BEHAVIOR OF INDICATORS AND OTHER WEAK BASES IN ACETIC ACID SOLUTIONS

BY

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To Charlie Brown

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I. INTRODUCTION

The quantitative measurement of the chemical property called basicity has engaged considerable attention for many decades. Most of the earlier research into the strengths of bases was conducted on aqueous solutions of the compounds. This emphasis on aqueous equilibria was natural and justified, in view of the extreme importance of water as a solvent in biological, geological, and man-made systems.

Recognition that basicity is not dependent upon reaction with water came early, but a quantitative measure of base strength required a more general theory of basicity than that provided by the water theory. The familiar definition of a base as a substance capable of accepting a proton, or, equivalently, as one which can donate an electron pair to an acid, furnishes the requisite foundation for a quantitative formulation of basicity. Although basicity is thus defined independently of a solvent, its quantitative evaluation will depend upon the presence of, and will be strongly affected by the nature of, a solvent.

An important limitation of water as a solvent in which to measure the strengths of bases is its own significant basicity. Clearly, any compound which is of the same base strength as water will appear to have no basic properties in this solvent, and the measurement of basicities which are only slightly greater than that of water is experimentally difficult. The study of such weakly basic compounds is therefore facilitated by the use of solvents which themselves are not noticeably basic. Two classes of such solvents are available: the acidic solvents, of which the carboxylic acids are useful representatives, and the "inert" solvents, for example the hydrocarbons. The study of basicity in nonaqueous solvents is motivated partly by the difficulties encountered in its study in aqueous solution, and partly by the increasing interest in the organic solvents per se, this interest being both of a theoretical and a practical nature.

The research reported in this thesis had as its aim the development of methods for the convenient and accurate determination of the relative strengths of very weak bases in nonaqueous solvents. Organic bases of varying strengths were studied, and one part of this program consisted of an elucidation of the basicities of several types of compounds in order to establish a useful correlation of structural type with base strength, although realization of such an extensive goal cannot come within the scope of the present effort. Because of its increasing analytical and preparative importance as a solvent, as well as for its desirable properties for the purpose at hand, acetic acid was chosen for the initial developmental work. Any quantitative measure of basicity of a compound must ultimately be founded upon the extent of reaction between the compound in question and a reference acid. The solvent, if acidic in nature, may be chosen as this reference acid; this is the common practice when dealing with aqueous solutions. Alternatively another acid may be added to the system to act as a reference; frequently an indicator acid is selected for this purpose, principally for the convenience it affords in measuring the extent of reaction. In the present work the reference acid is perchloric acid. The measure of basicity is then the equilibrium constant describing the reaction between perchloric acid and the base to form a perchlorate salt. This constant (the salt formation constant) is determined through the expedient of adding an indicator base to the system and observing the effect which the unknown base has upon the color of the indicator in the presence of perchloric acid.

After a brief presentation of the theory of ionic association, the theoretical section of this thesis will describe acid-base reactions in acetic acid, including discussion of the nature of indicator color changes in this solvent. The salt formation constant, already alluded to, will be defined more precisely and its significance as a basicity measure will be compared with other quantities. Three sections (III, IV, VI) will deal with the experimental evaluation of salt formation constants; the principles of the indicator measurements will be presented and the experimental techniques outlined. The results of these experiments on very weakly basic compounds, such as amides, are discussed in relation to the structures of the bases. The effect of changing the nature of the solvent upon the value of the salt formation constant has been studied, and is described in part V. In this case the acetic acid system was altered by the addition of benzene; this study represents an application of the methods developed in this work.

It is to be expected that research in such a relatively undeveloped field as the study of acid-base reactions in nonaqueous solvents should suggest many additional topics for investigation. A few of these problems are briefly described in section VI.

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II. THEORY OF ACID-BASE REACTIONS IN ACETIC ACID

A. Ionic Association

It is an experimental result that ionic equilibria in acetic acid are not completely explicable in terms of the concepts familiar in aqueous systems. Most of the difference in behavior is ascribable to incomplete dissociation of electrolyte species; consequently an introduction to current ideas concerning the process of ionic association is pertinent.

The Ion-pair. It has become commonplace to regard a solution of a strong electrolyte, for example a salt, as composed of the completely dissociated ions which comprise the salt in the crystalline state. The success of the Debye-Huckel theory of interionic attraction, particularly in dilute aqueous solution, provides a strong basis for such a view. The assumption of complete dissociation is not a valid one in general, however. The concept of the ion-pair was introduced in 1926 by Bjerrum to account for certain behavior of electrolyte solutions in systems other than the dilute aqueous solution (1). Bjerrum's definition of the ion-pair arises from the mathematical treatment of the assumed model.

A strong electrolyte AB is supposed to exist in equilibrium with its constituent ions; the equilibrium is governed by the mass action law.

$$AB \xrightleftharpoons{K} A^+ + B^-$$

The model assumed is a continuum characterized by a macroscopic dielectric constant D; the individual ions are considered to be charged spheres of finite radii. The equation obtained by Bjerrum for the dissociation constant, using a statistical treatment, is

$$1/K = (4\pi N/1000)\ (e^2/DkT)^3 Q(b) \qquad \text{(II-1)}$$

$$b = e^2/aDkT$$

In this expression N is Avogadro's number, k is the Boltzmann constant, T the absolute temperature, and e the electronic charge. The symbol a represents the "distance of closest approach" of the two ions, sometimes referred to as the contact distance. This quantity may best be regarded as an adjustable parameter.

The function Q(b) has been tabulated by Bjerrum (1) for b = 1-15, by Guggenheim (2) for b = 2-12, and by Fuoss and Kraus (3) for b = 15-80.

The evaluation of Q(b) leads to an arbitrary limit of $r = e^2/2DkT = ab/2$ as the dimension within which two ions are considered to exist as an ion-pair (4). This has the result that an ion-pair is defined even though the ions may not be in contact. Another mathematical result of the Q(b) function is that, for a given a value, a critical dielectric constant exists above which association is impossible (5). Despite these possible artificialities, the Bjerrum equation is useful in correlating the dissociation constant with the dielectric constant of the medium, and is capable of expressing log K of a salt to within one unit, without regard for the solvent (6). The relation between K and D is seen by expressing Q(b) in terms of a series approximation. Then Equation II-1 shows that 1/K changes in the same way that exp(b)/b does, and Equation II-1 takes the form

$$\log(1/K) = A/D + \log D + B \qquad \text{(II-3)}$$

The dissociation constant is very sensitive to dielectric constant, decreasing in magnitude as D decreases; such behavior is of course to be expected.

A simplified thermodynamic approach to ion-pair dissociation has been made by Denison and Ramsey (7). These authors consider the process

$$\begin{array}{lcl}\text{Ion-pair at contact} & \rightleftharpoons & \text{Separated ions} \\ (r = a)\text{ in medium} & & (r \gg a)\text{ in medium}\end{array}$$

That is, the ions are postulated to exist either as contact ion-pairs or as free ions at great distances from each other (great enough so that Coulomb forces become negligible). The free energy change for this process is

$$\Delta F^{\circ} = Ne^2/aD \qquad \text{(II-4)}$$

therefore

$$\ln(1/K) = e^2/aDkT \qquad \text{(II-5)}$$

so that $1/K = \exp(b)$. This equation predicts that log K is linear with 1/D, a relationship which is sometimes found to hold (7). A result of Equation II-5 is the assignment of the term ion-pair only to ions which are in contact. Equation II-5 also permits the possibility of association at any dielectric constant value, which is probably more realistic than the result imposed by the Bjerrum treatment (8).

An equation has been derived by Gilkerson based upon the free volumes available to the ions and the ion-pair (9). The contact distance a is considered a constant in this treatment, and two other quantities, which may be related to specific solvent effects but which function as adjustable parameters, are incorporated.

Ion-pair formation is noticeable in the intermediate ranges of dielectric constant (about 30-50) and becomes extensive in solvents of lower dielectric constant (5). The dissociation constants of substituted phenyltrimethylammonium perchlorates in ethylene chloride (D = 10.23) are representative of the values to be expected: these are of the order 10^{-5} (concentrations in equivalents per liter) (7).

Ion-pairs may be pictured in two forms of existence: the "intimate" ion-pair is one in which the two ions are in contact, while the non-intimate ion-pair has interposed between the ions at least one solvent molecule. This picture seems to fit the Bjerrum model more closely than it does the Denison-Ramsey theory; however, the contact distance a should thus be dependent upon the solvent, a dependence which is sometimes observed but which is not predicted by the Bjerrum theory. (Because of the strongly acidic nature of acetic acid, in this solvent the non-intimate type of ion-pairing would be expected to occur.)

Higher Ionic Aggregates. Most of our knowledge of electrolyte solutions is based upon conductance measurements; the ion-pair dissociation constant is usually evaluated in this way. Conductivity studies on salt solutions of very low dielectric constant have revealed behavior which is not adequately rationalized on the basis of ion-pair formation. To account for the experimental evidence (which consists of a minimum in the conductance-concentration curve) the formation of triple-ions has been postulated (10). A triple-ion results from the association of an ion-pair and a free ion, and in the simplest case of a 1:1 electrolyte two types are possible:

$$(ABA)^{+} \underset{}{\overset{k_1}{\rightleftharpoons}} A^{+} + AB$$

$$(BAB)^{-} \underset{}{\overset{k_2}{\rightleftharpoons}} B^{-} + AB$$

The equilibria are characterized by the dissociation constants k_1 and k_2, and lack of information concerning the factors governing the relative importance of the two cases (ion size, extent of solvation) suggests that k_1 and k_2 be taken equal. Using an approach similar to that employed in deriving the Bjerrum equation, Fuoss and Kraus obtained an expression for the triple-ion equilibrium.

$$1/k = (2\pi Na^3/1000)I(b) \qquad \text{(II-6)}$$

The quantity b is given by Equation II-2. Values of I(b) have been tabulated. This equation accounts satisfactorily for the conductance behavior of the salt tetraisoamylammonium nitrate in dioxane-water mixtures, in the dielectric constant range 2.38 to 5.84. The constant k varies from approximately 10^{-5} to 10^{-2} in this range (10).

In addition to ion-pairs and triple-ions, it may be expected that ionic aggregates containing even more ions may be stable in solutions of very low dielectric constant, particularly in concentrated solutions (11). Cryoscopic data have shown the existence of such aggregates; in some cases as many as 30-40 molecules of salt are believed to be involved (12).

It seems reasonable that, in solvents of extremely small dielectric constant, those ionic aggregates will preferentially exist which contain even numbers of ions (for a 1:1 electrolyte), since these aggregates do not carry a net charge.

B. Acid-Base Equilibria in Acetic Acid

Ionization and Dissociation. The dielectric constant of acetic acid is 6.195 at 25° C (13). This small value suggests that ionic association may be extensive in this solvent. Successful interpretation of ionic equilibria must take into account incomplete dissociation of electrolytes as well as the strong proton-donor nature (and weak basicity) of acetic acid (14).

It is convenient to separate the ionization and dissociation processes (though this separation may be only a paper-and-pencil operation, in some cases) (14). A strong acid is considered to react with the solvent according to these equations:

$$HA + HAc \rightleftharpoons H_2Ac^+A^- \rightleftharpoons H_2Ac^+ + A^-$$

This may be written conventionally without the solvent species indicated.

$$HA \rightleftharpoons H^+A^- \rightleftharpoons H^+ + A^-$$

The ionization constant K_i^{HA} and dissociation constant K_d^{HA} are defined*

$$K_i^{HA} = (H^+A^-)/(HA) \qquad \text{(II-7a)}$$

$$K_d^{HA} = (H^+)\ (A^-)/(H^+A^-) \qquad \text{(II-7b)}$$

The overall dissociation constant is

$$K_{HA} = (H^+)(A^-)/C_{HA} \qquad \text{(II-7c)}$$

Similar equations are written for bases.

$$B + HA_c \rightleftharpoons BH^+Ac^- \rightleftharpoons BH^+ + Ac^-$$

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* The maximum ionic strengths of the solutions to be considered in this work are of the order 0.001, hence activities in all equilibrium expressions are replaced by concentrations. A quantity in parentheses signifies the molar concentration of the indicated species; the symbol C represents the sum of the concentrations of ionized and unionized substance. E.g., $C_{HA} = (HA) + (H^+A^-)$.

$$K_i^B = (BH^+A\bar{c})/(B) \qquad \text{(II-8a)}$$

$$K_d^B = (BH^+)(A\bar{c})/(BH^+A\bar{c}) \qquad \text{(II-8b)}$$

$$K_B = (BH^+)(A\bar{c})/C_B \qquad \text{(II-8c)}$$

The relation between these constants is given by Equations II-9.

$$K_{HA} = K_i^{HA}\ K_d^{HA}\ /(1 + K_i^{HA}) \qquad \text{(II-9a)}$$

$$K_B = K_i^B\ K_d^B\ /(1 + K_i^B) \qquad \text{(II-9b)}$$

The constants K_{HA} and K_B are experimentally accessible by potentiometric (15) and conductometric (16) measurements. These constants are of the expected orders of magnitude. The values of pK_{HA} for some acids are (15): perchloric acid, 4.87; sulfuric acid, 7.24; and the pK_B for some bases are: diethylaniline, 5.78; urea, 10.24.

An overall dissociation constant for a salt is defined.

$$K_{BHA} = (BH^+)(A^-)/C_{BHA} \qquad \text{(II-10)}$$

Consideration of reactions between acids and bases in view of this very limited dissociation leads to several important differences between equilibria in acetic acid and in water. Two such examples are: (a) The common practice of estimating pK values from the point of half-neutralization on a potentiometric titration curve is unsound in acetic acid (17). (b) An unusual effect observed in acetic acid buffer solutions (base plus corresponding salt) is that a ten-fold dilution results in an 0.5 unit decrease in pH (18). Equations developed from the dissociation equilibria expressions explain this behavior (19). The potentiometric measurement of acidity and basicity has not been employed in the present work, and so the equations which relate pH to the several equilibrium constants and concentration variables will not be developed here.

The hydrogen ion concentration in acetic acid is low because of the limited dissociation. The hydrogen ion and acetate ion concentrations are related by the autoprotolysis constant, K_s.

$$HAc \rightleftharpoons H^+ + Ac^-$$

$$K_s = (H^+)(Ac^-) \qquad \text{(II-11)}$$

Kolthoff and Bruckenstein have found $pK_s = 14.45$ at 25°C. (15).

<u>Salt Formation</u>. In the absence of extensive dissociation the formation of a salt is written

$$B + HA \rightleftharpoons BHA$$

The molecules may exist in the unionized and ionized (ion-pair) forms; that is, higher ionic aggregates are not considered to be important. The <u>salt formation constant</u> is defined

$$K_f^{BHA} = C_{BHA}/C_B C_{HA} \qquad \text{(II-12)}$$

Combining Equation II-12 with Equations II-7c, IK-8c, II-10 and II-11 gives (20)

$$K_f^{BHA} = K_{HA}K_B/K_sK_{BHA} \qquad \text{(II-13)}$$

Although the salt formation constant (or formation constant) is expressible in terms of four dissociation constants, it can be shown to be dependent only upon ionization equilibria. This results from neglect of dissociation in its definition. If a significant degree of dissociation occurs, the experimental value of the formation constant will be affected only if the measurement of (say) C_{HA} also includes (H^+). In the case of very weak bases $C_B = (B)$ and the observed formation constant, K_f', is given by Equation II-14).

$$K_f' = \left[C_{BHA} + (BH^+)\right] / C_B \left[C_{HA} + (H^+)\right] \qquad \text{(II-14)}$$

These errors are partly compensating. When $K_{BHA} = K_{HA}$ no error results from including the free ion concentrations in the equilibrium expression. The dissociation effect did not reveal itself in terms of an inconstant "constant" in the present work, within the estimated experimental error.

The presence of equilibria involving ionic aggregates higher than the ion-pair would have the effect of increasing the observed formation constant. This will be discussed in more detail in Section V.

Behavior of Indicators. An indicator is a weak acid or base the conjugate forms of which exhibit different absorption spectra. The reaction of an indicator base with an acid is

$$I + HA \rightleftharpoons IHA$$

$$K_f^{IHA} = C_{IHA}/C_I C_{HA} \qquad (II\text{-}15)$$

The equilibrium is identical with that already described for the base B. The salt IHA displays the absorption spectrum of the acid form of the indicator and is indistinguishable spectrally from the dissociated ion IH^+. The ionized form of the indicator acetate, IH^+Ac^-

$$I + HA_c \rightleftharpoons IH^+Ac^-$$

also exhibits the acid spectrum.*

The principal feature which distinguishes indicator color change equilibria in acetic acid from color changes in water is the appearance of the concentration C_{HA} in the color change equilibrium expression. In acetic acid color change is governed by the free acid concentration and not by dissociation, that is, not by the pH or potentiometric acidity of the solution (14,21). This difference results in the indicator formation constant being a function of four other equilibrium constants as in Equation II-13; the analogous relation for aqueous solution involves only two constants (22).

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* This introduces some ambiguity into the indicator formation constant definition, II-15. The species IH^+Ac^- is spectroscopically a salt, but as we define it, it is a base; i.e., $C_I = (I) + (IH^+Ac^-)$. In the present study all indicators used were such weak bases that $(IH^+Ac^-) = 0$.

The experimentally determined quantity in indicator studies is the ratio of concentrations of indicator in the acid and base forms, I_a/I_b. From the preceding discussion it is clear that this indicator ratio is given by Equation II-16.

$$I_a/I_b = \left[C_{IHA} + (IH^+Ac^-) + (IH^+)\right]/(I) \qquad \text{(II-16)}$$

On the molecular level, it appears that color change is governed by degree of proton transfer to the indicator base (23). In pure acetic acid the indicator is present as the acetate, and the base color is exhibited. A hydrogen bond is probably involved in this form. In the perchlorate (acid) form the proton transfer is complete, or nearly so, because of the very weak basicity of the perchlorate anion (22).

C. Measurement of Basicity in Acetic Acid

The classical measure of basicity is the overall dissociation constant K_B (Equation II-8c). In a protogenic solvent of high dielectric constant, like water, this is a good measure of the proton-attracting power of the base.* In a medium of low dielectric constant, however, K_B is a function of not only the intrinsic strength of the base but also of the dissociating power of the solvent. These two factors can be roughly assigned to the ionization constant

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* Specific solvent effects or steric factors may modify the dissociation constant considerably.

K_i^B and the dissociation constant K_d^B, so that K_i^B is a better measure of base strength than is K_B (14); though it is the latter quantity which is usually measured.

The quantities K_i^B and K_B are, in acetic acid, measures of the extent of reaction of B with the reference acid acetic acid. It is possible to add a second acid to the system which will serve as the reference acid; then the base strength is measured by the equilibrium constant for the reaction: BASE + REFERENCE ACID $\rightleftharpoons$ SALT. This is the formation constant K_f^{BHA} (Equation II-12). One advantage to this method is that the study of base strength in the inert solvents is facilitated. Davis and coworkers, for example, have employed the technique to study acid-base reactions in benzene (23,24). In their work the reference acid was an indicator acid; this choice simplified the experimental determination of the formation constant (or association constant, as Davis, et al, prefer to call it). Other workers have used the same principle (25,26).

The reference acid selected may not be an indicator; this choice will alter the experimental technique, but may have other advantages. In the present study the reference acid is perchloric acid, so that the reaction studied and the constant determined are

$$B + HClO_4 \rightleftharpoons BHClO_4$$

$$K_f^{BHClO_4} = C_{BHClO_4}/C_B C_{HClO_4} \qquad \text{(II-17)}$$

In this case perchloric acid possesses some considerable advantages over other possible reference acids. It is the strongest acid available and so a greater range of base strengths can be measured without changing the reference. Such very weak bases as amides require the use of perchloric acid in order that the reaction proceed sufficiently toward salt formation.

The relative basicities of a series of compounds, measured by their reaction with a single acid, may conceivably depend upon the nature of the salt which is formed. The two extremes have already been mentioned: (1) weak hydrogen-bonding and, (2) complete proton transfer to form ion pairs. Intermediate bond types may occur, and the formation constant may depend upon the nature of the salt. Some evidence exists that indicates a tautomeric equilibrium between the extreme bond types in the intermediate cases (27), though it is possible that a single resonance form may be present. Use of perchloric acid as the reference ensures that the salts are in the ion-pair form to the greatest extent possible.

The above discussion suggests that some salts may exist in the unionized form in solution; that is, the several equilibria

$$B + HA \rightleftharpoons BHA$$

$$BHA \rightleftharpoons BH^{+}A^{-}$$

$$BH^{+}A^{-} \rightleftharpoons BH^{+} + A^{-}$$

represent, in the general case, the nature of salt solutions. This behavior has been observed in the case of picrates of tertiary amines in the solvent tricresylphosphate ($D = 6.92$) (28). It is unlikely that perchlorate salts exist in the unionized form to any significant extent.

One of the experimental techniques developed in this investigation for the evaluation of the formation constant yields the ratio of two such constants, one for an indicator and the other for a base. This ratio is called the <u>exchange constant</u> and its determination will be discussed in detail in the next section.

$$K_{ex} = K_f^{IHA} / K_f^{BHA} \qquad \text{(II-18)}$$

III. THE EXCHANGE CONSTANT

A. The Modified Type II Plot

Single Bases. The determination of the exchange constant of a base-indicator system, defined by Equation II-18, is based upon a linear extrapolation of photometric data obtained in the titration of the base-indicator system with the strong acid HA. In addition to the exchange constant this method yields the end point of the acid-base titration and so is useful analytically. The method to be developed here is a refinement of an earlier photometric titration technique (29), which will be discussed first.

The titration reaction is represented as a competition between the base B and the indicator I for the acid HA.

$$\mathrm{BHA} + \mathrm{I} \rightleftharpoons \mathrm{IHA} + \mathrm{B}$$

The indicator is present in such small concentration that the amount of acid held as indicator salt is considered negligible; for the present solvolysis effects are also neglected. The exchange constant is

$$K_{ex} = C_{IHA}\, C_B / C_{BHA}\, C_I = K_f^{IHA} / K_f^{BHA} \qquad \text{(III-1)}$$

The quantity X' is defined to be the total concentration of acid added to the system at any time before the end point of the titration. Then, neglecting dissociation,

$$X' = C_{BHA} \qquad \text{(III-2a)}$$

S' is the total base concentration initially present.

$$S' = C_B + C_{BHA} \qquad \text{(III-2b)}$$

The conversion equations III-3a and III-3b

$$X' = XN/V \qquad \text{(III-3a)}$$

$$S' = SN/V \qquad \text{(III-3b)}$$

transform the concentrations X' and S' to the volumes X and S of standard acid added at any point in the titration and at the end point, respectively. N is the normality of the acid titrant and V is the total volume of the titration solution. Combination of Equations III-1, III-2, and III-3 gives Equation III-4.

$$1/X = (K_{ex}/S)(I_b/I_a) + 1/S \qquad \text{(III-4)}$$

which is the basis of the so-called type II photometric titration plot (29). (When dissociation is negligible and a weakly basic indicator is employed, $C_I \ / \ C_{IHA} = I_b/I_a$. See Equation II-16).

A plot of $1/X$ <u>versus</u> I_b/I_a should yield a straight line, from which values of the end point and exchange constant may be determined. The validity of this graphical procedure has been established for several systems (29).

Applications of the type II plot to titrations of weak bases in acetic acid revealed significant and reproducible deviations from linearity when the sample size was very small. Recoveries in excess of 100% resulted when this curvature was observed. Similar deviations recently have led to the derivation of a more complete titration equation for the type III photometric plot (30,31); this treatment, which was developed for aqueous systems, takes into account hydrolysis of the salt formed during the titration. The equation developed for the aqueous system also describes the equilibrium in acetic acid, though not so exactly. This difference is apparent in the initial equations.

Let X' and S' have the meanings previously assigned. Then, taking into account both dissociation and solvolysis

$$X' = C_{HA} + C_{BHA} + (A^-) \qquad \text{(III-5a)}$$

$$S' = C_B + C_{BHA} + (BH^+) \qquad \text{(III-5b)}$$

If dissociation is neglected because of the small values of the dissociation constants in acetic acid, Equations III-5 may be expressed in the approximate forms

$$X' = C_{HA} + C_{BHA} \qquad \text{(III-6a)}$$

$$S' = C_B + C_{BHA} \qquad \text{(III-6b)}$$

These equations are analogous to those for the aqueous case. Combination of Equations III-1, III-3, and III-6 gives Equation III-7, which describes the titration equilibrium.

$$X = S + (V/K_f^{IHA}\,N)(I_a/I_b) - S/[1 + (I_a/I_b)(1/K_{ex})] \qquad \text{(III-7)}$$

Equation III-7 is the relation which Bodin and Higuchi found useful in describing the type III equilibria (31).

For the present purpose Equation III-7 can be put into usable form in the following manner: Consider the titration of two samples identical except for size; let sample 1 be the smaller of the two. The titration of sample 1 is described by Equation III-7, the volumes being denoted by X_1 and S_1. A similar equation involving X_2 and S_2 describes the titration of sample 2. Subtracting these two equations at constant I_a/I_b gives

$$X_2-X_1 = (S_2-S_1) - (S_2-S_1)/\left[1 + (I_a/I_b)(1/K_{ex})\right]$$

since the quantity $V/K_f^{IHA} N$ is practically constant in the two cases. This can be rearranged into the type II form.

$$1/(X_2-X_1) = \left[K_{ex}/(S_2-S_1)\right](I_b/I_a) + 1/(S_2-S_1) \qquad \text{(III-8)}$$

The quantity $1/(X_2-X_1)$ is calculated at given values of I_b/I_a by reading points from the smoothed plots of $1/X_1$ <u>vs</u> I_b/I_a and $1/X_2$ <u>vs</u> I_b/I_a. The end point, S_2-S_1, is that for the difference between the samples 2 and 1. This graphical treatment of data according to Equation III-8 will be referred to as the <u>modified type II plot</u>.

It is interesting to calculate the effect upon the indicator formation constant and upon the exchange constant to be expected when the indicator ionizes to a significant extent. The true formation constant is given by Equation II-15; the apparent constant is

$$K' = \left[C_{IHA} + (IH^{+}Ac^{-})\right] / (I)C_{HA}$$

It can be shown that the two are related by

$$K' = K_f^{IHA}\,(1 + K_i^I) + K_i^I/C_{HA} \qquad \text{(III-9)}$$

This suggests that K_f^{IHA} and K_i^I may be determined by plotting K' *vs* $1/C_{HA}$.

The observed formation constant of the sample base in a modified type II plot is not influenced by ionization; hence the apparent exchange constant is given by $K'_{ex} = K_{ex}\,K'/K_f^{IHA}$. Combination of this with Equation III-9 gives Equation III-10 for the variation of the observed exchange constant determined with an indicator possessing ionization constant K_i^I.

$$K'_{ex} = K_{ex}(1 + K_i^I) + K_{ex}\,K_i^I \,/\, K_f^{IHA}\,C_{HA} \qquad \text{(III-10)}$$

Mixtures of Bases. An equation describing the equilibrium in the titration of two bases B and C can be derived in a manner analogous to that used for a single base. The initial equations are

$$X' = C_{HA} + C_{BHA} + C_{CHA}$$

$$S'_B = C_B + C_{BHA}$$

$$S'_C = C_C + C_{CHA}$$

When the double titration technique is applied to the titration expression Equation III-11 results.

$$X_2 - X_1 = \frac{(S_2^B - S_1^B)(I_a/I_b)}{K_{ex}^B + I_a/I_b} + \frac{(S_2^C - S_1^C)(I_a/I_b)}{K_{ex}^C + I_a/I_b} \quad \text{(III-11)}$$

This equation has not yet been made useful for the general case of any two bases, but some special cases are of interest.

I. $K_{ex}^B = K_{ex}^C$

Under this restriction Equation III-11 reduces to Equation III-8 with the exception that the quantity $(S_2 - S_1)$ is replaced by $(S_2^B - S_1^B) + (S_2^C - S_1^C)$. The only situation which is non-trivial occurs when both exchange constants equal zero within the accuracy of the measurements. This situation can often be realized by proper choice of indicator, thus allowing determination of the total equivalents of base present.

II. $(S_2^B - S_1^B) > 0$, $(S_2^C - S_1^C) = 0$

In this case Equation III-11 becomes Equation III-8; The exchange constant and end point apply to base B. This case is an important one because it describes the titration of a base B in a solvent containing a basic impurity C. The solvent purity should not be critical, therefore, when the modified type II technique is used.

III. $K_{ex}^B \ll I_a/I_b$

Since I_a/I_b varies from about 0.5 to infinity in the region of interest $(0 < I_b/I_a < 2)$, K_{ex}^B should be less than about 0.02. Then Equation III-11 becomes

$$\frac{1}{(X_2 - X_1) - (S_2^B - S_1^B)} = \left[K_{ex}^C/(S_2^C - S_1^C)\right](I_b/I_a) + 1/(S_2^C - S_1^C) \qquad \text{(III-12)}$$

If the end point for the stronger base is known or can be found from an independent determination, the modified type II plot yields the exchange constant and end point for the weaker base.

B. Experimental Method

Apparatus. Bausch & Lomb Spectronic 20 colorimeter; two milliliter microburet, graduated to 0.01 ml and read with a magnifying glass; circulation apparatus for photometric titrations (32).

Indicators.*

Sudan III, recrystallized (4x) from 1:1 benzene-absolute ethanol; mp 203°.

p-Naphtholbenzein, recrystallized from glacial acetic acid; mp 236-241°.

Nile blue A and malachite green, used directly.

Bases. All compounds were from commercial sources. Data are given in the order: base; recrystallization solvent; melting point.

Acetamide; benzene; 79.5-80

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* The spectral characteristics of these indicators are described in Appendix A.

Acetophenetidin; water; 133-135

Aminopyrine; petroleum ether; 105-107

Antipyrine; water; 111-112

Caffeine; water; 236-238

2,6-Dimethyl-γ-pyrone; diethyl ether; 132-133

Isonicotinic acid; water; 317d

Thiourea; water; 173-174

Triphenylguanidine; toluene (2x), aqueous ethanol (1x) 148-149

Urea; absolute methanol; 132-134

Solvents. Glacial acetic acid, reagent grade. Purified acetic acid, prepared by refluxing glacial acetic acid with boron triacetate and distilling from an all-glass apparatus (33). Water content was determined by visual Karl Fischer titration in an equimolar quantity of pyridine.

Titration Procedure. Stock solutions of perchloric acid, indicator, and base were made in acetic acid. The titrant was prepared by taking aliquots of the indicator and acid solutions and diluting to give convenient concentrations of each. Standardization of the titrant was by visual titration of potassium biphthalate using p-naphtholbenzein indicator; the indicator contained in the titrant does not interfere with this visual end point. Sample solutions were composed of indicator and base aliquots diluted to a volume such that the indicator concentration was identical with that in the titrant.

All titrations were performed at 25 ± 2°C using a

Bausch & Lomb Spectronic 20 colorimeter. Titrant was delivered in increments of such size that 15-20 points were recorded in the range $0 < I_b/I_a < 2$. The calculation of the indicator ratio from spectral data is discussed in Appendix B.

C. Results

Titrations of Single Bases. Perchloric acid was used in 0.1 N solution for titrations with p-naphtholbenzein, Nile blue A, and malachite green, and 0.45N concentration for the Sudan III titrations. In most cases the sample weight in titration #1 was 5-7 mg and in titration #2 25-35 mg; the effective sample titrated (in 30 ml) was therefore in the range 20-30 mg. In subsequent discussion "sample size" will refer to the effective, or difference, sample.

The data for a typical titration (the system is urea-Nile blue A) are tabulated in Table I. The plots of $1/X_1$ and $1/X_2$ versus I_b/I_a are shown in Fig. 1. At the I_b/I_a values 0.2, 0.4, 0.6, 0.8, 1.0, 1.2, values of $1/X_1$ and $1/X_2$ were read from the respective curves. From these quantities the corresponding values of $1/(X_2-X_1)$ can be calculated and plotted vs I_b/I_a to give the line indicated as MODIFIED in the graph. The intercept is equal to $1/(S_2-S_1)$ and the slope to $(S_2-S_1)/K_{ex}$. The sample size was 19.36 mg; 19.30 mg was found. The observed exchange constant was 0.47.

A titration in which the experimental value of the

Table I

Typical Titration Data: Urea-Nile Blue A

($A_b = 0.530$; $A_a = 0.000$)

Titration #1: 4.84 mg urea

X_1 (ml)	$1/X_1$	A_{632}	I_b/I_a
0.602	1.661	0.290	1.22
0.653	1.531	0.260	0.97
0.704	1.420	0.233	0.78
0.754	1.326	0.208	0.65
0.805	1.242	0.178	0.50
0.857	1.167	0.158	0.43
0.902	1.109	0.138	0.351
0.954	1.048	0.122	0.297
1.006	0.994	0.109	0.258
1.100	0.909	0.090	0.201
1.203	0.831	0.070	0.152
1.303	0.767	0.061	0.127
1.503	0.665	0.050	0.102
1.702	0.588	0.039	0.078
2.000	0.500	0.028	0.053

Titration #2: 24.20 mg urea

X_2 (ml)	$1/X_2$	A_{632}	I_b/I_a
2.704	0.370	0.288	1.19
2.901	0.345	0.265	1.01
3.104	0.322	0.234	0.79
3.304	0.303	0.205	0.63
3.500	0.286	0.172	0.48
3.703	0.270	0.140	0.360
3.902	0.256	0.112	0.266
4.104	0.244	0.087	0.192
4.307	0.232	0.069	0.149
4.603	0.217	0.049	0.100
5.003	0.200	0.033	0.063
6.000	0.167	0.019	0.035

Modified Plot

I_b/I_a	$1/(X_2-X_1)$
0.2	0.336
0.4	0.365
0.6	0.390
0.8	0.417
1.0	0.447
1.2	0.476

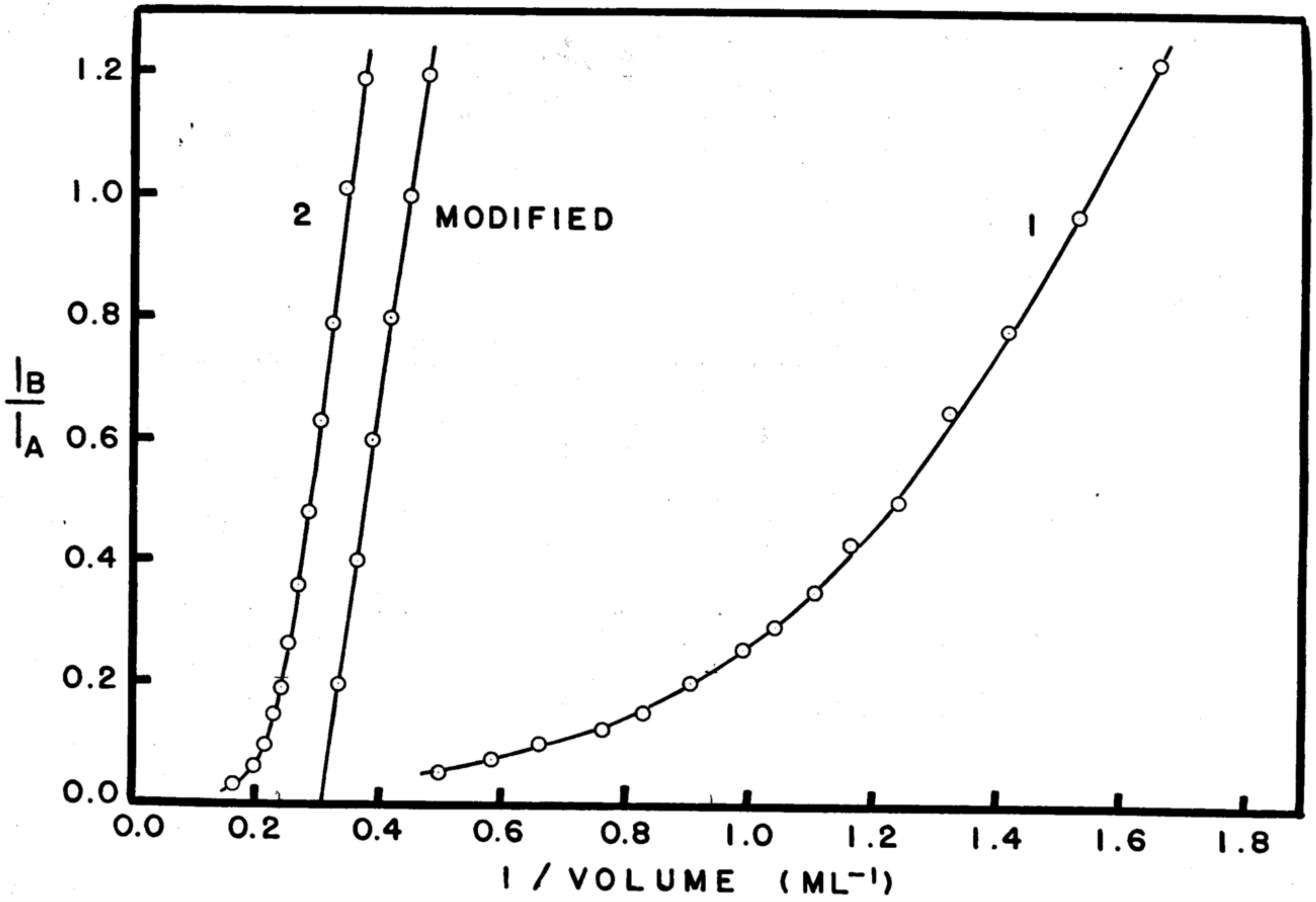

Fig. 1. Modified type II plot of urea-Nile blue A system. Line 1: I_b/I_a vs $1/X_1$; Line 2: I_b/I_a vs $1/X_2$; Modified line: I_b/I_a vs $1/(X_2-X_1)$. Titrant is 0.0980 N $HClO_4$. The data are given in Table I.

exchange constant is equal to zero is pictured in Figs. 2a and 2b. The formation constant of triphenylguanidine perchlorate is so much greater than that of Nile blue A perchlorate that the slope of the modified line is infinite. Figs. 3a and 3b show the titration of the urea-p-naphtholbenzein system, the exchange constant of which is greater than unity.

The behavior shown in Figs. 1, 2, and 3 is typical of the results observed. Some scatter of points occasionally was found to occur at lower indicator ratios, probably due to the large volumes being subtracted; the Sudan III systems exhibited this deviation to the greatest extent. Reduction of the sample size to 10-15 mg also increased the scatter and reduced the accuracy. Use of a sample of size zero for the titration #1 (equivalent to an indicator blank titration) is possible but not completely satisfactory because of poor reproducibility. Such a system is completely unbuffered and is very sensitive to trace impurities in the solvent.

The recovery values are summarized in Table II. Recoveries were satisfactory for every system, and only the titrations with Sudan III exhibited inconveniently large deviations from the mean. The very weak nature of this indicator base, necessitating a concentrated titrant solution, is responsible for the large mean deviation. A considerable part of the deviation observed in all cases is due to variations incurred in plotting the data. This

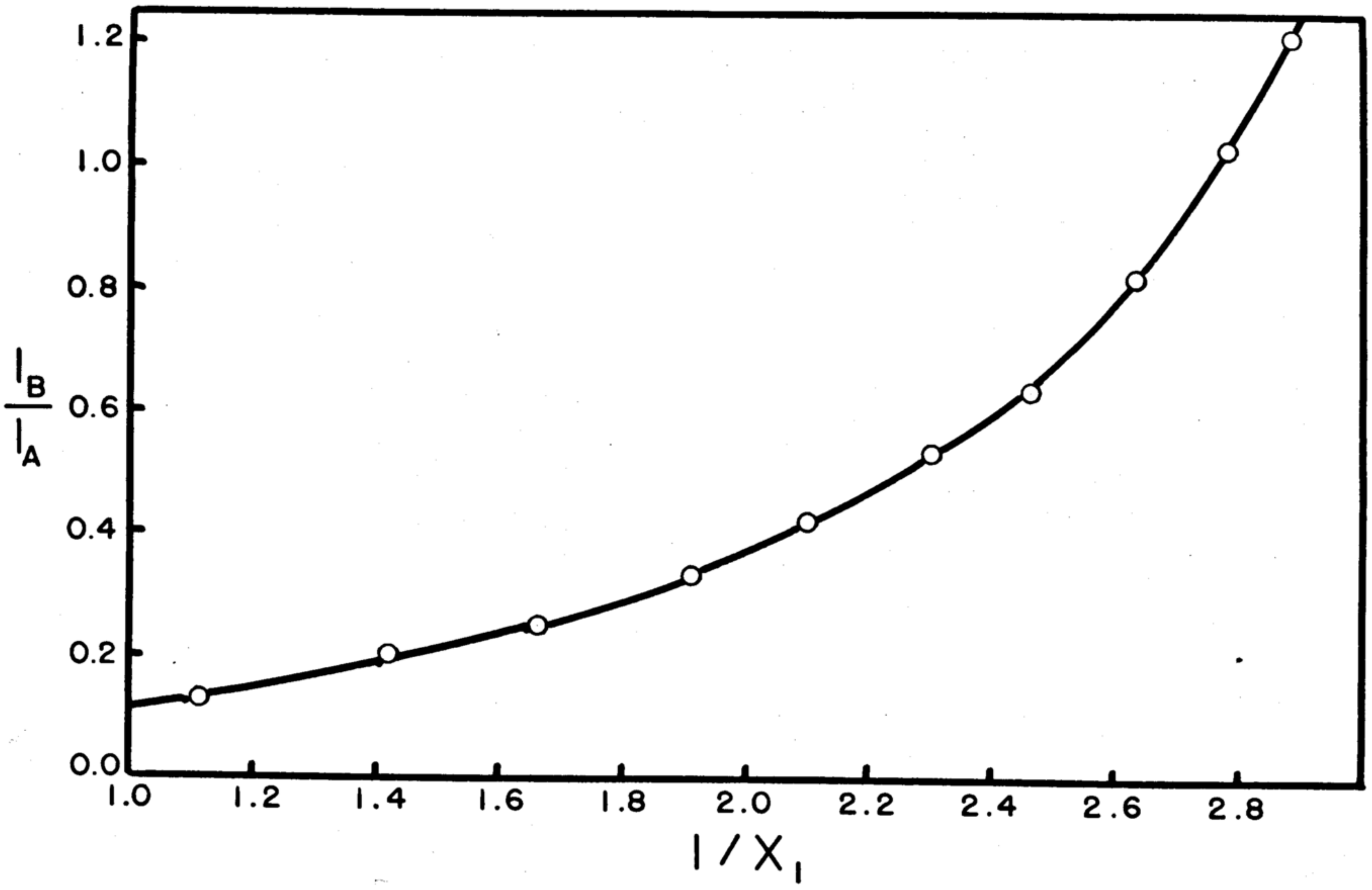

Fig. 2a. Titration (#1) of 7.66 mg of triphenylguanidine with 0.0982 N $HClO_4$; indicator is Nile blue A.

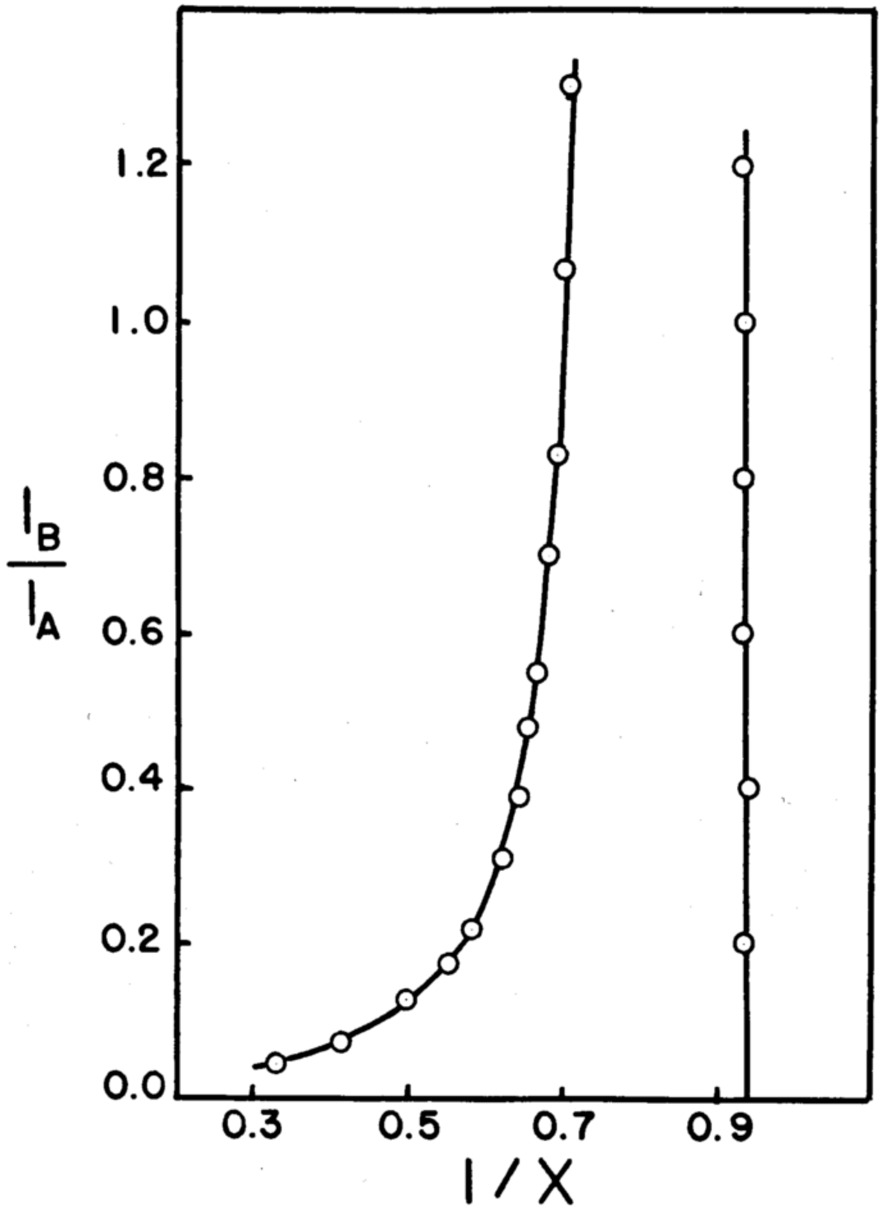

Fig. 2b. Curved line: titration (#2) of 38.29 mg of triphenylguanidine. Straight line: modified plot.

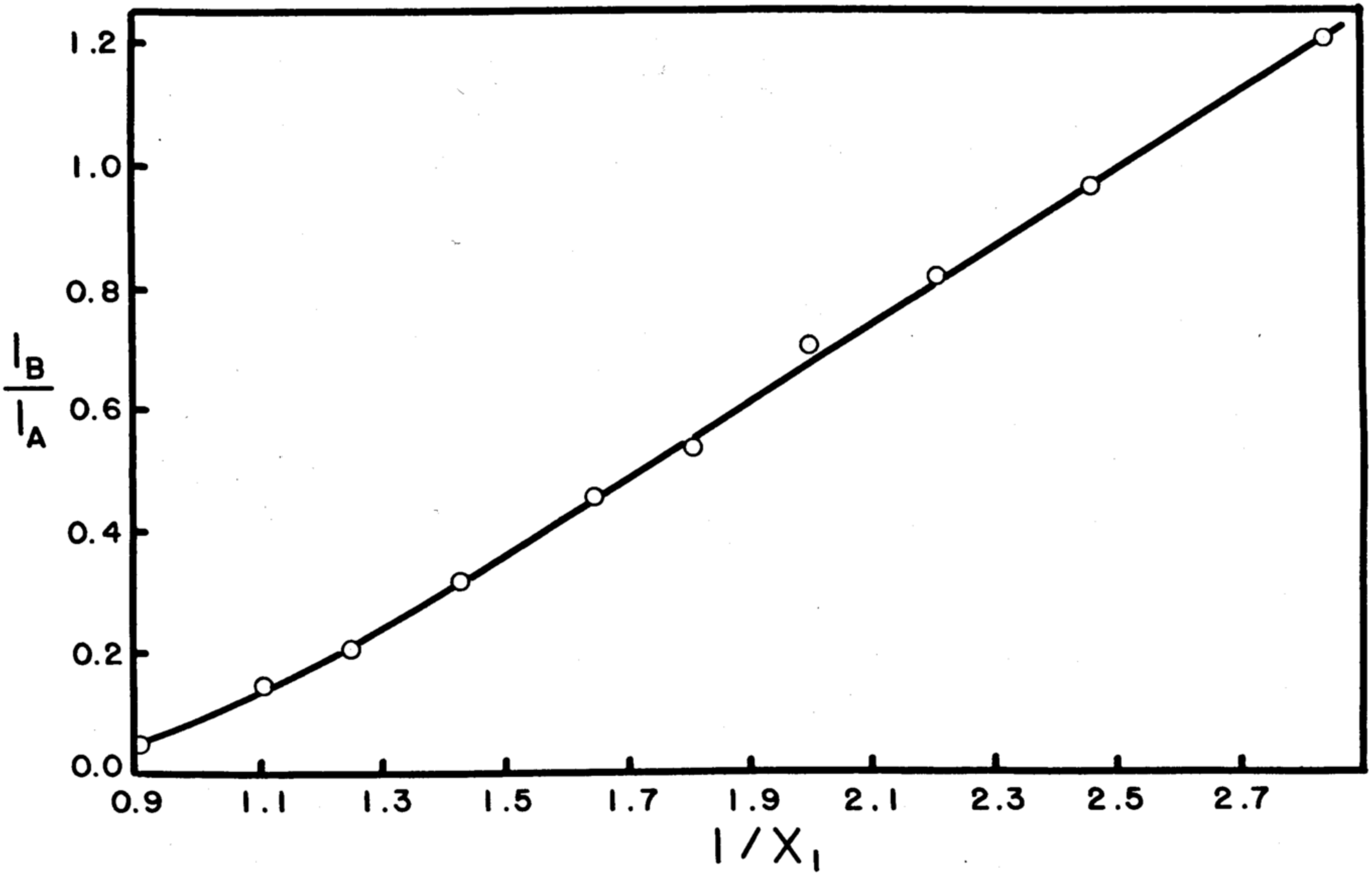

Fig. 3a. Titration (#1) of 5.4 mg of urea with 0.0982 N $HClO_4$; indicator is p-naphtholbenzein.

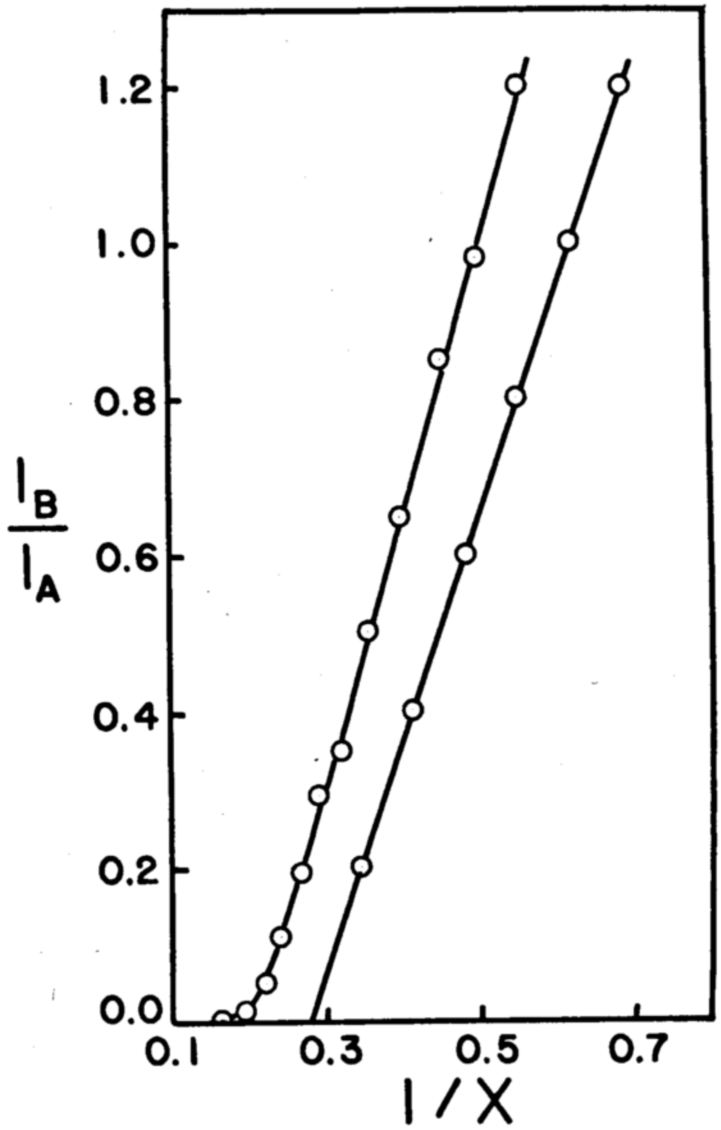

Fig. 3b. Curved line: titration (#2) of 27.2 mg of urea. Straight line: modified plot.

Table II

Recovery Values With the Modified Type II Plot

Base	Indicator (a)	Per Cent Recovery Mean	Per Cent Recovery Mean Deviation (b)	Number Det'ns
Acetamide	S-III	99.7	3.7	7
Acetamide	NBA	97.9	1.7	6
Antipyrine	NBA	97.9	0.8	4
Antipyrine	PNB	100.9	0.7	5
Caffeine	NBA	100.4	0.9	9
Caffeine	MG	99.0	1.0	5
2,6-Dimethyl-γ-pyrone	NBA	99.1	0.3	3
Thiourea	NBA	100.5	0.5	5
Thiourea	PNB	99.4	1.5	7
Triphenylguanidine	NBA	98.4	0.7	3
Urea	NBA	100.6	1.6	21
Urea	PNB	98.0	1.3	7
Urea	MG	98.0	1.5	6

(a) See Appendix A

(b) Calculated with formula: $M.D. = \frac{\sum |X_1 - \overline{X}|}{n-1}$

is evidenced by the data of Table III, which are the results several careful observers obtained plotting, independently, the experimental data of Table I.

The exchange constants found for these systems are listed in Table IV, together with the precision of the measurements, expressed both as the mean deviation and as per cent variation. The relative precision appears to be about 5% for all titrations using Nile blue A, p-naphtholbenzein, and malachite green. The number of determinations for each system is given in Table II.

By Equation III-1 the ratio of exchange constants for two bases with one indicator should equal the same ratio with another indicator. The data of Table IV provide two instances of this agreement. This ratio for urea: thiourea with the indicators Nile blue A and p-naphtholbenzein is 1.84 and 1.77, respectively; for urea: caffeine with the indicators Nile blue A and malachite green it is 2.87 and 2.83.

<u>Selection of Indicators</u>. As the data are plotted in Figs. 1, 2, and 3, the slope of the modified type II plot is equal to $(S_2-S_1)/K_{ex}$. The intercept, which yields the end point, is most accurately located when the slope of the type II line is steep. This slope can be increased in two ways for a given base: the sample size may be increased, and an indicator may be chosen to give a small exchange constant. This is the primary consideration in the choice of an

Table III

Graphical Variation in Modified Type II Results*

Observer	Intercept	End Point	Slope	K_{ex}
KAC	0.305	3.28	7.03	0.47
WJT	0.298	3.36	6.39	0.53
AD	0.307	3.26	7.41	0.44
RNH	0.301	3.32	6.45	0.52
JW	0.316	3.16	8.16	0.39
JKG	0.298	3.36	6.78	0.50

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* Results obtained by several observers from treatment of the experimental data given in Table I for the system urea-Nile blue A.

Table IV

Exchange Constants of Some Base-Indicator Systems

Base	Indicator (a)	Exchange Constant Mean	Exchange Constant Mean Deviation	Per Cent Variation (b)
Acetamide	S-III	0.12	0.03	
Acetamide	NBA	3.66	0.13	3.6
Antipyrine	NBA	0.00	0.01	
Antipyrine	PNB	0.03	0.01	
Caffeine	NBA	0.16	0.01	6.3
Caffeine	MG	0.75	0.03	4.0
Dimethylpyrone	NBA	0.28	0.01	3.6
Thiourea	NBA	0.25	0.01	4.0
Thiourea	PNB	0.73	0.04	5.5
Triphenyl-guanidine	NBA	0.00	0.01	
Urea	NBA	0.46	0.03	6.5
Urea	PNB	1.29	0.05	3.9
Urea	MG	2.12	0.04	1.9
			Mean:	4.4 ± 1.2

(a) See Appendix A

(b) Equal to $\left[(\text{Mean deviation})/K_{ex}\right] 100$

indicator for a titration in which the location of the end point is the most important factor. If, however, a finite value of the exchange constant is required in order to obtain a quantitative measure of basicity, then an indicator should be chosen which will provide an exchange constant greater than 0.1. Such an indicator would be a <u>differentiating</u> indicator, while an indicator which yields an exchange constant of zero, within the accuracy of measurement, is a <u>leveling</u> indicator. Nile blue A, for example, levels antipyrine and triphenylguanidine to, apparently, the same base strength.

Nile blue A is the most versatile of the indicators in the basicity range studied, being useful for the determination of all bases at least as strong as acetamide, and providing finite exchange constants for bases which do not greatly exceed caffeine in base strength. <u>p</u>-Naphtholbenzein and malachite green are stronger bases than Nile blue A. Sudan III is an extremely weak indicator base; it is not recommended for type II titrations unless the sample is too weak to titrate against Nile blue A.

The basicity relations of the indicators and bases are made clearer by arrangement of the exchange constants as in Table V.

<u>Titration of Mixtures</u>. The special cases of mixture analysis discussed earlier have been examined experimentally with the following results (the cases are enumerated

Table V

Exchange Constants of Base-Indicator Systems

Base	Indicator			
	S-III	NBA	PNB	MG
Acetophenetidin	0.24			
Acetamide	0.12	3.66		
Urea		0.46	1.29	2.12
Dimethylpyrone	[illegible]	0.28		
Thiourea		0.25	0.73	
Caffeine		0.16		0.75
Antipyrine		0.00	0.03	
Isonicotinic Acid				0.01
Triphenylguanidine		0.00		

as in the theoretical discussion).

Case I. Since Nile blue A levels antipyrine and triphenylguanidine to the same base strength (Table V), their mixture should yield total equivalents of base. Three determinations were made of a mixture containing 0.1291 milliequivalents of antipyrine and 0.0963 meq of triphenylguanidine (total, 0.2254 meq). The mean result was 0.2249 meq of base recovered, or 99.8%. The mean deviation was 1.3%. Observed K_{ex} was 0.01 ± 0.01.

Case II. The system urea-Nile blue A was chosen to provide an example for this case. The impurity (base C) was, variously, water, acetamide, or ammonia. The results, listed in Table VI, show that no significant interference was encountered in the urea determinations. Because acetic acid always contains water, and may absorb traces of volatile bases from laboratory air, this insensitivity to solvent impurities is an important advantage.

Case III. With Nile blue A as the indicator, antipyrine and urea satisfy the requirements of this special case. About 25 mg of each base was included in the titration sample. The end point for the antipyrine was calculated from knowledge of the sample size and titrant normality. The mean recovery for the titration of three samples was 97.9% of urea taken and the exchange constant observed was 0.46. Evidently Equation III-11 can be applied to such a mixture.

Table VI

Effect of Solvent Impurity on Titration of Urea-Nile Blue A System

Impurity	Impurity Concn (M)	Urea (mg) Taken	Urea (mg) Found(a)	Observed K_{ex}(a)
Water	0.01	20.5	20.6	0.47
Water	0.10	19.0	19.1	0.45
Acetamide (b)	0.005	21.8	22.2	0.49
Ammonia (b)	0.002	21.4	21.5	0.44

(a) Mean of three determinations

(b) Also 0.08 M with respect to water

An attempt to titrate aminopyrine as a monoacidic base by use of Equation III-8 yielded plots with reproducible curvature, indicating that a second basic function was consuming acid. Aminopyrine was consequently treated as a mixture of two bases, the exchange constant for the first group being estimated as 0.00. Equation III-11 was applied, yielding recovery values which were semiquantitative only, probably due to the extremely weak character of the second basic group. Nile blue A was the indicator in these titrations. The best estimate of the exchange constant for the second group is 5.0.

IV. THE SALT FORMATION CONSTANT

A. Determination of the Indicator Formation Constant

Theory. In order to calculate formation constant values from the exchange constants determined with the modified type II method, the formation constant of at least one indicator must be independently found. This presumably could be done on the basis of Equation III-7 by setting S equal to zero, that is, by including no base in the titration mixture. The slope of the line obtained by plotting X *versus* I_a/I_b should then yield K_f^{IHA}. (This is the type III plot (31)). Unfortunately, acetic acid cannot be made completely free of water, and water acts as a base in this solvent. Its basicity is so low that it cannot be titrated according to Equation III-7, but it does affect the slope of the type III plot. The magnitude of the effect depends upon the water concentration. The presence of water must therefore be taken into account in the evaluation of the indicator formation constant; this can be done as follows.

Let: W = initial water concentration

$Y = C_{H_2O.HA}$

H = total concentration of acid added

B = concentration of acid bound as salts

$Z = C_{IHA}$

Then: $C_{HA} = H - B \cong H - Z$

$$C_{H_2O} = W - Y \cong W$$

$$B = Y + Z$$

$$K_f^{IHA} = C_{IHA}/C_I C_{HA} = (I_a/I_b)/(H - B) \qquad \text{(IV-1a)}$$

$$K_f^{WHA} = C_{H_2O.HA}/C_{H_2O}\ C_{HA} = (B-Z)/W(H-B) \qquad \text{(IV-1b)}$$

$$K_f^{IHA}/\ K_f^{WHA} = (I_a/I_b)W/(B-Z) \qquad \text{(IV-2)}$$

Solving for B in Equation IV-1b and substituting into Equation IV-2 leads to Equation IV-3.*

$$K_f^{IHA} = (I_a/I_b)(1/C_{HA})(1 + K_f^{WHA}\ C_{H_2O}) \qquad \text{(IV-3)}$$

It is convenient to express the quantity $C_{HA} = (H-Z)$ in terms of volume of standard acid corresponding, respectively, to total acid added (X) and acid in the form of indicator salt (R). Then $X = HV/N$ and $R = ZV/N$ and Equation IV-3 is written

$$K_f^{IHA} = Q_f^{IHA}\ (1 + K_f^{WHA}\ C_{H_2O}) \qquad \text{(IV-4)}$$

$$Q_f^{IHA} = (I_a/I_b)V/N(X - R) \qquad \text{(IV-5)}$$

For *p*-naphtholbenzein and Sudan III, $R = VA/Na_a$; for Nile blue A and malachite green, $R = V(A_b-A)/Na_b$, where A = absorbance, A_b = absorbance of the indicator solution when

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* Bruckenstein and Kolthoff (34) have derived a relation which is equivalent to Equation IV-3.

the indicator is completely in its base form, a_a = molar absorptivity of the acid indicator species, and a_b = molar absorptivity of the basic species. The different expressions for the indicators result from the nature of their absorption spectra; these points are discussed in Appendix B.

Q_f^{IHA}, the apparent formation constant, is found from the slope of a plot of I_a/I_b versus $(X - R)$ according to Equation IV-5.

Equation IV-4 can be rearranged to the linear form

$$1/Q_f^{IHA} = K_f^{WHA} C_{H_2O}/ K_f^{IHA} + 1/ K_f^{IHA} \qquad (IV\text{-}6)$$

A plot of $1/Q_f^{IHA}$ against C_{H_2O}, the molar concentration of water, should give a straight line. From the intercept and slope the formation constants for water perchlorate and the indicator perchlorate may be evaluated.

Experimental Part. The indicators used in this study were the same as those used in the exchange constant determinations (Section III). Purified acetic acid was prepared as described in that section and the water content was varied by making a stock solution of water in acetic acid and taking appropriate aliquots. The titrations were conducted as before. Values of absorbance were recorded in the range $0 < I_a/I_b < 2$.

Results. Sudan III was chosen to test Equation IV-6. This indicator is such a weak base that the titrant normality

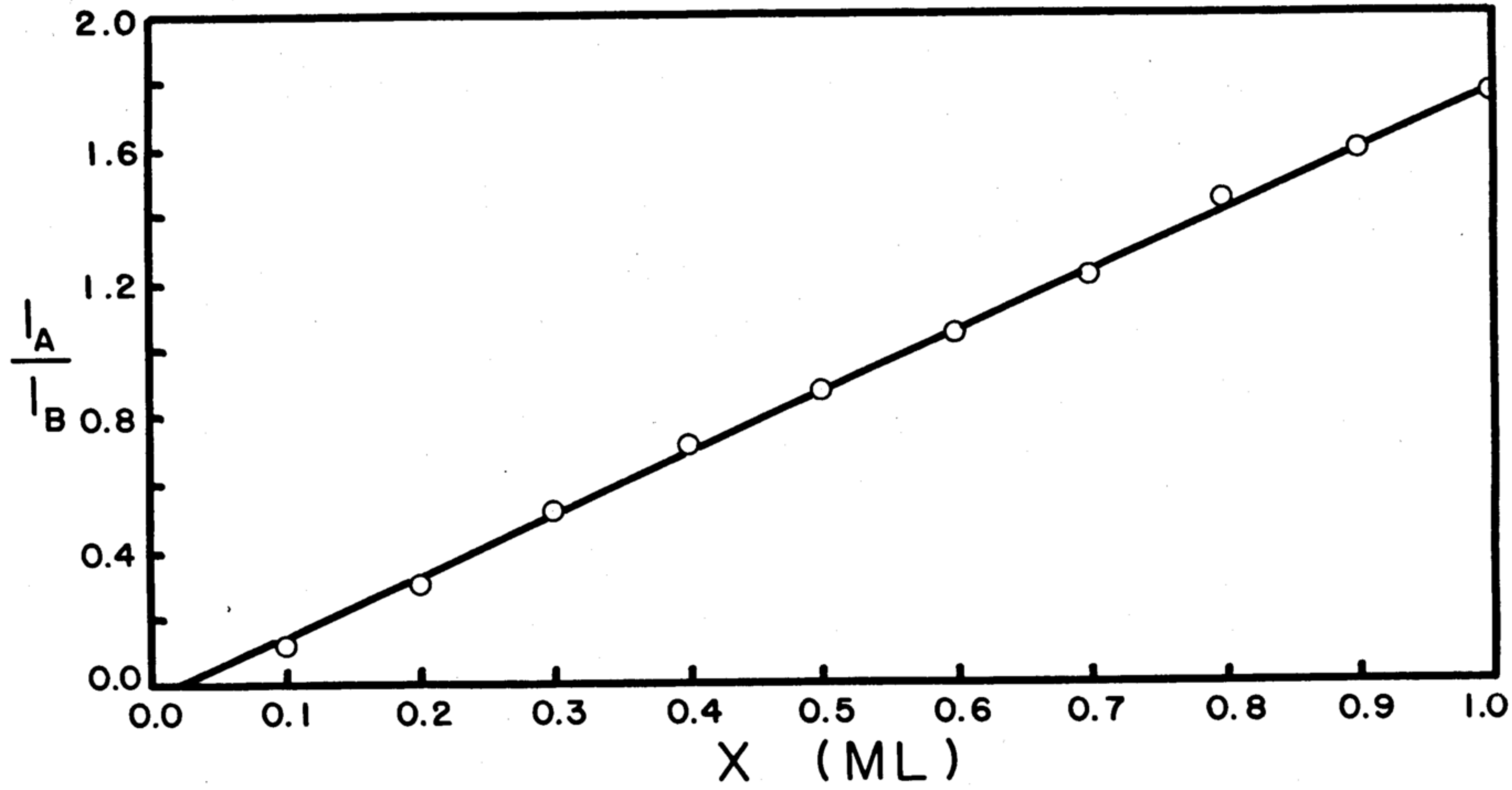

Fig. 4. Titration of Sudan III with 0.09901 N $HClO_4$. Water concentration was 0.013 M.

Table VII

Apparent Indicator Constants for Sudan III-Water System

C_{H_2O}	Q_f^{IHA}	$1/Q_f^{IHA} \times 10^3$
0.013	576	1.74
0.017	517	1.94
0.018	457	2.19
0.022	453	2.21
0.028	401	2.49
0.033	367	2.73
0.039	339	2.95
0.043	307	3.26
0.052	253	3.95

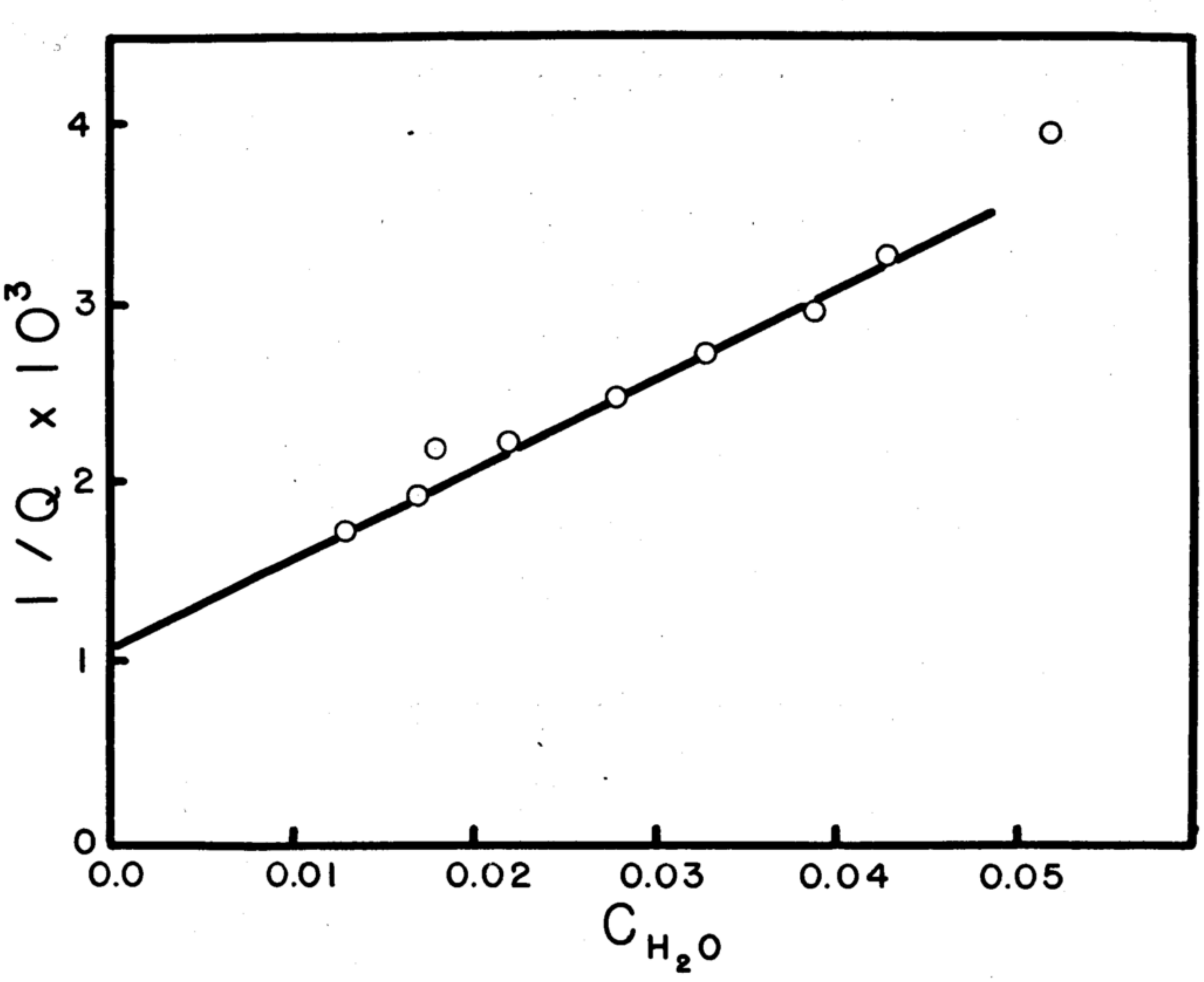

Fig. 5. Application of Equation IV-6 for Sudan III system. The data are given in Table VII.

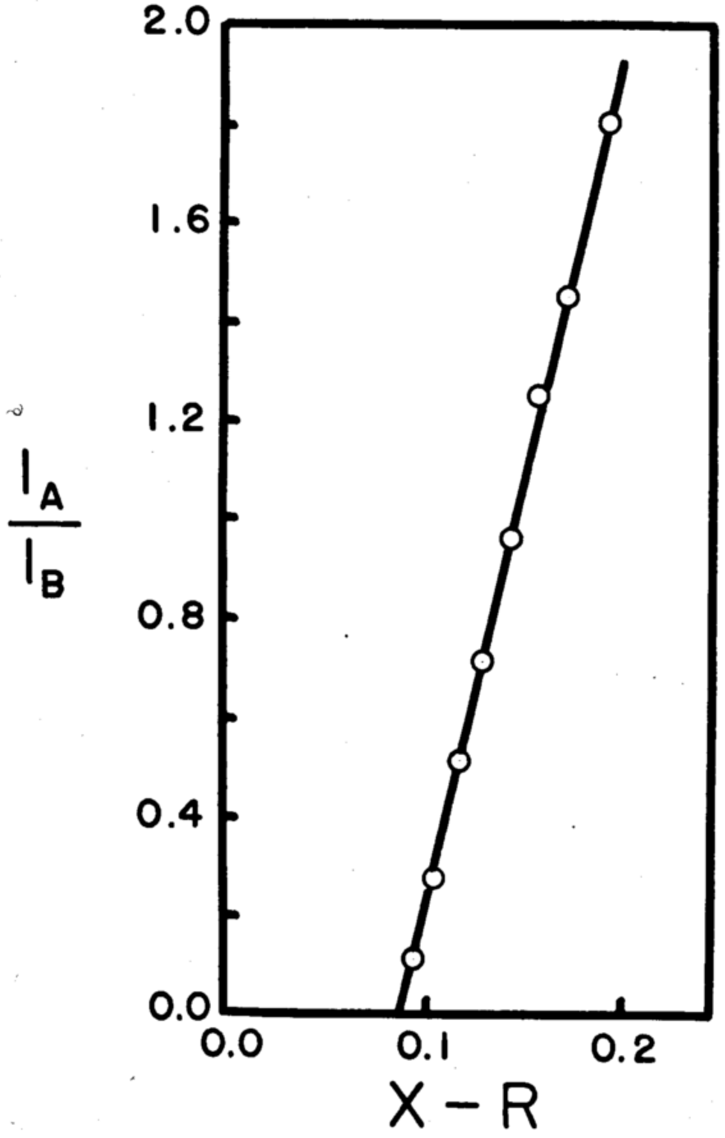

Fig. 6. Titration of p-naphtholbenzein with 0.00784 $\bar{N}$ $HClO_4$. Water concentration was 0.023 M.

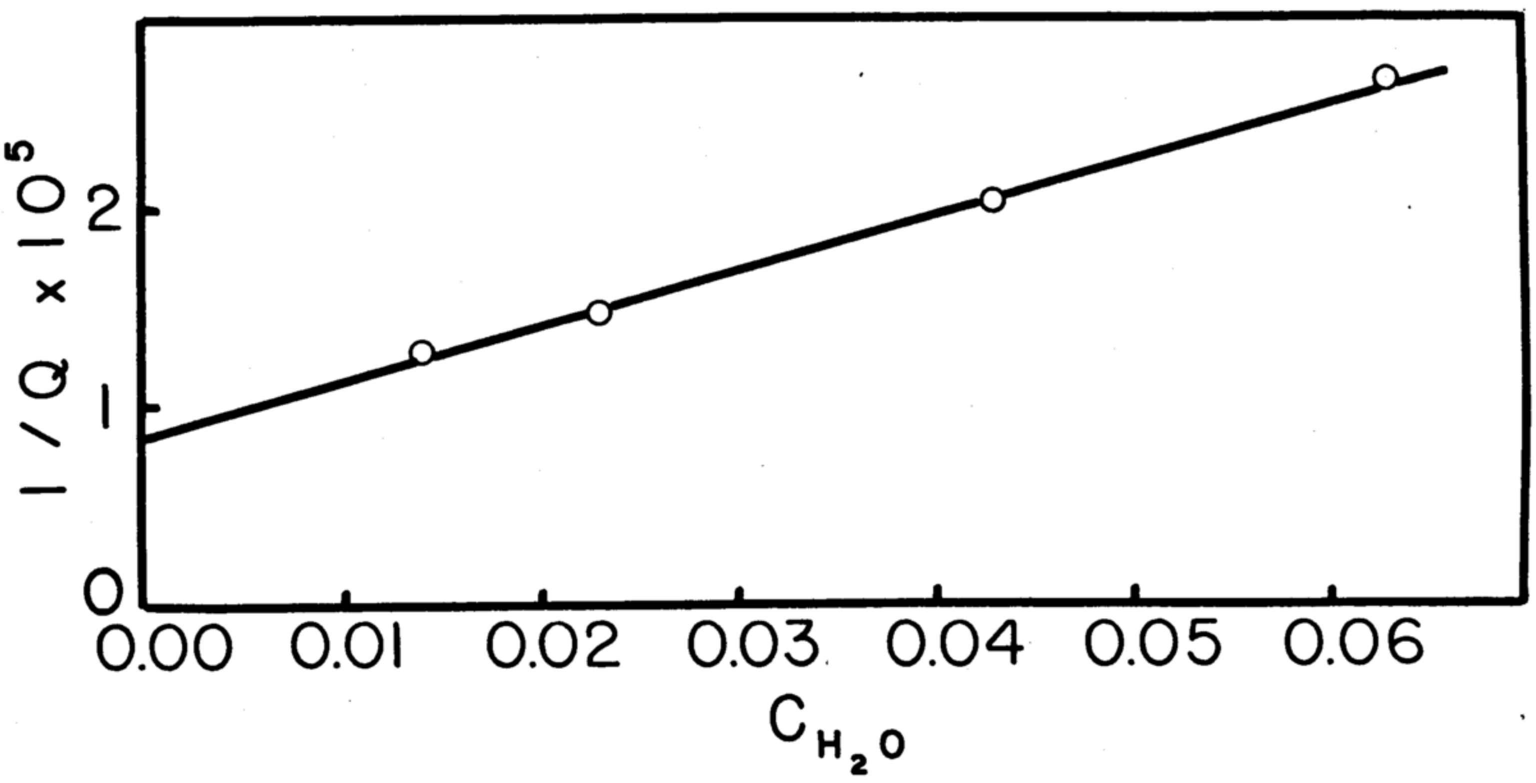

Fig. 7. Application of Equation IV-6 for p-naphtholbenzein system. The data are given in Table X.

constant for Nile blue A perchlorate was calculated from a determination of Q_f^{IHA}. K_f^{IHA} for this indicator is 3.4 x 10^4.

B. The Formation Constant for a Very Weak Base

Theory. If acetic acid could be rendered completely anhydrous, it should be possible to include a weak base in the indicator-solvent system and then to determine its salt formation constant in the same way that the formation constant for water was found in Section IV-A. Since in practice anhydrous acetic acid is not easily kept and used, it is desirable to determine the effect of small concentrations of water on such an experiment as that proposed. In much the same way that Equation IV-6 was derived it is possible to develop an equation which will be applicable in this more complex case. If C_B represents the concentration of weak base, the resulting expression is

$$1/Q_f^{IHA} = K_f^{BHA} C_B / K_f^{IHA} + (1 + K_f^{WHA} C_{H_2O}) / K_f^{IHA} \qquad (IV-7)$$

This equation is subject to some limitations in addition to those imposed in the derivation of Equation IV-6. The base B must be a considerably stronger base than is water, but it must be weaker than the indicator. Moreover, it is essential that the condition

$$(K_f^{WHA} C_{H_2O}) \ll (K_f^{BHA} C_B)$$

be met, so that the water concentration should be as small

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solution containing C_{H_2O} molar water and zero molar B. The slope depends upon the true formation constant of the indicator salt rather than upon the apparent constant.

Experimental Part. The titrant was 0.006 M perchloric acid in these titrations; the procedure was identical with that used earlier. The bases titrated are described below.

Phenobarbital; recrystallized from 50% ethanol; mp 172-174°

Salicylamide; recrystallized from water; mp 138-139°

Acetanilide; recrystallized from water; mp 112-113.5°

Acetophenetidine; recrystallized from water; mp 133-135°

Benzamide; prepared by shaking benzoyl chloride with aqueous ammonia. The precipitate was recrystallized three times from water; mp 127°

[illegible] titrations [illegible] utilize equation IV-7. This indicator is sufficiently strong to allow the study of a considerable [illegible] the bases titrated are listed in Table VIII and are shown graphically in Fig. 9. The water concentration was 0.[illegible] M in all of these titrations.

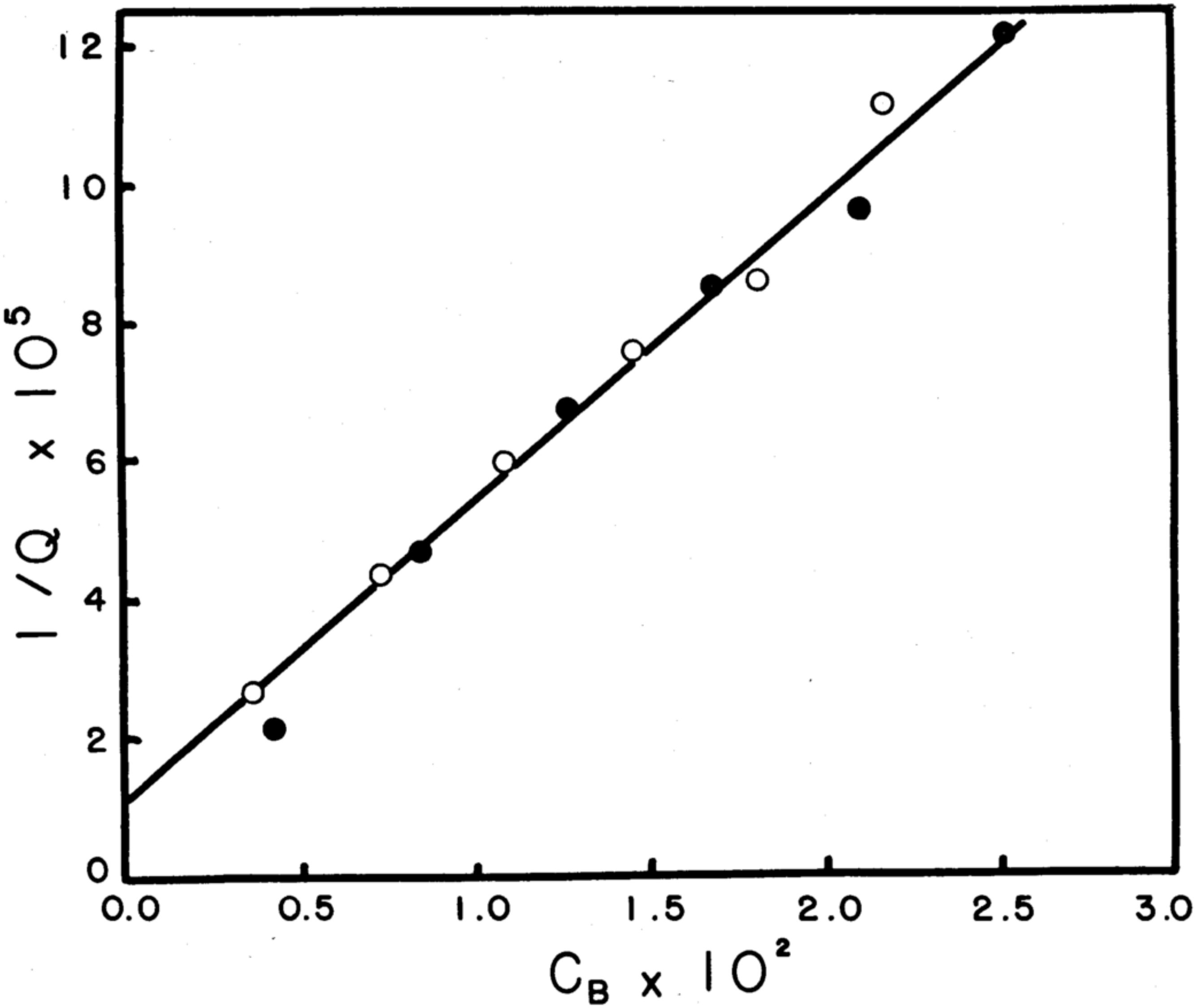

Fig. 8. Application of Equation IV-7 to the salicylamide-p-naphtholbenzein system. The data are given in Table VIII.

Table VIII

Experimental Data for PNB-Weak Base Systems

(C_{H_2O} = 0.018M; titrant is 0.008135N $HClO_4$)

C_B	Q_f^{IHA}	$1/Q_f^{IHA}$
	Salicylamide	
0.00364	3.74×10^4	2.67×10^{-5}
0.00728	2.31	4.33
0.0109	1.68	5.95
0.0146	1.33	7.52
0.0182	1.17	8.55
0.0218	0.90	11.1
0.00422	4.75	2.11
0.00844	2.13	4.69
0.0127	1.49	6.71
0.0169	1.18	8.47
0.0211	1.05	9.52
0.0253	0.82	12.2
	Benzamide	
0.00362	3.21×10^4	3.12×10^{-5}
0.00724	1.85	5.41
0.0108	1.22	8.20
0.0144	0.95	10.5
0.0181	0.80	12.5
0.0217	0.66	15.2
	Acetanilid	
0.00382	2.51×10^4	3.98×10^{-5}
0.00764	1.30	7.69
0.0115	0.99	10.1
0.0153	0.69	14.5
0.0191	0.55	18.2

Table VIII (Cont.)

Acetophenetidin

C_B	Q_f^{IHA}	$1/Q_f^{IHA}$
0.00000	8.27×10^4	1.21×10^{-5}
0.00374	1.11	9.01
0.00560	0.69	14.5
0.00748	0.50	20.0
0.0112	0.36	27.8

Phenobarbital

0.00177	8.27×10^4	1.21×10^{-5}
0.00354	8.79	1.14
0.00708	7.99	1.25
0.106	8.68	1.15

Base	K_f^{BHA} / K_f^{IHA}	K_f^{BHA}
Salicylamide	4.38×10^{-3}	4.8×10^2
Benzamide	6.48×10^{-3}	7.1×10^2
Acetanilid	8.35×10^{-3}	9.2×10^2
Acetophenetidin	2.35×10^{-2}	2.6×10^3
Phenobarbital	0	-

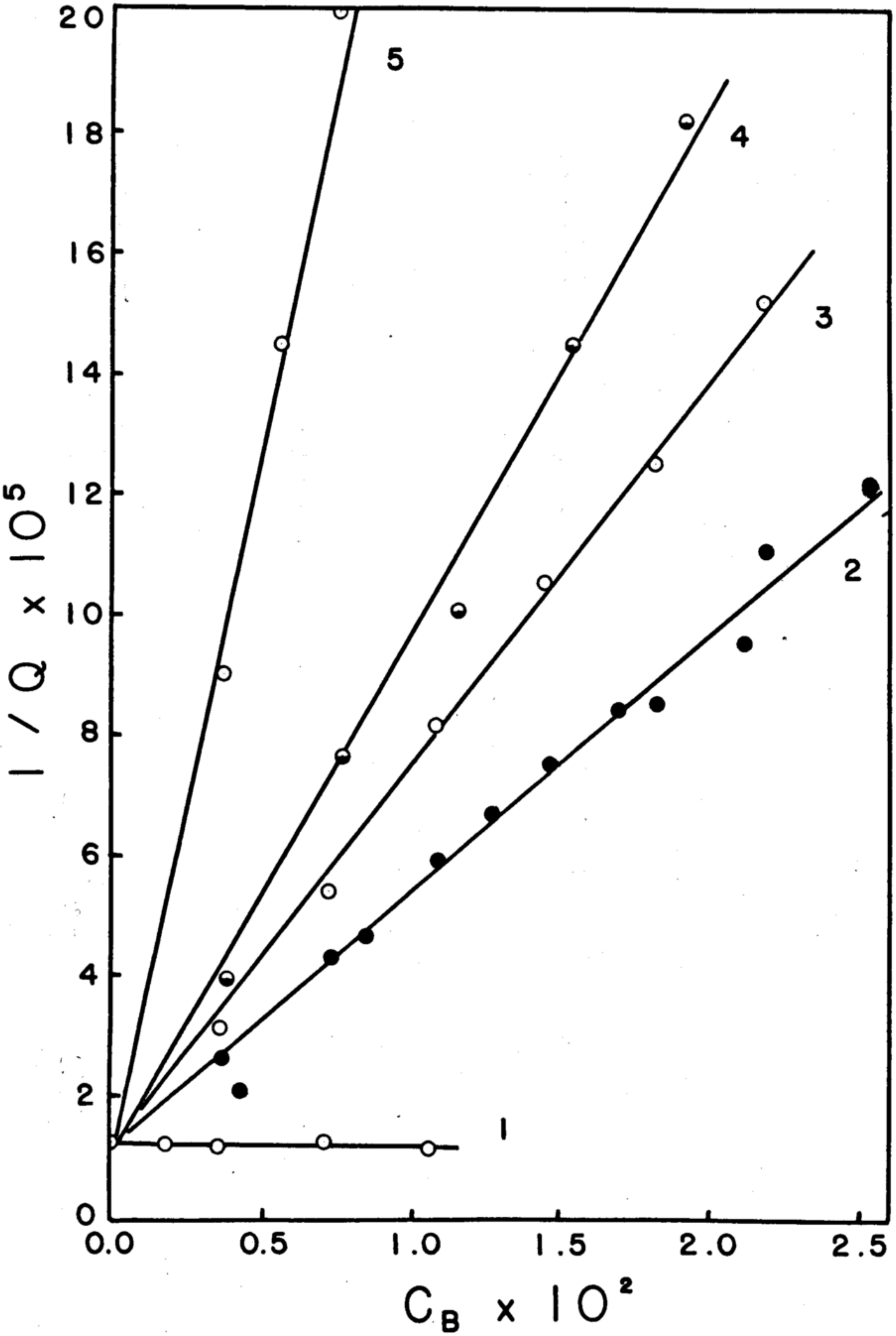

Fig. 9. Application of Equation IV-7 to some weak bases (p-naphtholbenzein is the indicator). (1) phenobarbital; (2) salicylamide; (3) benzamide; (4) acetanilid; (5) acetophenetidin. The data are given in Table VIII.

tration was increased to 0.043 M and a pronounced positive curvature was observed in the $1/Q_f^{IHA} - C_B$ plot.

It is evident that phenobarbital has no significant basicity in acetic acid according to this method of investigation.

The estimated error in the listed values of the formation constants will be discussed in Section VI.

V. EFFECT OF BENZENE ON SALT FORMATION IN ACETIC ACID

It has been observed that visual indicator end points of acid-base titrations in acetic acid are considerably sharpened by the addition of inert solvents of very low dielectric constant to the titration solution (35). This increased sensitivity may be due to suppression of solvolysis of the neutralization product (36), but it could be the result of a change in the indicator formation constant. In terms of the notation introduced in Section III, a sharper end point is associated with a smaller exchange constant; that is, the base appears to be stronger relative to the indicator.

The methods developed in Sections III and IV may be suitable for the investigation of such a phenomenon. A preliminary study has been made of a few base-indicator systems. Benzene was the inert solvent; because of solubility limitations the range of benzene concentrations studied did not include the very high values employed in the qualitative study noted above (35).

Reagent grade benzene was dried over calcium sulfate and distilled in an all-glass apparatus. The atmospheric boiling point was 79.3°. Water content was determined by visual Karl Fischer titration of an aliquot dissolved in methanol. Other materials employed have been described previously.

Two exchange constant systems have been investigated: the malachite green-caffeine system ($K_{ex} = 0.75$ in acetic acid) and Nile blue A - thiourea system ($K_{ex} = 0.25$). The modified type II technique was the experimental method used; the data are listed in Table IX. There is evidently no significant variation in exchange constant over the concentration range studied. The precision of the determinations is poorer in solutions containing benzene.

In order to determine the effect of benzene upon the formation constant the method developed in Section IV is required. Attempts to determine the variation in K_f^{IHA} of p-naphtholbenzein in accordance with this method showed that the formation constant of water perchlorate was also changing, consequently the entire $1/Q_f^{IHA} - C_{H_2O}$ plot had to be defined for each benzene concentration. The data are presented in Table X and the corresponding plots are shown in Fig. 10. The best straight lines were fitted to the points by the method of least squares; the equations of these lines are given in Table XI. The values of K_f^{WHA} / K_f^{IHA}, K_f^{WHA}, and K_f^{IHA} given by these equations are tabulated in Table XII. Because of the reciprocal nature of the vertical axis it is impossible to assign reliable values to the quantity K_f^{IHA} at the higher benzene concentrations; the scatter in the experimental points makes the location of the intercept uncertain. Although the individual formation constants of p-naphtholbenzein cannot be reliably determined from these data (this is a result of the inevitable presence of water in acetic acid) the ratios, corresponding to the slopes of the lines, are more accurately known.

Table IX

Effect of Benzene on Some Exchange Constants

Caffeine - Malachite Green

Mole Fraction Benzene	K_{ex}	Mean Deviation in K_{ex}	Number Determinations
0.000	0.75	0.03	5
0.067	0.80	0.05	10
0.139	0.76	0.04	5
0.216	0.78	0.09	4
0.300	0.80	0.08	5

Thiourea - Nile Blue A

Mole Fraction Benzene	K_{ex}	Mean Deviation in K_{ex}	Number Determinations
0.000	0.25	0.01	5
0.067	0.26	0.01	3
0.139	0.20	0.01	3
0.216	0.25	0.04	3
0.300	0.21	0.01	3
0.392	0.20	0.04	3

Table X

Experimental Data for *p*-Naphtholbenzein-Water-Benzene Systems

(N_b denotes mole fraction of benzene)

N_b	C_{H_2O}	Q_f^{IHA}	$1/Q_f^{IHA}$
0.000	0.014	7.73×10^4	1.29×10^{-5}
	0.023	6.76	1.48
	0.043	4.91	2.05
	0.063	3.76	2.66
0.067	0.018	7.12	1.40
	0.023	5.81	1.72
	0.033	4.83	2.07
	0.038	4.34	2.30
	0.043	3.79	2.64
	0.058	2.99	3.34
0.139	0.017	6.05	1.65
	0.021	6.37	1.57
	0.037	3.72	2.69
	0.047	3.15	3.17
	0.051	3.14	3.18
	0.057	2.67	3.75
0.300	0.015	6.69	1.49
	0.025	4.72	2.12
	0.045	2.58	3.88
	0.055	2.00	5.00
	0.065	1.77	5.65
0.491	0.014	7.29	1.37
	0.023	4.76	2.10
	0.034	2.91	3.44
	0.044	2.44	4.10
	0.054	1.79	5.59
	0.064	1.41	7.09

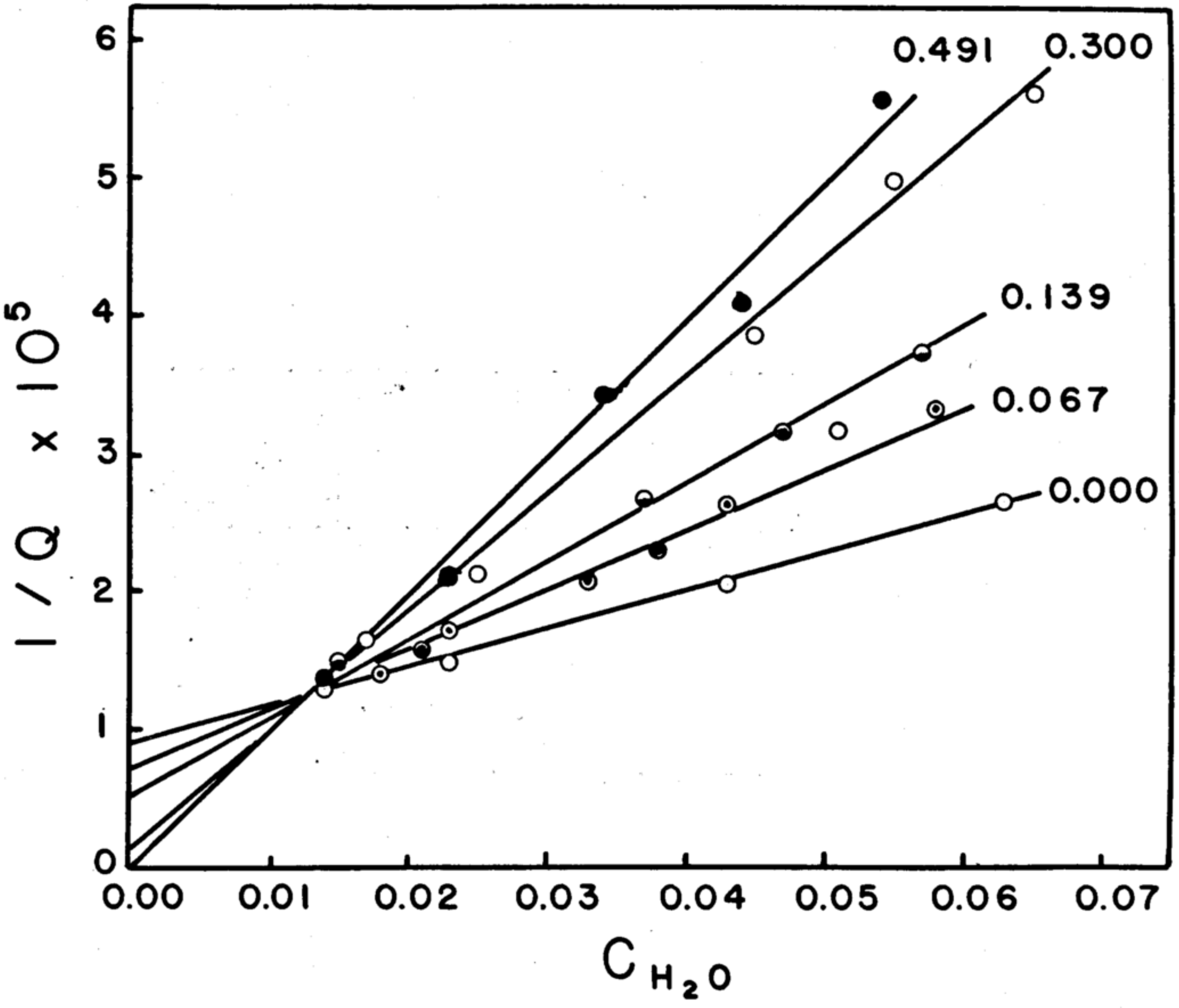

Fig. 10. Effect of benzene on the p-naphtholbenzein - water system in acetic acid. Mole fractions of benzene are indicated with the corresponding lines. These data are given in Table X.

Table XI

The Least Squares Equations for the p-Naptholbenzein-Water-Benzene System

N_b	Equation
0.000	$1/Q = 2.70 \times 10^{-4}\ c_{H_2O} + 0.90 \times 10^{-5}$
0.067	$1/Q = 4.12 \times 10^{-4}\ c_{H_2O} + 0.78 \times 10^{-5}$
0.139	$1/Q = 5.74 \times 10^{-4}\ c_{H_2O} + 0.49 \times 10^{-5}$
0.300	$1/Q = 8.69 \times 10^{-4}\ c_{H_2O} + 0.07 \times 10^{-5}$
0.491	$1/Q = 10.0 \times 10^{-4}\ c_{H_2O} - 0.06 \times 10^{-5}$

Table XII

Formation Constants for the p-Naphtholbenzein-Water-Benzene Systems

N_b	D	K_f^{WHA}/K_f^{IHA}	K_f^{IHA}	K_f^{WHA}
0.000	6.20	2.70×10^{-4}	1.1×10^{5}	30
0.067	5.50	4.12	1.3	5×10^{1}
0.139	4.80	5.74	2.0	1×10^{2}
0.300	3.58	8.69	$6 \cdot 10^{5}$ -	$5 \cdot 10^{2}$ -
0.491	2.83	10.0	-	-

The dielectric constants of the solvents are also recorded in Table XII.* The ratio K_f^{WHA} / K_f^{IHA} is linear with dielectric constant, as shown in Fig. 11. The values of the individual formation constants are not known with sufficient accuracy to determine the form of their dependence upon dielectric constant.

That the formation constant might be affected by small dielectric constant changes would not be expected from consideration of its definition (Equation II-12), which involves no free ions. The principal effect is probably due to the increased extent of higher ionic aggregate formation at the lower dielectric constants. (See Section I-A). In even the relatively simple case represented by the p-naphtholbenzein-water system the number of combinations of ions and ion-pairs to form aggregates is large. The species which may be involved are: H^+A^-, H^+, A^-, IH^+A^-, IH^+, $H_3O^+A^-$, H_3O^+. The experimental value of the indicator formation constant is affected only by those aggregates which include the indicator species. Consider the simple case in which the only pertinent aggregate is $A^-IH^+A^-$. The constant of formation of this triple-ion is

$$k = C_t / C_{IHA}(A^-) \qquad (V\text{-}1)$$

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* These dielectric constants at 25° were obtained by interpolation from the data of Smyth and Rogers (37). The dielectric constant-composition diagram deviates strongly from linearity.

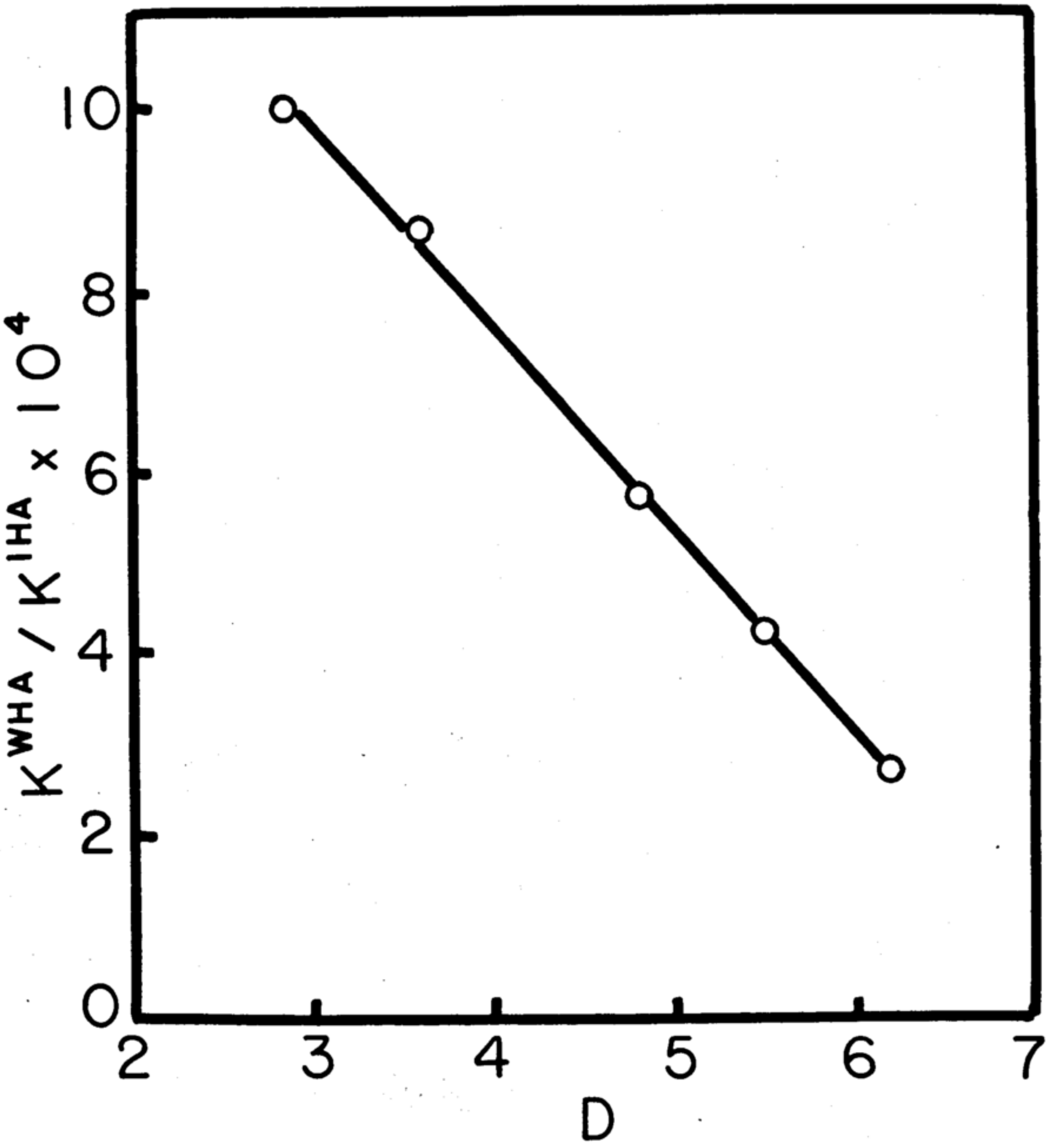


Fig. 11. Variation of the slopes of lines in Fig. 10 with dielectric constant of the solvent. The data are given in Table XII.

where C_t represents the concentration of triple-ion. K_f^{IHA} is defined by Equation II-15 and the apparent indicator constant, K', is

$$K' = (C_{IHA} + C_t) / C_I C_{HA} \qquad \text{(V-2)}$$

Combining Equations II-15, V-1, and V-2 gives

$$K' = K_f^{IHA} \left[1 + k(A^-) \right] \qquad \text{(V-3)}$$

In general the term within brackets will consist of a sum of products of aggregate formation constants and concentrations, each product being multiplied by an integer representing the number of indicator molecules contained in the aggregate. Evidently the apparent formation constant will be larger than the true constant, and the discrepancy will increase with decrease in dielectric constant. This problem might also be approached in terms of the variation in the activity coefficients in the thermodynamic formation constant expression.

A quantitative interpretation of these data is not possible at the present time. More accurate data, particularly relating to the behavior of individual formation constants, is necessary. This preliminary study serves to indicate the great effect which such a small change in the solvent may cause. It is unlikely that, at the benzene concentrations employed, the acetic acid concentration was sufficiently reduced to change markedly the acidic or solvating properties of the solvent. If the (assumed) molecule of solvent (acetic acid) released in the salt formation reaction is incorporated into the equilibrium expression the values of the individual formation constants will differ from those reported here, but the ratio K_f^{WHA} / K_f^{IHA} will remain unaltered.

VI. DISCUSSION OF THE RESULTS

A. The Salt Formation Constants

The technique outlined in Section IV-A permits the evaluation of the indicator formation constant; this value, together with the exchange constants determined by the modified type II plot, allows calculation of the formation constants of colorless bases. All of the constants determined in this way are compiled in Table XIII, which also includes formation constants found by the method of Section IV-B.

Most of the values tabulated are based upon the constant for p-naphtholbenzein, 1.1×10^5. Calculation via the exchange constants then yields the formation constant for any other indicator or base. The value thus calculated for Nile blue A is 3.9×10^4, while 3.4×10^4 was found experimentally (Section IV-A). In view of the estimated error of the determinations the calculated constant was taken as being more consistent with the other results, while it is in reasonable agreement with experiment. The formation constant of Sudan III was independently determined; the exchange constants of Sudan III - base systems are the least reliable of those reported because of the extremely weak character of this indicator.

The two methods developed for estimation of formation

Table XIII

Perchlorate Formation Constants for Some Bases and Indicators in Acetic Acid

Compound	$K_f^{BHClO_4}$	$\log K_f^{BHClO_4}$
Salicylamide	$4.8 \pm 0.4 \times 10^2$	2.68
Benzamide	$7.1 \pm 0.5 \times 10^2$	2.85
Acetanilid	$9.2 \pm 0.5 \times 10^2$	2.96
Acetophenetidin	$3.2 \pm 0.6 \times 10^3$	3.51
Acetamide	$1.1 \pm 0.2 \times 10^4$	4.04
Urea	$8.5 \pm 0.7 \times 10^4$	4.93
2,6-Dimethyl-γ-pyrone	$1.4 \pm 0.3 \times 10^5$	5.15
Thiourea	$1.5 \pm 0.2 \times 10^5$	5.18
Caffeine	$2.4 \pm 0.5 \times 10^5$	5.38
Sudan III	$9.1 \pm 0.5 \times 10^2$	2.96
Nile Blue A	$3.9 \pm 0.6 \times 10^4$	4.59
p-Naphtholbenzein	$1.1 \pm 0.05 \times 10^5$	5.04
Malachite Green	$1.8 \pm 0.2 \times 10^5$	5.26

constants of colorless bases, that is, the modified type II method (Section III-A) and the method based upon variation in apparent indicator constant with base concentration (Section IV-B) overlap slightly in the range of basicities accessible to each. Acetophenetidin falls in this intermediate zone, and its constant was accordingly determined by both methods. The method of Section IV-B gave $K_f^{BHA} = 2.6 \times 10^3$, while the modified type II plot, with Sudan III indicator, gave an exchange constant 0.24 which, combined with the formation constant of Sudan III, yields $K_f^{BHA} = 3.8 \times 10^3$. In view of the large uncertainty to be expected in Sudan III titrations these figures are taken to indicate good agreement between the two methods.

The estimated uncertainties listed in Table XIII are based upon the mean deviations in the exchange constants as shown in Table IV and upon the reasonable uncertainty assigned to the formation constant of p-naphtholbenzein, namely, $1.1 \pm 0.05 \times 10^5$. As mentioned earlier, much of the variation in experimental values results from the graphical treatment of the data, and is difficult to assess quantitatively.

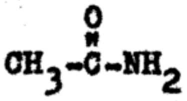
The estimated formation constant for the second basic function on aminopyrine is $8 \pm 2 \times 10^3$; this value is based upon the exchange constant of this group with Nile blue A ($K_{ex} = 5.0$).

B. Relative Strengths of Some Bases

The bases titrated during the course of the work described here were selected to cover the range of base strengths accessible with the four indicators used. An effort was made, at the same time, to choose bases which would provide interesting, though necessarily limited, information on structure-basicity relationships in this very low basicity range. Some of these particular examples will be discussed.

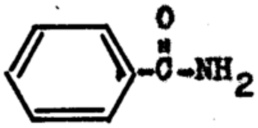
Table XIII includes the logarithm of the formation constant for each of the bases titrated; this quantity is proportional to the free energy change of the salt formation reaction, and gives an indication of the comparative strengths of the compounds and of the range of basicities studied. It has been pointed out, however, that the free energy change is not necessarily a valid measure of such structural features as bond energies, resonance energies, and electron displacements (38). These concepts relate directly to potential energy differences between structures while the free energy change represents contributions from both potential and thermal kinetic energy terms. The same may be said of the enthalpy change. Statistical arguments show that only when the entropy change of a process is equal to zero may the kinetic energy terms be neglected and the free energy and enthalpy changes be taken as valid measures of potential energy differences (38). The figures of Table XIII cannot, therefore, be related precisely to structural effects in the absence of additional information, but they serve to indicate the resultant of all effects on the basicity.

Three unsubstituted amides were among the compounds titrated: acetamide, I; benzamide, II; and salicylamide, III. It is interesting to compare the basicities of these

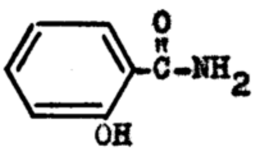


$CH_3-\overset{O}{\overset{\parallel}{C}}-NH_2$

I



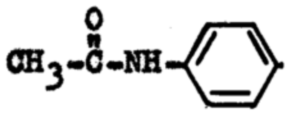
II



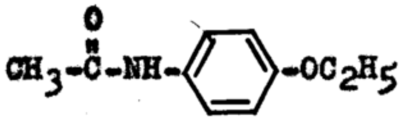
III

amides with the acidities of the corresponding acids. The logarithm of the formation constants for the amides are: I, 4.04; II, 2.85; III, 2.68. The pK_a values of the corresponding acids are 4.76, 4.20, and 2.97. The weaker the amide as a base, the stronger is the corresponding acid, as would be expected if the same effects are operative in the two cases, with the resultant negativity of the functional groups determining the extent of reaction. These three examples do not show a direct proportionality, the salicylic acid being much more acidic than would be expected from consideration of either the benzoic acid molecule or the amide series. This is probably due to internal hydrogen bonding from the phenolic hydrogen to the carboxylic oxygen (39). This effect would not be apparent in the amide studies because the solvent, acetic acid, would preferentially bond to the negative group. This negative group is, at least in aliphatic amides, the oxygen; nuclear magnetic resonance studies have shown that amides probably protonate on the oxygen (40).

Acetanilid, IV, is considerably less basic than acetamide, but this difference cannot safely be ascribed to relative electronegativity of the phenyl group; such an interpretation neglects the contribution of kinetic terms to the free energy change, as discussed earlier in this section. Comparison of acetanilid and acetophenetidin, V, which are very similar molecules, is more reasonable. Acetophenetidin, which contains the ortho-para directing ethoxy group para to the amide function, is more basic than acetanilid.

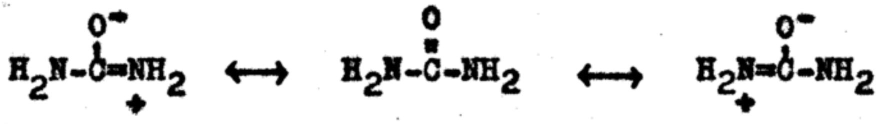


IV



V

The compounds urea and thiourea present an interesting case in this study. Thiourea is more basic than urea in acetic acid, according to the formation constant criterion (Table XIII). This is not the situation in some other solvents. In methanol, for example, urea is a stronger base than thiourea (K_b(urea) = 4.6×10^{-14}; K_b(thiourea) = 3.7×10^{-16}), and in water the same order is observed (K_b(urea) = 1.5×10^{-14}; K_b(thiourea) = 1.1×10^{-15})(41,42). Some possible reasons for this reversal can be suggested: (I) According to Equation II-13 the formation constant of a base depends upon the dissociation constant of its salt.* The dissociation constants of urea perchlorate and thiourea perchlorate may be sufficiently different, due to differences in ionic dimensions, perhaps, to account for the basicity relation. (2) The sites of protonation of the two compounds may not be the same in the two solvents. As with the aliphatic amides, it is probably the oxygen of urea which is protonated; if such is the case three resonance forms of the cation, two of them equivalent, can be drawn. The same argument applies to thiourea, which, due to the lesser electronegativity of sulfur, should then be a weaker base than urea. If in the acetic acid system protonation should occur on the nitrogen (for only urea, or for both molecules) such a reversal might occur. (3) It is believed that urea and thiourea both exist as resonance hybrids with contributions from ionic forms to the extent of 20-30% (43,44). The contribution of the polar form may be affected by the



$$H_2N\text{-}\overset{O^-}{C}{=}\underset{+}{N}H_2 \longleftrightarrow H_2N\text{-}\overset{O}{\overset{\|}{C}}\text{-}NH_2 \longleftrightarrow H_2\underset{+}{N}{=}\overset{O^-}{C}\text{-}NH_2$$

solvent to such a degree as to alter this percentage for the two compounds and thus induce changes in basicity. Such an effect might be due to the different polarizabilities of the sulfur and oxygen electronic systems. (4) The reversal could be due to some highly specific hydrogen-bonding

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* This is a disadvantage of the formation constant as a measure of basicity in solvents of low dielectric constant.

solvent effect; such an interpretation has been invoked to explain similar behavior observed with organic bases by other workers (45,46). These suggestions, however, are speculative only.

C. Further Studies Suggested by this Work

The first problem which must be met is of course the usefulness of the salt formation constant as a measure of basicity. The data obtained in the present work demonstrate that the formation constant is an accessible and useful quantity with which to characterize the neutralization reaction, but its limitations must be defined experimentally. One difficulty has been alluded to in connection with the basicities of urea and thiourea; that is, the formation constant depends upon the value of the dissociation constant of the salt. For a given solvent and a given acid, then, K_f^{BHA} varies directly with the ratio K_B/K_{BHA}. In a sense, the inclusion of K_{BHA} in the relation may cancel the effect which the solvent has through its dissociating power upon K_B.

The reproducibility observed in the present work is a resultant of the experimental measurements and the graphical treatment of the data. Volume measurements in the modified type II method were more than sufficiently accurate. For the titrations discussed in Section IV more sensitive volume measurement may increase the precision. Probably, however, spectral data from these very poorly buffered solutions are principally responsible for the deviations.

The accuracy of the Karl Fischer titrations is a factor in the determinations discussed in Section IV. The estimated uncertainty is 0.001 M; because of the technique used in preparing the solutions, this can affect the accuracy but not the precision of a series of determinations.

Until the precision of measurements is improved it is not important to consider the effect which ionic strength may have upon the value of the salt formation constant. The effect of temperature can be studied in order to determine, for practical reasons, the sensitivity of the constants. It is to be expected that exchange constants will not vary markedly with temperature, though the individual formation constants will. The usual thermodynamic functions can be obtained from these measurements.

The use of stronger indicators in these studies, perhaps with the application of relations such as Equations III-9 and III-10, will permit the study of moderately strong bases. Other acids than perchloric may be useful in such studies. In particular, diphenyl phosphate promises to be a useful titrant in organic solvents (47). This acid is soluble in inert solvents, as are many of its salts, and may help extend photometric methods to these media. Such an acid may be necessary in pursuing dielectric constant studies of the type described in Section V, since the solubility limitation may be overcome.

The determination of basicity of very weak bases is considerably facilitated by these photometric indicator methods. Some interesting applications of such determinations may involve, for example, the basicity of amides and its correlation with other amide reactions. The literature contains very few reliable values of amide basicities, and so extensive correlations of this type, which have been successful for other series of compounds, have not been possible. The strength of organic oxygen bases has not been sufficiently studied in a quantitative manner, and the present methods may allow such investigations to be made conveniently.

VII. SUMMARY

The salt formation constant, $K_f^{BHA} = C_{BHA}/C_B C_{HA}$, is defined for the neutralization reaction $B + HA \rightleftharpoons BHA$; this constant is taken to be a quantitative measure of the basicity of B against the reference acid HA in a given solvent. In the present investigation the reference acid was perchloric acid and the solvent was acetic acid. The purpose of the study was to develop methods for the evaluation of K_f^{BHA} for very weak bases. Two methods were devised, both involving photometric indicator titrations and thus measuring the formation constant through observation of the effect which the base has upon the indicator equilibrium. These methods are complementary with regard to their applicability to different ranges of base strength. The effect of structural changes in bases upon the salt formation constants was also studied to some extent, and the value of the formation constant in structural studies is suggested by the results of this work.

(1) For the investigation of bases at least as strong as acetamide the modified type II plot has been found to serve well. This graphical method, a refinement of an earlier technique, is based upon Equation VII-1.

$$1/(X_2-X_1) = [K_{ex}/(S_2-S_1)]\,(I_b/I_a) + 1/(S_2-S_1) \qquad \text{(VII-1)}$$

$K_{ex} = K_f^{IHA} / K_f^{BHA}$ where I is an indicator base, I_b/I_a is the ratio of base/acid forms of the indicator, X and S are milliliters of standard acid added at any point and at the equivalence point, respectively. Two samples, differing only in size and denoted by 1 and 2, are titrated. A graph of the quantity $1/(X_2-X_1)$ vs I_b/I_a is linear and yields the end point (S_2-S_1) and exchange constant (K_{ex}).

The indicators employed were Sudan III, Nile blue A, p-naphtholbenzein, and malachite green. Bases titrated were acetophenetidin, acetamide, urea, 2,6-dimethyl-γ-pyrone, thiourea, caffeine, antipyrine, isonicotinic acid, and triphenylguanidine. The last three bases are sufficiently strong so that their exchange constants with Nile blue A are equal to zero within the accuracy of the experimental measurements; Nile blue A is consequently termed a leveling indicator for these bases, while it is a differentiating indicator for the weaker bases. The relative precision of the exchange constant determinations is about 5%. The quantitative recoveries of 20-30 mg samples of all bases were 98-101%. Some special cases of binary base mixtures have been investigated with this technique also.

(2) A method has been developed which permits the evaluation of individual indicator formation constants. With acetic acid solvent, consideration of the indicator-acid equilibrium (taking into account water present as an impurity) leads to Equation VII-2.

$$1/Q_f^{IHA} = K_f^{WHA} C_{H_2O} / K_f^{IHA} + 1/K_f^{IHA} \qquad \text{(VII-2)}$$

K_f^{WHA} is the formation constant for water perchlorate, C_{H_2O} is the molar concentration of water, K_f^{IHA} is the indicator perchlorate formation constant, and Q_f^{IHA} is given by

$$Q_f^{IHA} = (I_a/I_b)V/N(X - R) \qquad \text{(VII-3)}$$

V is the total volume of titration solution, N is the titrant acid normality, X has the significance formerly assigned, and R is the volume of titrant equivalent to the acid bound as indicator salt; R is calculated from the spectral data and molar absorptivity of the indicator. Q_f^{IHA} is found from a plot of I_a/I_b vs $(X - R)$. According to Equation VII-2 values of K_f^{WHA} and K_f^{IHA} may be calculated from the slope and intercept of a $1/Q_f^{IHA}$ - C_{H_2O} plot. In this way K_f^{WHA} was found to be 38 ± 8.

In a variation on this method a weak base B is included in the system. If the condition $K_f^{WHA}C_{H_2O} \ll K_f^{BHA}C_B$ is satisfied an equation similar to Equation VII-2 may be used to evaluate K_f^{BHA}. Bases titrated in this way were salicylamide, benzamide, acetanilid, and acetophenetidin.

Combination of the results of the two methods permits the calculation of the formation constants for all of the weak bases studied. These bases and the logarithm of their perchlorate formation constants are: salicylamide, 2.68; benzamide, 2.85; acetanilid, 2.96; acetophenetidin, 3.51; acetamide, 4.04; urea, 4.93; 2,6-dimethyl- -pyrone, 5.15; thiourea, 5.18; caffeine, 5.38. The indicator perchlorate formation constants are: Sudan III, 2.96; Nile blue A, 4.59; p-naphtholbenzein, 5.04; malachite green, 5.26. The uncertainties in these values range from 0.04 to 0.1 unit.

In a preliminary study of the effect of benzene upon the formation constant in acetic acid, the exchange constants of the systems caffeine-malachite green and thiourea-Nile blue A were observed to remain unchanged over the accessible range of benzene concentrations. The p-naphtholbenzein-water system was investigated and the ratio K_f^{WHA} / K_f^{IHA} was found to change linearly with dielectric constant, the ratio increasing as dielectric constant decreases. The individual constants also increase, but the data are not sufficiently accurate to determine the form of this relationship. This increase in formation constant with decreasing dielectric constant has been attributed to an increased extent of formation of higher ionic aggregates.

VIII. APPENDIX A. SPECTRAL CHARACTERISTICS OF INDICATORS

The spectral properties of the indicators used in this work are recorded in Tables XIV and XV. Three of these indicators are tabulated in standard references as listed below.

Indicator	C.I. Number (2nd ed)(48)	C.I. Number (1st ed)	Schultz (7th ed)(49)
Malachite green	42000	657	754
Nile blue A	51180	913	1029
Sudan III	26100	248	532

p-Naphtholbenzein is not included in these works. It is commercially available from the Eastman Kodak Company (No. 924). The other indicators are from commercial sources also.

The spectral stabilities of the indicators were investigated by measuring the absorbance of their solutions at an absorption maximum as a function of time. Both the acid and base forms of each indicator were studied. Some of the indicators are stable for many weeks; all four of them undergo no significant change over a twelve hour period. The entire absorption spectrum, in the visible range, of each indicator was recorded on a Cary Model 11 spectrophotometer, and no change in the shape of the curves was noted during the time period considered.

Table XIV

Absorption Maxima of Indicators in Acetic Acid Solutions

Indicator	Abbreviation	Base Maxima (mu)	Acid Maxima (mu)
Malachite green	MG	425, 620	450
p-Naphtholbenzein	PNB	453	465, 623
Nile blue A	NBA	632	455
Sudan III	S-III	513	613

Underlined wavelengths are those used in photometric titrations.

Table XV

Absorptivities of Indicators in Acetic Acid Solutions

Indicator	Solvent	Wavelength (mu)	Absorptivity ($ml \cdot mg^{-1} \cdot cm^{-1}$)
MG	Glacial acetic acid	620	226
PNB	0.05N $HClO_4$	623	93
NBA	Glacial	632	150
S-III	0.05N $HClO_4$	613	193

All indicator solutions used in the photometric titrations discussed earlier were prepared fresh daily. The four indicators employed have all been used previously in acetic acid solutions (22,29).

IX. APPENDIX B. NOMOGRAPHS FOR THE EVALUATION OF INDICATOR RATIOS

Because the indicator concentration remains a constant throughout the course of the photometric titrations, the indicator ratio is given by Equation IX-1. (All absorbances are measured at the same wavelength).

$$R = I_b/I_a = (A - A_a)/(A_b - A) \qquad \text{(IX-1)}$$

All of the indicators concerned are practically unionized in acetic acid, hence the absorbance of the sample solution prior to titration gives the value of A_b. The absorbance of the titrant solution is A_a. Nile blue A and malachite green are indicators whose A_a value is very nearly zero at wavelengths used in photometric titrations; A_b is nearly zero for Sudan III and p-naphtholbenzein. Calculations are simplified by measuring all absorbances against the titrant solution in the first two cases and against an acetic acid solution of the indicator in the latter two. For Nile blue A and malachite green the equation then becomes

$$A(1/R + 1) = A_b$$

and for Sudan III and p-naphtholbenzein

$$A(R + 1) = A_a$$

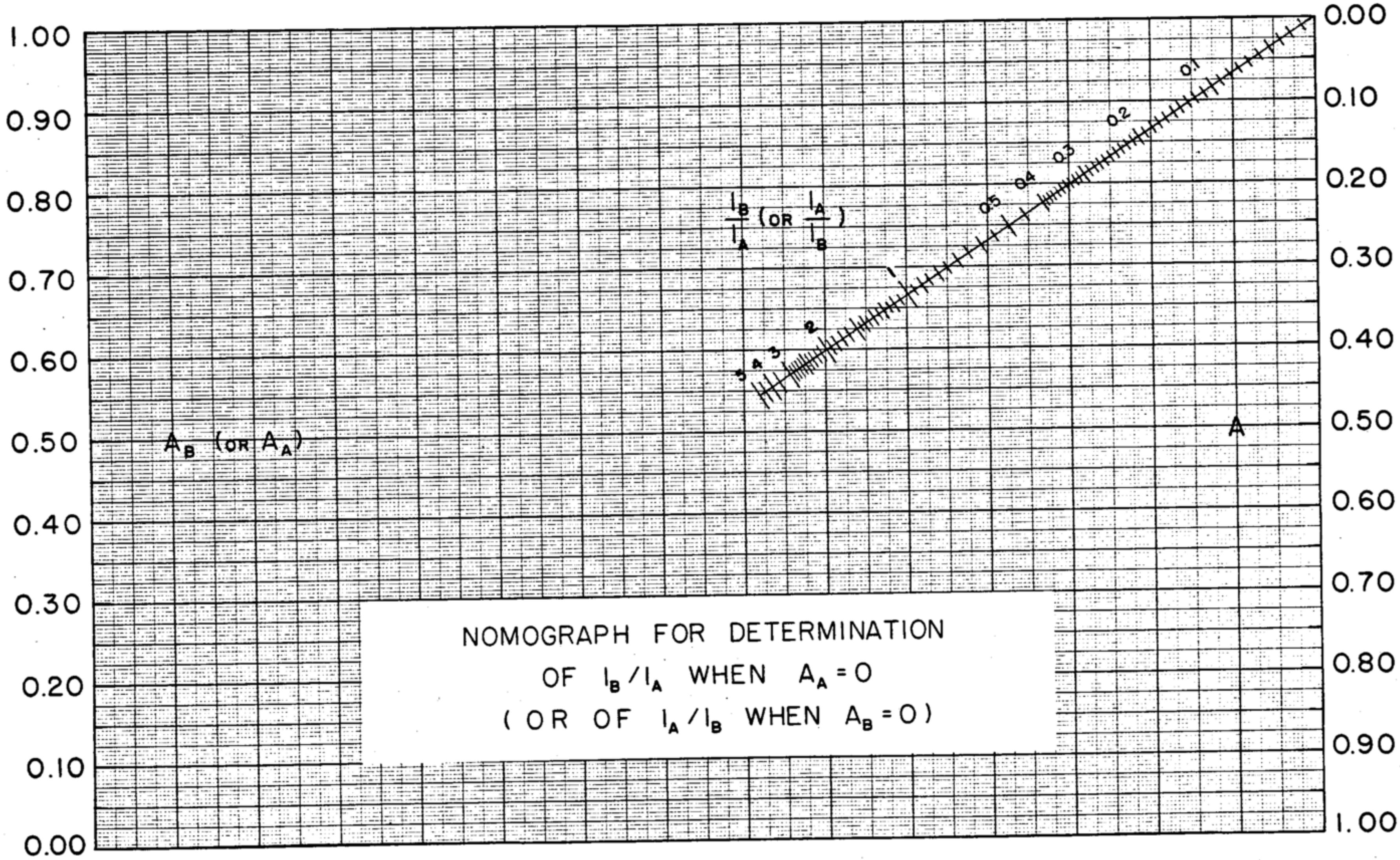
Both of these equations are of the form

$$f_1(A)f_2(R) = f_3(A_k) \qquad (k = a \text{ or } b)$$

and can be presented in nomographical form as a Z graph. When A and A_k are graphed according to the same scale, then the diagonal scale, representing values of the indicator ratio, may be calibrated with Equation IX-2 (50).

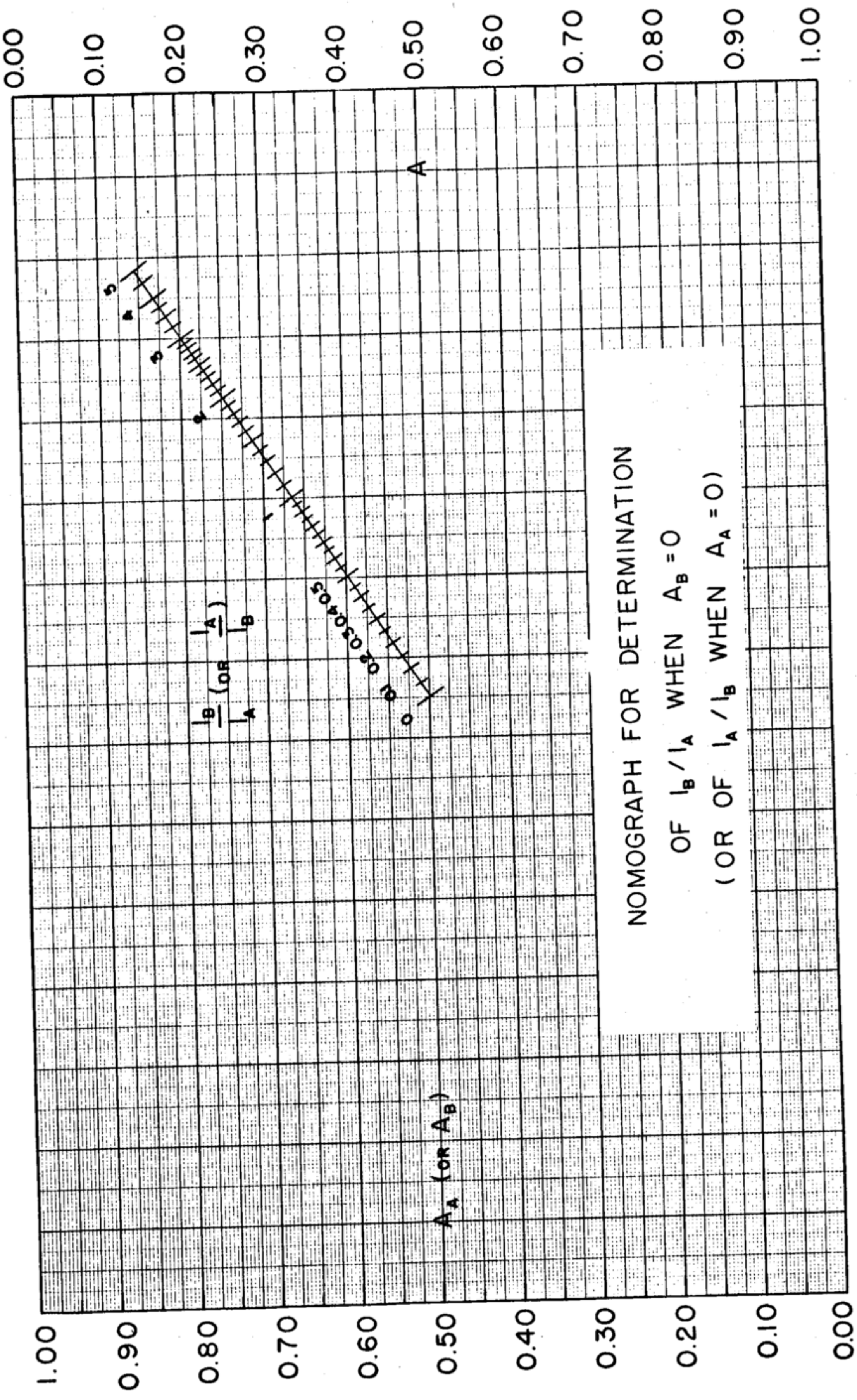
$$X_R = K/[f_2(R) + 1] \tag{IX-2}$$

where K is the total length of the diagonal and X_R is the distance of R along the diagonal, measured from the point $A = 0$. The nomographs are shown in Figs. 12 and 13. All indicator ratios were evaluated with these nomographs by connecting the experimental values of A and A_a (or A_b) with a straightedge; the point at which the straightedge intersects the diagonal gives the indicator ratio value.



NOMOGRAPH FOR DETERMINATION
OF I_B/I_A WHEN $A_A = 0$
(OR OF I_A/I_B WHEN $A_B = 0$)

Fig. 12



NOMOGRAPH FOR DETERMINATION

OF I_B / I_A WHEN $A_B = 0$

(OR OF I_A / I_B WHEN $A_A = 0$)

Fig. 13

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