions for several hours but cannot be isolated readily as it polymerizes rapidly at room temperature to $(SCN)_x$ when the solvent is removed. The corresponding selenocyanate is oxidized to $(SeCN)_2$, which does not polymerize but disproportionates to selenium metal and $Se(CN)_2$.[125] The voltammetric half-wave potentials are +0.32 V for thiocyanate and +0.06 V for selenocyanate versus the silver reference electrode.

The stability of acetonitrile to oxidation can be used to good advantage in investigations of substances such as aromatic hydrocarbons. Qualitative and rough quantitative (±5 to 20%) information can be obtained on the composition of hydrocarbon mixtures and on the nature and amount of undesirable impurities such as sludging components in oils by electrochemical oxidation in acetonitrile.[126]

Dimethyl sulfide is quantitatively oxidized to dimethyl sulfone by electrolysis at 1.2 V versus the silver reference if about 1% water is present in the acetonitrile solutions.[127] In anhydrous acetonitrile the reaction products are sodium methylsulfonate and carbon monoxide. When a perchlorate is present as the supporting electrolyte, the perchlorate anion appears to be a significant source of oxygen because chlorine in several oxidation states was detected in the reaction mixture. Similar reactions carried out using tetrafluoborate in place of perchlorate yielded no methanesulfonate product. The mechanism of the anhydrous oxidation is suggested to involve a one-electron oxidation yielding a cation radical that rapidly loses a proton and an electron to form a resonance stabilized sulfonium ion,

$$CH_3\overset{+}{S}{=\!=}CH_2 \rightleftarrows CH_3SCH_2^{\ +}$$

This ion then reacts with more dimethyl sulfide to give primarily $CH_3SCH_2S(CH_3)_2$, which slowly hydrolyses on standing to give CH_3SCH_3, CH_3SCH_2OH, and the corresponding protonated analogs. CH_3SCH_2OH then decomposes to HCHO and CH_3SH, the former being oxidized by air to formic acid and thereby to water and carbon monoxide, and the latter to methanesulfonic acid.

The oxidation of hydroquinone in acetonitrile is of interest because it is considered a classic case of an organic compound which can undergo reversible electron-transfer, and because it has been used to illustrate the effectiveness of various oxidizing reagents in this solvent. It was shown that the presence of a hydrogen-ion acceptor is necessary before copper(II), for example, will oxidize hydroquinone.[128] As a result the mechanism for oxidation may be quite complex when a proton acceptor is not available in sufficient concentration in the solution, and reversibility is not observed in pure acetonitrile.[129,130]

Phenothiazine, derivatives of which are powerful tranquilizing and antihistaminic drugs, is oxidized in two one-electron steps at 0.27 V and 0.78 V in 0.1 *M* perchloric acid at a platinum electrode in acetonitrile, the first oxidation product being a free radical.[131] A coulometric method has been suggested for the determination of phenothiazine by generation at constant current of the two-electron oxidation product, which then oxidizes unreacted phenothiazine to the point where all the material is converted to the intermediate free radical species.[132] With this procedure it is necessary to use a low current density to avoid undesirable side reactions, especially in the region of the equivalence point where the concentration of sample is low. Accuracies on the order of 1% were obtained for samples containing 2.4 mg of phenothiazine or more, and 2 to 3% for samples on the order of 0.24 mg.

Several other coulometric studies have been done in acetonitrile. Anthracene is oxidized quantitatively to bianthrone by controlled-potential coulometry.[133] Only two electrons are involved in the electrode process, although three are required per mole of anthracene for bianthrone formation. The electrode product is apparently 9-anthranol, which converts to the keto configuration and is oxidized to the final product. Although the reaction was not studied as an analytical method, there appears to be no reason why it could not be developed into a general procedure for anthracene-related compounds, for a large number of which polarographic half-wave potential data are available.[134]

Diphenylpicrylhydrazyl, one of the more stable free radicals, is both reduced and oxidized reversibly in one-electron steps in acetonitrile, and its concentration in solution can be determined readily by controlled-potential coulometry or voltammetry.[135] The potentials are relatively close together ($E_{1/2} = -0.12$ and $+0.39$ V versus a silver–0.01 *M* silver nitrate reference electrode in 0.1 *M* $NaClO_4$), so the range of electrochemical stability of the radical is limited.

Copper, lithium, and sodium can be determined at the micro level by controlled-potential coulometry in acetonitrile.[136] Copper is reduced only to the stable copper(I) species at the potential recommended, while lithium and sodium are reduced to the metals and deposited as amalgams in the mercury cathode. Analyses down to two microequivalents of each alone could be made at the 1% error level.

The standard potential of the gold(I) - (0)

couple in acetonitrile is about 1.05 V versus the silver reference electrode and gold(I) has been suggested by Goolsby and Sawyer as a possible coulometric titrant.[137] It is too unstable to use as a conventional titrant; a solution of gold(I) perchlorate, generated by oxidation of a gold electrode in tetraethylammonium perchlorate solution, has an initial decomposition rate of about 0.37% per hour. The reduction potential of the gold couple can be lowered by the addition of complexing agents such as the halides or pseudohalides if desired to allow selective oxidations. The gold metal formed in the analytical reactions could be easily recovered by filtration.

Hydrogen-ion generation from water by constant-current coulometry provides a method for the determination of weak bases in acetonitrile. Aliphatic amines and heterocyclic amines have been titrated in this way with an error of less than 2%.[138] About 0.3% water yields 100% current efficiency at a platinum electrode; this water level is conveniently provided by use of 0.05 *M* lithium perchlorate trihydrate in the acetonitrile. The method cannot be used with aromatic amines because oxygen produced at the platinum anode during current generation oxidizes the amines to nontitrable products. The addition of hydroquinone prevents this interference by reaction with electrogenerated oxygen.[139]

2. *Homogeneous Reactions in Acetonitrile*

Most analytical oxidation-reduction titrations in acetonitrile have to the present time involved oxidizing agents as titrants; of these copper(II) and cerium(IV) have been most studied. The reduction potential of the copper(II) - (I) couple is considerably higher in acetonitrile than in water because of increased stabilization of copper(I) by the solvent. An accurate thermodynamic potential for the couple has not been determined because of uncertainty in the extent of ion-association of copper(II) with perchlorate, but it is estimated to be about 0.81 V versus the silver electrode.[140] The formal potential for the couple is reported to be 0.65 V,[141] but this value, for which the ionic strength and water concentration were not specified, is probably too low by about 0.1 V. The presence of water appreciably decreases the potential of the couple. A decrease of 0.6 V is seen when 68% of the solvent is water, though the system remains reversible even at this high level.[142] Most anions also decrease the formal potential through preferential coordination of copper(II) over copper(I).

The potential of the copper(I) - (0) couple, −0.450 V, is considerably lower than that of the (II) - (I) system.[47] Again, the low value reflects the stability of the copper(I) -acetonitrile complex. Solutions of copper(II) perchlorate are stable for months in acetonitrile, and end-points in titrations are readily determined potentiometrically. Many of the compounds oxidized by copper(II) form colored reaction products, but for those that do not the osmium analogs of the ferroin indicators provide satisfactory visual end-points. Tris(5-methyl-1,10-phenanthroline)osmium(II) perchlorate is the best for titrations of thiourea and hydroquinone.[52] Solutions of copper(II) in acetonitrile can be standardized conveniently against ferrocene. A list of substances that have been titrated with this reagent is given in Table 5.

Ammonium hexanitratocerate, $(NH_4)_2Ce(NO_3)_6$, has a formal reduction potential of 0.755 V versus the silver reference electrode[143] and so is also a convenient analytical oxidant. Solutions of it in acetonitrile are relatively stable; no decrease in titer was observed over several days.[144] Some applications to analysis are shown in Table 6.

Oxidations by cerium(IV) are often slow in pure acetonitrile, but rates are generally increased if some acetic acid is added. This is caused by acetate-ion catalysis rather than by solvent effects because the addition of sodium acetate has the same rate-enhancing effect.[145] Acetate may replace nitrate in the first coordination sphere of cerium(IV) to yield a species capable of more rapid reaction, but other explanations may be possible. For example, nitrate has been proposed as the actual oxidant in the oxidation of cycloheptatriene to benzaldehyde, benzene, and carbon monoxide by cerium(IV) nitrate.[146] The reduction product of nitrate is then reoxidized by cerium(IV).

The iron(III) - (II) couple has a higher potential than the copper system, but the susceptibility of iron(III) to hydrolysis makes solutions of iron(III) unstable. The formal potential of the couple was estimated, by coulometric oxidation of half of the iron in a 4×10^{-3} *M* solution of iron(II) perchlorate in dry acetonitrile, to be 1.57 V versus the silver reference electrode.[147] This value may be somewhat high because another measurement in which the iron(III) and (II) ions were coulometrically generated from pure iron metal yielded a value of 1.18 V versus the silver – 0.01 *M* silver perchlorate reference couple.[148] The latter work also reported the anhydrous couple to be reversible. In a solution containing several moles of water per mole of iron(III) the potential is about 1.1 V versus the silver reference electrode, which is still 0.3 V greater than that of the copper(II) - (I) couple. All the compounds oxidized by copper(II) in acetonitrile are also oxidized by iron(III), as well as a number more. For example, thiocyanate is oxidized to thiocyanogen, $(SCN)_2$, tetrachlorohydroquinone to the corresponding quinone, and phenothiazine in two one-electron steps to a free radical and then the phenothiazonium cation.

Iron(III), in common with most other transition metals, coordinates readily with the halides, and anhydrous iron(III) chloride is easily prepared. The stability of the complex works against its effectiveness as an oxidant, however, and not only is the reduction potential lowered significantly but also the stability of solutions of iron(III) chloride in acetonitrile is poor because of hydrolysis and solvent attack. One third of the iron(III) is slowly reduced to iron(II) by acetonitrile to give the complex $[Fe(II)(CH_3CN)_6]$ $[FeCl_4]_2$.[125,149]

Added evidence for the stability of the Fe(II) $[FeCl_4]_2$ salt in acetonitrile is that it is formed when iron metal reacts with chloride in acetonitrile,[150] and that in titrations of readily oxidized materials with solutions of iron(III) chloride in acetonitrile only one third of the iron(III) initially

TABLE 5

Analytical Oxidations with Copper(II) in Acetonitrile

Substance Oxidized	Oxidation Product	Remarks	Ref.
Iodide	Iodine	Oxidized in two steps, first to triiodide, then to iodine.	155
Hydroquinone	Benzoquinone	Water necessary as base to accept protons produced in oxidation.	155
Thiourea	Diformamidine disulfide	One electron oxidation.	155, 156
N, N′-disubstituted thioureas	Corresponding disulfides	One electron oxidation in each case.	157
Potassium ethyl xanthate	Dixanthogen	One electron oxidation in two steps.	158
Diphenylbenzidine (DPB), tetramethylbenzidine (TMB)	DPB Violet, TMB Orange	Two electron oxidations in two steps in each case.	159
Phenothiazine drugs	Free radical	Photometric end point; some oxidation past one-electron free radical stage	160
Ferrocene derivatives	Ferricinium ion	One-electron oxidation	161

present acts as an oxidant.[151] A number of other metal chlorides are also reduced by acetonitrile, among them VCl_4, $CoCl_3$, $MoCl_5$, WCl_6, WCl_5, and $ReCl_5$. The natures of the oxidation products have not been determined. In all of these cases the metals are reduced completely to a lower oxidation state rather than partially, as is the case with iron(III). From a study of the rate of oxidation of the bipyridyl complex of cobalt(II) by copper(II) and iron(III) perchlorate in anhydrous acetonitrile[152] it appears that the reactions are fast enough to be analytically useful. The reaction of cobalt(II) with iron(III) has also been studied in the presence of excess bipyridine, and the rate was found to be inversely related to the bipyridine concentration. The rate decrease was not great, however, and the results suggest that it may be possible to determine cobalt by the addition of excess bipyridine and titration with copper(II), which is more stable and more convenient than iron(III).

Copper(I) in acetonitrile has been suggested as a reducing titrant in acetonitrile-acetic acid mixtures.[153] The substances determined – chromium(VI), vanadium(V), cerium(IV), manganese(VII), manganese(III), and hexacyanoferrate(III) – were dissolved, however, in aqueous sulfuric acid to yield a reaction medium containing water, acetonitrile, sulfuric acid, and acetic acid. The first four ions listed could be determined in the presence of iron(III). Both potentiometric and visual indicator end-point detection was used.

An interesting analytical method in acetonitrile, though not an oxidation-reduction reaction in the strict sense of the term, is the direct titration of aliphatic amines with cinnamic anhydride.[154] The

TABLE 6

Analytical Oxidations with Ammonium Hexanitratocerate in Acetonitrile

Substance Oxidized	Oxidation Product	Remarks	Ref.
Potassium ethyl xanthate	Dixanthogen	Accuracy of 1% at millimolar level; yellow cerium(IV) color used as endpoint.	144
Iodide Hydroquinone	Iodine Benzoquinone	Acetic acid present; potentiometric endpoint detection.	162
Ascorbic acid	Threonic and oxalic acid (postulated)	Four moles cerium(IV) used per mole of ascorbic acid; reaction conditions as for iodide.	163
Oxalic acid	Carbon dioxide	Acetic acid present; backtitration of excess cerium(IV) with hydroquinone; diphenylamine used as indicator.	164
Iron(II)	Iron(III)	Acetic acid present; N_2 atmosphere needed to prevent air oxidation of iron(II); potentiometric end point detection.	165

end point is determined photometrically by following the absorbance of unreacted cinnamic anhydride at 320 nm. Reactions are rather slow with many amines, but the method is sensitive and differences in rates of reaction can be used in some instances to provide a degree of selectively. The method could probably be adapted to differential kinetic analysis of mixtures.

C. Dimethylformamide

Dimethylformamide is a solvent for which only scattered applications as an analytical redox solvent have been reported but which has considerable promise. It has a dielectric constant close to that of acetonitrile, nitromethane, and dimethylacetamide; it dissolves many organic and inorganic compounds; it has a wide liquid range; it is stable thermally; it is readily available; and it has low toxicity upon inhalation or on contact with the skin. Table 2 lists some of its properties. It decomposes slowly upon exposure to ultraviolet radiation to dimethylamine and formaldehyde; if water is present hydrolysis is slight, but the reaction is catalyzed by acids, bases, and the hydrolysis products dimethylamine and formic acid.[166] Comprehensive reviews of the chemical properties and reactions of dimethylformamide,[167] and of its electrochemical solvent behavior,[168] are available.

The useful electrochemical range of dimethylformamide in the cathodic region extends past −2.5 V versus the aqueous saturated calomel electrode, making it useful for a variety of studies. Susceptibility to oxidation limits its utility in the anodic direction, however. The calomel electrode is not stable in this solvent, and an aqueous saturated calomel electrode with a suitable bridge or a silver – silver ion electrode is the best choice for electrochemical work.

Purification of dimethylformamide for careful work is fairly straightforward (Table 3). Sometimes potassium hydroxide is added before the distillation to neutralize any formic acid present.[169] Traces of water do not seem to interfere seriously with many electrochemical reactions in dimethylformamide, so rigorous precautions to exclude it may not always be necessary.

1. Electrochemical Systems in Dimethylformamide

Lithium, sodium, and potassium ions give well-defined polarographic waves in dimethylformamide, but rubidium and cesium exhibit maxima at low concentrations. The half-wave potential for lithium is somewhat more negative than for the other alkali metal ions. It is probably that a number of the alkaline earth and first-row transition metals can be determined polarographically in dimethylformamide.

Among organic compounds, anthraquinone has been determined with an accuracy within 2 to 3% of theoretical in organic mixtures by polarography in dimethylformamide.[170] A variety of other organic compounds gives well-defined polarographic waves, including styrene and several disulfides.

Phenol, resorcinol, and similar hydroxy compounds can be determined quantitatively in dimethylformamide by measurement of the effect they have on the height of the polarographic wave of butyl acrylate.[171] The overall two-electron reduction of butyl acrylate is facilitated by protonation of the one-electron reduction product by the acidic phenol, and the resulting increase in wave height is directly proportional to the phenol concentration. Benzophenone can be used in place of butyl acrylate; in this case two waves are observed in dimethylformamide, the first increasing and the second decreasing in height as a proton donor is added to the solution.

Potassium can be determined by precipitation as the tetraphenylborate salt in water, filtration, then redissolution of the precipitate in dimethylformamide and polarographic determination of the potassium ion.[172] Wave heights are proportional to concentration over the range 2×10^{-4} to 7.5×10^{-3} *M*. The solutions must be deoxygenated prior to the measurement step.

Oxygen is reduced to the superoxide ion in dimethylformamide[173] at about −0.80 V versus the aqueous saturated calomel electrode. A second reduction wave, presumably corresponding to reduction to peroxide, is seen at about −2.8 V. The first wave can be used to measure the concentration of dissolved oxygen over the range of 0.34 to 2.83 millimolar.[174] The system follows Henry's law, so a calibration curve can be prepared from solutions equilibrated with known partial pressures of oxygen.

The biphenyl radical anion can be quantitatively generated at platinum from a dimethylformamide solution 0.1 *M* in biphenyl and 0.1 *M* in tetrabutylammonium bromide.[175] It has been used for coulometric titrations of anthracene, benzophenone, nitrobenzene, nitromethane, and azobenzene. The biphenyl monoanion has the advantages of being a strong reductant, of reacting rapidly with a wide range of organic compounds and, since it is intense blue in color, of acting as its own indicator for the estimation of end points. Its principal disadvantage is that it may undergo reactions other than simple reduction with some organic substrates; also, in some instances the reduced sample may enter into complicating side reactions such as dimerization or reaction with the solvent. Surprisingly, water reacts relatively slowly with the biphenyl monoanion and so does not interfere.

2. *Homogeneous Systems in Dimethylformamide*

The first paper systematically exploring the use of oxidation-reduction titrations in dimethylformamide was that of Hinton and Tomlinson in 1961,[176] who showed that bromine, iodine, antimony(V) chloride, copper(II) chloride, and iron(III) chloride could be titrated potentiometrically with titanium(III) chloride. Chromium(II) chloride quantitatively reduced all of these substances and also titanium(IV) and iodine monochloride. In some cases the color change of the solution could be used for visual estimation of the end-point. Accuracies on the order of 1% were obtained.

More recently Hladky and Vrestal have investigated the use of copper(II) as an oxidant in dimethylformamide. Iron(II), titanium(III), and chromium(II) were quantitatively oxidized with an accuracy of about five parts per thousand.[177] Formal reduction potentials versus the aqueous saturated calomel electrode for some of the couples in 0.05 M HCl in dimethylformamide were: copper(II)-(I), 0.71 V; iron(III) - (II), 0.40 V; titanium (IV) - (III), 0.00 V; and chromium(III) - (II), -0.51 V. Mercaptan groups are also oxidized smoothly by copper(II) in dimethylformamide. Among the compounds determinable are thiolactic acid, thioglycolic acid, pentachlorothiophenol, thiophenol, and *o*-thiocresol.[178]

Lead(IV) chloride also can be employed as an oxidizing titrant in dimethylformamide.[179] Copper(I), iron(II), titanium(III), and chromium(II) are directly oxidized, as are iodide, a number of mercaptans, and glutathione. Phenylhydrazine hydrochloride and 2,4-dinitrophenylhydrazine must be determined indirectly by addition of excess lead(IV) and back-titration with titanium(III) chloride.

3. *Other Amides*

Amides other than dimethylformamide have been less thoroughly investigated as media for oxidation-reduction reactions. The chapter mentioned earlier[167] includes properties and reactions of several in addition to dimethylformamide, and a review on electrochemistry in the amides is also available.[180] The amides in general are excellent solvents for both electrolytes and covalent compounds; in fact, it has been suggested that N-methylacetamide is a more universal solvent than is water.[181] A disadvantage to more widespread study of the amides is the difficulty encountered in obtaining highly pure material, as traces of acetic acid or acetates, for example, are very difficult to remove.

Lead tetraformamide, $PbFm_4$, and trilead octaformamide, Pb_3Fm_8, have been used as analytical oxidants for the determination of tin(II), arsenic(III), antimony(III), cerium(III), iron(II), and thiosulfate in formamide.[182] Iodine and potassium dichromate are also satisfactory titrants for the same determinations. Water and oxygen had to be excluded during the titrations.

D. Dimethylsulfoxide

Dimethylsulfoxide (DMSO) has received considerable attention as an electrochemical solvent and has some promise for homogeneous analytical oxidation-reductions. Its excellent solvent properties for organic compounds and ability to act as a mild oxidant in conjunction with a number of reagents have made it of interest recently in organic synthesis.[183] Several of its physical properties are given in Table 1. It is also a good solvent for many inorganic compounds, and has a potential range of over 4.0 V.[184, 185] A thorough review of its properties as an electrochemical solvent that includes solubilities of a number of salts has been written by Butler.[186]

DMSO, though not very toxic in itself, penetrates the skin with astonishing rapidity, readily carrying with it material on the skin or dissolved in the DMSO.[187] Therefore, careful handling of toxic substances in conjunction with this solvent is imperative. Also, a number of compounds, including IF_5 and AgF_2,[188] NaH,[189] and H_5IO_6 [190], are reported to react violently with DMSO under some conditions, and several DMSO solvates of metal perchlorate salts, including aluminum and iron(III), have been patented as high explosives.[191] Aryl and acyl halides and compounds such as benzenesulfonyl chloride, $SOCl_2$, $POCl_3$, and P_2O_5 may react with DMSO to produce formaldehyde, which can polymerize explosively.[192]

Commercial DMSO as received typically contains 0.01 to 0.02% water, along with some dimethyl sulfide. Other organic impurities are undoubtedly present at low levels but have not been identified. Water appears to be the only contaminant likely to interfere in routine analytical use of DMSO as an analytical solvent; the water concentration can be lowered to 200 parts per million or so by passage through a column of Linde 5A molecular sieves.[196] The best procedure for the preparation of highly pure material is probably that given in Table 3.

1. Electrochemical Systems in Dimethylsulfoxide

As reference electrodes the silver – silver(I) and thallium amalgam – thallium(I) chloride[193] couples are recommended for careful work, though a number of other systems have been studied.[186] For practical work involving potentiometric end-point detection in titrations or in polarographic analyses the aqueous SCE is convenient. The junction potential associated with use of the SCE is appreciable but probably fairly constant. The mercury – mercury(I) halide reference couples in DMSO are apparently unsatisfactory because of mercury(I) disproportion.

Numerous electrochemical studies have been done in DMSO, but there have been few redox measurements in the analytical sense. From a survey of polarographic half-wave potentials the most promising analytical reagent for homogeneous oxidations seems likely to be iodine, for the formal potential of the $I_2 - I^-$ couple is +0.70 V versus the aqueous SCE.[194, 195] The half-wave potential for the $I_3^- - I^-$ couple is +0.48 V, and so for practical purposes the oxidant would be triiodide ion after the first third of the titrant had been added. Substances that would be expected to be quantitatively oxidized include hydroquinone ($E_{1/2} = -0.4$ V) and tetrachlorohydroquinone ($E_{1/2} = +0.08$ V), and also uranium(IV), and iron(II) ($E_{1/2} = -0.73$ V).

Several metals can be determined quantitatively in DMSO at the dropping mercury electrode. The alkali metals are reduced cleanly, but except for lithium their half-wave potentials are too close together to permit analyses of mixtures.[196] Water can be determined,[197] as can a number of halogenated silanes such as $RSiCl_3$.[198] Several gases give diffusion currents that are proportional to their concentrations; these include oxygen,[197, 199] HCl, H_2S, CO_2, SO_2, and $POCl_3$.[200] Other quantitative studies of CO_2 reduction have been made at the dropping mercury electrode[201] and at gold and amalgamated platinum electrodes.[202] The amalgamated platinum electrode appeared to be more satisfactory than gold; with it errors of less than 2% were found over the range CO_2 concentrations from 1 to 30% by volume in the saturating gas. Aluminum can be determined in the range of 0.2 to 2.5 m*M* at the dropping mercury electrode in 90% DMSO-10% acetylacetone mixtures,[203] and beryllium has also been determined in the same solvent mixture.[204] Water concentrations of up to 3% can be tolerated in either case.

Other electrochemical reactions that, though not reported as analytical methods, could probably be used for analytical determinations include the oxidations of hydroxylamine, formate, and oxalate, and the electrodeposition of americium. Hydroxylamine is oxidized irreversibly by a diffusion-controlled two-electron process at +0.5 V versus an aqueous SCE in DMSO.[205] The overall reaction is

$$2\ NH_2OH + 4\ OH^- \rightarrow 4\ e^- + N_2O + 5\ H_2O$$

If excess hydroxide ion is present, N_2 is also produced. Controlled-potential coulometry indicated a 1.99 ±0.04-electron oxidation at platinum for solutions containing neutralized $(NH_3OH)_2SO_4$.

Formate is oxidized to carbon dioxide and hydrogen ion at gold electrodes in DMSO.[206] Coulometric analysis shows that the overall reaction yields one half mole of carbon dioxide and one half mole of formic acid per mole of formate. On the basis of reverse chronopotentiometric and cyclic voltammetric experiments the mechanism proposed is

$$HCOO^- \rightarrow \cdot HCOO_{ad} + e^-$$

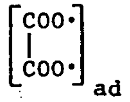
$$\cdot HCOO_{ad} \xrightarrow[\text{step}]{\text{slow}} CO_2 + \cdot H_{ad}$$

$$\cdot H_{ad} \rightarrow H^+ + e^-$$

$$\cdot HCOO_{ad} \rightarrow CO_2 + H^+ + e^-$$

$$H^+ + HCOO^- \rightleftarrows HCOOH$$

Oxalate is also oxidized under similar conditions to carbon dioxide.[207] The proposed mechanism involves a two-electron oxidation to a radical adsorbed on the electrode surface



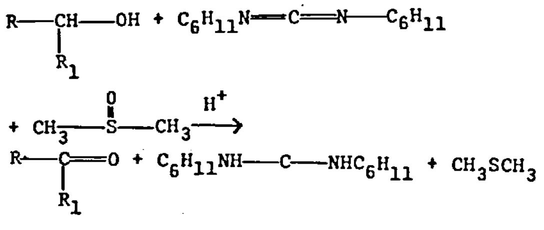
$$\left[\begin{array}{c}\mathrm{COO\cdot}\\ | \\ \mathrm{COO\cdot}\end{array}\right]_{ad}$$

which then decomposes to two molecules of carbon dioxide.

Americium is electrodeposited quantitatively from DMSO.[208] Up to 10% by volume of water in the DMSO does not interfere, nor do mineral acids such as HNO_3 or HCl up to 0.01 *M* or carboxylic acids such as oxalic acid up to 0.1 *M*. Sexivalent americium could be deposited selectively from fluoride-containing solutions in the presence of trivalent curium, apparently because of the greater stability of the curium complex with fluoride. In the absence of fluoride all metal cations are deposited to some extent, even lithium and sodium. By selection of appropriate conditions it may be possible from this solvent to do a number of analytical separations by electrodeposition.

2. *Homogeneous Reactions in Dimethylsulfoxide*

Some interesting homogeneous oxidations have been reported in DMSO. The solvent itself is more susceptible to oxidation than the electrochemical range might indicate; in fact, a proposed method for its determination is by oxidation in dilute aqueous solution with excess standard dichromate in sulfuric acid, the excess being titrated with standard iron(II) sulfate.[209] Oxidation is complete in less than a minute if the sulfuric acid concentration is 8 *M* or higher. On the other hand, DMSO itself will take part in many oxidations. Thus, in conjunction with carbodiimides it functions as an oxidant for a range of organic hydroxyl compounds.[210] The general reaction is



$$\underset{\displaystyle R_1}{R{-}\underset{|}{C}H{-}OH} + C_6H_{11}N{=}C{=}N{-}C_6H_{11} + CH_3{-}\overset{\displaystyle O}{\overset{\|}{S}}{-}CH_3 \xrightarrow{H^+} \underset{\displaystyle R_1}{R{-}\underset{|}{C}{=}O} + C_6H_{11}NH{-}C{-}NHC_6H_{11} + CH_3SCH_3$$

Pyridinium trifluoroacetate is recommended as the source of protons. The oxidation is mild and can be used on compounds such as steroids and alkaloids. Primary alcohols can be quantitatively oxidized to the corresponding aldehydes with no detectable formation of carboxylic acids. The method can also be used for the oxidation of thiols to the corresponding disulfides.[211]

E. Miscellaneous Solvents and Reactions

For a number of solvents only one or two quantitative reactions have been reported. Some of these systems were explored briefly and show little promise, but others merit further evaluation. In still other cases a particular reaction, such as the Karl Fischer titration, is uniquely useful. This section covers a range of solvents and reactions in the above categories.

The Karl Fischer method for the determination of water is probably the most widely used nonaqueous oxidation-reduction titration. The reactions involved have been thoroughly studied, and comprehensive discussions of the method are available.[212, 213] The titrant is a mixture of iodine and sulfur dioxide in pyridine and methanol (sometimes 1,2-dimethoxyethane is used in place of methanol); the sample is generally dissolved in methanol. The method may be used not only for the direct determination of water but for the indirect analysis of any functional group that will undergo a quantitative reaction either consuming or producing water. The system can also be modified to determine iodine or bromine in the presence of excess water. In this way N-chloro and N-bromo compounds have been determined with standard deviations on the order of 0.1%.[214]

An elegant application of nonaqueous solvents to analysis is the determination of elemental sulfur by dissolution in acetone and titration with sodium cyanide in isopropyl alcohol.[215] Thiocyanate is formed quantitatively and rapidly at 50° C. Mercaptans interfere, but aliphatic sulfides and disulfides do not. The same titrant can be used to determine selenium and heterocyclic quaternary ammonium salts.[216]

The lower aliphatic alcohols are excellent solvents and can be used for a number of nonaqueous oxidation-reduction reactions. In methanol, for example, alkyl and hydroxyalkyl ferrocenes can be titrated with iron(II) chloride with a precision of 0.2%.[217] Ferrocene derivatives with a carbonyl group adjacent to the cyclopentadienyl ring do not react, so differentiating titrations of mixtures are feasible. Titration with copper(II) in acetonitrile is somewhat simpler and more precise, however.[161]

8,8′-Diquinolyldisulfide is reduced electrochemically in methanol through an electroactive $Hg(RS)_2$ intermediate to 8-mercaptoquinoline,[218] which has been proposed as an analytical reagent analogous to 8-hydroxyquinoline.[219] Coulometric generation of this reagent, which is rather unstable, would make its use more practicable.

Europium and ytterbium can be determined at the micromolar level by controlled-potential coulometry in methanol.[220] In each case a one-electron reduction to the plus two oxidation state occurs. Organic acids can also be titrated coulometrically in nonaqueous solvents by generation of hydroxide from low concentrations of water. Errors on the order of 1% were found in the titrations of *p*-toluenesulfonic acid, benzoic acid, and 2,4-dinitrophenol separately in acetone.[221]

Nitromethane and nitrobenzene have dielectric constants of about the same magnitude, 35, and have many similarities from an electrochemical point of view. The potential range in nitromethane extends from +2.7 to −2.4 V versus the aqueous saturated calomel electrode when $LiClO_4$ is the supporting electrolyte.[222] The potential limits are determined by the generation of lithium metal and perchlorate radicals. Maxima were observed, however, at −0.3 and −0.8 V, perhaps from traces of water in the system. The polarographic behaviors of a number of metal ions in nitromethane have been surveyed and the results are not encouraging from an analytical point of view.[223] The alkali metals and alkaline earths are not determinable, and many salts of the transition metals are either insoluble or only very slowly soluble. Also, the effects of water on the half-wave potentials are great. Nevertheless, this solvent may still have some utility for organic systems, and some preliminary information on the reactivities of a number of positive chlorine compounds has been obtained.[244]

Precautions should be taken in the handling of nitromethane as it presents an explosion hazard, especially if small amounts of bases or heavy metal salts are present.

Triphenylmethylarsonium permanganate is soluble in nitrobenzene and chloroform (saturated solutions are about 0.8 *M* and 1.0 *M*, respectively). In chloroform 2-propanol is quantitatively oxidized to acetone.[225] Several other low-molecular-weight alcohols and nitro compounds are oxidized but toluene, diethyl ether, ethyl acetate, and *t*-butanol are not. Oxidation studies in nitrobenzene were not reported.

Tetrahydrofuran is a widely used solvent for reductions in organic synthesis; lithium aluminium hydride and sodium borohydride are particularily important reagents.[226, 227] The low dielectric constant of tetrahydrofuran, 7.6, slows many ionic reactions, but the possibility of developing useful analytical methods in this solvent seems promising. Among the direct analytical procedures published to date is the use of sodium naphthalide to reduce cobalt(II) quantitatively to the metal.[228] A conductometric end-point is best. Aldehydes and ketones can be determined by addition of an excess of lithium aluminum hydride in tetrahydrofuran to the sample, allowing a few minutes for reaction, then back-titrating the remaining hydride with a standard solution of an alcohol in an inert solvent such as benzene.[229]

Dioxane has been used as a medium for reductions with chromium(II) acetate.[230] Sulfuric acid must be present; otherwise the reducing power of the chromium(II) is significantly lowered. Copper(II) and vanadium(IV) or (V) were titrated in a 1:1 chloroform mixture, copper being reduced to copper(I) and vanadium(V) to vanadium(III) in two steps. Mixtures of the two metals are determinable in a single potentiometric titration, the first break corresponding to formation of vanadium(IV) and the second to formation of vanadium(III) plus copper(I). If sulfuric acid is not added, only the vanadium(V) - (IV) reduction is seen. Uranium(VI) can also be titrated in ethanol solutions.[231] Oxygen must be carefully excluded in all of these systems.

Morpholine (tetrahydro-1,4-oxazine) is an interesting solvent, though the dielectric constant is low (7.2). It is readily available commercially, has excellent solvent properties toward a wide range of organic compounds, and is relatively nontoxic.[232] Susceptibility of the secondary amine group to chemical reaction with a variety of functional groups somewhat limits the scope of applicability, however.

Sulfolane is a solvent of moderately high dielectric constant, 43, that has been suggested for acid-base titrations, and which may have some utility for oxidation-reduction systems. The potential range for electrochemistry extends from +2.4 to −3.5 V versus the silver – 0.01 *M* silver perchlorate reference electrode in sulfolane.[233] The high viscosity (9.9 cp) is somewhat inconvenient.

A number of solvents have in recent years been receiving intensive study for application to high-energy-density battery systems. Some of those singled out for particular study include solvents known for some time, such as acetonitrile and dimethylformamide, but some are relatively new in terms of our knowledge of their solvent properties; these include propylene carbonate, γ-butyrolactone, dimethylsulfoxide, and methyl formate. Each of the above compounds has many properties desirable in a solvent for electrochemical and analytical electron-transfer studies, and future work will likely incorporate them to a much greater extent than has been the case thus far. A considerable amount of qualitative information is now available in reports of various contractors to the U. S. government. (A bibliography of U. S. government reports on organic electrolyte batteries over the period 1961 to 1968, when most of the work in this area was done, is available.[234])

Propylene carbonate has been used for a number of electrochemical studies. In addition to the silver – silver ion reference electrode, the system Hg;Hg_2Cl_2, KCl (saturated), $(C_2H_5)_4NClO_4$(0.10 *F*) has been studied[235] as a reference. Polarographic data are available for a number of metal ions; for example, the analytical determination of the alkali metals and the alkaline earths by polarography is reported to be feasible,[236] as is the determination of uranium by measurement of the (VI) - (V) reduction wave.[237]

A number of metal ions are reduced polarographically to the zero oxidation state in one step in propylene carbonate. These include thallium(I), iron(III), cobalt(II), nickel(II), copper(II), zinc(II), and cadmium(II), as well as the chlorides of aluminum(III), tin(IV), and tin(II).[238] Diffusion currents in each case are reported to be proportional to concentration in the 10^{-4} to 10^{-3} *M* concentration range. The waves corresponding to the reduction of titanium(IV) to (III), vanadium(IV) and (III) to (II), and chromium(III) to (II) also may have analytical utility.[239]

Mercaptans can be titrated with either copper(II) or iron(III) in pyridine[182] instead of dimethylformamide, but there seems to be no real advantage over dimethylformamide, at any rate not enough to overcome the disagreeable handling properties of pyridine. The plus one oxidation state of copper is stable in pyridine as well as in acetonitrile and dimethylformamide. The copper(II) – (I) couple is reversible and has been suggested as a reference electrode.[240]

A variety of mercaptans can be titrated with copper(II) butyl phthalate in hydrocarbon solvents.[241] Hydrogen cyanide, organic thiocyanates, organic sulfides, thiocyanoacetates, and terpenes do not interfere, but hydrogen sulfide cannot be present. Thioglycolic acid and dithioethylene glycol form insoluble copper salts.

2,4,6-Tri-*tert*-butylphenoxy free radicals are produced in a number of organic solvents by oxidation of the corresponding phenol with lead dioxide[242] and are stable for several days in solutions protected from oxygen. A suggested application is the determination of oxygen at the part-per-million level in solvents such as acetone, benzene, cyclohexane, and ethyl acetate. Ascorbic acid is also quantitatively oxidized. End-points in the titrations could be determined either potentiometrically or spectrophotometrically.

The determination of oxygen in organic solvents can be readily accomplished by electrochemical methods. In addition to the titrimetric method just described, polarographic reduction to the superoxide ion in dimethylformamide has been suggested,[243] and other aprotic solvents may probably be used. For example, superoxide ion is formed in pyridine, acetonitrile, acetone, dimethylsulfoxide, and methylene chloride, as well as in dimethylformamide.[244] Alternative methods such as modifications of the Winkler procedure[243] and mass spectroscopic isotopic dilution procedures[245] are considerably slower and more complex.

Ammonium hexanitratocerate quantitatively oxidizes hydroquinone, iodide, ascorbic acid, ferrocyanide, and iron(II) chloride in a 1:4 by volume mixture of tri-*n*-butyl phosphate and carbon tetrachloride.[83] Carbon tetrachloride is added to reduce the viscosity of tributyl phosphate, which is appreciable (3.885 cp at 20° C). Conventional visual indicators do not function, and potentiometric end-point location is difficult because of the high resistances of the solutions. Glass reference electrodes are more satisfactory than antimony. Because of the difficulty in locating end-points and because the titrant is not very stable in the solvent mixture, the system does not appear to offer any advantage over solvents such as acetic acid or acetonitrile for analytical use.

A variety of monosubstituted hydrazines can be determined with a precision of about 1% by titration with coulometrically generated bromine in an acetic acid-methanol-water solvent system (60-25-15 ratio).[246] Unsymmetrically disubstituted hydrazines react stoichiometrically but consume six equivalents of bromine per mole rather than four as do the monosubstituted compounds. Symmetrically disubstituted hydrazines do not react stoichiometrically.

V. CONCLUSIONS

The structure of liquid water, the solvent in which most analytical reactions have been performed, is still unknown. Current evidence points to the existence in liquid water at room temperature of clusters of water molecules hydrogen-bonded in loose structures whose lifetimes are on the order of 10^{-10} to 10^{-11} sec, along with some interstitial monomeric water. It has been pointed out by Brank that the concept of water as a mixture has been over the years attractive to chemists and repugnant to physicists.[247] The concept of a mixture conveniently explains some of the properties of aqueous solutions and of water as a reaction medium. On the other hand, it complicates comparison of information on reaction rates and mechanisms between water and other solvents. Therefore, more data on fundamental solvent-solute interactions in representative solvents are needed. Once it becomes possible to deduce the bulk properties of a solvent from correlations with its molecular structure, it should be relatively easy to select solvents that will answer the needs of particular analytical problems.

The replacement of water by another solvent in an analytical oxidation-reduction reaction presumes that one or more advantages outweigh the inconvenience necessarily accompanying the change. Advantages may arise from the solubilization of samples that are insoluble in water or that react with it through hydrolysis or oxidation-reduction, from the formation of a stronger oxidant than is available in water, or from the occurrence of solvent-solute interactions that shift an equilibrium to a more favorable position. Some disadvantages associated with the nonaqueous solvents now most widely used include problems in purification, storage, and handling of the pure solvent; a lack of reagents of sufficient strength, solubility, and stability to be of general application; and the relatively low rates of reaction often encountered. Further progress in this area will depend on the development of new solvents and possibly new reagents.

It has now been established that oxidation-reduction titrations can be performed in nonaqueous solvents with the precision and accuracy of conventional aqueous titrations. For some compounds rapid and convenient quantitative procedures have been developed. Prospects for this picture's changing through future developments in fundamental and applied research are good as new solvents, reagents, and techniques steadily expand the range and utility of these methods. In particular the possibilities for organic analysis by direct electrochemical oxidation or reduction at an electrode, or by homogeneous reaction in solution with a reagent, show considerable promise.

VI. SUMMARY

Nonaqueous solvents may be used in place of water to extend the scope of oxidation-reduction reactions. The solvent dielectric constant and Lewis acid-base character are important in establishing the magnitude of solute solubilities, equilibria, and reaction rates. Important factors in the practical use of these systems include solvent purification, choice of reference electrodes, and the effects of solvent volatility, viscosity, and thermal coefficient of expansion on the accuracy and precision of analytical work. The present status of electroanalytical and homogeneous oxidation-reduction analytical methods in organic solvents is still in an early stage of development.

Acknowledgments

The author gratefully acknowledges the permission of Kresge-Hooker Science Library Associates to reprint a portion of Table 4 from *Record of Chemical Progress*, and the assistance of Richard Krause and Barbara Butterwick in preparation of the manuscript.

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