THE THEORY OF REVERSIBLE TWO-STEP OXIDATION INVOLVING FREE RADICALS

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In a previous review (9) there was presented the evidence for the existence of free radicals, designated as semiquinones, which are intermediate products formed in organic oxidation–reduction reactions. At that time emphasis was placed on the experimental basis of the theory. Since then, with the accumulation of more actual examples in other laboratories as well as in this one, it has been possible to extend and to simplify the whole underlying theory. Because the importance of the problem has become more generally recognized, it is worth while now to present this theory comprehensively, and to develop it not from the historical but from a purely logical point of view. Since it is the purpose of this review to unify work scattered through various publications (8, 10 to 19, 21) changes have been made in some of the equations, but the equivalence of the new forms with the earlier ones will easily be recognized. Another problem to be discussed in this review is the relation between the equations for this stepwise oxidation and the equations for the stepwise ionization of dibasic acids.

I. THE FUNDAMENTAL REDUCTION PROCESS

If a substance, A, can undergo a reversible reduction by accepting an electron,[1] the process may be represented thus:

$$A + \epsilon \rightleftharpoons A^- \tag{1}$$

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[1] List of symbols used:

ϵ = electron,
H^+ = proton,
a = total amount of the substance, in moles,
r = amount of R, the reduced form,
s = amount of S, the semi-oxidized form as semiquinone,
t = amount of T, the totally oxidized form,
d = amount of D, the semi-oxidized form as dimer,
x = equivalents of added oxidizing agent,
k = formation constant of the intermediate semiquinone form,

If the product, A^-, happens to be the ion of a weak acid it will tend to combine with a proton furnished either by the oxonium ion OH_3^+, if the solvent contains water, or by any other acid in Brönsted's generalized terminology:

$$A^- + H^+ \rightleftharpoons AH \tag{2}$$

κ = dismutation constant = $1/k$,

$\gamma = 4\kappa - 1 = \frac{4 - k}{k}$

$\xi = \frac{x}{a}$

$\mu = \xi - 1 = \frac{x - a}{a}$

$\lambda = 1 - \mu^2$

$\tau = \frac{t}{s}$

$\rho = \frac{r}{s}$

$q = \sqrt{1 + \gamma\lambda} = \sqrt{1 + (4\kappa - 1)(1 - \mu^2)}$

E = potential,

E_m = mean normal potential,

E_1 = normal potential of the lower step,

E_2 = normal potential of the higher step,

$E_i = E_{(\text{at } 50\% \text{ oxidation})} - E_{(\text{at } 25\% \text{ oxidation})}$ = index potential,

K_1, K_2 = the two ionization constants of a bivalent acid,

RT = product of gas constant and absolute temperature (printed in italics, in distinction to the above R and T),

v = volume of solution containing total substance, a,

$Q = \frac{vd}{rt}$

$G = \frac{vd}{s^2}$

$L = \frac{Qa}{v}$

δ = slope of titration curve at midpoint where $\mu = 0$,

$N = t/r = 10^{\frac{\Delta E}{0.03}}$

$\alpha = \frac{E_i F}{RT}$

$k' = \frac{K_1}{K_2}$

ΔE is the difference between any observed potential and the midpoint potential.

If these two processes occur simultaneously the net effect can be represented by the combined reaction:

$$A + \epsilon + H^+ \rightleftharpoons AH \qquad (3)$$

or

$$A + H \rightleftharpoons AH \qquad (3a)$$

Only in such a case is the term "reduction" entirely equivalent to hydrogenation.

Exactly the same argument applies to the bivalent oxidation–reduction process of a substance B when the two steps occur simultaneously. The corresponding reactions are:

$$B + 2\epsilon \rightleftharpoons B^{--} \qquad (4)$$

$$B + 2\epsilon + 2H^+ \rightleftharpoons BH_2 \qquad (4a)$$

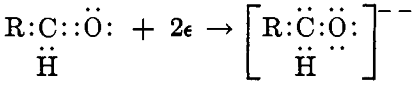
$$B + 2H \rightleftharpoons BH_2 \qquad (4b)$$

There are other variations in the form in which these reactions sometimes need to be written. For example, the reduction of an ester is represented by:

$$RCOOEt + 2\epsilon + H^+ \rightarrow RCHO + (OEt)^- \qquad (5)$$

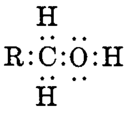
However, the common feature of all these equations and the essential characteristic of the reduction process is that the compound undergoing reduction accepts electrons, as expressed in equations 1 and 4. This process may be, and in most cases is, accompanied by changes in the condition of ionization of products first formed. That is to say, the product resulting from reaction 1 or 4 may immediately attach or detach protons or hydroxyl ions, depending on its acidity and on the medium in which it is formed. Any such changes in state of ionization, although usually accompanying the reduction, must be kept logically distinct. It is often convenient to write reduction reactions in the forms of equations 3a or 4b, but for the purposes of developing a unified and consistent theory and a set of equations to describe the electrochemical facts of reduction, equations 3a and 4b must be thought of as broken into the two parts represented by equations 1 and 2.

A few examples will illustrate this idea. Consider the reduction of an aldehyde. The electronic structures corresponding to equation 4 are:



$$\mathrm{R}{:}\underset{\ddot{\mathrm{H}}}{\mathrm{C}}{::}\ddot{\mathrm{O}}{:} + 2\epsilon \rightarrow \left[\mathrm{R}{:}\underset{\ddot{\mathrm{H}}}{\ddot{\mathrm{C}}}{:}\underset{\cdot\cdot}{\ddot{\mathrm{O}}}{:}\right]^{--} \qquad (6)$$

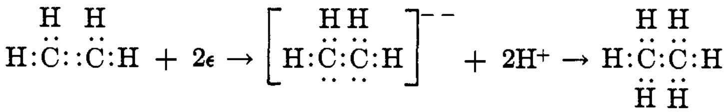
The product formed would be the divalent ion of an unmeasurably weak acid and would immediately attach protons to form the alcohol:



$$\mathrm{R}:\overset{\mathrm{H}}{\underset{\mathrm{H}}{\ddot{\underset{\cdot\cdot}{\mathrm{C}}}}}:\ddot{\underset{\cdot\cdot}{\mathrm{O}}}:\mathrm{H}$$

But this addition of protons has nothing to do with the reduction process, which is entirely contained in equation 6.

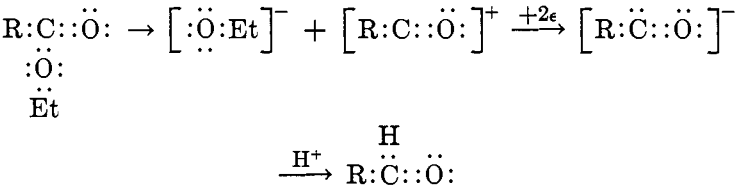
A similar case is afforded by the reduction of ethylene to ethane, in which the reduction and proton-attaching processes are:



$$\mathrm{H}:\overset{\mathrm{H}}{\ddot{\mathrm{C}}}::\overset{\mathrm{H}}{\ddot{\mathrm{C}}}:\mathrm{H} + 2\epsilon \rightarrow \left[\mathrm{H}:\overset{\mathrm{H}}{\ddot{\underset{\cdot\cdot}{\mathrm{C}}}}:\overset{\mathrm{H}}{\ddot{\underset{\cdot\cdot}{\mathrm{C}}}}:\mathrm{H}\right]^{--} + 2\mathrm{H}^{+} \rightarrow \mathrm{H}:\overset{\mathrm{H}}{\underset{\mathrm{H}}{\ddot{\underset{\cdot\cdot}{\mathrm{C}}}}}:\overset{\mathrm{H}}{\underset{\mathrm{H}}{\ddot{\underset{\cdot\cdot}{\mathrm{C}}}}}:\mathrm{H} \quad (7)$$

The pairs of molecules AH and A^- or BH_2 and B^{--} of equations 2 and 4 may be said to be two states of ionization of the same acid, of which the ionized form in some cases may be practically incapable of existence.

Other cases also arise in which the ionization process involves hydroxyl or alkoxyl ions instead of protons. For example, the reduction represented by equation 5 can be written electronically:



$$\underset{\underset{\mathrm{Et}}{:\ddot{\underset{\cdot\cdot}{\mathrm{O}}}:}}{\mathrm{R}:\mathrm{C}}::\ddot{\mathrm{O}}: \rightarrow \left[:\ddot{\underset{\cdot\cdot}{\mathrm{O}}}:\mathrm{Et}\right]^{-} + \left[\mathrm{R}:\mathrm{C}::\ddot{\mathrm{O}}:\right]^{+} \xrightarrow{+2\epsilon} \left[\mathrm{R}:\ddot{\mathrm{C}}::\ddot{\mathrm{O}}:\right]^{-} \xrightarrow{\mathrm{H}^{+}} \mathrm{R}:\overset{\mathrm{H}}{\ddot{\mathrm{C}}}::\ddot{\mathrm{O}}:$$

In this case the attachment of the electron pair and the detachment of the ethoxyl group may occur simultaneously, but again the latter is an ionization step and must not be confused with the reduction itself.

In what follows equations 1 and 4 are considered as the elementary reduction process. The changes represented by equations 2, 3, 3a, 4a, and 4b contain features not belonging to the process proper of oxidation–reduction.

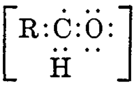
II. STEPWISE REDUCTION AND THE EXISTENCE OF FREE RADICALS

Usually in organic compounds reduction is bivalent, that is, it involves taking up two electrons, as represented in equation 4. This is because almost without exception the compounds which have been considered as stable organic molecules contain an even number of electrons. But it now appears that there is no reason why this must be so. In carrying out the reduction represented by equation 4, by gradually adding a reductant to **B**, the process may take place in steps:

$$\begin{aligned} B + \epsilon &\rightleftharpoons B^- \qquad (8) \\ B^- + \epsilon &\rightleftharpoons B^{--} \end{aligned}$$

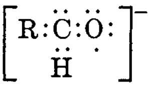
In the reduction represented by equation 4 each molecule of B takes up two electrons simultaneously and only two molecular species, **B** and B^{--}, are involved in the equilibrium. In the reduction represented by equation 8, however, each molecule of B first takes up one electron to form B^-. When such a reduction is performed by titrating with a reducing agent, three molecular species, B, B^-, and B^{--}, will be present in equilibrium with each other. It is a detailed analysis of this equilibrium which is one of the major objects of this review. From simple mass law equations, functions are derived which express the amounts of B, B^-, and B^{--} present at successive stages throughout such a reduction. One of the consequences of the existence of this equilibrium is that it is in general impossible to isolate the intermediate form or even to study it alone in solution. It is an essential property of these intermediate oxidation levels that they are always in a mobile equilibrium with the compounds on the next higher and the next lower step of oxidation, whereas ordinary valence-saturated organic compounds are usually inert with respect to establishing equilibria with other valence-saturated compounds. Acetaldehyde does not dismute to ethyl alcohol and acetic acid in an acid or neutral solution, although it would be possible, speaking purely thermodynamically. In contrast, the establishment of the equilibrium of a radical of the type mentioned with an electron donor or acceptor is just as unhampered as that of an acid or base with a proton donor or acceptor. If a large part of B is converted to B^- before B^- begins to accept electrons to form B^{--}, then the two steps of reduction of equation 8 will be separated. But if B^- begins to accept electrons while much B is left, then the steps will be said to overlap. In the reduction represented by equation 4 the overlapping is complete, and equation 4 is a limiting case of equation 8.

If B is a common organic molecule such as an aldehyde or a quinone it will have an even number of electrons and so B^- must have an odd number. For example, if the reduction of the aldehyde in equation 6 were to proceed in separated steps, it would be necessary to consider the existence of molecular species such as:



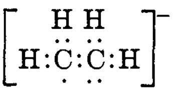
$$\left[\begin{matrix} R:\underset{\cdot\cdot}{\dot{C}}:\underset{\cdot\cdot}{\ddot{O}}: \\ H \end{matrix}\right]^-$$

or



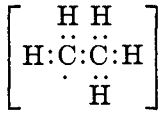
$$\left[\begin{matrix} R:\underset{\cdot\cdot}{\dot{C}}:\underset{\cdot}{\ddot{O}}: \\ H \end{matrix}\right]^-$$

Likewise, the intermediate step in the reduction of ethylene (equation 7) would have to be



$$\left[\begin{matrix} & & \mathrm{H} & & \mathrm{H} & & \\ & & \cdot\cdot & & \cdot\cdot & & \\ \mathrm{H} & : & \mathrm{C} & : & \mathrm{C} & : & \mathrm{H} \\ & & \cdot & & \cdot\cdot & & \end{matrix}\right]^-$$

or, on adding a proton,



$$\left[\begin{matrix} & & \mathrm{H} & & \mathrm{H} & & \\ & & \cdot\cdot & & \cdot\cdot & & \\ \mathrm{H} & : & \mathrm{C} & : & \mathrm{C} & : & \mathrm{H} \\ & & \cdot & & \cdot\cdot & & \\ & & & & \mathrm{H} & & \end{matrix}\right]$$

that is, the ethyl radical would be the result. These particular radicals are not capable of existence to any measurable extent as components of equilibrium systems, at least not at ordinary temperatures. However, the compound of styrene and sodium probably has some such structure.

Outside the gas phase studies, there have been two approaches from which free radicals have been considered in the past. The first deals with actual isolation of radicals and determination of their molecular weights as shown, for example, in the extensive studies on compounds of the types of triphenylmethyl, diphenylnitrogen, triphenylhydrazyl, or diphenylnitric oxide. Radicals of these types have rarely been studied in aqueous solutions, because they are often very unstable in water. In organic solvents the equilibria involved in the combination of such radicals with themselves (dimerization) or with other radicals have been studied. On the other hand, reactions of such radicals to form simultaneously molecules of a higher and a lower oxidation level (dismutation), although known to occur, have not been so extensively studied.

The second approach to a study of free radicals included both organic and inorganic radicals and applies to such radicals in aqueous solutions; on the other hand, the studies are not on equilibrium systems and the existence of the radicals is not based on such direct evidence. Radicals of this sort are discussed by Franck and Haber (5) and by Haber and Willstätter (7, 6). As an example of the type of system studied, there is the oxidation of sulfurous acid by oxygen catalyzed by copper ion. Radicals are postulated as the primary molecular species formed. They are supposed to have a very short life time, since they are either oxidized or reduced immediately as they arise, or they are supposed rapidly to undergo irreversible side reactions such as dimerization to valence-saturated compounds. The radicals are members of a chain of reactions which may break sooner or later according to conditions and so lead to different final states of the system. The formation of the radical is supposed to require a considerable activation energy, and the course of the process depends on kinetic factors. Thus the existence of radicals as intermediate steps in bivalent oxidations is studied, but the reactions considered are not sequences of continuously shifting thermodynamical equilibria but are in part irreversible processes.

The experimental basis on which the semiquinone theory is built supplies a new method for the study of radicals. Semiquinones are free radicals. They also frequently happen to be ions, because the substances dealt with have acid–base properties. They are stable molecules existing as intermediate oxidation levels in thermodynamic equilibrium in reversible bivalent reductions in aqueous solution. A measure of their stability is afforded by the steadiness of the electric potentials which can be obtained in systems of which they are components at precious metal electrodes. That such odd electron molecules can be stable is no more surprising than the stability of many other organic radicals whose radical nature is based on direct determinations of molecular weight. Direct determination of the molecular weight of semiquinones by any of the usual methods is in general not possible, since they exist in equilibrium with their oxidized and reduced forms.

Most of the substances in which semiquinone formation has definitely been shown to occur to a well-measurable extent are aromatic or heterocyclic compounds. In all cases the reduction can be interpreted as the stepwise addition of two electrons to atoms at the ends of a system of conjugated double bonds. The atoms at the ends of this system are usually oxygen or nitrogen atoms. In the first case the semiquinone level is favored in alkaline solutions, and in the second case it is favored in acid solutions. In all such examples the stability of the odd electron semiquinone molecule is due to the formation of a more or less symmetrical resonance system. It seems likely that the reason the formation of semiquinones has so far been observed only in molecules containing a conjugated system of double bonds is that such a system can act as an electron reservoir or electron "buffer". In accepting a single electron there exist a number of different ways of rearranging the whole electronic system of the molecule to accommodate the added electron. In each such arrangement of the electrons one atom of the conjugated system must be associated with an odd number of electrons. If the structure of the molecule is symmetrical, or at least nearly symmetrical, the odd electron may be imagined to oscillate between the two symmetrical moieties, just as the electron of the hydrogen molecule ion, resulting in resonance, which has been recognized, since Heisenberg's work, as a stabilizing factor.

On the other hand, consider the reduction of a simple aldehyde as represented by equation 6, or of a simple ethylenic compound as represented by equation 7. Such molecules might similarly be imagined to accept electrons singly, giving rise to the radicals represented on page 8. Owing to lack of symmetry, there is a smaller chance of stability. This is just a general principle which we cannot yet survey in detail. Even without such a symmetrical structure, intermediate oxidation levels might still exist in concentrations extremely low indeed, but sufficient to play an important rôle in the kinetics of oxidation–reduction reactions.

III. DISMUTATION AND DIMERIZATION

The reaction $2B^- \rightarrow B + B^{--}$ will be referred to as dismutation. This is analogous to the Cannizzaro reaction or disproportionation, insofar as a given molecular species gives rise simultaneously to a higher and a lower state of oxidation. But in the Cannizzaro reaction both the oxidation and the reduction are bivalent as in the case of an aldehyde, considered in its hydrated form:

$$2R\cdot CH(OH)_2 \rightleftharpoons R\cdot CH_2OH + R\cdot COOH$$

In a dismutation, on the other hand, the oxidation and reduction are univalent, such as might occur with the hypothetical radical, $R\cdot C(OH)_2$, namely:

$$2R\cdot C(OH)_2 \rightleftharpoons R\cdot CH(OH)_2 + R\cdot COOH$$

Among other reactions beside dismutation, which radicals can undergo, the process of dimerization is particularly important. In fact, triphenylmethyl is more usually looked upon as a dissociation product of its dimer, hexaphenylethane, than as an oxidation product of triphenylmethane. Although from the standpoint of classical organic chemistry dimerization is the most probable reaction for a radical to undergo, this reaction is not so general as was believed. It is true that radicals such as CH_3 easily dimerize rather than dismute. Furthermore, the first oxidation product of sulfhydryl compounds (hydrogen sulfide, sulfites, thiosulfates, and mercaptans) that can be detected is a disulfide:

$$2RSH \rightleftharpoons RSSR + 2H$$

This may be accounted for by assuming that a radical first forms which immediately dimerizes. Franck and Haber (5) presented good evidence for this assumption in the case of the oxidation of sulfurous acid.

Until quite recently the semiquinones seemed to differ from other known organic radicals in that the examples known showed no tendency to dimerize. There are two conditions which may account for this. In the first place, studies of the semiquinones have been made potentiometrically on aqueous solutions of electrolytes. To get titration curves that could easily be interpreted thermodynamically the work was always carried out in dilute solution, ranging from 10^{-3} to 10^{-5} molar. Such dilute solutions are of course not favorable to the formation of dimers. In the second place, while the equilibria of dimerization of organic radicals have usually been studied in non-associated organic solvents, semiquinones are always studied in aqueous solution, which might favor the dissociation. However, there have recently been found several cases in which it has been possible to show that semiquinones can dimerize, and the extent of the dimerization has been measured (14, 19).

In general, a radical may be said to be capable of two kinds of reaction, —dismutation and dimerization. Sometimes the one prevails, sometimes the other. Unless the tendency to dimerize is very strong, as it is in the formation of disulfides, experimental conditions can be arranged to make the dimerization negligible. For, since dimerization is a bimolecular reaction, its extent depends on the concentration of the substances involved. At a sufficient dilution the dimerized form will practically completely dissociate into radicals. So, working in sufficiently dilute solutions, we can, as a rule, approach a condition where dimerization can be neglected (15, 19). Thus in what follows, if we sometimes speak of processes as if no dimerization occurred, we mean only that quantitatively it is negligible in comparison with dismutation.

A radical, of course, may be able to undergo various other chemical reactions, e.g., biphenylnitride can combine with nitric oxide. Such reactions need not be considered here at all. We always suppose that the system is exposed to no other chemical reagents than such as are just capable of changing its level of oxidation–reduction.

In what follows, those cases will be dealt with principally where dismutation is the only change to which the radical is subjected. This is the more fundamental situation. On the basis of the theory for this uncomplicated case, the adjustment of the theory to the case of dimerization can easily be presented in a short subsequent section. The first problem will be to express the equilibrium which exists among the three levels of oxidation–reduction whenever the substance is present in a not entirely oxidized or reduced state. For this purpose we imagine the mixture of which we are to study the equilibrium to be made up by partially oxidizing the reduced form. The gradual change of the level of oxidation–reduction of the system is imagined to be accomplished by titrating the reduced form with an oxidizing agent.

IV. THE EQUILIBRIUM OF THE THREE LEVELS OF OXIDATION–REDUCTION

First we shall consider only what we have defined as the elementary process of bivalent oxidation–reduction. Suppose that there is given a solution of a substance in its reduced form and we titrate it with a strong oxidizing agent. Provided the potential range of the oxidizing agent is much more positive than that of the substance to be oxidized, the following relations hold: Let the total molar amount of the substance, which is originally present in its reduced form, be a. Let the amount of the oxidizing agent added at a given stage of the titration be x, expressed in equivalents so that at the endpoint of titration $x = 2a$. At any point of the titration there will be a mixture of the reduced form R, of the semi-oxidized form, S, and of the totally oxidized form T. The molar amounts of these substances are designated by r, s, t. Then, at any point of the titration,

$$r + s + t = a \tag{9}$$

$$s + 2t = x \tag{10}$$

For the purpose of solving the equations for r, s, and t we need a third equation. This is given by considering the equilibrium

$$2\text{S} \rightleftharpoons \text{T} + \text{R}$$

expressing the process of dismutation. The equilibrium of this reaction is

$$\frac{r \cdot t}{s^2} = \kappa = \frac{1}{k} \tag{11}$$

κ will be designated as the dismutation constant. Its reciprocal value, k, will be referred to as the semiquinone-formation constant. We shall use either one or the other term according to convenience.

From equations 9, 10, and 11 we could express r, s, and t in terms of a, x, and κ. Since all molecules arising or disappearing during the titration are supposed to have the same molecular size and a dimerization reaction involving the formation of a bimolecular form is supposed not to occur, the absolute values of concentrations are irrelevant and only their ratios are significant. So it will be found more convenient to choose instead of the variables r, s, t and x, the set r/a, s/a, t/a and ξ where $\xi = x/a$. Then from equation 9,

$$\frac{r}{a} + \frac{s}{a} + \frac{t}{a} = 1 \tag{12}$$

The solutions of these equations will be more symmetrical if a further substitution is made defined by the relation:

$$\mu = \xi - 1 \tag{13}$$

This substitution places the zero point of the functions at the midpoint of the titration where ξ is equal to 1, which is a point of symmetry, instead of at the beginning of the titration where ξ is equal to zero. During the titration μ varies from -1 to $+1$. A further substitution which will help to simplify the final results is:

$$\gamma = 4\kappa - 1 = \frac{4 - k}{k} \tag{14}$$

The solution of equations 9, 10, and 11 with the substitutions given in equations 13 and 14 then leads to the result:

$$\frac{r}{a} = \frac{1 - \mu}{2} - \frac{\sqrt{1 + \gamma(1 - \mu^2)} - 1}{2\gamma} \tag{15}$$

$$\frac{s}{a} = \frac{\sqrt{1 + \gamma(1 - \mu^2)} - 1}{\gamma} \tag{16}$$

$$\frac{t}{a} = \frac{1 + \mu}{2} - \frac{\sqrt{1 + \gamma(1 - \mu^2)} - 1}{2\gamma} \tag{17}$$

The functions r/a and t/a are antisymmetric in μ with respect to each other, since on changing μ for $-\mu$ either one becomes the other. The function s/a, on the other hand, is itself symmetric in μ, since changing μ for $-\mu$ does not change its value. The sum of the three functions is unity, as required by equation 12. The form in which these functions were written in the previous review (reference 9, p. 252) did not bring out the symmetry that exists among them and that is reflected in the symmetry of the experimental potentiometric titration curves. The older form of these functions has also the disadvantage that the choice of the sign before the square root depends on the value of k, whereas the present form is unambiguous. Purely mathematically, of course, there is a second series of solutions such that in equations 15, 16, and 17 a negative sign must be used before the square root. But such solutions have no physical significance. To show this the functions may be plotted for various assumed values of the parameter γ. When γ is any positive number the functions are ellipses, and when γ is a negative number they are hyperbolae. Physically, of course, negative values of γ are restricted to the range between -1 and 0. Physically also we are only interested in the segments of these functions in the range of μ between -1 and $+1$. In each case it will be found by actual plotting of the curves that of the two segments of each curve which fall within this physically significant range of μ, only that segment corresponding to the choice of the positive sign before the root of equations 15, 16, or 17 gives acceptable values of r/a, s/a, or t/a. The only physically acceptable values of these functions are positive values in the range of 0 to 1. Instead of plotting the functions direct consideration of the equations leads to the same conclusion. If it can be shown for one particular value of μ that the positive segment must be chosen, this holds for all values of μ, since the function is continuous and cannot jump during the titration from one segment to the other. Let us take, for instance, $\mu = 0$, and consider equation 16. This then appears in the form

$$\frac{s}{a} = \frac{\pm\sqrt{1+\gamma} - 1}{\gamma}$$

Since k is always a positive number, γ is always > -1. If γ is a positive number, the choice of the negative value of the square root would give a negative value for s/a; if γ is negative, s/a would become > 1 on choosing the negative square root. Neither of these values has any physical significance.

In the special case that $\kappa = \frac{1}{4}$, or $\gamma = 0$, these functions are useless, because they contain a term of the form 0/0 and so are indeterminate. If, however, in equations 9, 10, and 11 we substitute for κ the value $\frac{1}{4}$ directly, the solution appears in the form:

$$\frac{r}{a} = \frac{1}{4}(1 - \mu)^2 \tag{18a}$$

$$\frac{s}{a} = \frac{1}{2}(1 - \mu^2) \tag{18b}$$

$$\frac{t}{a} = \frac{1}{4}(1 + \mu)^2 \tag{18c}$$

These latter functions are parabolic and have only one branch. As regards the manner of symmetry with respect to μ, the same holds as for equations 15, 16, and 17.

First formulation of the potential

Our main problem is to express the potential E as a function of x, or ξ, or μ. According to the principles of thermodynamics, the potential can be expressed in three different ways:

$$E = E_m + \frac{RT}{2F} \ln \frac{t}{r} \tag{19a}$$

or

$$E = E_1 + \frac{RT}{F} \ln \frac{s}{r} \tag{19b}$$

or

$$E = E_2 + \frac{RT}{F} \ln \frac{t}{s} \tag{19c}$$

E_m, E_1, and E_2 are constants characteristic of the particular chemical compound. E_m is the potential when $t = r$. It may be called the mean normal potential and is always the potential at the midpoint of titration, when $\mu = 0$. It is analogous to the normal potential of a bivalent oxidation–reduction system without step formation. E_1 is the potential at that point of the titration where $r = s$. It may be designated as the normal potential of the lower step. E_2 is the potential when $t = s$. It is the normal potential of the higher step.

To express E as a function of μ we could substitute the values of r, s, and t as obtained from equations 15, 16, and 17. The function resulting would be found awkward to manipulate in subsequent developments. We shall obtain more amenable forms in the following section. However, the equations 19 are useful for the following argument. Subtracting 19a and 19b, we obtain

$$E_m - E_1 = \frac{RT}{2F} \ln \frac{s^2}{rt}$$

or

$$E_1 = E_m - \frac{RT}{2F} \ln k \tag{20a}$$

and similarly

$$E_2 = E_m + \frac{RT}{2F} \ln k \tag{20b}$$

furthermore

$$E_m = \frac{E_1 + E_2}{2} \tag{21}$$

So it can be seen that the mean normal potential, E_m, lies halfway between E_1 and E_2. If two of the three potentials E_1, E_m, and E_2 are known, the third is also unambiguously defined.

Alternative formulation of the potential

Regarding equation 11, we can write it in a more symmetrical form by making the substitutions:

$$\frac{r}{s} = \rho$$

and

$$\frac{t}{s} = \tau$$

we then obtain

$$\rho\tau = \kappa \tag{22}$$

In order to introduce the variables ρ and τ instead of r and t in equation 9 and 10, we divide both by s and obtain

$$\rho + 1 + \tau = \frac{a}{s}$$

$$1 + 2\tau = \frac{x}{s}$$

To eliminate the remaining s, we divide the second of these two equations by the first:

$$\frac{1 + 2\tau}{1 + \rho + \tau} = \xi = \mu + 1 \tag{23}$$

Equations 22 and 23 are two equations for the two unknowns ρ and τ. By putting the value of ρ from equation 22,

$$\rho = \frac{\kappa}{\tau}$$

into equation 23 we obtain, writing only the solution with a positive sign before the square root,

$$\tau = \frac{1}{2(1 - \mu)}\left[\mu + \sqrt{\mu^2 + 4\kappa(1 - \mu^2)}\right] \tag{24a}$$

$$\rho = \frac{1}{2(1 + \mu)}\left[- \mu + \sqrt{\mu^2 + 4\kappa(1 - \mu^2)}\right] \tag{24b}$$

The other solutions, having a minus sign before the root, can be ruled out, for the absolute magnitude of the square root is always $> \mu$. Therefore both τ and ρ would be always negative on choosing the negative sign and so without physical significance. Now from equation 19a,

$$E - E_m = \frac{RT}{2F} \ln \frac{t}{r} = \frac{RT}{2F} \ln \frac{\tau}{\rho}$$

So we obtain

$$E - E_m = \frac{RT}{2F} \ln \frac{1 + \mu}{1 - \mu} + \frac{RT}{2F} \ln \frac{\sqrt{1 + \gamma(1 - \mu^2)} + \mu}{\sqrt{1 + \gamma(1 - \mu^2)} - \mu} \tag{25}$$

where, as before, γ stands for $(4\kappa - 1)$. This function shows the symmetry of the potential around the midpoint of titration quite clearly. By exchanging $+\mu$ for $-\mu$ we obtain a value for $E - E_m$ of the same absolute magnitude but with reversed sign. So the function is antisymmetric

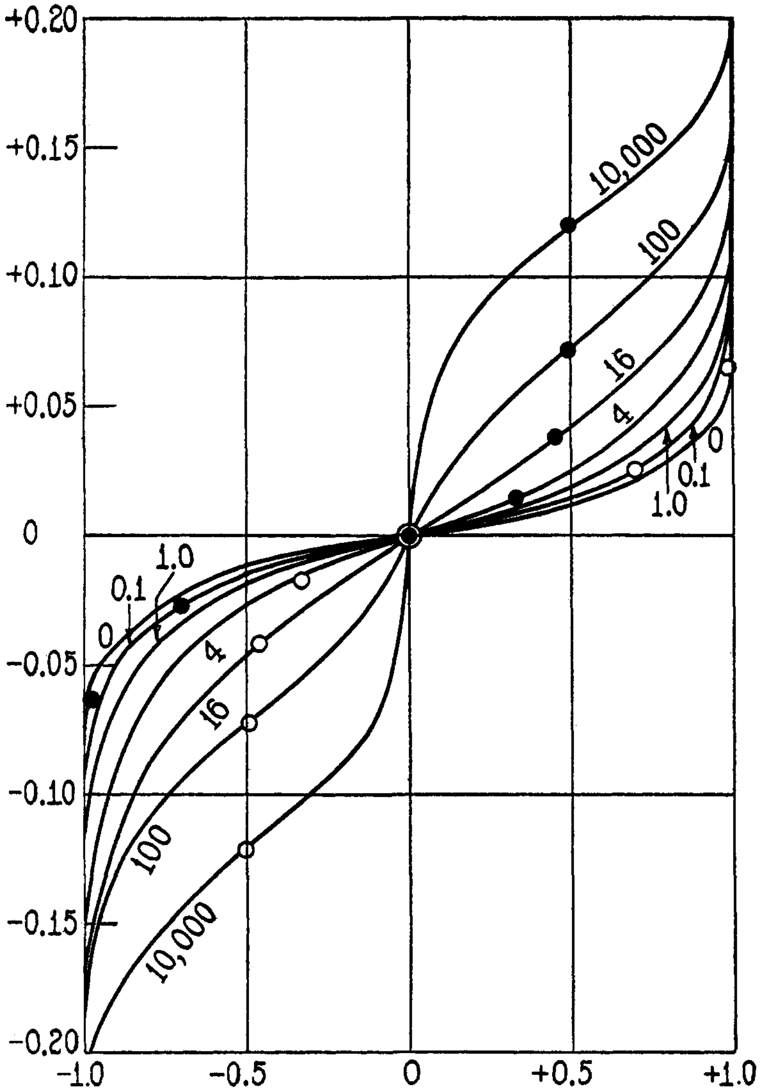


FIG. 1. Two-step titration curves involving formation of semiquinone radical. Abscissa: μ. $\mu = 0$ means 50 per cent of the total oxidation; $\mu = 1$ means 100 per cent of the total oxidation. Ordinates: $E - E_m$, the potential, referred to the mean normal potential E_m, in volts. Each curve holds for the value of k (semiquinone-formation constant) as indicated. White circle: that point of the titration curve where $E = E_1$ (the normal potential of the lower step). Black circle: that point where $E = E_2$ (the normal potential of the higher step). The black *and* white circle in the center belongs to the curve for $k = 1$; here E_m, E_1, and E_2 coincide at $\mu = 0$. White circles are on the left side for curves with $k > 1$; they are on the right side when $k < 1$. Both the white and the black circle in the curve for $k = 0$ belong actually to a curve for k intermediate between 0 and 0.1. When k is precisely 0, the circles would lie at $\mu = \pm 1$ and at potential $\pm \infty$. The lateral points of inflection begin to appear only when $k > 16$.

with respect to μ. Another convenience of this equation is that the first logarithmic term is the one holding if no intermediate form arises. In this case, γ is very large and the second logarithmic term vanishes. The second logarithmic term is the correction due to step formation and the dismutation constant appears only in this term. This equation (equation 25) is also the most suitable for the differentiation which we will have to execute presently.

The shape of this function varies with the value of γ or from the relation 14 with the values of κ or k. Figure 1 shows the variation in shape for different values of k. If k is very small then the potential approaches the value

$$E - E_m = \frac{RT}{2F} \ln \frac{1+\mu}{1-\mu} \tag{26}$$

as it should be for a system with no intermediate step of oxidation.

When $\kappa = \frac{1}{4}$, or $\gamma = 0$ and $k = 4$, then

$$E - E_m = \frac{RT}{F} \ln \frac{1+\mu}{1-\mu} \tag{27}$$

a curve in which all ordinates are double the size of those in equation 26. This is the same curve as for a univalent oxidation system. These curves (equations 26 and 27) have a point of inflection at $\mu = 0$. When κ becomes much smaller, two more points of inflection appear. So a jump in the middle part of the curve appears which indicates a more distinct separation of the curve into two parts or two successive steps. For vanishingly small κ, or large k, these two points of inflection lie at $\mu = \pm\frac{1}{2}$. It is an important problem to study the existence and the location of these lateral points of inflection generally. This problem will be discussed by differentiation.

The first derivative of E

On differentiating E with respect to μ we obtain

$$\frac{dE}{d\mu} = \frac{RT}{F} \frac{1}{1-\mu^2} \left(1 + \frac{1}{\sqrt{1+\gamma(1-\mu^2)}}\right) \tag{28}$$

When κ is not too small (say $>10^{-2}$), the middle part of the potential curve where μ lies in the range from $+0.3$ to -0.3, is for all practical purposes a straight line. So it is very easy to determine graphically from an experimentally obtained curve the slope at $\mu = 0$. The slope, δ, at this point, is

$$\delta = \frac{RT}{F}\left(1 + \frac{1}{\sqrt{1+\gamma}}\right) \tag{29}$$

In the special case that k becomes very small (or γ very large) this approaches the form:

$$\delta = \frac{RT}{F} = 0.02606 \text{ volt per unit of } \mu \tag{29a}$$

This is the slope of a titration curve in its midpoint (where $\mu = 0$), if no intermediate compound is formed.

On solving equation 29 for γ, we obtain

$$\gamma = \frac{1}{\left(\frac{F}{RT}\cdot\delta - 1\right)^2} - 1$$

or

$$k = 4\left(\frac{F}{RT}\cdot\delta - 1\right)^2 \tag{30}$$

This equation serves to calculate k from the slope of a titration curve. Elema (4) has expressed this as follows: Draw the tangent at the midpoint of titration and extend it to intersection with the ordinate of the endpoint of titration. Read the magnitude of the ordinate at this point of intersection in volts. Subtract the voltage of the midpoint of titration. This difference equals δ (expressed in volts) and has the following relation to k, at 30°C.:

$$k = (76.63\delta - 2)^2 \tag{31}$$

The second derivative of E; points of inflection

From equation 28 we derive:

$$\frac{d^2E}{d\mu^2} = 2\frac{RT}{F}\cdot\frac{\mu}{\lambda}\left[\frac{1}{\lambda}\left(1 + \frac{1}{\sqrt{1+\gamma\lambda}}\right) + \frac{\gamma}{2}\cdot\frac{1}{(\sqrt{1+\gamma\lambda})^3}\right] \tag{32}$$

by first making the substitution:

$$\lambda = 1 - \mu^2$$

By equating this to zero we obtain the abscissae of the points of inflection. One such value directly evident from equation 32 is

$$\mu = 0$$

This gives the point of inflection at the midpoint of titration which is always present independent of the magnitude of κ. Furthermore, by equating the term in brackets to zero, we obtain

$$q^3 + \frac{3}{2} q^2 - \tfrac{1}{2} = 0$$

where

$$q = \sqrt{1 + \gamma\lambda} \tag{33}$$

This equation of third degree in q has three real roots, of which two are alike and equal to -1, and the third is $\frac{1}{2}$. Only the latter root gives a result of physical significance. Retracing the definition of q back to the original variables (14, 33) we find that when q is $\frac{1}{2}$,

$$\mu = \pm \frac{1}{2} \sqrt{\frac{16\kappa - 1}{4\kappa - 1}} \tag{34a}$$

or, in terms of k,

$$\mu = \pm \frac{1}{2} \sqrt{\frac{k - 16}{k - 4}} \tag{34b}$$

Only when $k \geqq 16$ is μ real, and then it must lie in the range of μ from $-\frac{1}{2}$ to $+\frac{1}{2}$.

When $k < 16$, no acceptable solutions can be obtained. For, when $k < 16$ but >4, μ is imaginary; and when $k < 4$, μ will always lie outside the range from -1 to $+1$. In neither of these cases have the solutions any physical significance. Furthermore, when the root $q = -1$ is chosen, the corresponding values of μ are found to be ± 1. But at these values of μ the potential is $\pm \infty$, and at values of μ greater than 1 or less than -1, the potential assumes complex values. So the vanishing of the second derivative cannot have the significance of a point of inflection.

The physically significant results can be summarized as follows: There is always one point of inflection at $\mu = 0$. Only when $k > 16$ are there two more lateral points of inflection, symmetrically situated at either side of the midpoint. As k increases from the value 16 the abscissae of these two lateral points of inflection move symmetrically from zero in a positive and negative sense and at large values of k approach the abscissae $\pm\frac{1}{2}$.

The fact that the threshold value of k is 16 was not recognized until recently (17). Both Elema and writers erroneously believed it to be 4, not having executed the necessary calculations and being misguided by the fact that the value 4 had been found to have another singular significance as discussed above (see equations 18).

Elementary and composite constants

All these considerations hold for the elementary process of oxidation–reduction as described by equations 8. To extend the theory to real conditions in which ionization phenomena appear we have to adapt the fundamental equations adequately. Equations 9 and 10 need not be changed at all if r means the amount of the R form in all its states of ionization, and similarly for s and t. Only equation 11 has to be modified. This equation holds for varying acidity only if we understand by r, s, and t the elementary forms B^{--}, B^-, and B. At any given pH the elementary B is a constant fraction of the total amount of B including such molecules also as BH^+, BH_2^{++}, etc., and the same holds for B^- and for B^{--}. Suppose then that as in equations 9 and 10 we allow r, s, and t to mean the total amounts of these several forms in all their states of ionization. The effect would be that k would be a constant only for a given pH and would vary with pH. Such a k is not a constant depending only on the chemical nature of the substance but is a parameter depending also on the hydrogen-ion concentration. The constant k or κ, such as is defined in equation 11, may be designated as the elementary constant, whereas this new parameter may be termed the effective constant. Experimentally only effective constants have been considered, so from now on we shall use the letters k and κ for effective constants. Then all our above considerations and formulas hold true. For a given oxidation–reduction system k may vary to an enormous extent with the pH depending on the ionization constants of each of the substances R, S, and T. The largest constant that has been observed is about 50 (9) (for oxyphenazine in very acid solution). The smallest that could be measured with satisfactory accuracy is about 0.05 (in lactoflavin at pH 4.6) (19). Many cases are now known for which in a certain pH range $k > 1$ and in another pH range $k < 1$. In general the curve for E_m as plotted against pH will not be parallel to those for E_1 or E_2. If k is unity, E_m, E_1, and E_2 coincide, and at this pH there is a crossing point of the three normal potential curves. But E_m for any one pH will always lie halfway between E_1 and E_2. When k becomes very small, say $<1/20$, the potentiometric method is no longer suitable for its precise determination. Practical methods for estimating k will be discussed later. Whenever $k < 1/20$, an error of, say, 1/10 of a millivolt in the index potential, or an exceedingly small error in the determination of the midpoint-tangent would involve a great error in the evaluation of k. In such a case it can only be recognized that k is very small. In fact, by this method all values of $k < 0.05$ are undistinguishable from $k = 0$. This situation prevails in many dyestuffs in ordinary pH ranges, and this is one of the reasons why the existence of a small amount of the intermediate radical has been overlooked until recently. Yet it might be foolish to disregard a constant <0.05 just because the present potentiometric methods are unsuitable for its precise determination. It is much more likely that the difference in the magnitude of k in various systems is only a quantitative one and that the really simultaneous addition of two electrons in one step is not the common process in organic reduction, but an extreme limiting case which perhaps is never strictly realized. This is just about the opposite to what organic chemists have believed so far. We have to consider that, e.g., even for $k = 10^{-4}$, as much as $\frac{1}{2}$ per cent of the substance would be in the radical form at the half-reduced state. This follows from equation 49.

The location of E_1 and E_2 on the titration curve

On considering a titration curve it will be important to know at which point the potential equals E_m, at which point it equals E_1, and at which point it equals E_2. E_m is always the potential at 50 per cent oxidation, as is apparent from equation 25 on setting μ equal to zero, that is, $E_m = E_{\mu=0}$. Only when k is extremely large (>1000, say) is it easy to see that $E_1 = E_{\mu=-\frac{1}{2}}$ and $E_2 = E_{\mu=\frac{1}{2}}$. Generally, the location of E_1 and E_2 can be arrived at in the following way.

In order to locate E_1 we have to find that value of μ where $E = E_1$, that is to say, where r/a equals s/a. Equating the expression for r/a of equation 15 to that of s/a in equation 16, we obtain:

$$\mu_{E_1} = -\frac{k-1}{2k+1} \tag{35a}$$

In the same way, by equating equations 16 and 17, we obtain:

$$\mu_{E_2} = +\frac{k-1}{2k+1} \tag{35b}$$

This shows that for very large k we approach the limit:

$$\mu_{E_1} = -\tfrac{1}{2}$$

$$\mu_{E_2} = +\tfrac{1}{2}$$

For $k = 1$ we have

$$\mu_{E_1} = \mu_{E_2} = 0$$

In the latter case all three normal potentials coincide in the midpoint of titration.

For any $k > 1$, μ_{E_1} (that value of μ where $E = E_1$) is negative, and μ_{E_2} is positive. This may be designated as the natural order of the normal potentials. For any $k < 1$, μ_{E_1} is positive, and μ_{E_2} negative. This may be said to be the inversed order of the normal potentials. For k approaching 0, this inversion is so complete that the normal potential of the higher step lies, in the limit, at the zero point of titration, i.e., at the point where only the reduced form exists, and the normal potential of the lower step at the endpoint of titration. In this limiting case the radical is incapable of existence and we have the completely overlapping bivalent oxidation which was formerly taken as the only possible case of bivalent oxidation in organic compounds.

V. THE PROBLEM OF DIMERIZATION

The entire analysis has so far been restricted to the case where the only molecular species intermediate between the oxidized form T and the reduced form R is the semiquinone radical S. This is the case which has been most thoroughly explored experimentally.

It has been pointed out earlier in this review that a semiquinone radical may dimerize to form a compound of double its molecular weight. Such a reaction may be represented by the equation:

$$2\mathrm{S} \rightleftharpoons \mathrm{D} \tag{36}$$

The same dimerization product could also be formed by combination of one molecule of the oxidized with one molecule of the reduced form of the given substance:

$$\mathrm{R} + \mathrm{T} \rightleftharpoons \mathrm{D} \tag{37}$$

The dimeric molecule D is at the same oxidation level as the semiquinone molecule S. It will be shown in the subsequent analysis that the effect of the existence of such a dimeric molecule in equilibrium with the other molecules, R, S, and T, is to increase the slope of the titration curve at the midpoint. This is similar to the effect produced by semiquinone formation, as is evident from figure 1. Therefore methods must be found to decide in the case of a given titration curve with a midpoint slope greater than RT/F (equation 29a), whether this larger slope is due to semiquinone formation, dimerization, or a combination of both. General equations may be set up, analogous to equations 9, 10, and 11, to cover cases of both semiquinone formation and dimerization.

At any point of the titration curve we have

$$r + s + 2d + t = a \tag{38}$$

$$s + 2d + 2t = x \tag{39}$$

where x is the equivalent amount of the oxidizing agent. As before:

$$\frac{s^2}{rt} = k \tag{11}$$

In addition there are two equations for the equilibria 36 and 37.

$$\frac{vd}{s^2} = G \qquad \text{(``constant of dimerization'')} \tag{40}$$

$$\frac{vd}{rt} = Q \qquad \text{(constant of ``dimeric formation'')} \tag{41}$$

where v is the volume of solution containing the total amount of substance, a. The last three equations are of course not independent, the three equilibrium constants being related by the equation:

$$k \cdot G = Q \tag{42}$$

The general solution of this set of equations in terms of r, s, d, and t is, however, so complicated as to be quite impractical. But there is another special case which has been realized in practice and which can be subjected to analysis. This is the case where the semiquinone radical is completely or almost completely dimerized. One example (15) is phenanthrenequinonesulfonate in acid solution. In this case during a titration there are only three molecular species which need to be considered in equilibrium, that is R, D, and T. Neglecting s we have from equations 38, 39, and 41:

$$r + 2d + t = a \tag{43}$$

$$2d + 2t = x \tag{44}$$

$$vd = Qrt \tag{41}$$

This set of equations is analogous to the set 9, 10, and 11, which formed the basis of the analysis of the case in which semiquinone formation occurs but dimerization is negligible. There is an important difference in the two sets of equations. It is this difference which must be responsible for the difference in the two titration curves derived from the two sets of equations. Equation 11 is homogeneous in the three variables r, s, and t, but equation 41 is not homogeneous in r, d, and t. It is thus not possible to set up the equation for the potential in terms of variables analogous to ρ and τ as was done in equations 22 to 25. However, solving equations 43, 44, and 41 for r and t and substituting these values in equation 19a, it is found that:

$$E = E_m + \frac{RT}{2F} \ln \frac{L\mu - 1 + \sqrt{L(L\mu^2 + 2) + 1}}{-L\mu - 1 + \sqrt{L(L\mu^2 + 2) + 1}} \tag{45}$$

in which

$$L = \frac{Qa}{v}$$

In figure 2 are plotted a series of curves analogous to those of figure 1. For large values of L step formation occurs as in the case of semiquinone formation with large k. The important difference between the two cases

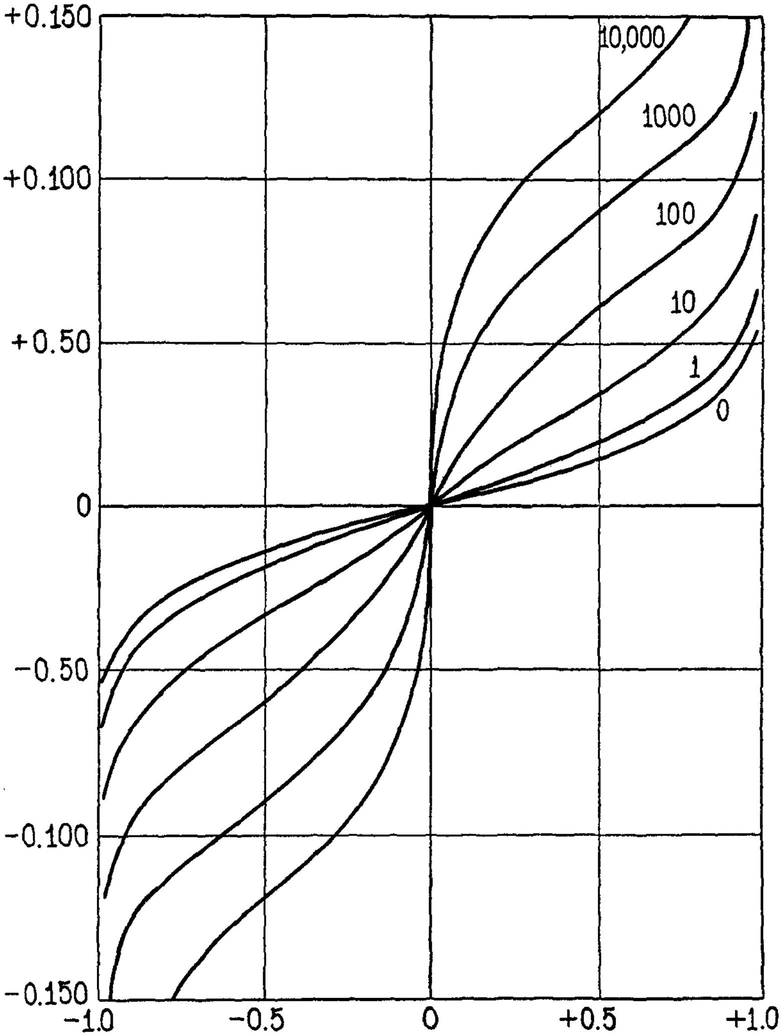


Fig. 2. Two-step titration curves involving formation of the dimeric intermediate compound alone. Abscissa and ordinates as in figure 1. Each curve holds for the value of L as indicated. $L = Q \times a/v$, the product of the dimeric formation constant and the molar concentration of the substance. Theoretically the two lateral points of inflection appear when $L > 4$. The figure shows that even for $L = 10$ these points of inflection are scarcely noticeable.

is that while the semiquinone curves are independent of concentration the dimer curves vary with the concentration of the substance titrated. This is evident since the particular curve obtained depends on

$$L = \frac{Qa}{v}$$

which varies directly with the concentration.

There is another difference between the semiquinone curves of figure 1 and the dimer curves of figure 2. It was shown that the abscissae of the lateral points of inflection of the semiquinone curves for large values approached the values $\mu = \pm 0.5$. In the case of the dimer curves (45) it can be shown by similar methods that when L is very large the abscissae of the lateral points of inflection approach $\mu = \pm\sqrt{2(3 + 2\sqrt{2})} = \pm 0.586$. Thus while the semiquinone curves for high values of k can be broken into two parts, each of which is symmetrical around its own midpoint, the dimer curves for high values of L separate into two parts each of which is an unsymmetrical curve. The two lateral points of inflection appear only when $L > 4$.

However, it must be emphasized that although these differences between the two families of curves can be deduced from an examination of the potential equations, if one had only a single titration curve at hand it would be difficult or practically impossible to decide whether it belonged to the semiquinone family or the dimer family. The more general case in which both semiquinone and dimer formation occur would of course lie in between the two special cases discussed.

VI. THE ANALYSIS OF EXPERIMENTAL CURVES, AND THE DETERMINATION OF CONSTANTS

A single titration curve can be interpreted only if the midpoint slope is accurately RT/F (equation 29a). In this case it can be said that neither semiquinone nor dimer formation occurs to an extent greater than about 1 or 2 per cent.

In practice there is an easier criterion than the midpoint slope, namely, the index potential, E_i, which is defined as the potential difference between 50 per cent oxidation and 25 per cent (or 75 per cent) oxidation, or the difference of the potential at $\mu = 0$ and $\mu = \pm\frac{1}{2}$;

$$E_i = E_{50\%} - E_{25\%} = E_{75\%} - E_{50\%}$$

or

$$E_i = E_{\mu=0} - E_{\mu=-\frac{1}{2}} = E_{\mu=+\frac{1}{2}} - E_{\mu=0}$$

In the limiting case, with no intermediate compound formed, $E_i = 0.0143$ volt at 30°C., for the ratio of r to t equals 3 at this point, and so

$$E_i = \frac{RT}{2F} \ln \frac{3}{1} = 0.0143 \text{ volt at } 30°\text{C.}$$

If an index potential greater than 14.3 millivolts is found, it must first be determined whether this is due to semiquinone formation, dimer formation, or both. From the analysis of the preceding section it is clear that the simplest test is to run a series of titrations at different total concentrations, a/v, of the substance titrated. If these curves are all identical when E is plotted against μ, then the only intermediate form is a semiquinone radical

Another test based on the same principle has been called the "dilution test" (11, 14). We designate the molar amount (not the concentration) of the totally oxidized form as t, that of the reduced form as r, and that of the intermediate, if it is a bimolecular meriquinone, as d. The equivalent of the equations 9, 10, and 11 is equations 43, 44, and 41. Solving for d we obtain:

$$d = \tfrac{1}{2}\left(a + \frac{v}{Q} \pm \sqrt{\left(a + \frac{v}{Q}\right)^2 + x(x - 2a)}\right)$$

So d depends on the volume v. If the color of D differs sufficiently from that of R and S, one can observe whether or not the maximum amount of D, as it exists at 50 per cent oxidation when $x = a$, will decrease with increasing volume of the solvent. If this is not the case, the intermediate compound is not a bimolecular meriquinone but a semiquinone radical. The variation of d with v may, however, sometimes be small and lie within the limits of error. This depends on the magnitude of v/Q. If this is $<<a$, the above equation approaches the form

$$d = \frac{x}{2} \quad \text{or } d = \tfrac{1}{2}(2a - x)$$

or, at 50 per cent oxidation when $x = a$, we obtain

$$d = \frac{a}{2}$$

and d is independent of the volume. If, however, $v/Q >>a$, the following equation is approximately fulfilled:

$$d = \frac{x(2a - x)}{4v}$$

and d will be inversely proportional to the volume. This is the condition best suited for the test. The amount of the unimolecular radical, s, would not depend on the volume at all, as shown by equation 16. It must be remembered that Q is what was previously called an effective constant and so in general varies with pH. So we have to choose a pH such that v/Q is very large in comparison with a. This is accomplished by choosing such a pH that the total amount of the intermediate compound at 50 per cent oxidation is so small as just to be noticeable. Since the color of the intermediate form is in most cases much more intense than that of the R or T form, it is easy to detect even a very small amount of the intermediate form in a mixture with a large excess of the others. So, when at a properly chosen pH the dilution test shows that the total amount (not concentration!) of the intermediate substance is independent of the volume of the solvent, it is sufficient evidence that we have to deal with an S-form, not with a D-form.

This dilution test is very sensitive. Even if a precise colorimetry may be difficult, it is always easy to decide whether on increasing the volume tenfold the total amounts of the intermediate form are approximately unchanged, or tenfold decreased.

Thus it is possible either by running a series of titrations at different concentrations or by the application of the dilution test to decide whether the intermediate form consists only of a semiquinone radical. If this is the case then from the characteristics of the curve the semiquinone formation constant can be calculated. There are several ways to evaluate k from the experimental titration curve.

One method is based on equation 30 or equation 31. From the slope of the midpoint of titration k can be evaluated. This method is of value only when k is not too large and the slope not too steep. In the latter case the limits of error are rather great. So it should be used when the curves have no lateral inflection points at all, or at least when the jump in the middle part of the curve is not too great.

Another method is based on the determination of the index potential E_i. To express E_i as a function of k or κ, use is made of equation 25. By successively substituting the values $\frac{1}{2}$ and 0 for μ and finding the difference between the two resulting values of E we have:

$$E_i = \frac{RT}{2F}\left[\ln 3 + \ln \frac{\sqrt{1 + 12\kappa} + 1}{\sqrt{1 + 12\kappa} - 1}\right]$$

Let $\alpha = E_iF/RT$ and solve in terms of k instead of κ. Then:

$$k = (e^{\alpha} - 3e^{-\alpha})^2$$

or, at 30°C. and transferring to the base 10,

$$k = \left(10^{\frac{E_i}{0.06}} - \frac{3}{10^{\frac{E_i}{0.06}}}\right)^2 \tag{46}$$

Values of this function are tabulated in table 1 of the review (9). When E_i is large, say >0.2 volt, equation 46 reduces to

$$\log k = \frac{E_i}{0.06}$$

The index potential method of determining k does not take full advantage of the titration curve, since only two points are used. To obtain a more accurate estimate of k a whole series of points of the experimental curve can be used to calculate the constant. In any bivalent titration curve, regardless of the form of the intermediate, we have the relation:

$$\Delta E = \frac{RT}{2F} \ln \frac{t}{r} = 0.03 \log \frac{t}{r} \qquad \text{(at 30°C.)}$$

where ΔE is the difference in potential at the midpoint of titration and at that point whose abscissa is x (which varies during the titration from 0 to 2a). Further, by setting $t/r = N$ this equation can be rewritten in the form

$$\frac{t}{r} = N = 10^{\frac{\Delta E}{0.03}} \tag{47}$$

Using this equation, together with the two equations,

$$r + s + t = a$$

$$s + 2t = x$$

we can solve for r, s, and t, giving

$$\begin{aligned} r &= \frac{a - x}{1 - N} \\ s &= \frac{x(1 + N) - 2Na}{1 - N} \\ t &= \frac{N(a - x)}{1 - N} \end{aligned} \tag{48}$$

From these values of r, s, and t in terms of the experimental variables of a titration curve it is possible to calculate k from equation 11 for a whole series of points of the curve.

It is an important problem to calculate the maximum amount of s which can arise during the titration. It is easy to see that the maximum amount of the S-form always exists at 50 per cent of the oxidation, when $\mu = 0$. This statement scarcely needs a proof, but it can be proved by differentiation of equation 16 with respect to μ. It is often of great importance to calculate this maximum amount, which of course depends on the value of k. Now, when $\mu = 0$,

$$r = t = \tfrac{1}{2}(a - s)$$

Then equation 11 appears in the form

$$\frac{(a - s)^2}{4s^2} = \kappa$$

which gives

$$\left(\frac{s}{a}\right)_{\text{max.}} = \frac{1}{1 + 2\sqrt{\kappa}} = \frac{\sqrt{k}}{2 + \sqrt{k}} \tag{49}$$

If the tests outlined above indicate the existence of a dimeric compound, there are still two cases to distinguish. In the first case, case A, the dimeric form exists in measurable amounts but the amount of semiquinone is negligible and in the second case, case B, both semiquinone and dimer exist in measurable amounts.

Case A. In this case dimerization occurs but no appreciable semiquinone formation. The titration curves belong to the family of figure 2. Since s is very small, k cannot be calculated but can only be said to be less than 0.05, say. To show that a given curve belongs to this family it is necessary to run a series of curves at progressively higher dilutions. This is equivalent to decreasing L in the curves of figure 2. The limiting curve at sufficiently high dilution will be the usual curve for a two-electron change with no intermediate step and will have an index potential of 14.3 millivolts. Within a range of concentration which is low enough the form of this curve will not depend on concentration.

The dimer formation constant Q (equation 41) can be calculated from those experimental curves run at concentrations high enough so dimerization occurs. From the set of equations:

$$r + 2d + t = a$$

$$2d + 2t = x$$

$$\frac{t}{r} = N = 10^{\frac{\Delta E}{0.03}}$$

are found the values:

$$\begin{aligned} r &= \frac{a - x}{1 - N} \\ d &= \frac{x(1 + N) - 2Na}{2(1 - N)} \\ t &= \frac{N(a - x)}{1 - N} \end{aligned} \tag{50}$$

From these Q can be calculated.

Case B. The last case to consider is the most general of all. It will be presented here not so much in accordance with one paper (15), but in the form shown in another paper (19), which is both easier and more general. During a titration both semiquinone and dimer are formed in appreciable amounts. In this case the shape of the curve is a composite of those of figures 1 and 2. The shape of the curve varies with concentration, but as curves are run at higher and higher dilution a limiting curve will be approached at which the dimerization becomes negligible and only the effect of semiquinone formation remains. At a dilution that is high enough the shape of the curve may be independent of concentration over a considerable range. In this range the curve has been designated as the "limiting curve for infinite dilution" and is one of the family of figure 1. This situation has already been experimentally realized in two cases (14, 19) and on further investigation may turn out to be quite common. In this case the constant k can be calculated from the limiting curve by the methods described for the simple semiquinone curves. With this constant determined it becomes possible to use the curves at higher concentration, where semiquinone and dimer are both formed, for the calculation of both Q and G. At these higher concentrations there are in equilibrium during a titration four molecular forms, R, S, D, and T. The amounts present at any point during a titration can be calculated from the equations:

$$r + s + 2d + t = a$$

$$s + 2d + 2t = x$$

$$\frac{t}{r} = N = 10^{\frac{\Delta E}{0.03}}$$

$$\frac{s^2}{rt} = k$$

From these it is found:

$$\left.\begin{aligned} r &= \frac{a - x}{1 - N} \\ s &= \frac{(a - x)\sqrt{kN}}{1 - N} \\ d &= \frac{x(1 + N) - 2aN - (a - x)\sqrt{kN}}{2(1 - N)} \\ t &= \frac{N(a - x)}{1 - N} \end{aligned}\right\} \qquad (51)$$

From these values both Q and G, as defined in equations 40 and 41, can be calculated from experimental curves and should be found constant both for different points of a particular curve and for a set of curves at different concentrations.

A glance at the expressions for r and t in the solutions (equations 48, 50, and 51) shows that in each case they have the same form. Since the potential can always be expressed by equation 19a it might appear that in all cases considered the potential curve would have the same shape. This is only so in appearance, however, since the expressions for r and t contain N, which from equation 47 is derived from the potential curve and carries in itself the difference in shapes of the curves of the three types discussed.

It may be emphasized in conclusion that we have always dealt in this review with systems in homogeneous solution. The decision whether a solid, crystalline quinhydrone is a radical, a dimer, or a compound of R and T in a ratio different from 1:1 requires entirely different methods. The very concept of molecular size, involving the decision between the assumption of a radical or a polymer, cannot simply be taken over from the theory of the dissolved state. The molecular size within a crystal is ambiguous. Which elementary unit, repeated periodically in a crystal, should be preferably considered as the molecular unit, can be decided in such a case only by measurement of the paramagnetic susceptibility. Although not the subject of this review, it may be emphasized that the method has been used successfully. In the crystalline state, in a number of cases, the paramagnetic susceptibility was that of a molecule with one magnetically unbalanced electron, in other cases it was smaller. In such a case, we might speak of a partial dimerization. It would, however, be more adequate, for the crystalline state, to speak about a state intermediate between unimolecular and bimolecular units, a resonance between two adjacent molecules, between a free and a combined condition.

VII. TWO-STEP ACIDIC DISSOCIATION

All these formulas, except those concerned with dimerization, can be easily extended to the field of ionization of bivalent acids. The theory of the titration curve for bivalent acids, especially with respect to the points of inflection, has been developed exhaustively by Auerbach and Smolczyk (1) in a very different way. It is, however, important to show that the method used in the present paper can also be extended to this problem in order to show the analogy between the problems of oxidation and of dissociation. It is gratifying to see that the results of that other method agree with what follows.

Consider a solution of a weak acid AH_2 at such a pH that it exists entirely in the form of the secondary ion A^{--}, and suppose that it is titrated with a strong acid. Then the anion will successively attach two protons.

$$\begin{aligned} A^{--} + H^+ &\rightleftharpoons AH^- \\ AH^- + H^+ &\rightleftharpoons AH_2 \end{aligned} \tag{52}$$

Equations 52 are analogous to equations 8. At any point during the titration a pair of equations similar to equations 9 and 10 will hold good.

$$A^{--} + AH^- + AH_2 = a \tag{53}$$

$$AH^- + 2AH_2 = x \tag{54}$$

In this case a is the total amount of the weak acid in all its stages of ionization and x is the amount of strong acid added, in equivalents. To continue the analogy, the ion AH^- may be said to be in equilibrium with the other forms by a kind of "acidic dismutation":

$$2AH^- \rightleftharpoons AH_2 + A^{--}$$

and this equilibrium may be characterized by a constant analogous to the semiquinone formation constant:

$$\frac{[AH^-]^2}{[AH_2][A^{--}]} = k' \tag{55}$$

The more usual treatment of the equilibria in equation 52 is in terms of the two dissociation constants K_1 and K_2 defined by the relations:

$$K_1 = \frac{[H^+][HA^-]}{[HA_2]} \quad \text{and} \quad K_2 = \frac{[H^+][A^{--}]}{[HA^-]} \tag{56}$$

From equations 55 and 56 it is evident that

$$k' = \frac{K_1}{K_2} \tag{57}$$

Thus the three basic equations, 9, 10, and 11, of the semiquinone theory from which all subsequent formulas and relations were deduced are identical in form with a corresponding set, 53, 54 and 55, that could be used to develop the theory of the titration of dibasic acids. The equivalence of the two theories is established by this identity in form of the three basic equations and the relation (57) which shows the "acidic dismutation" constant k' to be the ratio of the classical ionization constants. In particular, it may be pointed out that the potentiometric titration curve of a dibasic acid has no jump in its middle section unless the ratio K_1/K_2 is greater than 16, a result which was obtained in a different way by Auerbach and Smolczyk (1) in 1924.

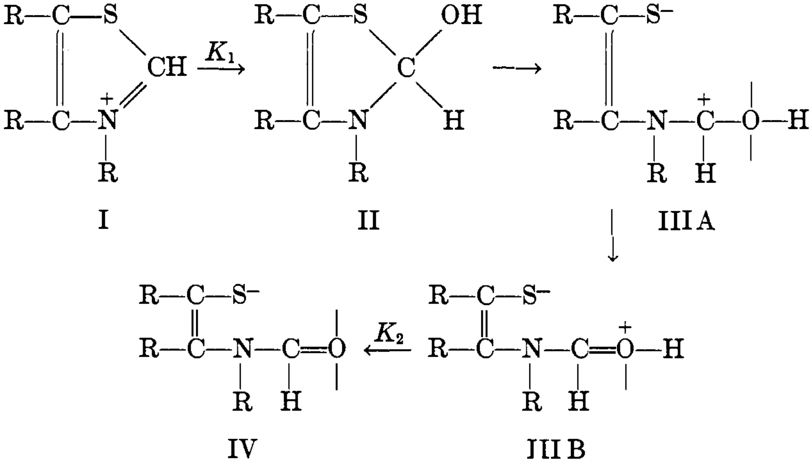
But although the physical pictures as described by equations 8 and 52 are so similar and the mathematical deductions from these equilibria are identical there nevertheless appear to be fundamental differences between two-step oxidation and two-step ionization. The semiquinone formation constant of the two-step oxidation theory may assume any positive value between zero and infinity. The corresponding constant of the ionization theory given in equations 55 or 57 appears, however, practically never to be less than about 5.

To understand this difference we must examine in more detail the effects of electron addition to a molecule as represented by equation 8 and of proton addition as represented by equation 52. Suppose we have the anion of a dibasic acid or, what is even more general, suppose we have a molecule which can accept two protons; the acceptance of one proton may be represented by equations such as:

$$\begin{gathered} A^{--} + H^+ \rightarrow AH^- \\ B^- + H^+ \rightarrow BH \\ C + H^+ \rightarrow CH^+ \end{gathered} \tag{58}$$

The acceptance of this proton may bring about a more or less profound rearrangement of the electrons of the molecule accepting the proton. Usually it does not. For example, if the doubly charged succinate ion accepts one proton it is probable that this does not greatly affect the electronic arrangement of the second carboxylate group. Actually, practically all studies of titration curves of dibasic acids have been of this type. In such cases each acid group functions independently and the only influence of one on the other is due to electrostatic forces. If the groups are widely separated in the molecule this electrostatic effect becomes small. In the further case that both acid groups are identical, as in the cases of dicarboxylic acids or diammonium salts, the statistical theory can be applied and it appears that K_1/K_2 approaches 4 as a lower limit, as shown by Wegscheider (23; see also 2). Such a limit is realized in practice in the titration of the two phenolic groups of phenolphthalein, which Thiel and Diehl (22) find to differ by approximately half a pH unit. In the case of molecules with such independently functioning acid groups it is of course necessary that K_1 be greater than K_2, merely because K_1 is defined as the greater constant.

It is, however, imaginable that the acceptance of a proton by a molecule such as shown in equation 58 may bring about a radical rearrangement of the electronic structure, resulting in the formation of a new molecule which could actually attach a proton more readily than the first molecule. In such a case K_2 would be greater than K_1 and k' of equation 57 would be less than 1. An example illustrating this already occurs in the literature, but now that the principle is realized additional ones may be discovered. The chemistry of this curious case was first described by Mills, Clark, and Aeschlimann (20) and later shown to be generally true of thiazolium salts (3). A titration curve showing the lack of formation of any intermediate step of ionization was given by Williams and Ruehle (24) for 4-methylthiazolethiode. We may interpret this type of ionization as follows:



III is a zwitter ion with a negative charge at the sulfur atom and a positive charge either at the carbon atom or at the oxygen atom, as at III A or III B. In either case III is a very strong acid and at the pH prevailing at its formation is entirely converted to IV. Obviously K_2 is very much greater than K_1.

Turning now to the case of two-step reduction, it appears clear why values of k, the semiquinone-formation constant of equation 11 and the analogue of equation 55, may readily take on values less than unity. The acceptance by a molecule of a single electron necessarily brings about an electronic rearrangement, and because of the tendency of electrons to pair the resulting molecule may take up a second electron more readily. In such cases k is less than 1. That this is not always the case is clear, however, from the large number of cases now known where the semiquinone-formation constant is much greater than 1.

There is another respect in which the reduction reactions of equation 8 differ in practice from the ionization reactions of equation 52. This may be traced to what was defined early in this review as the elementary reduction process. Actually, as was subsequently pointed out, elementary reduction processes are generally complicated by simultaneous ionization processes, so a distinction had to be made between the elementary semiquinone-formation constant and the effective constant which is usually measured.

This circumstance can very easily cause the practical dismutation constant to become much smaller than 1, and even undistinguishable from 0, without resorting at all to the effect of electronic rearrangement mentioned before. In the field of ionization theory, however, the acceptance of protons is the analogue of the elementary reduction process. This is usually not complicated by any gain or loss of electrons. The reason for this is clear. Both oxidation–reduction and acid–base titrations are usually carried out in aqueous solution or in solvents such as acetic acid or alcohol which are similar in that they can act as acceptors or donors of protons. Solvents which can act as acceptors or donors of electrons are never used. So while oxidation–reduction titrations are complicated by acid–base equilibria, acid–base titrations are not complicated by oxidation–reduction equilibria.

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