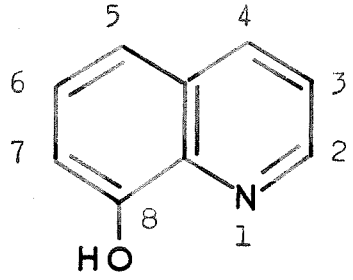
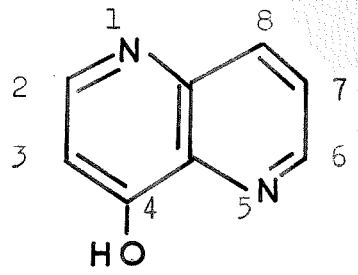
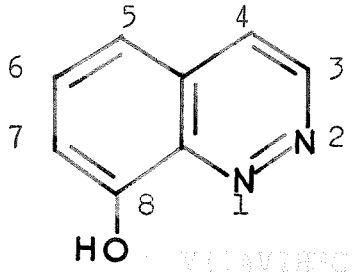
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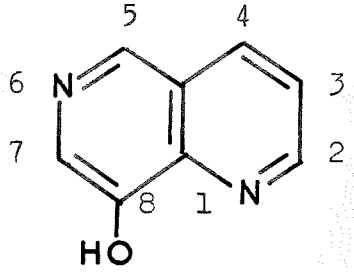
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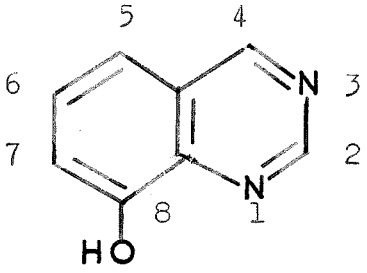
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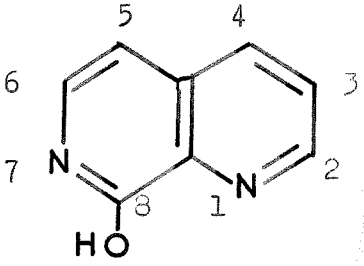
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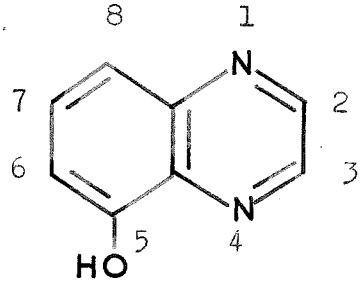
8-Hydroxy-1:6-naphthyridine.



8-Hydroxyquinazoline.



8-Hydroxy-1:7-naphthyridine.



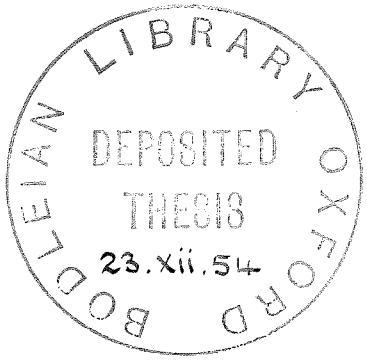
5-Hydroxyquinoxaline.

Trinity Term, 1954.

SOME INVESTIGATIONS OF

ORGANIC REAGENTS FOR METALS.

A Thesis submitted for the Degree of Doctor of Philosophy.



H. S. Rossotti,
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Oxford.

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Abstract.

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NOTE ON SYMBOLISM.

In this work, K_n refers to the stability constant of the complex ML_n relative to ML_{n-1}, and corresponds to the symbols k_n and K_{ML_n} used by Bjerrum and Schwarzenbach respectively. The overall stability constant of the species ML_n will be written β_n (Fronaeus), which corresponds to K_n (Bjerrum), $\bar{K}^L_{ML_n}$ (Schwarzenbach) and χ_n (Sillen). Thus $\beta_n = K_1K_2\ldots K_n$.

No right-hand superscript is used for terms refering to metal-ligand complexes. The right-hand superscript, H, refers to ligand-proton complexes, so that the overal stability constant of the species H_jL is $\beta^H_j = K^H_1.K^H_2\ldots.K^H_j$, and the degree of formation of the ligand-proton system is written $\bar{n}^H$. The right-hand superscript, A, refers to conventional acid dissociation constants, which can be simply related to the terms K^H_1, K^H_2... (see pages 12 and 25).

The left-hand superscript, T, c, and B refer to thermodynamic, stoicniometric and Brønsted constants, respectively, e.g.

$$^cK_n = [ML_n]/[ML_{n-1}][L] \qquad ^c\beta_n = [ML_n]/[M][L]^n$$

$$^TK^H_j = \{H_jL\}/\{H_{j-1}L\}\{H\} \qquad ^T\beta^H_j = \{H_jL\}/\{L\}\{H\}^j$$

and, for the species, HL,

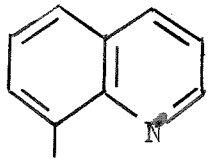
$$^BK^A = \{H\}[L]/[HL].$$

SECTION 1.

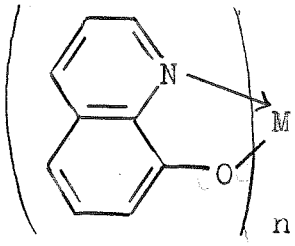
INTRODUCTION.

1(a) THE SCOPE OF THE PRESENT WORK.

8-Hydroxyquinoline ('oxine',I) is widely used in analytical chemistry, as it reacts with a variety of metal ions to form chelate complexes of the type II.



I.



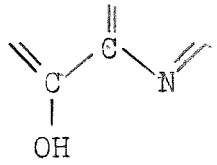
II.

Its use as a precipitant for metals depends on the low solubility of the chelates in water [1]. The precipitates have a high molecular weight, and a fixed stoichiometric composition over a wide range of temperature [2], and are widely used in gravimetric analysis. The chelates are also freely soluble in polar organic solvents, and so find application in partition chromatography [3-5], and in solvent extraction [6]. As the chelates are highly coloured, the metal content of the organic phase may be determined absorptiometrically [7].

The main disadvantage of oxine as an analytical reagent is that it reacts with a very large number of metals [8], so that rigorous control of experimental conditions, and the use of masking agents, are necessary to obtain any degree of selectivity. Separation of two metals by selective precipitation of the oxinates is only possible if the two complexes differ appreciably either in stability or in 'intrinsic solubility' in water (i.e. the maximum concentration of undissociated molecules of the complex in a solution in equilibrium with the solid complex). Similar separations by solvent extraction or partition chromatography depend on large differences in either stability or in partition coefficient. Greater selectivity might therefore be expected with reagents which form metal complexes of more varied stability than the corresponding oxinates; but there is little quantitative knowledge of the factors which determine the stability of such complexes. Of the many derivatives

of oxine which have been investigated semi-quantitatively, the only observed trend towards selectivity was the failure of the 2-substituted reagents to precipitate aluminium ions [9,10].

In this work, some of the factors influencing the stability of complexes of oxine derivatives have been investigated. The inductive effects acting on the functional group in oxine,



have been modified both by the replacement of one =CH- group by =N- in all six possible positions, and also by alkyl substitution in some positions of oxine, and of some of the aza-oxines. Steric hindrance to complex formation was studied using reagents having substituents adjacent to the chelating nitrogen atom. The stability constants of complexes of these reagents with Mg^{++}, Zn^{++}, Ni^{++}, Cu^{++}, and UO_2^{++} ions were determined in 50% v/v aqueous dioxan, as both the reagents and their complexes are very sparingly soluble in water.

The calculation of the stability constants is based on Jannik Bjerrum's treatment of step equilibria, which is outlined in Section 1(b). As the existing methods for obtaining formation curves (see p. 5) of metal complexes from pH titration curves are not strictly applicable to mixed solvents, a new method has been evolved, and is described in Section 2(b). It is generally applicable to all ligands which are conjugate bases to weak acids, both in aqueous and in mixed solvents. The calculation of successive stability constants from the experimental formation curve is discussed in Section 2(c). Some of the current methods are unsatisfactory, and two new methods for computing constants for 2:1 complexes are described.

Some measure of the inductive effects acting on the functional group of a reagent is given by its dissociation constants. New methods for determining these constants from pH titration data in water or in mixed solvents, and from variation of optical absorbancy with pH in water are given in Sections 2(b) and 2(c) respect-

ively; both methods may be applied to reagents having two groups with similar dissociation constants. The experimental values of the dissociation constants in water, and in 50% v/v aqueous dioxan, are given in Section 3(a). The absorption spectra of oxine and of the aza-oxines were determined in acidic, neutral and alkaline solution in an attempt to elucidate the position of the more basic nitrogen atom in the aza-oxines. Other physical properties of the reagents discussed in Section 3(a) include the absorption spectra in water and in amyl alcohol, values of wet and dry melting points, and solubility data.

Some thermodynamic aspects of metal complex formation are considered in Section 3(b), where possible relationships between the stability of a complex and the dissociation constants of the reagent, the ionisation potential of the metal, and the stability of related complexes, are discussed. Conditions for the existance of 'stability orders' of metals are also considered. Applications of the above treatment to the constants obtained in this work are discussed in Section 3(c).

Intercomparison of results obtained by different authors is often complicated by the fact that different solvent mixtures have been used. In an attempt to elucidate the influence of the nature of the solvent on the stability of metal complexes, some stability constants have been determined in series of mixed solvents of varying composition. The results are reported and discussed in Section 3(a).

1(b). INTRODUCTION TO REVERSIBLE STEP EQUILIBRIA.

The formation of metal complexes in solution is conveniently discussed in terms of Jannik Bjerrum's Theory of Step Equilibria [11,12]. Consider a complex ML_N, in which the central group, M, is surrounded by a maximum number, N, of ligands, L. In solution, the species M, L, and ML_N will be in equilibrium with intermediate species such as ML, ML_2 ....ML_{N-1},(all charges being omitted for the sake of clarity).

The formation of the ultimate complex, ML_N, is considered to take place by a series of consecutive reactions, each involving two of the intermediate species. The following equilibria are therefore concerned in the formation of ML_N :—

$$\begin{aligned} M + L &= ML \\ ML + L &= ML_2 \ .... \\ .... \ ML_{N-1} + L &= ML_N \end{aligned} \qquad ....(1)$$

The equilibrium constants for these consecutive reactions are known as the 'step equilibrium constants' of the system, and as the 'stability' (or 'formation','complexity') constants of the individual species formed. The stoichiometric stability constant, ${}^cK_n$, for the species ML_n is given by

$${}^cK_n = [ML_n]/[ML_{n-1}][L] \qquad ....(2)$$

The product ${}^cK_1{}^cK_2....{}^cK_n$ is written as ${}^c\beta_n$

$$\prod_1^n {}^cK_n = {}^c\beta_n = [ML_n]/[M][L]^n \qquad ....(3)$$

When n=N, the maximum number of ligands attached to a central group, ${}^c\beta_N$ is the overall equilibrium constant for the system

The 'degree of formation' of the system, $\bar{n}$, is defined as average number of ligands attached to one central group.

$$\bar{n} = \sum(\text{bound ligand})/\sum(\text{central group})$$

If no polynuclear species are present,

$$\bar{n} = \frac{[ML] + 2[ML_2] \ldots + n[ML_n] \ldots + N[ML_N]}{[M] + [ML] + [ML_2] \ldots + [ML_n] \ldots + [ML_N]}$$

$$= \sum_{n=1}^{n=N} n[ML_n] \; / \; \sum_{n=0}^{n=N} [ML_n] \qquad \ldots(4)$$

Substituting from equation (2),

$$\bar{n} = \frac{{}^{c}K_1[M][L] + 2{}^{c}K_1{}^{c}K_2[M][L]^2 \ldots + n{}^{c}K_1{}^{c}K_2 \ldots {}^{c}K_n[M][L]^n \ldots \ldots}{[M] + {}^{c}K_1[M][L] + {}^{c}K_1{}^{c}K_2[M][L]^2 \ldots + {}^{c}K_1{}^{c}K_2 \ldots {}^{c}K_n[M][L]^n}$$

$$\sum_{n=1}^{n=N} n{}^{c}\beta_n[L]^n \; / \; \sum_{n=0}^{n=N} {}^{c}\beta_n[L]^n \qquad \ldots(5)$$

where ${}^{c}\beta_0 = 1$, by definition.

Equation (5) is known as the 'formation function' of the system, and the plot of $\bar{n}$ against $pL = -\log_{10}[L]$ is known as the 'formation curve'. If the formation curve can be obtained experimentally, the values of the stability constants may be calculated from it (see Section 2(c)). An experimental method for obtaining the formation curve is describes in Section 2(b).

SECTION 2

NEW METHODS OF COMPUTATION.

2(a). THE SPECTROPHOTOMETRIC DETERMINATION OF DISSOCIATION CONSTANTS.

The dissociation constants of 8-hydroxycinnoline, 8-hydroxy-4-methylcinnoline, 8-hydroxyquinazoline, 8-hydroxy-2:4-dimethylquinazoline and 5-hydroxyquinoxaline were determined spectrophotometrically, as the reagents are very sparingly soluble in water, and absorb strongly in the near ultra-violet region of the spectrum. Several methods have been described for calculating dissociation constants from measurements of optical absorbancy, [13-17], but these are either inaccurate or tedious if the ratio of the dissociation constants of the two groups is less than 10^4. The following simple graphical method offers certain advantages.

The absorbancy $A_{s(j)}$ of a solution containing only the species H_jL, in a cell of length 1 cms., is given by the Beer-Lambert Law,

$$A_{s(j)} = 1.\varepsilon_j.[H_jL] \qquad \ldots.(6)$$

where ε_j is the molecular extinction coefficient of the species H_jL. As oxine and its analogues may exist in the forms L^-, HL, and H_2L^+, the total concentration of the reagent is given by

$$T_L = [L] + [HL] + [H_2L]$$
$$= [L]\{1 + {}^cK_1^H[H] + {}^cK_1^H.{}^cK_2^H[H]^2\} \qquad \ldots.(7)$$

where the stability constant of the species H_jL is defined as

$${}^cK_j^H = [H_jL]/[H_{j-1}][H]$$

and charges are omitted for clarity.

Then, the total absorbancy of the solution is given by

$$A_s = 1\{\varepsilon_o[L] + \varepsilon_1[HL] + \varepsilon_2[H_2L]\}$$
$$= 1[L]\{\varepsilon_o + \varepsilon_1K_1[H] + \varepsilon_2K_1K_2[H]^2\}$$

$$A_s = l.T_L \left\{ \frac{\varepsilon_o + \varepsilon_1 K_1[H] + \varepsilon_2 K_1 K_2 [H]^2}{1 + K_1[H] + K_1 K_2 [H]^2} \right\} \quad \ldots.(8)$$

where the superscripts c and H are omitted for clarity in this Section.

In practice, a plot of A_s against pH is obtained for a series of solutions of the same total concentration of ligand. The slope of this plot is given by

$$\frac{dA_s}{dpH} = -2.303 T_L \left\{ \frac{K_1[H]}{(1 + K_1[H] + K_1 K_2 [H]^2)^2} \right\} \quad \ldots.(9)$$
$$\left\{ (\varepsilon_1 - \varepsilon_o) + 2(\varepsilon_2 - \varepsilon_o) K_2 [H] + (\varepsilon_2 - \varepsilon_1) K_1 K_2 [H]^2 \right\}$$

and so, at a maximum, minimum, or point of deflection in the curve, $dA_s/dpH = 0$, and

$$(\varepsilon_1 - \varepsilon_2) + 2(\varepsilon_2 - \varepsilon_o) K_2 [H]_{max} + (\varepsilon_2 - \varepsilon_1) K_1 K_2 [H]^2_{max} = 0 \quad \ldots.(10)$$

Whence

$$[H]_{max} = \frac{(\varepsilon_o - \varepsilon_2) K_2 \pm \sqrt{(\varepsilon_2 - \varepsilon_o)^2 K_2^2 - (\varepsilon_1 - \varepsilon_o)(\varepsilon_2 - \varepsilon_1) K_1 K_2}}{(\varepsilon_2 - \varepsilon_1) K_1 K_2} \quad \ldots.(11)$$

Similarily, the condition that the slope, dA_s/dpH, is maximal or minimal, is given by $d^2 A_s / d(pH)^2 = 0$, and

$$(\varepsilon_1 - \varepsilon_o) + \left\{ (\varepsilon_1 - \varepsilon_o) K_1 + 4(\varepsilon_2 - \varepsilon_o) K_2 \right\} [H'] + 3(\varepsilon_2 - 2\varepsilon_1 + \varepsilon_o) K_1 K_2 [H']^2$$
$$+ \left\{ (\varepsilon_2 - \varepsilon_1) K_1^2 K_2 - 4(\varepsilon_2 - \varepsilon_o) K_1 K_2^2 \right\} [H']^3 - (\varepsilon_2 - \varepsilon_1) K_1^2 K_2^2 [H']^4 = 0$$
$$\ldots.(12)$$

Two special cases may be considered.

Case I. $K_1 \gg K_2$, and $\varepsilon_o, \varepsilon_1$ and ε_2 are of the same order.

Equation (11) then becomes

$$[H]_{max} = \sqrt{(\varepsilon_o - \varepsilon_1)/(\varepsilon_2 - \varepsilon_1) K_1 K_2} \quad \ldots.(11a)$$

and from equations (6) and (11a),

$$A_{s(max)} = lT_1\varepsilon_1 \qquad \ldots.(6a)$$

Also, if $K_1/K_2 \gg (\varepsilon_2-\varepsilon_o)/(\varepsilon_2-\varepsilon_1)$, equation (12) becomes

$$(\varepsilon_1-\varepsilon_o) + (\varepsilon_1-\varepsilon_o)K_1[H'] + 3(\varepsilon_2-2\varepsilon_1+\varepsilon_o)K_1K_2[H']^2 + (\varepsilon_2-\varepsilon_1)K_1^2K_2[H']^3 - (\varepsilon_2-\varepsilon_1)K_1^2K_2^2[H']^4 = 0 \qquad \ldots.(12a)$$

Now as $K_1 \gg K_2$, the first three terms in equation (12a) are negligible in comparison with the other terms when [H] is large, and dA_s/dpH is maximal (or minimal) at the point

$$[H'] = 1/K_2 \qquad \ldots.(13a)$$

At this point,

$$A'_s = \left\{\frac{\varepsilon_o + \varepsilon_1(K_1/K_2) + \varepsilon_2(K_1/K_2)}{1 + 2(K_1/K_2)}\right\} lT_1$$

and since ε_o, ε_1 and ε_2 are of the same order,

$$A'_s = \tfrac{1}{2}lT_1(\varepsilon_1+\varepsilon_2) = \tfrac{1}{2}(A_{s(max)} + A_{s2}) \qquad \ldots.(8b)$$

where the absorbancy of a solution, in which all the reagent is in the form H_2L^+ is given by $A_{s2} = lT_L\varepsilon_2$ (see page 6).

Similarily, if [H] is small, the last three terms in equation (12a) are negligible compared with the first two terms, and dA_s/dpH is maximal at the point

$$[H'] = 1/K_1 \qquad \ldots.(13b)$$

At this point

$$A'_s = \tfrac{1}{2}lT_1(\varepsilon_o+\varepsilon_1) = \tfrac{1}{2}(A_{so} + A_{s(max)}) \qquad \ldots.(8c)$$

where $A_{so} = lT_1\varepsilon_o$.

As $A_{s(max)}$ may be determined experimentally, the two values of A'_s may be calculated directly from equations (8b) and (8c) if values of A_{so} and A_{s2} are also available. Values of K_1 and K_2

may then by calculated from the corresponding values of [H'], using equations (13a) and (13b) (see Fig.1). If values of A_{so} and A_{s2} cannot be determined, the two values of [H'] corresponding to $1/K_1$ and $1/K_2$ may be obtained from a plot of dA_s/dpH against pH (see Fig.2)

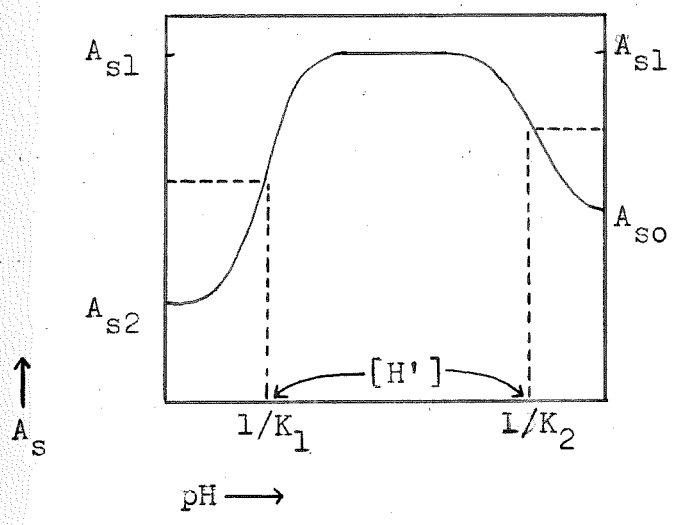


Fig.1.

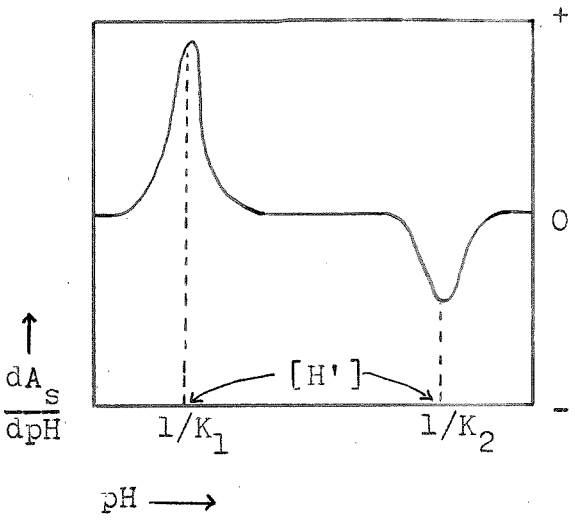


Fig.2.

Case II. $\varepsilon_o = \varepsilon_2$.

If the wavelengths chosen for measurement are those at which the species L^- and H_2L^+ have the same molecular extinction coefficients, the dissociation constants may readily be determined, even in cases where $K_1 \leqq K_2$.

When $\varepsilon_o = \varepsilon_2$, equation (11) becomes

$$[H]_{max} = \sqrt{1/K_1K_2} \qquad \ldots.(11b)$$

and from equation (8)

$$A_{s(max)} = 1T_L \frac{2\varepsilon_o + \varepsilon_1\sqrt{K_1/K_2}}{2 + \sqrt{K_1/K_2}} \qquad \ldots.(8d)$$

The condition for maximal or minimal slope now becomes,

$$1 - K_1[H'] - 6(K_1K_2)[H']^2 - K_1(K_1K_2)[H']^3 + (K_1K_2)^2[H']^4 = 0 \quad \ldots\ldots(12b)$$

The values of $[H']$ for which $d^2A_s/d(pH)^2 = 0$ may be obtained graphically and combined with values of (K_1K_2) obtained from equations (11b). Equation (12b) may then be solved for K_1 and K_2, (see Figs. 3 and 4).

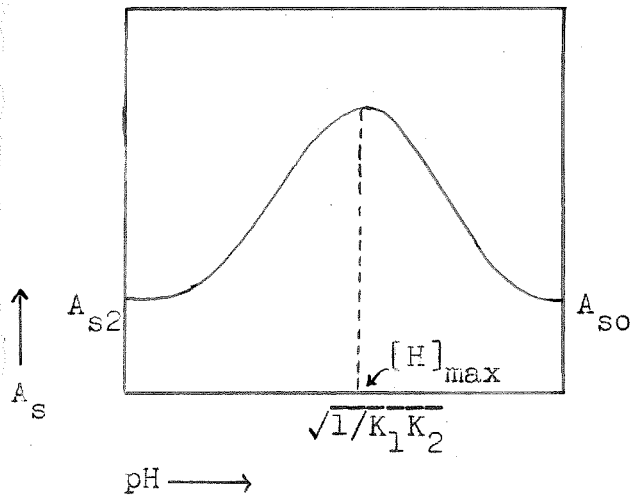


Fig. 3.

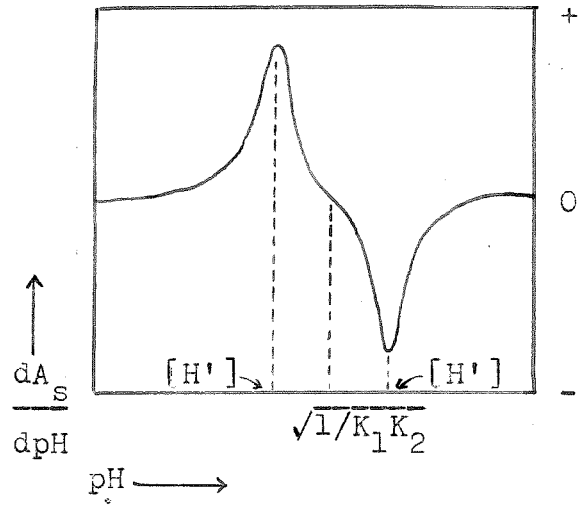


Fig. 4.

Application to the Present Work.

For all the reagents studied in this work, $K_1 \gg K_2$, and values of A_{so} and A_{s2} were obtainable from absorbancy measurements in strongly alkaline and acidic solutions, respectively. Values of K_1 and K_2 were therefore obtained using equations (8b), (8c), (13a) and (13b). Measurements were made at wavelengths such that, over the whole pH range, $0.1 < A_s < 0.8$, so that the extinction coefficients ε_o, ε_1 and ε_2 were of the same order. The experimental results are plotted in Graphs 5-9, and the dissociation constants obtained are given in Table II.

Application to Other Physical Measurements.

The above treatment need only be slightly modified if the absorbancy readings are to be replaced by other physical measurements, such as electrical conductivities, solubilities, or distribution ratios. The last case will be taken as an example.

It may be assumed that, if an aqueous solution of an oxine derivative be shaken with an organic solvent, such as chloroform, only the uncharged species, HL, will be extracted. The distribution ratio of the reagent is then defined

$$q = \frac{[HL]_o}{[L] + [HL] + [H_2L]} \qquad \ldots\ldots(14)$$

$$= p\left\{\frac{K_1[H]}{1 + K_1[H] + K_1K_2[H]^2}\right\}$$

where $[\ ]_o$ refers to concentrations in the organic phase, and p is the partition coefficient of the species HL between water and the organic solvent. Thus $p = [HL]_o/[HL]$.

The plot of the distribution ratio against pH may be determined experimentally, and the value of its slope may be shown to be

$$\frac{dq}{dpH} = -2.303p\left\{\frac{K_1[H]}{(1 + K_1[H] + K_1K_2[H]^2)^2}\right\}(1 - K_1K_2[H]^2) \qquad \ldots\ldots(15)$$

Thus, the curve passes through a maximum at the isoelectric point where

$$[H]_{max} = \sqrt{1/K_1K_2} \qquad \ldots\ldots(16)$$

Similarily, dq/dpH is maximal or minimal at the points where

$$1 - K_1[H'] - 6(K_1K_2)[H']^2 - K_1(K_1K_2)[H']^3 + (K_1K_2)^2[H']^4 = 0 \quad \ldots(17)$$

It is seen that equations (16) and (17) are identical with (11b)

and (12b), and they may be solved for K_1 and K_2 as indicated on page 10.

Now if $K_1 \gg K_2$ equation (17) reduces to $[H'] = 1/K_2$ at large values of [H], and to $[H'] = 1/K_1$ at small values of [H]. At each of these points, $q = p/2$, and the method of obtaining K_1 and K_2 is analogous to that described on page 9.

The Relationship between ${}^{c}K_1^H, {}^{c}K_2^H$ and Conventional Dissociation Constants.

The conventional stoichiometric dissociation constants of the species H_2L^+ and HL respectively are defined

$${}^{c}K_1^A = [H^+][HL]/[H_2L^+] \qquad {}^{c}K_2^A = [H^+][L^-]/[HL]$$

and are simply related to the stability constants, ${}^{c}K_2^H$ and ${}^{c}K_1^H$, which are defined on page 6. Thus

$${}^{c}K_1^H = 1/{}^{c}K_2^A \qquad {}^{c}K_2^H = 1/{}^{c}K_1^A$$

In practice, however, measurements of pH in aqueous solution give values of the activity $\{H^+\}$ of the hydrogen ion, rather than its concentration, $[H^+]$, and the above methods give values of the Brønsted dissociation constants, defined as

$${}^{B}K_1^A = \{H^+\}[HL]/[H_2L^+] \qquad {}^{B}K_2^A = \{H^+\}[L^-]/[HL]$$

The thermodynamic constants, ${}^{T}K_1^A$ and ${}^{T}K_2^A$, may be obtained from the corresponding Brønsted constants if the relevant activity coefficients, f, are known.

$${}^{T}K_1^A = \{H^+\}\{HL\}/\{H_2L^+\} = {}^{B}K_1^A \cdot f_{HL}/f_{H_2L^+} \qquad {}^{T}K_2^A = \{H^+\}\{L^-\}/\{HL\} = {}^{B}K_2^A \cdot f_{L^-}/f_{HL}$$

In the present work, it was assumed that the activity coefficient for the uncharged molecule was unity, and for the singly

charged ions H_2L^+ and L^- are given by the extended Debye-Hückel equation for a 1:1 electrolyte,

$$\log f_{H_2L^+} = \log f_{L^-} = \frac{-A\sqrt{\mu}}{1 + ab\sqrt{\mu}} \quad \ldots(18)$$

where μ is the ionic strength $= \frac{1}{2}\Sigma cz^2$.

a is the ionic radius in Å.

$A \propto DT^{-3/2}$, = 0.5 in water at room temperature.

$b \propto DT^{-1/2}$, =3.29 x 10^7 in water at room temperature.

Taking a to be 2.5Å, equation (18) gives $\log f_{L^-,H_2L^+} = -0.19$ in a solution of ionic strength 0.3M.

2(b) THE CALCULATION OF FORMATION CURVES OF METAL COMPLEXES FROM pH TITRATION CURVES IN MIXED SOLVENTS.

Calvin and Wilson [18] have shown that pH measurements made while titrating with alkali a solution of a chelating agent, in the presence and in the absence of metal ions, can be used to calculate the free ligand exponent, pL, the degree of formation of the system, $\bar{n}$, and hence the stability constants, K_n, of the metal-ligand complexes present (see Section 1(b).) Explicit equations have since been deduced at length by Maley and Mellor [19] for acetylacetone, salicylaldehyde, 8-hydroxyquinoline and its 5-sulphonic acid, and glycine and its analogues. Albert has dealt with amino-acids with two or more ionising groups [20-21], Vickery with ethylenediaminetetra-acetic acid [22], while other authors have treated, for example, diamines [23-24], polyamines [25-26], and complex polyamino-acids [27]. Owing to the variety of symbols employed, the equivalence of the different equations relating $\bar{n}$ and pL with experimentally determinable quantities is not immediately obvious. The following treatment is simpler, shorter, and quite generally applicable.

Omitting charges for the sake of clarity, the stoichiometric stability constant of the metal-ligand complex, ML_n, is defined by ${}^{c}K_n = [ML_n]/[ML_{n-1}][L]$, and that of the ligand-proton complex LH_j, is defined by ${}^{c}K_j^H = [LH_j]/[LH_{j-1}][H]$. The corresponding overall stability constants are respectively defined as ${}^{c}\beta_n = {}^{c}K_1 {}^{c}K_2 \ldots {}^{c}K_n$ and ${}^{c}\beta_j = {}^{c}K_1^H . {}^{c}K_2^H \ldots . {}^{c}K_j^H$.

Let the total concentration of ligand, metal and dissociable hydrogen in the system be T_L, T_M, T_H respectively.
Then for the degree of formation of metal-ligand complexes,

$$\bar{n} = \frac{\text{total concentration of ligand bound to metal}}{\text{total concentration of metal}}$$

$$\bar{n} = \{T_L - (\text{concentration of ligand not bound to metal})\}/T_M \quad \ldots.(19)$$

Similarily for ligand-proton complexes,

$$\bar{n}^H = \frac{\text{total concnetration of proton bound to ligand}}{\text{total concentration of ligand not bound to metal}}$$

$$= (T_H - [H])/(T_L - \bar{n}T_M) \quad \ldots.(20)$$

Whence, from equation (19),

$$\bar{n} = \{T_L - (T_H - [H])/\bar{n}^H\}/T_M \quad \ldots.(21)$$

But from equation (5), page 5,

$$\bar{n}^H = \frac{\sum_{j=1}^{j=J} j[LH_j]}{\sum_{j=0}^{j=J} [LH_j]} = \frac{\sum_{j=1}^{j=J} j\ {}^c\beta_j^H [H]^j}{\sum_{j=0}^{j=J} {}^c\beta_j^H [H]^j} \quad \ldots.(22)$$

Finally,

$$T_L - \bar{n}T_M = \text{concentration of ligand not bound to metal}$$

$$= [L] \sum_{j=0}^{j=J} {}^c\beta_j^H [H]^j \qquad (\text{where } {}^c\beta_0^H = 1)$$

and

$$pL = \log_{10}\left\{\sum_{j=0}^{j=J} {}^c\beta_j^H [H]^j / (T_L - \bar{n}T_M)\right\} \quad \ldots..(23)$$

Consider now the value of T_H in the general case. If to a concentration of mineral acid E is added sufficient ligand carrying dissociable hydrogen in the form H_yL to give a total ligand concentration T_L, then the total concentration of dissociable proton will be $E + yT_L$. Thus for ligands such as ammonia or ethylenediamine, y=0; for glycine, oxine, acetylacetone or salicylaldehyde, y=1; for oxalic acid, or the disodium salt of ethylenediaminetetra-acetic acid, y=2.

Addition of alkali in the form NaOH, to give a sodium ion concentration Na (in excess of any due to neutral salt initially present) will reduce the total acidity to a value

$$T_H = E + yT_L - Na + [OH] \quad \ldots.(24)$$

where the last term, usually negligible in comparison with the others, appears on account of hydrolysis.

Calculations of $\bar{n}^H$, $\bar{n}$ and pL from equations (20),(21) and (23) require an accurate knowledge of [H], and two difficulties may arise.

(i) If data are taken from a single titration curve for mineral acid and ligand, with or without metal present, in the more acidic solutions the terms Na and [OH] are negligible in comparison with the others, and if E $\ll T_L$, E = [H]. The calculated value of T_H - [H] will then be very sensitive to small errors in [H]. The following procedure largely overcomes this difficulty.

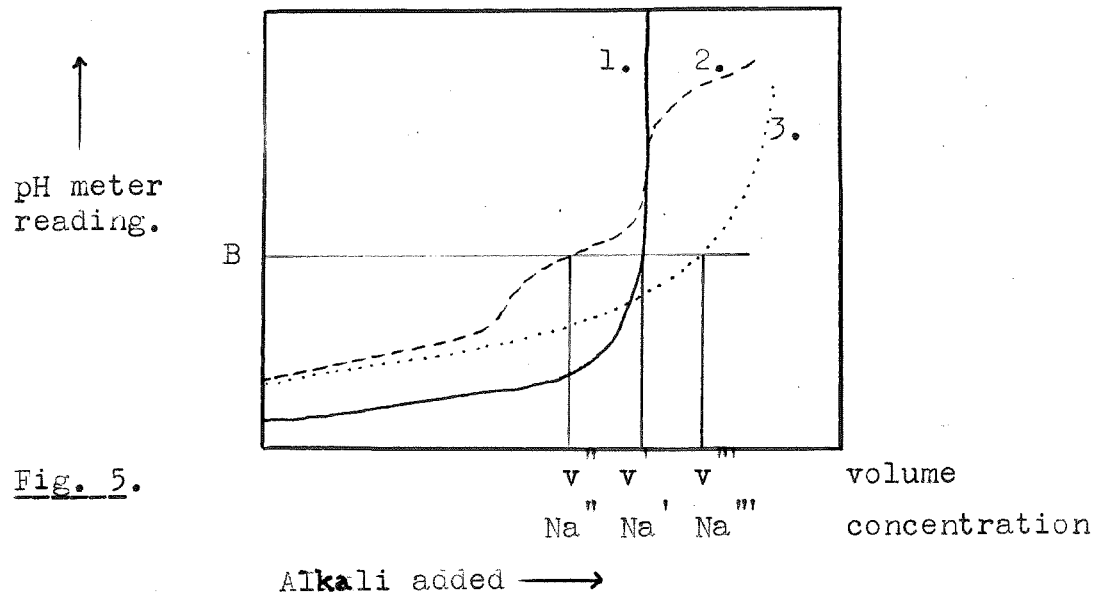


Fig. 5.

Fig.5, curve 1, shows the pH titration curve for mineral acid alone, and curve 2 shows that for a mixture of mineral acid and a ligand of the oxine type.(Although the relative positions of the curves depend on the nature of the ligand, the argument remains unchanged).

Points on curve 1 are given by

$$[H]' = E' + [OH]' - Na' \qquad \ldots.(25)$$

and from equation (20), points on curve 2 are given by

$$[H]'' = E'' + [OH]'' - Na'' + yT_L'' - \bar{n}^{H}{}'' T_L'' \quad \ldots.(26)$$

At ordinate B, the pH meter readings are the same for both solutions and $\{H\}' = \{H\}''$ and $\{OH\}' = \{OH\}''$, and if further the solutions have the same ionic strength, $[H]' = [H]''$ and $[OH]' = [OH]''$. It then follows that

$$\bar{n}^{H}{}'' = \left\{(E'' - E') - (Na'' - Na') + yT_L''\right\}/T_L'' \quad \ldots.(27)$$

Suppose that the initial volumes, V^o, and mineral acid concentrations, E^o, were the same in each titration, and that volumes v', v'', of alkali, of concentration N, were added to reach the points Na', Na''. If the initial concentration of ligand in curve 2 was T_L^o, then

$$E'' = V^o E^o/(V^o + v'')$$
$$Na'' = v''N/(V^o + v'')$$
$$T_L'' = V^o T_L^o/(V^o + v'')$$

Similar equations may be obtained for E' and Na'. Then from (27),

$$\bar{n}^{H}{}'' = \left\{yT_L^o + \frac{(v' - v'')(N + E^o)}{(V^o + v')}\right\} / T_L^o \quad \ldots.(28)$$

If, as in the work described in Section 3, $N \gg E^o$, and $V^o \gg v'$, then,

$$\bar{n}^{H}{}'' = \left\{yT_L^o + \frac{v' - v''}{V^o}.N\right\} / T_L^o \quad \ldots.(28a)$$

Values of $\bar{n}^{H}$ may thus readily be calculated from equations (28) or (28a). These values correspond to pH meter readings, rather than to true hydrogen ion activities or concentrations, but it will be shown later that they may be used directly to calculate stoichiometric stability constants of metal-ligand complexes.

(ii) A second difficulty which arises is the calculation of values of the ligand-proton stability constants, ${}^{c}K_j^{H}$ from equation (22). To obtain j such constants, at least j widely separated values of n must be known (see Section 2(c)), but in every case

the corresponding value of [H] is required. Now in aqueous solution we assume that $-\log_{10}\{H\} = p\{H\} = B$, the reading of the pH meter, since its readings have been correlated with known $p\{H\}$ values of the buffer solutions used in 'standardising' the instrument. Van Uitert and Haas [28] have recently shown that the more general relationship,

$$-\log_{10}[H] = B + \log f + \log U_H^o \qquad \ldots.(29)$$

is equally valid for water and for water-dioxan mixtures. Its use can be extended even to pure ethanol [29]. Here f is the activity coefficient of hydrogen ions in water at the same temperature and ionic strength, and U_H^o corresponds to the correction at zero ionic strength for the solvent mixture under consideration. For water, $U_H^o = 1$, and at unit activity coefficient, $[H] = 1/\text{antilog } B$. If then values of $1/\text{antilog } B = [H]fU_H^o$ (in the general case) are substituted into equation (22) in place of the less easily determinable values of [H], there will result values of the proton-ligand stability constants which will be termed 'practical constants', denoted by ${}^{P}K_j^H$. These are related to the desired stoichiometric constants by the expression

$${}^{C}K_j^H = f.U_H^o.{}^{P}K_j^H \qquad \ldots.(29a)$$

Further $${}^{C}\beta_j^H = (f.U_H^o)^j.{}^{P}\beta_j^H \qquad \ldots.(29b)$$

$\log(f.U_H^o)$ may be obtained as the intercept of the linear plot of p[H] against B, using solutions of known hydrogen ion concentration, and used to convert 'practical constants' into stoichiometric constants. It will be shown later (p.20) that these refinements are not, in fact, necessary for calculating the stability constants of metal-ligand complexes.

Fig. 5, curve 3, shows a typical titration curve for a mixture of mineral acid, ligand, and metal ions. For any point on the curve,

$$[H]''' = E''' + yT_L''' + OH''' - Na''' - \bar{n}^{H'''}.T_L + \bar{n}^{H'''}.n'''.T_M''' \quad ...(30)$$

If the pH meter reading, B, and the ionic strength of this solution are the same as those given by equation (26) for a point on curve 2 (i.e., at the same ordinate, B), then $[H]''' = [H]''$, $[OH]''' = [OH]''$ and $\bar{n}^{H'''} = \bar{n}^{H''}$, so that

$$\bar{n}''' = (E''' - E'') + (T_L''' - T_L'')(y - \bar{n}^{H''}) - (Na''' - Na'') / \bar{n}^{H''}.T_M''' \quad ...(31)$$

If the initial volumes, V^o, and concentrations of acid, E^o, and of ligand, T_L^o, were the same in each solution, and volumes v'' and v''' of alakli, of concentration N, were added to reach the points Na'' and Na''' respectively, then from equation (31)

$$\bar{n}''' = (v''' - v'')\{N + E^o + T_L^o(y - \bar{n}^{H''})\}/(V^o + v'')\bar{n}^{H''}.T_M^o \quad ...(32)$$

where T_M^o is the initial concentration of metal. Now if $N \gg E^o$, and $V^o \gg v''$, then

$$\bar{n}''' = (v''' - v'')N/V^o.\bar{n}^{H''}.T_M^o \quad ...(32a)$$

Table 1, page 20, shows some computations illustrating the agreement between results obtained using the approximate equations (28a) and (32a), and the rigorous equations (28) and (32). It is seen that values of $\bar{n}^H$ and $\bar{n}$ obtained using the approximate equations seldom differ significantly from those obtainwith the rigorous equations, unless the volume of alkali added is a considerable fraction of V^o.

Values of $\bar{n}^H$ appropriate to each pH meter reading, B, have been previously obtained from equation (28), so that $\bar{n}$ may be calcuated directly from pH meter readings without any exact knowledge of the corresponding hydrogen ion activities or concentrations. The calcuation of pL from equation (23) would again appear to require a knowledge of [H], but, by a simple transform-
ation,

TABLE 1. Titration Data for Some Complexes of 2-Methyl-oxine.

B	4.00	4.00	5.25	6.25	9.50	11.00	11.50
$10^2 v'$, ml.	1.667	1.667	1.683	1.683	1.693	1.707	1.721
$10^2 v''$, ml.	1.197	1.197	1.450	1.643	1.721	1.898	2.100
$10^2 v'''$, ml.	1.647	1.279	1.643	2.066	1.815		
Metal ion.	Cu^{++}	UO_2^{++}	Ni^{++}	Ni^{++}	Mg^{++}		
$\bar{n}^H$ (i)	1.935	1.935	1.463	1.077	0.944	0.620	0.242
(ii)	1.921	1.921	1.456	1.076	0.943	0.625	0.262
Diff.	0.014	0.014	0.007	0.001	0.001	0.005	0.014
$\bar{n}$ (i)	0.930	0.169	0.527	1.560	0.503		
(ii)	0.918	0.167	0.520	1.538	0.496		
Diff.	0.012	0.002	0.007	0.022	0.007		

Values in the rows preceeded by (i) and (ii) are those calculated by equations (28),(32) and (28a) and (32a) respectively. v', v'', and v''' refer to points on curves of the type 1, 2 and 3 in Fig.5. The concentrations of the reactants are given in the Experimental Section of this work. V^o = 9.85 ml. in each case, and for 2-methyl-oxine, y = 1.

$$pL = \log \sum_{j=0}^{j=J} \frac{{}^{c}\beta_j^H}{(f.U_H^o)^j} ([H]f.U_H^o)^j/(T_L - \bar{n}T_M)$$

$$= \log \sum_{j=0}^{j=J} {}^{P}\beta_j^H \, (1/\text{antilog } B)^j / (T_L - \bar{n}T_M) \qquad \ldots.(23a)$$

Hence equation (23) remains of the same form provided that (i) values of 1/antilog B are again used in place of [H], and (ii) the 'practical' overall stability constants ${}^{P}\beta_j^H$, previously obtained for the ligand-proton complexes (cf. page 18) are used instead of the stoichiometric values ${}^{c}\beta_j^H$.

Having thus obtained corresponding values of $\bar{n}$ and pL, the formation curve of the metal-ligand system can be drawn, and values of the stablity constants calculated by the methods described in Section 2(c).

Titrations in which the Total Concentration of Ligand is Varied.

In early studies of the stability of metal ammines [12] Bjerrum obtained variations in pL by varuing the total concentration of ligand in the system by discrete steps. Later workers [30] have carried out pH titrations with the amine as titrant. Here a solution containing metal ion and mineral acid is titrated with a solution of ligand, and as in the method described above $\bar{n}^H$ and $\bar{n}$ may be obtained directly from the horizontal displacement of titration curves.

In Fig6, curves 1 and 2 represent those in which solutions of mineral acid of initial concentrations $E^{o'}$ and $E^{o''}$ are titrated severally with a solution of ligand H_yL of molar concentration L. When the ligand is added as the free base, e.g. as ammonia or ethylenediamine, y = 0. Points on the two curves are given by

Curve 1. $[H]' = E' - [OH]' - (\bar{n}^{H'} - y)T_L'$ ....(33a)

Curve 2. $[H]'' = E'' - [OH]'' - (\bar{n}^{H''} - y)T_L''$ ....(33b)

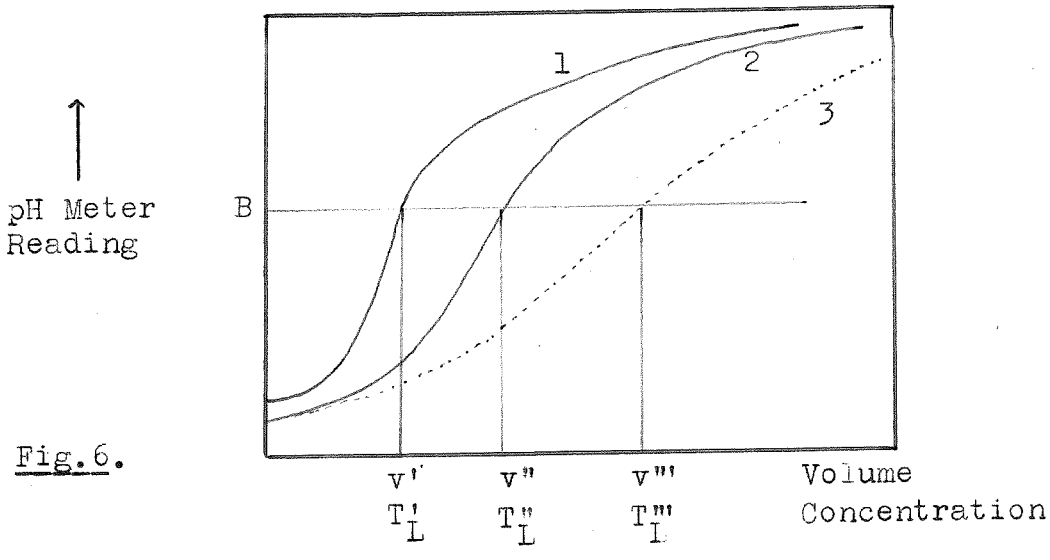


Fig.6.

Now for the same values of the ordinate, B, if the solutions have the same ionic strength, $[H]' = [H]''$, $[OH]' = [OH]''$, and

$$\bar{n}^{H'} = \bar{n}^{H''} = (E'' - E')/(T_L'' - T_L') + y \qquad \ldots.(34)$$

If the initial volumes of both solutions were V^o, and if volumes v' and v'' of ligand solution were required to give the same pH meter reading, B, on curves 1 and 2 respectively, then

$$\bar{n}^H = \frac{E^{o''}(V^o + v') - E^{o'}(V^o + v'')}{L(v'' - v')} + y \qquad \ldots.(35)$$

and if $V^o \gg v', v''$,

$$\bar{n}^H = y + (E^{o''} - E^{o'})V^o/L(v'' - v') \qquad \ldots.(35a)$$

Fig.6, curve 3 represents the titration curve of a volume V^o of a solution containing metal ions and acid, of initial concentrations T_M^o and $E^{o'''}$ respectively, with a ligand solution of concentration L. For any point on curve 3,

$$[H]''' = E''' + [OH]''' - (\bar{n}^{H'''} - y)T_L''' + \bar{n}'''.\bar{n}^{H'''}.T_M''' \qquad \ldots.(36)$$

If a volume v''' of ligand solution is required to give a pH meter reading of B, then from equations (35b) and (36)

$$\bar{n}''' = (v''' - v'')\{E^{o''} + (\bar{n}^{H''} - y)L\}/(V^o + v'')\bar{n}^{H''}.T_M^o \qquad ..(37)$$

and if $V^o \gg v''$, and $(\bar{n}^{H''} - y)L \gg E^{o''}$, then

$$\bar{n}''' = (v''' - v'')(\bar{n}^{H''} - y)L/V^o\bar{n}^{H'''}.T_M^o \qquad \ldots.(37a)$$

which reduces to

$$\bar{n}''' = (v''' - v'')L/V^oT_M^o \qquad \ldots.(37b)$$

when the ligand is added as free base. Thus the use of equations (35) and (37) to give corresponding values of $\bar{n}^H$ and $\bar{n}$ for a series of pH meter readings resembles the proceedure using equations (28) and (32) (page 19). In practice, however, it is often more convenient to obtain values of $\bar{n}^H$ from the titration of an acidic solution of the ligand with alkali (using equation 10)

and then to obtain values of $\bar{n}$ at the same pH meter reading by the method just described, using equation (37). All solutions must have the same ionic strength. In order to construct the formation curve, values of pL are calculated from equation (23), page 15.

The Relationship between Values of ${}^{c}K_{j}^{H}$ and Conventional Acid Dissociation Constants.

The stability constants ${}^{c}K_{j}^{H}$ for ligand-proton complexes have been defined on pages 6 and 14, and may be generally related to the classical dissociation constants of the various acids derived from L. It is customary to use the subscript 1 to denote the dissociation constant of the most acidic species, LH_J, so that

$$ {}^{c}K_{1}^{A} = [H][LH_{J-1}]/[LH_J] = 1/{}^{c}K_{J}^{H} $$

For the next strongest acid species,

$$ {}^{c}K_{2}^{A} = [H][LH_{J-2}]/[LH_{J-1}] = 1/{}^{c}K_{J-1}^{H} $$

For the dissociation of the final species,

$$ {}^{c}K_{J}^{A} = [H][L]/[LH] $$

In general, then, ${}^{c}K_{j}^{H} = 1/{}^{c}K_{J+1-j}^{A}$.

Thermodynamic Stability Constants.

The above methods have given stoichiometric stability constants which could be converted to thermodynamic constants were the appropriate activity coefficients available. For the uncharged complex, ML_2, of a monvalent ligand, L^-, and a divalent cation, M^{++}, the second thermodynamic stability constant is given by

$$ {}^{T}K_2 = \{ML_2\}/\{ML^+\}\{L^-\} = {}^{c}K_2 . f_{ML_2} / f_{ML^+} . f_{L^-} = {}^{c}K_2 / f_{\pm}^2 $$

if it is assumed that the activity coefficient of the uncharged species, ML_2, is unity, and independent of salt concentration, and that the product $f_{ML^+} . f_{L^-}$ may be replaced by the square of the mean activity coefficient for hydrochloric acid in the same medium at the same ionic strength. Measurements by Van Uitert and Haas [28] justify this assumption that the species ML^+ behaves as the cation of a strong electrolyte in aqueous dioxan, at least when M is a transition metal, and HL is a 1:3-diketone. For the first stability constant,

$$ {}^{T}K_1 = \{ML^+\}/\{M^{++}\}\{L^-\} = {}^{c}K_1 . f_{ML^+} / f_{M^{++}} . f_{L^-} = {}^{c}K_1 / f_{\pm}^4 $$

if we assume that the ratio f_{ML^+}/f_{L^-} is unity and unaffected by change of ionic strength, and that the activity coefficient $f_{M^{++}}$ for the doubly charged ion equals the fourth power of the value for a singly charged ion under the same conditions. Hence

$$ \log {}^{T}K_1 = \log {}^{c}K_1 - 4 \log f_{\pm 1\text{-}1} $$

and since measurements were made in the presence of a large concentration of neutral salt providing an excess of monovalent anions, an equivalent expression can be shown to be

$$ \log {}^{T}K_1 = \log {}^{c}K_1 + \log f_{\pm 1\text{-}1}^2 / f_{\pm 2\text{-}1}^3 $$

where the superscripts refer to 1-1 and 2-1 electrolytes respectively. In a basically similar treatment of thermodynamic stability constants, Van Uitert and Haas [28] deduce that

$$ \log {}^{T}K_1 = -\log {}^{T}K_1^H + \log \frac{[ML^+]}{[M^{++}]} + \log \frac{[H^+]}{[HL]} + \log \frac{f_{\pm 1\text{-}1}^2}{f_{\pm 2\text{-}1}} $$

(in the nomenclature of this work) and note that the last term becomes zero and thus independent of ionic strength when the limiting case of the Debye-Huckel law is applied. Of the two

assumptions made in this derivation, viz.

(i) $f_{ML^+} = f_{H^+} = f_{L^-} = f_{\pm 1-1}$ and (ii) $f_{M^{++}} = f_{\pm 2-1}$

the latter is incorrect, and the last term of their equation should read $\log f^4_{\pm 1-1}/f^3_{\pm 2-1}$, and will be a function of ionic strength.

Similar calculations may be used to obtain thermodynamic stability constants for ligand-proton complexes, and for metal-ligand complexes of different charge type. These assumptions can only be logically justified in dilute solutions, and may lead to considerable error where ions of multiple charge are involved. In this work, values of the stoichiometric constants are reported, together with the details of the salt background used.

2(c) METHODS FOR COMPUTING SUCCESSIVE STABILITY CONSTANTS FROM EXPERIMENTAL FORMATION CURVES.

Experimental methods for the determination of stability constants developed by Leden [31], Bjerrum [12] and Fronaeus [32] have been discussed by Sullivan and Hindman [33]. In this work, stability constants are obtained from the formation curve of the system, in which the degree of formation, $\bar{n}$, is plotted against the free ligand exponent, pL (see page 5). Bjerrum has shown that $\bar{n}$ and [L] are related by the 'formation function' of the system,

$$\bar{n} = \sum_{n=1}^{n=N} n\beta_n[L]^n \Big/ \sum_{n=0}^{n=N} \beta_n[L]^n \qquad \ldots\ldots(5)$$

where $\beta_n = {}^c\beta_n$, and $\beta_o = 1$.

Whence

$$\sum_{n=0}^{n=N} (\bar{n} - n)\beta_n[L]^n = 0 \qquad \ldots\ldots(38)$$

Sullivan and Hindman point out that sets of equations of the type (38) can be solved for unique, non-trivial values of K_1, K_2 and K_n if the determinant

$$\begin{vmatrix} (\bar{n}_1-1)[L_1] & \ldots\ldots\ldots & (\bar{n}_N-N)[L_1]^N \\ (\bar{n}_1-1)[L_N] & \ldots\ldots\ldots & (\bar{n}_N-N)[L_N]^N \end{vmatrix} \neq 0$$

This expresses the condition that N inhomogeneous equations of the type (38) are needed for the evaluation of N stability constants in systems where the highest complex has the formula ML_N. In practice, experimental data often exceed these minimal requirements, and the real problem is to find those values for the constants, K_n, which will best express all the experimental results. Two difficulties may arise. (i) The substitution of experimentally determined values of $\bar{n}$ and [L] into (38) will give a set of $m > N$ equations, which will probably be inconsistent owing to experimental errors. (ii) The data obtained experimentally may

not be fully representative of the whole function. As a particular case, linear equations formed from neighbouring points may be ill-conditioned. The work described in this section deals with this problem of obtaining the best set of stability constants from experimental values of $\bar{n}$ and [L], and will be mainly restricted to systems for which N=2, and the equation

$$\bar{n} + (\bar{n}-1)K_1[L] + (\bar{n}-2)K_1K_2[L]^2 = 0 \qquad \ldots.(38a)$$

is applicable.

The current methods for obtaining K_1 and K_2 from the formation curve are discussed below, and additional methods for computing stability constants are suggested, and applied to some formation curves in the literature.

Method A. Successive Approximations.

From equation (38a)

$$K_1 = \frac{1}{[L]} \cdot \frac{\bar{n}}{(1-\bar{n}) + (2-\bar{n})K_2[L]} \qquad \ldots.(39a)$$

$$K_2 = \frac{1}{[L]} \cdot \frac{n + (n-1)K_1[L]}{(2-\bar{n})K_1[L]} \qquad \ldots.(39b)$$

Equations (39a) and (39b) emphasise that the calculation of K_1 depends on the value of K_2 and vice versa. Bjerrum [12] applies these equations to the refinement by successive approximations of 'temporary' constants obtained by other methods. If m experimental points are determined on the formation curve, there are m(m-1)/2 pairs of values which could be treated in this way; but some judgement would be necessary since several combinations would yield ill-conditioned equations and the resulting values of K_1 and K_2 would have to be omitted from the general average.

Method B. Solution of Simultaneous Equations.

When N=2, the required stability constants can be obtained by solving pairs of simultaneous equations derived from (38a). The criticisms of Method A apply equally here.

Method C. Interpolation at Half $\bar{n}$ Values.

From equations (39a) and (39b),

$$\log K_1 = pL_{1/2} + \log 2/(1 + \sqrt{1 + 12K_2/K_1}) \quad \ldots.(40a)$$

$$\log K_2 = pL_{3/2} - \log 2/(1 + \sqrt{1 + 12K_2/K_1}) \quad \ldots.(40b)$$

where pL_a represents the free ligand exponent when $\bar{n} = a$. Provided that $K_{n-1} \gg K_n$, approximately equal amounts of ML_{n-1} and ML_n will be present in solution, and the contributions of ML_{n-2} and ML_{n+1} may be neglected. Following Bjerrum [12], we may write

$$\log K_n = pL_{n-\frac{1}{2}} \quad \ldots.(41)$$

Unless $K_1/K_2 \gg 10^{2.5}$, this very commonly used approximation can introduce considerable error (see page 40) and in any case it has the disadvantage of using only two points on the formation curve.

Method D. Interpolation at Various $\bar{n}$ Values.

Rewriting equation (38a) for the point $\bar{n} = 1-d$,

$$\log K_1 = pL_{1-d} + \log 2(1-d)/[d + \sqrt{4(1-d^2)K_2/K_1 + d^2}\ ] \quad \ldots.(42)$$

which reduces to

$$\log K_1 = pL_{1-d} + \log(1-d)/d \quad \ldots.(43a)$$

when $K_1 \gg K_2$. Similarly,

$$\log K_2 = pL_{1+d} - \log(1-d)/d \quad \ldots.(43b)$$

The use of these equations over the whole range of the formation curve ($0<d<1$) is only justified if $K_1/K_2 > 10^4$, though in this case Method D is preferable to Method C as it can be applied at several points along the formation curve, and the mean values of K_1 and K_2 obtained from the results. If $K_1/K_2 < 10^4$, calculated valued of the stability constants show a drift which is more pronounced the lower the value of d. Albert [20] averages constants obtained in this manner, while Jonassen et al. [34] take the most probable value to be that obtained from the point where $d=\frac{1}{2}$; this is, in effect, employing Method C.

Method E. The Use of the Mid-point.

(i) At the mid-point of the formation curve, $\bar{n} = 1$, and

$$K_1K_2[L_1]^2 = 1$$

or $$\log K_1K_2 = 2pL_1 \quad \ldots.(44)$$

The abscissa of the mid-point will therefore give a value of the overall stability constant, β_2, whose precision is limited only by that of the experimental measurements. The common practice of evaluating individual values of K_1 and K_2 from the product K_1K_2 so obtained, together with equation (41) demands full appreciation of the implicit approximations, and does not make full use of the experimental data.

(ii) For a system in which N=2, Bjerrum [12] defines a 'spreading factor',

$$x = \sqrt{K_1/4K_2}$$

and relates it to the mid-point slope, D, of the formation curve at the point where $\bar{n}=1$ by the expression

$$D = -2.303/(1+x)$$

From the measured mid-point slope the ratio K_1/K_2 may be calculated and individual values of K_1 and K_2 obtained from this and equation (44). This method is only applicable where K_1/K_2 lies between 10^3 and 10^{-2} (as $K_1/K_2 \rightarrow \infty$, $D \rightarrow 0$, and as $K_1/K_2 \rightarrow 0$, $D \rightarrow -2.303$) and it uses only a very small portion of the formation curve in the region of the mid-point. Significant errors may be introduced both in plotting the 'best' formation curve to pass through the experimental points, and in measuring its mid-point slope.

Method F. Schwarzenbach's Graphical Method.

Schwarzenbach, Nilli and Bach [35] describe a graphical method for computing the dissociation constants of dibasic acids from data obtained by potentiometric titrations; this was later applied to the computation of stability constants of metal complexes [36].

The method can be applied to computing stability constants from experimental values of $\bar{n}$ and [L] by plotting values of $A = (\bar{n}-1)[L]/\bar{n}$ and $B = (\bar{n}-1)/(2-\bar{n})[L]$ as abscissae and ordinates respectively. All lines passing through the pairs of points (A,B) should intersect when extrapolated at the point $(1/K_1, K_2)$. This proceedure is unreliable if lengthy extrapolation is necessary, and is only suited to experimental data of high precision.

General Comments.

It is seen that the choise of computational method depends on the ratio K_1/K_2 in the system under consideration. An approximate value of this ratio may rapidly be obtained from the mid-point slope, D, of the formation curve, without introducing the concept of the spreading factor. For systems in which N=2, D is given by,

$$D = -4.606/(2 + \sqrt{K_1/K_2})$$

and values of D for given K_1/K_2 ratios are given in Table 2 and in Graph 1a.

TABLE 2. The Mid-point Slope, D, for Systems in which N=2.

$\log K_1/K_2$	5.0	4.0	3.0	2.0	1.0	0
D	-0.0145	-0.0451	-0.137	-0.384	-0.892	-1.535
$\log K_1/K_2$	-1.0	-2.0	-3.0	-4.0	-5.0	-∞
D	-1.989	-2.193	-2.267	-2.292	-2.300	-2.303

Thus, if Method C is to be used, K_1/K_2 must be $>10^{2.5}$ and D must be > -0.23. The form of the curve is then wavelike. For Method D, K_1/K_2 must be $>10^4$, and D must then be >-0.04, giving rise to a formation curve showing two very distinct steps. Method E is applicable to systems where $10^{-2} < K_1/K_2 < 10^3$, and $-2.2 < D < -0.14$ It is seen that, in the 'normal' case, where $K_1 > K_2$, $0 > D > -1.535$ while if $K_2 > K_1$ (e.g. for the ammines of Ag^+ in water) $1.535 > D > -2.303$.

Additional Methods for Computing Stability Constants.

The ideal method should minimise the subjective 'smoothing' implicit in most graphical proceedures and ought to employ the experimental data as fully as possible. The two methods presented below do not fully attain to this ideal, but represent a real improvement on existing methods.

Method G. The 'Correction Term' Method.

In a system in which N=2, the theoretical formation curve is symmetrical about its mid-point, so that,

$$pL_{1-d} + pL_{1+d} = 2pL_1 = \log K_1K_2 \qquad \ldots.(45)$$

from equation (42) $\log K_1 = pL_{1-d} + y$ ....(46a)

and $\log K_2 = pL_{1+d} - y$ ....(46b)

where the 'correction term', y, is given by

$$y = \frac{2(1-d)}{d + \sqrt{d^2 + 4(1-d^2)K_2/K_1}} \qquad \ldots.(47)$$

and depends both on d, and on the ratio K_2/K_1. If $K_1/K_2 > 10^4$, equation (47) reduces to $y \simeq \log (1-d)/d$, and the correction term depends only on the value of d (Method D) and becomes zero in the special case $d=\frac{1}{2}$ (Method C).

If pL_{1-d} and pL_{1+d} are two points on the formation curve disposed symmetrically about the mid-point, then from equations (45) and (46),

$$\Delta pL_d = pL_{1-d} - pL_{1+d} = \log K_1/K_2 + 2y \qquad \ldots.(48)$$

Using equations (47) and (48) corresponding values of y and ΔpL have been calculated for nine values of d for each of a series of values of K_1/K_2 ranging from 10^5 to 10^{-2}. The relationship between y and ΔpL is shown in Table 3,, and in Graph 2.

The correction term method is applied as follows to pairs of points $(\bar{n}, pL)$ symmetrically disposed about the mid-point. Suppose that the experimental values were $pL_{0.4} = 9.50$ and

$pL_{1.6}$ = 8.00. The value of the correction term, y, is read off from the curve for d = 0.6 as the ordinate corresponding to ΔpL = 1.50. Thence $\log K_1$ = 9.50 - 0.23 = 9.27, and $\log K_2$ = 8.00 + 0.23 = 8.23. The process is repeated for several values of d, and the mean value of the calculated stability constants is taken. In practice, it is convenient to draw the best formation curve through the experimental points, and to read off values of $pL_{1\pm d}$ for those values of d tabulated.

TABLE 3. The Relationship between y and ΔpL.

	d = 0.1		d = 0.2		d = 0.3	
$\log K_1/K_2$	y	ΔpL	y	ΔpL	y	ΔpL
5.000	0.954	3.092	0.602	3.796	0.368	4.264
4.000	0.954	2.092	0.602	2.796	0.369	3.264
3.523	0.942	1.639	0.599	2.325	0.366	2.789
3.000	0.916	1.167	0.592	1.816	0.364	2.272
2.523	0.861	0.802	0.574	1.376	0.355	1.812
2.000	0.746	0.507	0.523	0.954	0.330	1.341
1.523	0.593	0.336	0.430	0.663	0.273	0.976
1.000	0.388	0.225	0.274	0.452	0.159	0.682
0.523	0.178	0.167	0.093	0.336	0.004	0.515
0.000	-0.065	0.130	-0.131	0.262	-0.202	0.405
-0.477	-0.296	0.116	-0.354	0.231	-0.413	0.349
-1.000	-0.551	0.101	-0.602	0.204	-0.656	0.312
-1.477	-0.786	0.095	-0.835	0.193	-0.885	0.294
-2.000	-1.046	0.091	-1.092	0.184	-1.141	0.282
	d = 0.4		d = 0.5		d = 0.6	
5.000	0.176	4.648	0.000	5.000	-0.176	5.352
4.000	0.176	3.648	0.000	4.000	-0.176	4.352
3.523	0.175	3.173	0.000	3.523	-0.176	3.876
3.000	0.174	2.652	-0.001	3.003	-0.177	3.354
2.523	0.169	2.185	-0.004	2.531	-0.178	2.880
2.000	0.158	1.684	-0.012	2.025	-0.184	2.367
1.523	0.120	0.976	-0.035	1.592	-0.198	1.918
1.000	0.036	0.928	-0.094	1.188	-0.238	1.477
0.523	-0.085	0.693	-0.196	0.916	-0.317	1.158
0.000	-0.278	0.556	-0.362	0.725	-0.459	0.917

TABLE 3. (continued)

	d = 0.4		d = 0.5		d = 0.6	
$\log K_1/K_2$	y	pL	y	pL	y	pL
-0.477	-0.477	0.477	-0.549	0.621	-0.633	0.789
-1.000	-0.715	0.430	-0.778	0.556	-0.852	0.705
-1.477	-0.940	0.402	-1.000	0.523	-1.069	0.661
-2.000	-1.193	0.278	-1.251	0.502	-1.317	0.634
	d = 0.7		d = 0.8		d = 0.9	
5.000	-0.368	5.736	-0.602	6.205	-0.954	6.908
4.000	-0.368	4.736	-0.602	5.205	-0.954	5.908
3.523	-0.368	4.260	-0.602	4.727	-0.954	5.431
3.000	-0.368	3.737	-0.602	4.204	-0.954	4.909
2.523	-0.369	3.261	-0.603	3.728	-0.954	4.432
2.000	-0.372	2.745	-0.604	3.209	-0.955	3.910
1.523	-0.381	2.285	-0.609	2.741	-0.957	3.437
1.000	-0.407	1.815	-0.615	2.230	-0.964	2.928
0.523	-0.465	1.452	-0.662	1.846	-0.980	2.482
0.000	-0.582	1.164	-0.794	1.497	-1.032	2.064
-0.477	-0.736	0.996	-0.879	1.281	-1.123	1.770
-1.000	-0.944	0.887	-1.066	1.133	-1.279	1.557
-1.477	-1.154	0.831	-1.268	1.060	-1.459	1.441
-2.000	-1.398	0.796	-1.506	1.012	-1.690	1.359

Although the method involves some 'smoothing' of the experimental data, the correction term proceedure is very rapid and reliable as it taked fully into account the complicating factors introduced by the absolute magnitude of the ratio K_1/K_2 which may vitiate the application of Methods C and D. On the other hand, small changes in ΔpL correspond to large changes only when the ratio K_1/K_2 becomes low. This is especially marked in the central part of the curve, and if $K_1 < K_2$, values calculated from d smaller than 0.5 will not be reliable.

The value of the correction term, y, may also be calculated from the exact equation,

$$y = \log \frac{1-d}{d} + \log \left[1 - \frac{(1+d)[L]_{1-d}}{(1-d)[L]_{1+d}} \right] \quad \ldots\ldots(49)$$

which is useful in the absence of Graph 2, if only occaisional use is to be made of the correction term at values of d which are not tabulated.

Since the above treatment postulates the symmetry of the formation curve about its mid-point, it cannot be used for complex systems where $N > 2$. Lack of symmetry may, however, also appear in some systems where $N=2$ if polydentate ligands are involved. In the system Cu^{++} and diethylenetriamine ('dien'), $\bar{n}$ increasses slowly with [L] over the range $1 < \bar{n} < 2$, and does not approach 2 asymptotically [34]. This is explicable if the second ligand molecule is not co-ordinated through each of its nitrogen atoms. Ligands such as $\alpha\beta$-diaminocarboxylate ions could chelate with metal ions in three different ways [21] to give three different 1:1 complexes and six different 2:1 complexes. In these circumstances the formation curve would not be represented by equation (38a). Unsymmetrical formation curves may also result if polynuclear complexes are involved. Many unsymmetrical formation curves are, however, depicted in the literature for systems where N=2 and where none of these complications is expected. In such cases the experimental work must be regarded as suspect, and only limited confidence can be placed on the stability constants calculated from it by any of the methods described in this section, since they all postulate that the results may be represented accurately by equation (38a).

Method H. Least Squares Treatment.

Equation (38a) can be rewritten,

$$\frac{\bar{n}}{(\bar{n}-1)[L]} = \frac{(2-\bar{n})[L]}{(\bar{n}-1)} K_1K_2 - K_1 \qquad \ldots.(50)$$

which is the equation to a straight line. Since, in practice, the term [L] may vary by several powers of ten, it is seldom convenient to plot $\bar{n}/(\bar{n}-1)[L]$ directly against $(2-\bar{n})[L]/(\bar{n}-1)$ to obtain the slope, K_1K_2, and the intercept, $-K_1$, of the best straight line. The constants are best evaluated by the method of 'least squares' which makes use of all the experimental data and avoids subjective 'smoothing' of data incidental to plotting the 'best straight line'. A minor disadvantage arises from the properties of the functions $\bar{n}/(\bar{n}-1)$ and $(2-\bar{n})/(\bar{n}-1)$, which become very large in the centre of the curve ($0.95 < \bar{n} < 1.05$) and very sensitive to slight experimental errors in $\bar{n}$ (see Graph 1b). Points in this small region are therefore best neglected in this treatment.

This method was tested using three systems with widely different values of the ratio K_1/K_2, and as many experimental points as possible. Using the values of $\bar{n}$ K_1 and K_2 obtained by Method H, values of $\bar{n}$ corresponding to the experimental values of pL were calculated. Values of pL, $\bar{n}_{expt.}$, and $\Delta\bar{n}$ ($= \bar{n}_{calc.} - \bar{n}_{expt.}$) are given in Tables 4-6, together with the standard deviation $\sigma = [\Sigma(\Delta\bar{n})^2/\text{number of readings}]^{\frac{1}{2}}$. The stability constants calculated by Method H are compared with those obtained by the original workers, and those calculated by Method G.

TABLE 4. Cu^{++} and Dimethyethylenediamine in Water, at 25°C [30]. ($K_1/K_2 \sim 10^3$).

pL	10.889	10.351	10.074	9.954	9.835	9.726	9.607	9.518
$\bar{n}_{expt}$:	0.048	0.192	0.313	0.374	0.433	0.493	0.553	0.614
$\Delta\bar{n}$	+0.011	-0.013	-0.021	-0.021	-0.016	-0.014	-0.005	-0.016

TABLE 4. (continued).

pL	9.270	8.942	8.414	7.727	7.311	7.163	7.025	6.907
$\bar{n}_{expt.}$	0.773	0.853	0.971	1.088	1.202	1.259	1.319	1.376
$\Delta\bar{n}$	-0.046	+0.001	-0.002	-0.007	-0.004	+0.015	+0.004	+0.029

pL	6.799	6.701	6.593	6.496	6.271	6.009	5.672
$\bar{n}_{expt.}$	1.432	1.491	1.547	1.604	1.716	1.821	1.918
$\Delta\bar{n}$	+0.013	+0.011	+0.017	+0.020	+0.013	+0.012	-0.003

	$\log K_1$	$\log K_2$	$\log \beta_2$	σ
Method A	9.69	6.65	16.34	
Method G	9.69	6.69	16.38	
Method H	9.69	6.71	16.40	±0.017

TABLE 5. Cu^{++} and Glycine in Water at 25°C [30]. ($K_1/K_2 \sim 10^{1.4}$)

pL	9.612	8.667	8.607	8.549	8.492	8.423	8.358	8.294
$\bar{n}_{expt.}$	0.008	0.250	0.270	0.296	0.326	0.351	0.365	0.426
$\Delta\bar{n}$	-0.005	-0.025	-0.019	-0.018	-0.009	-0.009	-0.008	+0.008

pL	8.221	8.150	8.076	7.993	7.902	7.803	7.715	7.630
$\bar{n}_{expt.}$	0.463	0.511	0.564	0.620	0.681	0.749	0.807	0.872
$\Delta\bar{n}$	+0.001	0.000	-0.003	-0.002	0.000	0.001	+0.005	-0.001

pL	7.530	7.423	7.318	7.215	7.084	6.975	6.838	6.708
$\bar{n}_{expt.}$	0.938	1.012	1.088	1.169	1.251	1.339	1.425	1.515
$\Delta\bar{n}$	+0.001	0.000	-0.004	-0.014	-0.005	-0.016	-0.007	-0.009

pL	6.565	6.380	6.192	6.886	5.034
$\bar{n}_{expt.}$	1.606	1.697	1.788	1.880	1.972
$\Delta\bar{n}$	-0.015	+0.002	-0.013	+0.002	+0.010

	$\log K_1$	$\log K_2$	$\log \beta_2$	σ
Method A	8.16	6.73	14.89	
Method G	8.13	6.78	14.91	
Method H	8.12	6.77	14.89	±0.010

TABLE 6. Ag^+ and Ammonia in 2N Aqueous Ammonium Nitrate at 30°C. [12]. ($K_1/K_2 \backsim 10^{-0.6}$)

pL	4.051	3.816	3.656	3.523	3.385	3.232	3.030
$\bar{n}_{expt.}$	0.247	0.495	0.741	0.988	1.230	1.477	1.711
$\Delta\bar{n}$	+0.002	-0.003	-0.002	+0.002	-0.004	-0.002	-0.006

	Log K_1	Log K_2	Log β_2	σ
Method A	3.20	3.83	7.03	
Method G	3.18	3.84	7.02	
Method H	3.19	3.84	7.03	±0.004

Method A was used by the original workers in the cases considered. In these three systems, it is seen that the stability constants calculated by Methods G and H are in very good agreement with those obtained by the original workers, and that the standard deviations of $\Delta\bar{n}$ are low. As a further test of Method H, stability constants were calculated for some systems where the workers' own method of calculation seemed suspect, or where the experimental formation curve was incomplete. The results are given in Tables 7-10, and in Graph 3.

TABLE 7. Cd^{++} and l-Asparagine in Water. — Albert [20]. ($K_1/K_2 \backsim 10^{0.6}$)

pL	4.75	4.40	4.10	3.80	3.62	3.45	3.30
$\bar{n}_{expt.}$	0.10	0.20	0.40	0.57	0.74	0.93	1.11
$\Delta\bar{n}$(Method D)	+0.019	+0.040	+0.008	+0.033	+0.041	+0.012	-0.033
$\Delta\bar{n}$(Method H)	-0.014	-0.017	-0.067	-0.003	-0.003	+0.006	-0.007

pL	3.16	3.05	2.92
$\bar{n}_{expt.}$	1.26	1.42	1.56
$\Delta\bar{n}$(Method D)	-0.057	-0.121	-0.152
$\Delta\bar{n}$(Method H)	+0.002	-0.051	-0.067

	Log K_1	Log K_2	Log β_2	σ
Method D	3.87	2.90	6.77	±0.069
Method H	3.71	3.07	6.78	±0.036

The stability constants obtained using Method H lead to a much lower standard deviations of $\Delta\bar{n}$, than do those obtained by Albert using Method D, which is only applicable to systems in which $K_1/K_2 > 10^4$.

The magnitude of σ is a measure of the precision, rather than of the accuracy, of the experimental data. It is seen that the values of σ obtained using Method H are very small in the centre of the curve, but increase as d increases. This effect, which is observed with several of the systems studied, is due to the 'weighting' of the central terms by the least squares treatment. It is fortunate that the points where d is small may be determined with greater experimental precision than those where $d \rightarrow 1$.

TABLE 8. Ni^{++} and Oxine in 70% Aqueous Dioxan at 25°C. — Maley and Mellor [19]. ($K_1/K_2 \backsim 10^{1.2}$)

pL	11.71	11.68	11.63	11.56	11.54	11.27
$\bar{n}_{expt.}$	0.37	0.47	0.53	0.63	0.70	0.85
$\Delta\bar{n}$(Method C)	+0.128	+0.046	+0.020	-0.030	-0.084	-0.043
$\Delta\bar{n}$(Method H)	+0.131	+0.052	+0.014	-0.020	-0.075	-0.017

pL	11.08	10.83	10.51	10.39	10.28	9.94
$\bar{n}_{expt.}$	1.04	1.20	1.42	1.48	1.53	1.60
$\Delta\bar{n}$ (MethodC)	-0.061	-0.079	-0.070	-0.003	-0.019	-0.095
$\Delta\bar{n}$ (MethodH)	-0.021	-0.021	+0.004	+0.080	+0.033	-0.035

	Log K_1	Log K_2	Log β_2	σ
Method C	11.65	10.35	22.00	±0.068
Method H	11.64	10.47	22.11	±0.056

This system is a case where the experimental points do not lie on a smooth curve, and even with Method H, a high value of σ is obtained, indicating a low precision of the data. The constants calculated using Method H, do however fit the experimental curve appreciably better than do those obtained by Maley and

Mellor, using Method C. It has been seen that the use of Method C is unjustified unless $K_1/K_2 > 10^{2.5}$.

TABLE 9. Ni^{++} and 'Dien' in Water at 30°C.— Jonassen at al. [34] ($K_1/K_2 \backsim 10^{2.7}$).

pL	11.10	11.05	10.97	10.68	10.51	10.39
$\bar{n}_{expt.}$	0.376	0.406	0.443	0.582	0.639	0.689
$\Delta\bar{n}$(Method C)	-0.015	-0.018	-0.011	+0.016	+0.051	+0.055
$\Delta\bar{n}$(Method H)	-0.023	-0.035	-0.025	+0.002	+0.038	+0.047

pL	8.55	8.32	8.16	8.09	7.93	7.78
$\bar{n}_{expt.}$	1.295	1.399	1.502	1.532	1.604	1.679
$\Delta\bar{n}$(Method C)	-0.019	-0.003	-0.015	-0.004	+0.014	-0.015
$\Delta\bar{n}$(Method H)	-0.019	-0.003	-0.014	-0.004	+0.015	+0.018

	Log K_1	Log K_2	Log β_2	σ
Method C	10.85	8.14	18.99	±0.025
Method H	10.82	8.14	18.96	±0.024

Values of $\bar{n}$ (= 1±d) are only recorded in the two regions where $d \simeq 0.5$, but it is seen that, even with such a very incomplete formation curve, Method H gives satisfactory results, which are in good agreement with those obtained by Jonassen et al., using, in effect, Method C. This would be expected in such a system, where $K_1/K_2 > 10^{2.5}$.

TABLE 10. Cu^{++} and Oxine in 50% Aqueous Dioxan. — Johnston and Freiser [37]. ($K_1/K_2 \backsim 1$)

pL	13.18	13.16	13.07	13.05	12.89	12.74	12.72	12.50
$\bar{n}_{expt.}$	0.84	0.90	1.05	1.11	1.33	1.48	1.55	1.75
$\Delta\bar{n}$(J. & F.)	+0.087	+0.048	-0.037	-0.048	-0.103	-0.109	-0.160	-0.16
$\Delta\bar{n}$(Meth.H)	+0.035	+0.009	0.000	+0.035	-0.014	-0.013	-0.020	-0.02

	Log K_1	Log K_2	Log β_2	σ
J. & F.	(13.49)	12.73	26.22	±0.108
Method H	13.05	13.15	26.20	±0.021

This system is also represented by an incomplete formation curve ($0.65 < \bar{n} < 1.75$). Johnston and Freiser used Method C to obtain K_2, but do not indicate how K_1 was calculated. From the value they obtained, it seems possible that equation (44) was used. This indicates the misleading results which may be obtained when Method C is applied to a formation curve where $K_1 \cong K_2$. Values of $\bar{n}$ calculated from the stability constants given by the authors differ considerably from the experimental values. Not only are the deviations large, but there is an unmistakable trend in their magnitude. On recalculation by Method H, a satisfactory fit is obtained with $\log K_1 = 13.05$ and $\log K_2 = 13.15$, values which differ considerably in magnitude from those calculated by the authors, who, moreover, report $\log K_1 > \log K_2$. It is significant that the revised overall constant, β_2 is in good agreement with that previously obtained; this emphasises that calculated values of K_1 and K_2 may together satisfy equation (44), although the individual constants may both be in error.

Systems of Higher Complexity.

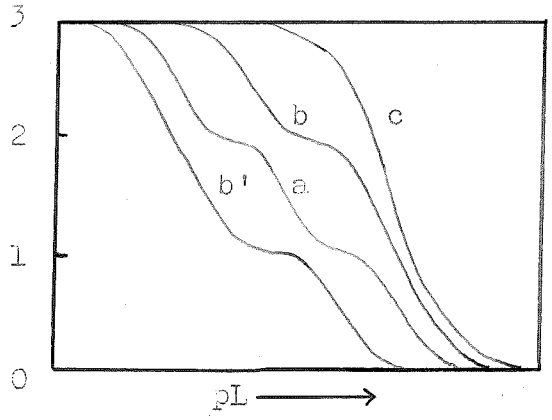


Fig. 7.

There are no simple methods of calculating stability constants in systems where $N \geqslant 3$. If all the successive constants differ greatly in magnitude the formation curve has N distinct steps (cf. Fig.7a for the case where N=3) and Method C can be

used. When N=3, and $K_1 \simeq K_2 \gg K_3$, the formation curve will show only two steps, corresponding to $0 < \bar{n} < 2$ and $2 < \bar{n} < 3$ (Fig.7b.). Here $\log K_3 = pL_{2\frac{1}{2}}$ (Method C) and K_1 and K_2 may be calculated by treating the lower step as a complete formation curve of a system where N=2, using one of the appropriate methods described above. Fig.7b' represents a formation curve where $K_1 \gg K_2 \simeq K_3$ which again can be treated as if it consisted of two separate portions. When the successive complexes are of similar stability the curve loses its wavelike character (Fig.7c.) and a set of trial constants, obtained appropriately from equation (41), must be refined by successive approximation using the following equation

$$\log K_n = pL_{\bar{n}} + \log \left\{ \sum_{t=0}^{t=n-1} (\bar{n}-t)\,\beta_t [L]^t \Big/ \sum_{t=n}^{t=N} \frac{(t-n)\beta_t [L]^{t-1}}{K_n} \right\} \quad \ldots.(51)$$

The general form, equation (38), may be written

$$\sum_{n=0}^{n=N} \frac{(\bar{n}-n)}{(\bar{n}-1)} \cdot [L]^{n-1} \beta_n = 0 \quad \ldots.(52)$$

of which equation (50) is a particular case for N=2. If there are m experimental points $(\bar{n}, pL)$ substition of the appropriate values of $\bar{n}$ and pL in equation (52) will give m inhomogeneous linear equations in $\beta_1, \beta_2 \ldots \beta_N$. The normal equations obtained the therefrom by the usual methods form a set of N simultaneous linear equations which can be solved for $\beta_1, \beta_2 \ldots \beta_N$ by matrix or other methods.

The Method used in This Work.

As it was found that N=2 for all the systems studied in this work, the 'correction term' method (G) was used throughout. In all cases, the constants obtained were used to calculate the theoretical formation curves, which are plotted in Graphs 17-28, and show good agreement with the experimental points. The theoretical curves were calculated very rapidly with the aid of Graph

4, in which the correction term, y, is plotted against $\log K_1/K_2$ for nine values of d; thus for a given ratio of K_1/K_2 values of y corresponding to various values of d may be obtained. Now from equations (46a) and (46b)

$$pL_{1-d} = \log K_1 - y$$
$$pL_{1+d} = \log K_2 + y$$

and as K_1 and K_2 are known, values of pL correspondong to values of $\bar{n} = 1 \pm d$ may rapidly be calculated for the given values of d.

SECTION 3.

RESULTS AND DISCUSSION.

3.(a). SOME PHYSICAL PROPERTIES OF THE REAGENTS.

(i) DISSOCIATION CONSTANTS.

In the absence of steric, entropy, and orbital change effects some quantitative relationship might be expected between the strengths of metal-ligand and proton-ligand bonds. The eff- of aza-substitution in oxine and the strength of its proton-ligand bonds was therefore investigated by determining the acid dissociation constants of 8-hydroxycinnoline (and its 4-methyl- derivative), 8-hydroxyquinazoline (and its 2:4-dimethyl- derivative) and 5-hydroxyquinoxaline in water. Thermodynamic constants were obtained spectrophotometrically (see Section 2a) at room temperature, 14 ± 3°C, and are shown in Table 11, together with relevant values from the literature. The constants obtained for 8-hydroxycinnoline, 8-hydroxyquinazoline, and 5-hydroxyquinoxaline are in fairly good agreement with the Brønsted constants obtained by Albert and Hampton [38] from pH titrations at 20°C and unspecified ionic strength. Before determining the stability constants of metal-ligand complexes in 50% v/V aqueous dioxan, the dissociation constants of the reagents were determined by pH titration in this medium (see pp. 17-21). The stoicniometric constants, given in Table 11, are valid for a salt background of 0.3M sodium perchlorate at 20°C.

Notes to Table 11.

$pK_{OH} = \log {}^{c}K_1^H$ and $pK_{NH} = \log {}^{c}K_2^H$, as defined on p.6.

* This work. Stoicniometric constants obtained from pH titrations at 20°C and ionic strength 0.3M.

+ This work. Thermodynamic constants obtained spectrophotometrically at 14 ± 3°C.

[13]. Thermodynamic constants obtained spectrophotometrically at room temperature,

[37]. Brønsted constants obtained by pH titration at 25°C and unspecified ionic strength,

Notes to Table 11. (continued).

[38] Brønsted constants obtained by pH titration at 20°C and unspecified ionic strength.

[39] Brønsted constants obtained spectrophotometrically at 25 ±3° and ionic strength 0.1M.

[40]. No details given.

TABLE 11. Dissociation Constants of Organic Reagents.

		Water.			50% aq. dioxan.		
No.	Reagent.	pK_{OH}	pK_{NH}	Ref.	pK_{OH}	pK_{NH}	Ref.
1.	8-Hydroxyquinoline.	9.85	5.00	[13]	10.80 11.54	4.48 3.97	* [37]
2.	8-Hydroxy-2-methyl-quinoline.	10.31	5.54	[39]	11.01 11.69	5.01 4.51	* [37]
3.	8-Hydroxy-5-methyl-quinoline.	-	-	-	11.11	4.71	*
4.	8-Hydroxy-6-methyl-quinoline.	-	-	-	10.71	4.76	*
5.	8-Hydroxy-7-methyl-quinoline.	-	-	-	11.31	4.26	*
6.	1:2:3:4-Tetrahydro-10-hydroxyacridine.	-	-	-	11.39	5.49	*
7.	5-Fluoro-8-hydroxy-quinoline.	-	-	-	10.11	3.03	*
8.	8-Hydroxycinnoline.	8.20 8.15	2.70 2.06	[38] +	8.84	1.77	*
9.	8-Hydroxy-4-methyl-cinnoline.	8.67	3.28	+	9.00	2.59	*
10.	8-Hydroxyquinazoline.	8.65 8.54	3.41 3.36	[38] +	9.59	3.30	*
-	8-Hydroxy-4-methyl-quinazoline.	8.75	2.90	[38]	-	-	-
11.	8-Hydroxy-2:4-di-methylquinazoline.	9.41	3.79	+	10.14	3.15	*
12.	8-Hydroxy-4-methyl-2-phenylquinazoline.	-	-	-	10.33	<1	*
13.	5-Hydroxyquinoxaline.	8.65 8.56 7.98	0.9 0.97 2.05	[38] + [40]	9.29	<1	*

TABLE 11.(continued)

No.	Reagent.	Water. pK_{OH}	Water. pK_{NH}	Ref.	50% aq. dioxan. pK_{OH}	50% aq. dioxan. pK_{NH}	Ref.
14.	4-Hydroxy-1:5-naphthyridine.	10.01	2.85	[38]	10.16	2.41	*
15.	8-Hydroxy-1:6-naphthyridine.	8.33	4.08	[38]	9.16	3.86	*
16.	8-Hydroxy-1:7-naphthyridine.	12;01	2.64	[38]	12	2.51	*

The structural formualae of the reagents are shown on the flap attached to the front cover.

Apart from the entropy change which accompanies the dissociation of an H — L bond, the value of pK for an acid is decreased by the following factors, [41].

(i) A low energy for the purely covalent H—L link.

(ii) A high electron affinity of L.

(iii) A high resonance energy of L as compared with HL.

As factor (i) is constant for a series of reagents in which changes in either pK_{OH} or pK_{NH} are being considered, the discussion will be limited to factors (ii) and (iii).

A. pK_{OH}.

It is seen that pK_{OH} is increased by alkyl substitution in the 2-, 5-, 7-, and 2:3-positions of oxine, but is almost unchanged by the presence of a 6-methyl substituent. This is in accordance with the expected inductive effect. pK_{OH} is also increased by methyl-substitution in the aza-oxines studied.

The observed lowering of the pK_{OH} of oxine by aza-substitution at C_2 and C_3 has also been reported for the corresponding 4-hydroxyquinolines [42], and may be attributed to the electron-attracting power of the nitrogen atom [43]. pK_{OH} is also lowered by aza-substitution at C_4 and C_6, but is increased by aza-substitution at C_5 and C_7. Similar effects are observed if aza-substitution occurs in the positions α- or γ- to the hydroxyl group

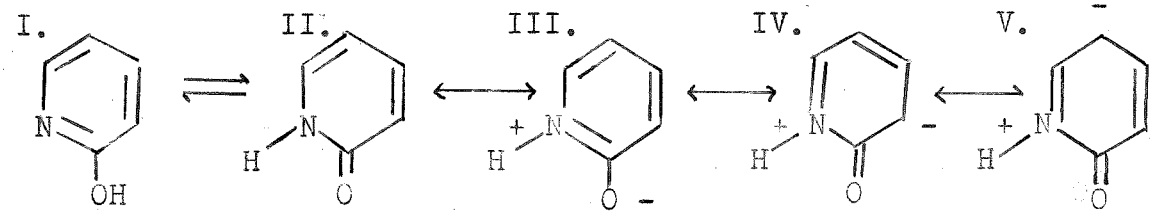
in phenol or in 5-hydroxyquinoxaline, but substitution of two nitrogen atoms $\alpha-\alpha'$ or $\alpha-\gamma$ to the hydroxy group cause a decrease in pK_{OH}. (See Table 12.)

TABLE 12. Values of pK_{OH} in Water.

Reagent.	N	pK_{OH}.	Ref.
8-Hydroxyquinoline.	-	9.89	[38]
4-Hydroxy-1:5-naphthyridine.	(γ)	10.01	[38]
8-Hydroxy-1:6-naphthyridine.	(β)	8.33	[38]
8-Hydroxy-1:7-naphthyridine.	(α)	12.01	[38]
4-Hydroxypyridino-(2':3'-5:6)-pyrimidine.	($\alpha-\gamma$)	8.95	[38]
Phenol.	-	9.98	[45]
2-Hydroxypyridine.	(α)	11.62	[38]
3-Hydroxypyridine.	(β)	8.72	[38]
4-Hydroxypyridine.	(γ)	11.09	[38]
2-Hydroxypyrimidine.	($\alpha-\alpha'$)	9.17	[44]
4-Hydroxypyrimidine.	($\alpha-\gamma$)	8.59	[44]
5-Hydroxyquinoxaline.	-	8.65	[38]
4'-Hydroxypyridino-(2':3'-2:3)-pyrazine.	(γ)	8.78	[38]
2'-Hydroxypyridino-(3':4'-2:3)-pyrazine.	(α)	11.05	[38]
4-Hydroxypteridine.	($\alpha-\gamma$)	7.69	[44]

'N' refers to the position of the nitrogen atom(s) relative to the hydroxyl group.

The high value of pK_{OH} in compounds in which a nitrogen atom is α- or γ- to the hydroxyl group may be explained in terms of the tautomerism (I $\rightleftharpoons$ II) of the neutral molecule [38]. The resonance energy of the neutral molecule, relative to the anion, would



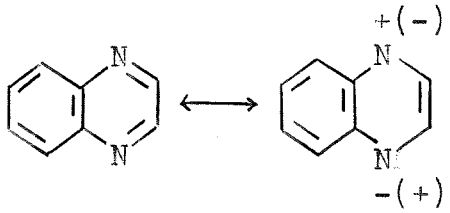
be increased by the zwitterion contributions, III, IV, V, to the amido tautomer, II; this would lead to an increase in pK_{OH} (factor iii, p.45). This type of tautomerism would be impossible if the nitrogen atom were β- to the hydroxyl group, and would be more likely to occur in α-aza-derivatives than in γ-aza-derivatives; it is seen that the values of pK_{OH} for compounds with a nitrogen atom in the α-position are higher than those for γ-aza-compounds. The high melting points of the 4-hydroxy-1:5- and 8-hydroxy-1:7- naphthyridines, and their appreciable solubility in water would suggest that they exist predominantly in zwitterion forms. If two nitrogen atoms are present in positions α-α' or α-γ to the hydroxyl group, only one of them can take part in tautomerism, and the electron-attracting power of the other may account for the lower value of pK_{OH} relative to that in the parent compound.

The increase in pK_{OH} observed on changing from water to a mixed organic solvent has frequently been noted for compounds in which a hydroxyl group dissociates (e.g.[46],[47]) and will be considered in more detail in Section 3(d).

B. pK_{NH}.

As expected from the inductive effect, pK_{NH} is increased by alkyl substitution in the 2-, 5-, and 2:3-positions of oxine, the 4-position of 8-hydroxycinnoline, and the 2:4-positions of 8-hydroxyquinazoline. The very low value of pK_{NH} in 8-hydroxy-4-methyl-2-phenylquinazoline may be attributed to blocking of the basic nitrogen atom by the large phenyl group. Similar effects have been observed for substituted acridines [48]. The lowering of pK_{NH} in oxine by the substitution of a methyl group in the 7-position may be due to a displacement of the hydroxyl group towards the basic nitrogen atom, thus hindering the approach of solvated protons.

Aza-substitution in oxine invariably leads to a decrease in the value of pK_{NH}, as would be expected from the electron attracting powers of the nitrogen atom. The order of values of pK_{NH} for oxine, 8-hydroxycinnoline, 8-hydroxyquinazoline and 5-hydroxyquinoxaline is the same as that for the parent heterocyclics [43]. The very low value obtained for 5-hydroxyquinoxaline differs widely from that obtained by Freeman and Spoerri [40], but is in good agreement with that of Albert and Hampton [38], and comparable with the very low value of pK_{NH} for the parent quinoxaline, for which Albert, Goldacre and Phillips [43] postulate very favourable resonance possibilities for the neutral molecule, compared with those for the cation. Such resonance would be less likely for cinnoline, where the unlike charges would be less well separated. It would be impossible for quinazolines.



The observed decrease in pK_{NH} on changing from water to a mixed organic solvent has only been reported for N—H dissociation in some amines [49-50], and will be discussed more fully in Section 3(d).

The influence of pK_{NH} on metal complex formation in the aza-oxines is somewhat obscured by the lack of conclusive evidence for the position of the more basic nitrogen atom (to which pK_{NH} refers), which might no longer be that one involved in chelation.

(ii). THE POSITION OF THE MORE BASIC NITROGEN ATOM.

The calculations of Longuet-Higgins and Coulson [51] indicate that N_1 is the more basic nitrogen atom in all the parent mono-aza-quinolines (except for quinoxaline and 1:5-naphthyridine, which are symmetrical), but the position of the basic centre may

well be changed by the presence of substituents. This is particularly likely for quinazoline in which the relative distributions of charge on the two nitrogen atoms are very similar.

The absorption spectra of the cationic, neutral, and anionic species of oxine, and of the aza-oxines were measured in the hope of elucidating this problem (see p. 97). The spectra of the cation and anion of oxine both show a bathochromic shift relative to the spectrum of the uncharged species (Graph 11a), similar to those shown by the quinolinium and β-naphtholate ions, relative to the appropriate neutral molecules [52]. Sets of spectra similar to that for oxine might also be expected for those aza-oxines in which the more basic nitrogen atom is that one adjacent to the hydroxyl group, and in which the hydroxyl group dissociates to form an anion.

Cinnoline Derivatives. It has been found [53-54] that N_1 is the basic centre in 4-methyl- and 4-aminocinnoline. The large increase in pK_{NH} produced by the substitution of a methyl group in the 4-position of 8-hydroxycinnoline also indicates that the more basic centre is in the γ-position to the 4-substituent. (See Table 13).

TABLE 13. Values of pK_{NH} in Water.

Reagent.	pK_{NH}	Ref.
8-Hydroxyquinoline.	4.92	[39]
8-Hydroxy-2-methylquinoline.	5.54	[39]
8-Hydroxy-3-methylquinoline.	4.94	[39]
8-Hydroxy-4-methylquinoline.	5.56	[39]
8-Hydroxycinnoline.	2.65	+
8-Hydroxy-4-methylcinnoline.	3.28	+

For conditions of measurement, see Notes to Table 11, pp. 43, 44.

The bathochromic shift and slight increase in intensity of the long wavelength band shown by the spectra of the cations of 8-hydroxycinnoline and 8-hydroxy-4-methylcinnoline relative to the spectra of the neutral molecules (graph 12) are very similar to those observed for oxine, and may be taken as further indication that N_1 is the basic centre in these compounds.

Quinazoline Derivatives. It has been shown that quaternary salt formation takes place at N_3 in quinazoline [55] and in 8-hydroxyquinazoline[38], but at N_1 in some 4-substituted derivatives [56]. Albert and Hampton [38] have found that the value of pK_{NH} of 8-hydroxy-4-methylquinazoline (2.90) is unexpectedly lower than that of 8-hydroxyquinazoline (3.41). The spectra of 8-hydroxy-2:4-dimethylquinazoline and 8-hydroxy-4-methyl-2-phenylquinazoline in acidic and neutral solution (Graph 13) resemble those of oxine, but the spectrum of the cation of the parent 8-hydroxyquinazoline (Graph 11b) shows a hypsochromic shift relative to that of the neutral molecule, and a slight increase in intensity. These observations might suggest that the basic centre is N_3 in 8-hydroxyquinazoline, but is N_1 in its 2:4-dimethyl- and 4-methyl-2-phenyl-derivatives.

5-Hydroxyquinoxaline. The position of the basic centre is uncertain as the ability of the methiodide derivative to form complexes with nickel ions indicates that quaternary salt formation takes place at N_1, while the relative positions of the spectra in acidic and neutral solutions (Graph 14a) are very similar to those for oxine, and might suggest that the basic centre is N_4. The measurement of values of pK_{NH} for the 2-methyl- and 3-methyl-derivatives might elucidate this problem.

Naphthyridine Derivatives. The spectra of the cations of 4-hydroxy-1:5-naphthyridine and 8-hydroxy-1:7-naphthyridine (Graph 15) show bathochromic shifts relative to those of the neutral molecules, but only a slight bathochromic shift is observed for

8-hydroxy-1:6-naphthyridine (Graph 14b); this might indicate that the more basic centres of these compounds are N_4, N_1 and N_6 respectively. As much of the evidence for the positions of the basic centres in these compounds concerns metal complex formation further discussion will be deferred until p.75. The spectra of the anions of both 4-hydroxy-1:5-naphthyridine and 8-hydroxy-1:7-naphthyridine are very like those of the neutral molecules; this is further indication that the neutral molecules of these compounds exist mainly in the form of amido zwitterions [52,57]. The spectrum of the anion of 8-hydroxy-1:6-naphthyridine shows the expected bathochromic shift relative to that of the neutral molecule, in which tautomerism is impossible.

(iii) WET AND DRY MELTING POINTS.

Knowledge of the occurence of hydrogen bonding between the hydroxyl group and the adjacent nitrogen atom might give further evidence for the positions of the more basic centres in the azaoxines. The melting points of the solids were therefore measured both dry, and in the presence of water, which would be expected to depress the melting points of compounds with intermolecular hydrogen bonding to a much greater extent than those of compounds with intramolecular hydrogen bonding [58-60]. The reults are given in Table 13.

TABLE 13. Wet and Dry Melting Points, and Partition Coefficients.

Reagent.	Ref.	m.p °C.	Δ °C.	p.
8-Hydroxyquinoline.		74	3	67
8-Methoxyquinoline.	[61]	45	25	-
8-Hydroxy-2-methylquinoline.	[61]	74	3	-
8-Methoxy-2-methylquinoline.	[61]	124	37	-
5-Bromo-8-hydroxyquinoline.	[61]	126	2	-

TABLE 13 (continued).

Reagent.	Ref.	m.p.°C	Δ°C	p.
1:2:3:4-Tetrahydro -10-hydroxy-acridine.	[61]	89.5	3	-
8-Hydroxycinnoline.		180	42	6.3
8-Hydroxy-4-methylcinnoline.		178	39	-
8-Hydroxyquinazoline.		150	22	5.4
8-Hydroxy-2:4-dimethylquinazoline.		112	7	-
8-Hydroxy-4-methyl-2-phenyl-quinazoline.		110	3	-
8-Methoxyquinazoline.		90	42	-
5-Hydroxyquinoxaline.		100	20	8.1
4-Hydroxy-1:5-naphthyridine.		>240	>65	<.02
8-Hydroxy-1:6-naphthyridine.		162	70	1.1
8-Hydroxy-1:7-naphthyridine.		239	130	.14

Δ refers to the depression in the melting point causes by the presence of water, ±2°C.

p refers to the partition coefficient between water and oleyl alcohol, (see p.54.)

The very small differences (< 6°C) between the wet and dry melting points of oxine (and its 2-methyl- and 5-bromo- derivatives) and of 1:2:3:4-tetrahydro-10-hydroxyacridine indicate that strong internal hydrogen bonding occurs in these solids; water causes a much greater depression of the melting points of 8-methoxyquinoline and 8-methoxy-2-methylquinoline, in which such bonding is impossible. Water also causes a large depression in the melting points of all the aza-oxines studied except for 8-hydroxy-2:4-dimethylquinazoline and 8-hydroxy-4-methyl-2-phenylquinazoline. The occurence of internal hydrogen bonding in these two compounds, but not in 8-hydroxyquinazoline, is further evidence that the more basic centre is N_1 in the 4-substituted 8-hydroxyquinazolines but is N_3 in the parent. The absence of internal hydrogen bonding in 8-hydroxycinnoline and in 5-hydroxyquinoxaline is no

conclusive evidence for the positions of the basic centres; the low values of pK_{NH} in these compounds suggest that even the more basic nitrogen atoms would have little tendency to form hydrogen bonds. As the value of pK_{NH} for 8-hydroxy-1:6-naphthyridine is relatively high, the observed depression in melting point is some evidence that the basic centre is N_6. The very high dry melting points of 4-hydroxy-1:5-naphthyridine and 8-hydroxy-1:7-naphthyridine, and the large depressions in the presence of water, support the suggestion that these compounds exist predominantly as zwitterions.

(iv) ABSORPTION SPECTRA IN WATER AND IN AMYL ALCOHOL.

The keto-enol tautomerism postulated for 4-hydroxy-1:5- and 8-hydroxy-1:7- naphthyridine is also possible for 8-hydroxycinnoline and for 5-hydroxyquinoxaline, but not for oxine, 8-hydroxyquinazoline or 8-hydroxy-1:6-naphthyridine. If tautomerism occurred, the position of tautermeric equilibrium, and hence the absorption spectrum, might be expected to be sensitive to the nature of the solvent. Absorption spectra of the neutral species of oxine and of its aza-derivatives were therefore measured in water and in amyl alcohol (Graph 16) as the reagents were insoluble in less polar solvents. As anticipated, change of solvent leads to slight changes in the spectra of 8-hydroxyquinazoline and of 8-hydroxy-1:6-naphthyridine, and to major changes in the spectra of 4-hydroxy-1:5- and 8-hydroxy-1:7- naphthyridine. The spectrum of 5-hydroxyquinoxaline is also slightly sensitive to change of solvent, and some tautomerism may occur in this compound; only slight changes are observed for 8-hydroxycinnoline. The spectrum of oxine shows an anomolous bathochromic shift, and decrease in intensity, on changing from water to amyl alcohol. Tautomerism is impossible here, and the effect may be due to a different degree of internal hydrogen bonding of oxine in the two solvents.

(v) SOLUBILITY.

Most of the reagents discussed in this section are appreciably soluble in polar organic solvents and very sparingly soluble in water, but the reverse is true of 4-hydroxy-1:5- and 8-hydroxy-1:7- naphthyridine, Albert amd Hampton [38], repott values of the 'partition coefficient' of the aza-oxines between oleyl alcohol and an aqueous buffer of pH 7.3, but their values really refer to the distribution ratio, defined as

$$q = [HL]_o / \left\{ [H_2L^+]_w + [HL]_w + [L^-]_w \right\}$$

where HL represents the neutral species, and the subscripts o and w refer to the organic and aqueous phases respectively. The true partition coefficient of the species HL is given by

$$p = [HL]_o / [HL]_w$$

Thus

$$p = \left\{ \frac{1 + {}^{c}K_1^H[H^+] + {}^{c}K_1^H \cdot {}^{c}K_2^H[H^+]^2}{{}^{c}K_1^H[H^+]} \right\} \cdot q$$

where ${}^{c}K_1^H$, ${}^{c}K_2^H$ are defined on page 6. Now as $[H^+]$ is known, and as

$$\log {}^{c}K_1^H \cong {}^{B}pK_{OH} \text{ and } \log {}^{c}K_2^H \cong {}^{B}pK_{NH}$$

approximate values of p may be calculated from those of q using values of the Brønsted dissociation constants in water. The results are shown in Table 13, pp.51,52.

If the two phases are completely immiscible and the partitioned species is not solvated, the partition coefficient of a species is the ratio of its solubilities in the two solvents considered. The high partition coefficient of oxine is compatible with the internal hydrogen bonding in the molecule, and the absence of keto-enol tautomerism. Lower partition coefficients are observed for 8-hydroxycinnoline, 8-hydroxyquinazoline and 5-hydroxyquinoxaline, which are not internally hydrogen-bonded, and have two nitrogen atoms which may be hydrated. The solubility

of 8-hydroxy-1:6-naphthyridine in water is similar to that in in amyl alcohol. The very low partition coefficients observed for 4-hydroxy-1:5- and 8-hydroxy-1:7- naphthyridine are further evidence of the zwitterion structure of these compounds.

3(b). SOME FACTORS INFLUENCING THE STABILITY OF METAL COMPLEXES.

Before discussing the stability constants of some metal complexes of the reagents studied in this work (see Section 3c), some general factors which influence the stability of metal complexes will be considered. If the reaction

$$M + L = ML$$

occurs in water, the accompanying change in standard free energy is given by

$$-\Delta F^{o} = RT\ln {}^{T}K_{1} = \bar{F}^{o}_{M} + \bar{F}^{o}_{L} - \bar{F}^{o}_{ML} \qquad .....(53)$$

where charges are omitted, and where $\bar{F}^{o}_{M}$, $\bar{F}^{o}_{L}$, and $\bar{F}^{o}_{ML}$ are the standard partial molar free energies of the species M, L, and ML respectively. Similarily for the reaction

$$H + L = HL$$

$$-\Delta F^{o} = RT\ln {}^{T}K^{H}_{1} = \bar{F}^{o}_{H} + \bar{F}^{o}_{L} - \bar{F}^{o}_{HL} \qquad .....(54)$$

whence

$$RT\ln {}^{T}K_{1} = RT\ln {}^{T}K^{H}_{1} + (\bar{F}^{o}_{M} - \bar{F}^{o}_{H}) - (\bar{F}^{o}_{ML} - \bar{F}^{o}_{HL}) \qquad ...(55)$$

where the formation constants ${}^{T}K_{1}$ and ${}^{T}K^{H}_{1}$ are defined on p. 23,24 and for clarity will be written as K_{ML} and K_{HL} in this section. Equation (55) was first derived by Duncan [62], and may be extended to form the basis for a discussion of the stability of metal complexes. If the appropriate activity coefficients were available, the terms K_{ML} and K_{HL} could be determined experimentally, and data for $(\bar{F}^{o}_{M} - \bar{F}^{o}_{H})$, the standard free energy of formation of the hydrated metal ion, are available in many cases [63]. The value of the term $\bar{F}^{o}_{ML}$ would be decreased by an increase in the ionisation potential of the metal, and , unless steric factors were involved, by a decrease in the radius of the metal ion, (see p. 64) It would also depend on the co-ordination number and stereochemistry of the metal ion, and the possibility of favourable hybridisation changes accompanying complex formation. Both $\bar{F}^{o}_{ML}$ and $\bar{F}^{o}_{HL}$ would be influenced by the number and nature of the donor atoms of the ligand, ~~and~~ by the inductive effects acting on

them , by the size and stereochemistry of the ligand molecule, and by the entropy changes accompanying the reactions

$$M + L \rightarrow ML$$
$$H + L \rightarrow HL \ .$$

In practice, stability constants must often be determined in mixed aqueous/organic solvents, for which equation (55) must be rewrittem,

$$RT\ln K'_{ML} = RT\ln K'_{HL} + (\bar{F}^{o'}_{M} - \bar{F}^{o'}_{H}) - (\bar{F}^{o'}_{ML} - \bar{F}^{o'}_{HL}) \qquad \ldots(55a)$$

where thersuperscript dash refers to constants appropriate to the solvent mixture. For each species,s,

$$\bar{F}^{o'}_{s} = \bar{F}^{o}_{s} + \bar{F}^{t}_{s}$$

where $\bar{F}^{t}_{s}$ is the free energy of transfer of the species from the standard state in water to the same concentration in the solvent mixture. In a binary mixed solvent in which n_X is the molar fraction of an organic solvent, X, a relationship , $\bar{F}^{t}_{s} \propto n_X$, might be expected at low values of n_X;this relationship has been observed for the transfer of chlorides of the alkali metals from water to aqueous ethanol [64-65a]. If such a relationship held for each species in solution, then

$$\bar{F}^{t}_{s} = a_s . n_X$$

and

$$\bar{F}^{o'}_{s} = \bar{F}^{o}_{s} + a_s . n_X \ .$$

where the value of the 'transfer constant',a_s, would depend both on the nature of the solute species and of the organic solvent. Thus, from (55a),

$$\ln K'_{ML} = \ln K'_{HL} + 1/RT\left\{(\bar{F}^{o}_{M} - \bar{F}^{o}_{ML} + \bar{F}^{o}_{HL} - \bar{F}^{o}_{H}) + n_X(a_M - a_{ML} + a_{HL} - a_H)\right\}$$

$$\ldots.(56)$$

In aqueous solution, $n_X = 0$, $K'_{ML} = K_{ML}$ and $K'_{HL} = K_{HL}$ and equation (56) reduces to (55).

APPLICATIONS OF EQUATION (56).

(i) The Relationship between the Stability of a Metal Complex and the Dissociation Constant of the Reagent.

Although the relationship between K'_{ML} and K'_{HL} for a given metal ion with a series of ligands has been considered [18,66,67] no quantitative treatment has been proposed. Now $\bar{F}^{o}_{H} = 0$, by definition, and rearranging equation (56),

$$\ln K'_{ML} = \ln K'_{HL} + 1/RT\left\{(\bar{F}^{o}_{HL}-\bar{F}^{o}_{ML}-n_X(a_{HL}-a_{ML}) + 1/RT(\bar{F}^{o}_{M}-n_X(a_M-a_H)\right\} \quad \ldots.(56a)$$

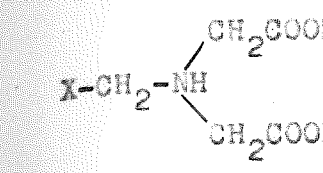
where the last term is a constant for a given metal ion with a series of ligands. The plot of $\ln K'_{ML}$ against $\ln K'_{HL}$ will be linear if the third term is (a) negligible compared with the other terms, or (b) constant throughout the series of ligands, or (c) itself is a linear function of $\ln K'_{HL}$. If a linear plot is obtained, its slope will be unity in cases (a) and (b), but in case (c) will be (1+k), where k is a constant, such that

$$1/RT\left\{\bar{F}^{o}_{HL}-\bar{F}^{o}_{ML}-n_X(a_{HL}-a_{ML})\right\} = k.\ln K'_{HL} + b.$$

It is possible to distinguish between the cases (a) and (b) for data obtained in water; the intercept for case (a) is then $\bar{F}^{o}_{M}/RT$, which may be calculated if $\bar{F}^{o}_{M}$ is known. For case (b), the intercept is the term $(\bar{F}^{o}_{M}+\bar{F}^{o}_{HL}-\bar{F}^{o}_{ML})/RT$, which cannot be calculated. No such distinction can be made in mixed solvents, as the relevant transfer constants are not known.

Equation (56a) accounts for the empirical relationships between $\ln K'_{ML}$ and $\ln K'_{HL}$ which have been observed for complexes of various metal ions with sets of closely related ligands. A replot of data for the cupric complexes of some substituted salicylaldehydes in 50% v/v aqueous dioxan [18] gives an approximately straight line of unit slope (case (a) or (b)). The slopes of the two lines obtained for the silver complexes of primary, and

secondary amines in water [67] are both much less than unity, indicating that $(\bar{F}^{o}_{HL}-\bar{F}^{o}_{ML})$ is a linear function of $\ln K'_{HL}$ in these systems (case (c)). Similar results are obtained for the copper, nickel and cerous complexes of some diketones in 50% v/v aqueous dioxan [66]. The complexes formed by ligands of the type



with ions of the alkaline earth metals and with zinc in water [66] show an exactly linear relationship between $\ln K'_{ML}$ and $\ln K'_{HL}$ and the slopes of the lines were found to be a linear function of the ionisation potential, I, of the metal. Thus, for these systems, the slope is given by $(1+k) = cI + d$; thus

$$(\bar{F}^{o}_{ML}-\bar{F}^{o}_{HL}) = RT\{(cI+d-1)\ln K'_{HL} + b\}$$

where b, c, and d are constants.

Plots of $\ln K'_{ML}$ against $\ln K'_{HL}$ for systems investigated in this work are shown in Graphs 33,34, and are discussed on p. 69.

<u>(ii)The Relationship between the Stabilities of the Complexes of a Series of Metals with Two Ligands.</u>

If a metal ion, M, forms complexes with two ligands, P and Q, then from equation (56),

$$\ln K'_{MP} = \ln K'_{MQ} - \{(\bar{F}^{o}_{MP}-\bar{F}^{o}_{MQ})-n_X(a_{MP}-a_{MQ})\}/RT + \ln\frac{K'_{HP}}{K'_{HQ}} + \{(\bar{F}^{o}_{HP}-\bar{F}^{o}_{HQ})+n_X(a_{HP}-a_{HQ})\}/RT \quad \ldots.(57)$$

as the last two terms are independent of M, a plot of $\ln K'_{MP}$ against $\ln K'_{MQ}$ for a series of metal ions will be linear if the term $\{(\bar{F}^{o}_{MP}-\bar{F}^{o}_{MQ})-n_X(a_{MP}-a_{MQ})\}$ is negligible compared with the other terms, or is independent of the nature of M, or is a linear function of $\ln K'_{MQ}$. Moreover, if the ligands P and Q are very similar, it might be expected that $(\bar{F}^{o}_{MP}-\bar{F}^{o}_{MQ}) \simeq (\bar{F}^{o}_{HP}-\bar{F}^{o}_{HQ})$ and that $(a_{MP}-a_{MQ}) \simeq (a_{HP}-a_{HQ})$. Equation (57) would then become

$$\ln K'_{MP} = \ln K'_{MQ} + \ln \frac{K'_{HP}}{K'_{HQ}}$$

$$\text{or} \quad \log K'_{MP} = \log K'_{MQ} + pK'_{(HP)} - pK'_{(HQ)} \qquad \ldots.(57a)$$

A plot of $\log K'_{MP}$ against $\log K'_{MQ}$ would then be a straight line of unit slope and of intercept $pK'_{(HP)} - pK'_{(HQ)}$. Major deviations from such a line for a pair of very similar ligands would indicate that some specific factor, such as steric hindrance, was operative. Some plots of $\log K'_{MP}$ against $\log K'_{MQ}$ for oxine derivatives are shown in Graphs 35-39, and are discussed in Section 3c.

(iii) The Relationship between the Stabilities of the Complexes of Two Metals with a Series of Ligands.

Similarily, if a ligand, L forms complexes with two metals, M and N, then from equation (56),

$$\ln K'_{ML} = \ln K'_{NL} - \{(\bar{F}^{\circ}_{ML} - \bar{F}^{\circ}_{NL}) - n_X(a_{ML} - a_{NL})\}/RT + \{(\bar{F}^{\circ}_{M} - \bar{F}^{\circ}_{N}) + n_X(a_M - a_N)\}/RT \qquad \ldots.(58)$$

The last term is independent of L, and a plot of $\ln K'_{ML}$ against $\ln K'_{NL}$ for a series of ligands will be a straight line of unit slope if the term $\{(\bar{F}^{\circ}_{ML} - \bar{F}^{\circ}_{NL}) - n_X(a_{ML} - a_{NL})\}$ is negligible compared with the other terms, or is independent of L. This might be expected to be the case for two very similar metals with a series of closely related reagents. A linear plot, not of unit slope, will be obtained if the term $\{(\bar{F}^{\circ}_{ML} - \bar{F}^{\circ}_{NL}) - n_X(a_{ML} - a_{NL})\}$ is itself a linear function of $\ln K'_{NL}$. Plots of $\log K_1$ for the copper complex against $\log K_1$ for the nickel complex for series of substituted ethylenediamines [30] and β-diketones [66] are shown in Graph 40. It is seen that, in both cases, the majority of points do lie approximately on a straight line of unit slope. The deviations probably reflect the effect of the different geometry of the metal ions on their reactions with sterically hindered reagents. Similar plots of constants obtained in this work are shown in Graph 41 and discussed on page 71.

(iv) The Relationship between the Stability Constant of a Metal Complex and the Ionisation Potential of the Metal.

Van Eck [69] has obtained linear plots of $\log K'_{ML}$ for complexes of a few metals with one ligand against the ionisation potential, I, of the metal, and some authors have obtained similar plots of $\log \beta_N$ against I [70,71]. Fig.s 8 and 9 illustrate such plots for complexes of glycine in water, and of salicylaldehyde in 50% v/v aqueous dioxan, [19,69,71].

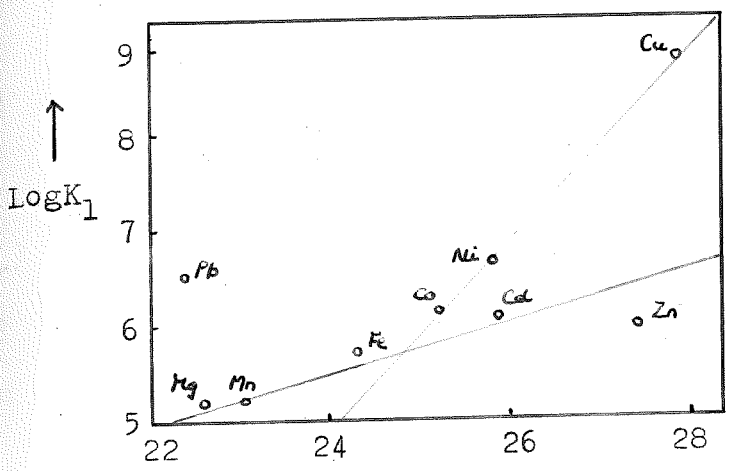


Fig. 8.

Salicylaldehyde Complexes.

50% Aqueous Dioxan.

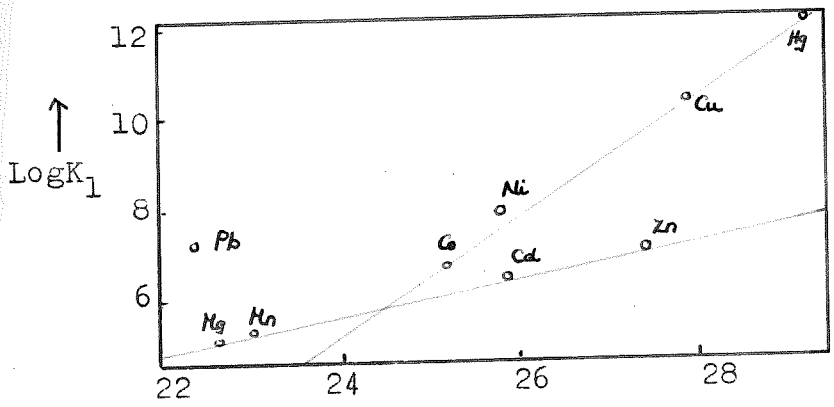


Fig. 9.

Glycine Complexes.

Water.

For a divalent metal, I is the heat required for the reaction

$$M(gas) \longrightarrow M^{++}(gas)$$

and there seems to be no obvious reason why $\log K'_{ML}$ should be a linear function of I.

From equation (56a)

$$\ln K'_{ML} = \left\{(\bar{F}^{o}_{M}-\bar{F}^{o}_{ML})+n_X(a_M-a_{ML})\right\}/RT + \ln K'_{HL} + \left\{\bar{F}^{o}_{HL}+n_X(a_{HL}-a_H)\right\}/RT$$

As the last two terms in this equation are independent of M, the existance of a linear relationship between I and $\log K'_{ML}$ would imply that such a relationship must also exist between I and $\left\{(\bar{F}^{o}_{M}-\bar{F}^{o}_{ML})+n_X(a_M-a_{ML})\right\}$. Numerical values of I and $\bar{F}^{o}_{M}$ [63] for some divalent metals are plotted in Graph 32, and it is seen that $\bar{F}^{o}_{M}$ is an approximately linear function of I for some sets of metals. If $\bar{F}^{o}_{M} = eI + f$, and $\bar{F}^{o}_{M}$ and I are expressed in Kcals./mole, numerical values of the parameters e and f are given in Table 14.(59)

TABLE 14. Linear Relationships between I and $\bar{F}^{o}_{M}$.

Metals.	e.	f.	
Ca, Sr, Ba.	0.038	-144	Determined graphically.
Mg, Mn, Fe(II).	2.2	-1207 ± 10	" "
Co, Ni, Cu.	0.473	-290 ± 2	Least Squares Method.
Cu, Cd, Hg.	0.84	-525 ± 3	" " "
Fe(II), Co, Ni, Cu.	0.403	-247 ± 3	" " "
Hg, Co, Ni, Cu.	0.586	-358 ± 4	" " "

In water, $n_X=0$, and $\ln K'_{ML}$ will be a linear function of I for these sets of metals provided that $\bar{F}^{o}_{ML}$ is largely independent of M, or is itself a linear function of I. If ML is predominantly covalent and there is little entropy change accompanying complex formation, the ionisation potential will be a measure of the energy of the M — L bond. In such cases, it is probable that for some sets of metal complexes

$$\bar{F}^{o}_{ML} = gI + h \qquad \ldots.(61)$$

If both $\bar{F}^{o}_{M}$ and $\bar{F}^{o}_{ML}$ are linear functions of I, then

$$\ln K'_{ML} = \{(e-g)I+n_X(a_M-a_{ML})\}/RT + \ln K'_{HL} + \{\bar{F}^{o}_{HL}+n_X(a_{HL}-a_H)+f-h\}/RT \quad \ldots.(61)$$

The last two terms will be constant for complexes of different metals with the same reagent, and $\ln K'_{ML}$ will be a linear function of I if $n_X=0$ (i.e. in pure water) or if $n_X(a_M-a_{ML}) \ll (e-g)I$, (i.e. in a mixed solvent). Fig.s 8 and 9 show that linear plots are indeed obtained for some complexes of Hg, Cu, Ni, and Co, and of Mg, Mn, Fe, but that points for other metals, such as cadmium, to which the same values of the parameters e and f are not applicable, may also fall on these lines.

Consider a series of metals, M, all having the same values of the parameters e, f, g and h, and a metal M', not belonging to this series. It is possible that, for M', the differences (e-g) and (f-h) may fortuitously be very similar to the corresponding terms for the series of metals, M, even though the values of the individual parameters are different. In water, the point for the metal M' will then lie on the same line as points for the series of metals; but in mixed solvents, this will only be the case if $(a_{M'}-a_{M'L})=(a_M-a_{ML})$ or if $(e-g)I \gg n_X(a_M-a_{ML})$, $n_X(a_{M'}-a_{M'L})$. Even if all these conditions are not strictly fulfilled, the point for M' may still appear to lie on the line within the limits of experimental error. This may account for the position of Cd on the same line as Mg, Mn, and Fe in Fig.8, even though the equation $\bar{F}^{o}_{M} = 2.2I - 1207$ does not apply to Cd.

(v) Stability Orders of Metals.

Maley and Mellor [71,72] observed that, with a limited range of ligands, the stability of a series of metal complexes often fell in the order, Pd > Cu > Ni > Co > Zn > Cd > Fe > Mn > Mg. Irving and Williams [73,74] have since shown that, if a stability order

is to be valid for complexes of a wide range of ligands, the heat change for the reaction M + L $\longrightarrow$ ML must be much greater than the corresponding entropy change, and that the order of increasing strength of the M—L bond must be independent of bond type. They postulate that a stability order for purely covalent complexes would follow the order of increasing ionisation potential, I, of the metal, and that an order for purely ionic complexes would follow the order of decreasing (crystal) ionic radius, r, of the metal ion. They would therefore expect a universal stability order for a series of metals for which the order of increasing ionisation potential is the same as that of decreasing ionic radius, provided that the entropy changes on complex formation are negligible compared with the heat changes. If appreciable entropy changes are involved, a universal stability order would only be expected if, for each ligand, these changes are either independent of the nature of the metal, or else follow the same order as the corresponding heat changes.

From equation (66),

$$\ln K'_{ML} = \{(\bar{F}^{o}_{M}-\bar{F}^{o}_{ML})+n_X(a_M-a_{ML})\}/RT + \ln K'_{HL} + \{\bar{F}^{o}_{HL}+n_X(a_{HL}-a_H)\}/RT \quad \ldots\ldots(56)$$

$$= \{(\bar{F}^{o}_{M}-\bar{F}^{o}_{ML})+n_X(a_M-a_{ML})\}/RT + \text{constant} \quad \ldots\ldots(56b)$$

for a given ligand. Thus a high value of $\ln K'_{ML}$ is favoured by a high value of $\bar{F}^{o}_{M}$ and a low value of $\bar{F}^{o}_{ML}$, and in mixed solvents, by a high value of $n_X(a_M-a_{ML})$. The term $\bar{F}^{o}_{ML}$, which is the only one considered in the Irving-Williams treatment, is decreased by an increase in the strength of the M—L bond, and hence by increases in I and 1/r. A general stability order in water would therefore only be expected for those metals in which the terms $\bar{F}^{o}_{M}$, I and 1/r all increased in the same order. If the term (a_M-a_{ML}) varies widely with change of M or L, the stability

order might be changed by change of solvent. The stability order might also be changed if there are large entropy changes on complex formation.

For the divalent ions of the first transition series, the terms $\bar{F}^{o}_{M}$, I, and 1/r fall in the order,

$\bar{F}^{o}_{M}$ Mn < Zn < Fe < Co < Ni < Cu

I Mn < Fe < Co < Ni < Zn < Cu

1/r Mn < Fe < Co < Ni < Zn < Cu (small variation)

On the basis of the Irving-Williams treatment, the stabilities of the zinc complexes should always fall between those of the corresponding complexes of nickel and copper; this is only found to be the case for the hydroxide, cyanide, and riboflavin complexes [75-78]. If the contribution of the term $\bar{F}^{o}_{M}$ is considered, the stability order, Mn < Fe < Co < Ni < Cu > Zn > Mn would be expected and is found to be valid for a large number of ligands [75].

The orders of the terms $\bar{F}^{o}_{M}$, I and 1/r for the ions of the alkaline earth metals are given by

$\bar{F}^{o}_{M}$ Ba < Sr < Ca < Mg

I Ba < Sr < Ca < Mg

1/r Ba < Sr < Ca < Mg (large variation)

The stability order Ba < Sr < Ca < Mg would therefore be expected, and is indeed observed for ligands which are the anions of weak acids. The reverse order is observed for anions of strong acids, and is explained by the preferential hydration of the smaller ions [79,80]. The inverse effective radius of the solvated ions would then fall in the order Mg < Ca < Sr < Ba. As complexes formed by the anions of strong acids would be mainly ionic in character, it is to be expected that their stabilities would follow this order. No such complications arise for ions of the first transition series, for which there are only small variations in 1/r.

The orders of the terms $\bar{F}^{o}_{M}$, I and 1/r for the divalent ions of Group IIB metals and the trivalent ions of Group IIIB metals are given by

$\bar{F}^{o}_{M}$	Zn < Cd < Hg	Ga < In < Tl
I	Cd < Zn < Hg	In < Ga < Tl
1/r	Hg < Cd < Zn	Tl < In < Ga

As the three terms increase in different orders, no general stability orders would be expected in these groups. If, however, the complexes are predominantly covalent, the contribution of 1/r is unimportant, and the expected stability orders would be Hg > Cd, Zn and Tl > In, Ga.

3(c). THE STABILITIES OF SOME METAL COMPLEXES IN 50% v/v AQUEOUS DIOXAN.

The effect of changes in the environment of the functional group on the complexing power of oxine derivatives was investigated by determining the stability constants $^{c}K_1$ and $^{c}K_2$ (see page 14) of the complexes formed by the available reagents and a series of metal ions. The divalent ions Mg^{++}, Zn^{++}, Ni^{++}, Cu^{++} and UO_2^{++}, were selected for diversity of size and electronic configuration. Measurements were made in 50% v/v aqueous dioxan as many of the reagents and complexes are very sparingly soluble in water. A salt background of 0.3M sodium perchlorate was used, since in this mixed solvent the rate of change of activity coefficient with ionic strength is likely to be small at this concentration ([46], p.548), and the perchlorate ion would be expected to form less stable complexes than other inorganic anions with the metal ions. The dissociation constants of the reagents and the stability constants of the metal complexes were determined at 20.0 ± 0.2°C by pH titration (see Sections 2(b) and 2(c));the titration and formation curves obtained are plotted in Graphs 17-31, and values of the stoichiometric stability constants are given in Table 15. Values in parentnesis are those reported by Johnston and Freiser [37], obtained by pH titration at 25°C and unspecified ionic strength. While there is a systematic variation between the two sets of stability constants obtained for the oxine complexes, there is little agreement between the two sets of values for the complexes of 2-methyl-oxine.

TABLE 15. The Stability Constants of Metal Complexes at 20°C in 50% v/v Aqueous Dioxan.

		Mg^{++}	Zn^{++}	Ni^{++}	Cu^{++}	UO_2^{++}
1.	8-Hydroxyquinoline.					
	$\log^c K_1$	5.04 (6.38)	9.34 (9.96)	10.43 (11.44)	13.03 (13.49)	11.25
	$\log^c K_2$	4.29 (5.34)	8.22 (8.90)	9.97 (9.94)	12.35 (12.73)	9.64
2.	8-Hydroxy-2-methylquinoline.					
	$\log^c K_1$	3.73	8.66 (10.10)	8.52 (9.50)	10.22 (13.00)	~9.4
	$\log^c K_2$	3.13	8.10 (9.07)	7.96 (8.50)	9.32 (11.64)	~8.0
3.	8-Hydroxy-5-methylquinoline.					
	$\log^c K_1$	5.21	9.46	insol.	13.55	11.25
	$\log^c K_2$	4.47	8.40	"	12.35	9.52
4.	8-Hydroxy-6-methylquinoline.					
	$\log^c K_1$	5.09	insol.	insol.	insol.	10.09
	$\log^c K_2$	4.31	"	"	"	9.26
5.	8-Hydroxy-7-methylquinoline.					
	$\log^c K_1$	4.64	9.31	insol.	insol.	11.28
	$\log^c K_2$	4.12	8.11	"	"	9.78
6.	1:2:3:4-Tetrahydro-10-hydroxyacridine.					
	$\log^c K_1$	3.98	8.80	insol.	11.78	10.10
	$\log^c K_2$	3.56	7.86	"	10.40	8.20
7.	5-Fluoro-8-hydroxyquinoline.					
	$\log^c K_1$	4.15	insol.	insol.	insol.	10.04
	$\log^c K_2$	3.33	"	"	"	8.42
8.	8-Hydroxycinnoline.					
	$\log^c K_1$	3.02	6.93	8.25	9.49	8.68
	$\log^c K_2$	2.18	5.80	7.23	8.59	7.16

TABLE 15 (continued).

	Mg^{++}	Zn^{++}	Ni^{++}	Cu^{++}	UO_2^{++}
9. 8-Hydroxy-4-methylcinnoline.					
$\log^c K_1$	3.66	7.23	~8.5	insol.	9.00
$\log^c K_2$	2.58	6.47	~8.2	"	7.30
10. 8-Hydroxyquinazoline.					
$\log^c K_1$	3.89	7.48	insol.	10.56	8.99
$\log^c K_2$	2.91	6.96	"	9.54	7.70
11. 8-Hydroxy-2:4-dimethylquinazoline.					
$\log^c K_1$	3.81	7.77	7.88	10.26	8.77
$\log^c K_2$	3.09	7.01	7.00	9.74	7.33
12. 8-Hydroxy-4-methyl-2-phenylquinazoline.					
$\log^c K_1$	~0	7.03	insol.	8.83	8.53
$\log^c K_2$		5.87	"	8.31	7.85
13. 5-Hydroxyquinoxaline.					
$\log^c K_1$	3.44	7.07	7.79	9.66	8.40
$\log^c K_2$	2.95	5.71	7.02	8.84	7.51

DISCUSSION OF RESULTS.

(i) The Relationship between the Stability of a Metal Complex and the Dissociation Constant of the Reagent.

As $\log^T K_1 = \log^c K_1 + \text{constant}$,

equation (56a), page 58, predicts that a plot of $\log^c K_1$ against pK_{OH} for a given metal ion with a series of ligands will be linear if the term $\{\bar{F}^o_{HL} - \bar{F}^o_{ML} - n_X(a_{HL} - a_{ML})\}/2.303RT$ is negligible compared with the other terms of the equation, or is independent of the nature of L, or is a linear function of pK_{OH}. If the ligands are very closely related, it might be expected that the term $\{\bar{F}^o_{HL} - \bar{F}^o_{ML} - n_X(a_{HL} - a_{ML})\}$ would be constant for a given metal and a plot of $\log^c K_1$ against pK_{OH} would be a straight line of

unit slope. The plot of $\log^c K_1$ against pK_{OH} for complexes of magnesium is shown in Graph 35, together with the best straight line of unit slope. There are two types of deviation from the theoretically predicted behaviour:

(a). Major deviations where $\log^c K_1$ is always smaller than predicted. These are associated with reagents having substituents adjacent to the chelating nitrogen atom, and the stabilities of the metal complexes are clearly decreased by steric hindrance. There is no evidence for complex formation between the magnesium ion and 8-hydroxy-4-methl-2-phenylquinazoline.

(b). Minor deviations in which $\log^c K_1$ may be either smaller or larger than predicted. Since both oxygen and nitrogen atoms are involved in the chelation, the magnitude of pK_{OH} is not the only factor which influences $\log^c K_1$. The observed minor deviations may be due to differences in the co-ordinating power of the chelating nitrogen atoms.

Plots of $\log^c K_1$ against pK_{OH}, for zinc and nickel complexes are also shown in Graph 35, and large negative deviations are again observed for complexes of sterically hindered reagents. The minor deviations are much more marked than in the case of magnesium, and it seems probable that variations in the inductive effects acting on the chelating nitrogen atoms have a much greater influence on the stability of complexes formed by zinc and nickel, which form fairly strong metal-nitrogen bonds, than on the stability of complexes of magnesium, which only forms weak links to nitrogen. Indeed, if the metal ion is very strongly bound to one of the chelating atoms, it may appreciably modify the inductive effects acting on the other chelating atom, so that any simple theoretical predictions of stability based on the values of pK_{OH} and pK_{NH} would be unjustified. Such an effect would be most noticeable for the uranyl ion, which forms very

strong links with oxygen, and for the cupric ion, which forms strong links to both oxygen and nitrogen. Plots of $\log^{c}K_1$ against pK_{OH}, for the complexes of uranyl and copper are shown in Graph 34, and it is seen that a small increase in pK_{OH} gives rise to an abnormally large increase in $\log^{c}K_1$; the slope of the best straight line is 1.3 for the uranyl complexes, and 2.2.for the copper complexes. The expected large negative deviations are again observed for complexes of sterically hindered reagents.

(ii).The Relationship between the Stabilities of Related Series of Metal Complexes.

Equation (57), page 59, indicates that, if a series of metal ions form complexes with two very similar ligands, P and Q, then a plot of $\log K'_{MP}$ against $\log K'_{MQ}$, or of $\log^{c}K_{1(MP)}$ against $\log^{c}K_{1(MQ)}$, would be a straight line of unit slope, and of intercept $pK_{OH(MP)}-pK_{OH(MQ)}$. Some plots of this type, together with the theoretically predicted lines, are shown in Graphs 35-39.

In Graph 35, values of $\log^{c}K_1$ for complexes of 5-methyl-oxine and of 6-methyl-oxine are plotted as the ordinates, and values of $\log^{c}K_1$ for oxine complexes as the abscissae. The experimental points fall closely on the theoretical lines, as might be expected for pairs of reagents which differ only slightly in their structure and in their values of pK_{NH}. The complexes of 7-methyl-oxine (Graph 35) are, however, consistently somewhat less stable than predicted. This may be due either to the lower value of pK_{NH} of this reagent, or to steric effects. Since the deviation occurs even with the magnesium complex, the latter seems the more likely.

Other ordinates in Graph 35 are values of $\log^{c}K_1$ for the complexes of 2-methyl-oxine, all of which are much less stable than the value of pK_{OH} of the reagent would suggest; this is

undoubtedly due to steric effects. Similar plots are obtained for complexes of 1:2:3:4-tetrahydro-10-hydroxyacridine (Graph 35) 8-hydroxy-2:4-dimethylquinazoline, and 8-hydroxy-4-methyl-2-phenylquinazoline (Graph 36). The decrease in stability is most marked with complexes of the last reagent, probably on account of the size of the 2-substituent. The lower values of $\log {}^{c}K_{1}$ observed for complexes of every 2-substituted reagent as compared with those of the parent reagent and the same metal provide clear evidence that steric factors hinder the formation of the 1:1 complexe. This supplements results obtained recently for derivatives of oxine [70], 1:10-phenanthroline,[81] and ethylenediamine [30].

Values of $\log {}^{c}K_{1}$ for complexes of 8-hydroxycinnoline, 8-hydroxy-4-methylcinnoline, 8-hydroxyquinazoline, and 5-hydroxyquinoxaline form the ordinates in Graph 37, and values of $\log {}^{c}K_{1}$ for oxine complexes form the abscissae. Although the stability constant for the magnesium complex of 8-hydroxycinnoline lies on the theoretical line, that for the copper complex lies well below it. Points for other complexes lie in intermediate positions. The low value of pK_{NH} for 8-hydroxycinnoline compared to that for oxine would be expected to reduce the stability of the copper complex, but to have little effect on that of the magnesium complex. The plots for the complexes of 8-hydroxy-4-methylcinnoline, 8-hydroxyquinazoline and 5-hydroxyquinoxaline are similar. If values of $\log {}^{c}K_{1}$ for these reagents are plotted against those for 8-hydroxycinnoline (Graph 38), the experimental points lie much near the theoretical line than when the complexes of oxine are made the basis of comparison. . This is doubtless because the variation in the inductive effects acting on the chelating nitrogen atom is smaller among these reagents.

Graph 39 shows values of $\log {}^{c}K_{1}$ for complexes of sterically

hindered reagents, plotted against values of $\log {}^{c}K_{1}$ for complexes of 2-methyl-oxine. If the value of pK_{NH}, and the size and position of the hindering group were the same for each reagent, the points should again lie on a straight line of unit slope and of intercept ΔpK_{OH}. The points for the magnesium, zinc and uranyl complexes of 1:2:3:4-tetrahydro-10-hydroxyacridine are seen to lie on the theoretical line, but the copper complex ~~mf~~ is more stable than predicted, doubtless due to the high value of pK_{NH} of the reagent, and the tendency for copper to form strong links to nitrogen. The points for the zinc, nickel and uranyl complexes of 8-hydroxy-2:4-dimethylquinazoline also lie near the appropriate theoretical line, but the stabilities of the copper and magnesium complexes are anomolously high. The magnesium, zinc, and copper complexes of 8-hydroxy-4-methyl-2-phenylquinazoline are considerably less stable than predicted, probably on account of the size of the hindering group in this reagent.

It has been shown on page 60 that a plot of $\log {}^{c}K_{1(ML)}$ against $\log {}^{c}K_{1(NL)}$ for complexes of two very similar metals with a series of closely related reagents might be expected to give a straight line of unit slope. In Graph 41, values of $\log {}^{c}K_{1}$ for zinc, nickel, uranyl and copper complexes are plotted against values of $\log {}^{c}K_{1}$ for the corresponding magnesium complexes. As none of these ions is very similar to the magnesium ion, linear plots would not be expected, and are not, in fact, obtained. The complexes of zinc would be expected to show the closest resemblance to those of magnesium, and it is seen that, while points for the zinc complexes of the aza-oxines do fall approximately on a straight line of unit slope, those for complexes of substituted oxines appear to fall on a different straight line, which has a slope of about 0.7, and lies well above the line for the aza-oxine complexes. The increase in the value of pK_{NH} on passing

from the aza-oxines to the substituted oxines doubtless causes a greater increase in the stability of the zinc complexes than in those of the magnesium complexes. Approximately straight lines of unit slope are also obtained for the complexes of the aza-oxines with copper and uranyl ions, but not with nickel ions. That points refering to complexes of these ions with reagents with higher values of pK_{OH} and pK_{NH} do not lie on straight lines may be due either to the influence of small changes in pK_{NH} on the stability of these complexes, or to the modification of the inductive effects acting on one of the atoms in the chelating group by the attachment of the metal ion to the other atom, (see p.70).

(iii). General Considerations.

Irrespective of the nature of the ligand, the stability of these metal complexes always follows the order $Mg^{++} < Zn^{++} < Ni^{++} < UO_2^{++} < Cu^{++}$, whether steric hindrance occurs or not. The only exception is 2-methyl-oxine where the nickel complex is slightly less stable than the zinc complex. The extent of steric hindrance to complex formation may be estimated from the deviations from the theoretical straight lines in Graphs 35,36, but cannot be simply related to any properties of the ions or ligands investigated. Thus the order of increasing deviation is $Zn^{++} < Mg^{++} < UO_2^{++} < Cu^{++}$ for 1:2:3:4-tetrahydro-10-hydroxyacridine, $Zn^{++} < Mg^{++} < Ni^{++} \sim UO_2^{++} < Cu^{++}$ for 2-methyl-oxine, but $Mg^{++} < Zn^{++} < Ni^{++} \sim UO_2^{++} < Cu^{++}$ for 8-hydroxy-2:4-dimethylquinazoline, and $Zn^{++} < UO_2^{++} < Ni^{++} \sim Cu^{++} < Mg^{++}$ for 8-hydroxy-4-methyl-2-phenylquinazoline. Thus, smaller deviations are observed for the less stable complexes of magnesium and zinc, than for the more stable complexes of nickel, uranyl and copper. An exception is 8-hydroxy-4-methyl-2-phenylquinazoline, which appears to form no complex with magnesium. Zinc ions form tetrahedral bonds, and might be less effected by steric hindrance than nickel, uranyl and copper ions, which probably form coplanar bonds. The geometry favoured by 4-covalent magnesium is unknown.

The differences $\log^c K_1 - \log^c K_2$ for the metal complexes studied do not indictae a purely statistical addition of the second ligand [12]. The observed differences show no definite trend and it seems probable that the hydrated cation is so modified by the addition of the first ligand that the forces leading to the interaction of the singly charged 1:1 complex with a second ligand molecule are of rather a different type from those operating between the solvated divalent ion and the first molecule of the ligand [29,47]. In none of the complexes investigated is $K_2 > K_1$. The values of K_1/K_2 are consistently high for the uranyl complexes, and it may be that the 1:1 complexes formed by the large, linear uranyl ions are less hydrated than the 1:1 complexes formed from the smaller spherical cations. The addition of a second ligand molecule might then be expected to liberate fewer water molecules from the 1:1 uranyl complex than from those of the other metals; this would result in a smaller positive entropy change for the reaction $ML^+ + L^- \rightarrow ML_2$, and hence lower the value of K_2 relative to K_1.

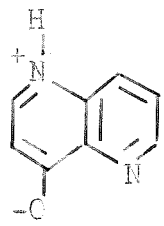
SOME METAL COMPLEXES OF THE HYDROXYNAPHTHYRIDINES.

(i) Metal Complexes of 4-Hydroxy-1:5-naphthyridine and of 8-hydroxy-1:7-naphthyridine.

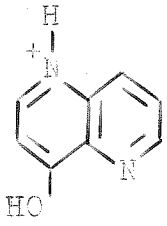
Albert and Hampton [58] have found that 4-hydroxy-1:5-naphthyridine and 8-hydroxy-1:7-naphthyridine form complexes with metal ions in aqueous acid solutions, but that the complexes are decomposed as the pH is raised. The relative positions of the titration curves obtained in this work (Graph 29) show that similar reactions occur in 50% v/v aqueous dioxan. Albert and Hampton report that, at still higher values of pH, complexes analogous to the oxinates are formed. The graph shows that, except for the magnesium complex of 4-hydroxy-1:5-naphthyridine, the titration curves for the reagents in the presence of metal ions differ

appreciably from those for the reagents alone, only in the pH range where there is considerable hydrolysis of the metal ions (see Graph 30); the precipitates obtained had the appearance of metallic hydroxides, and there is little evidence that these compounds form stable complexes of the oxinate type in the solvent mixture used in this work.

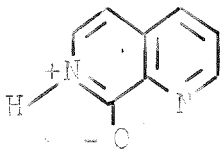
The nature of the complexes formed is obscure. Albert and Hampton suggest that the zwitterions (I) and (III), derived from the cations (II) and (IV), act as ligands in acid solution; as the pH is increased, the concentration of cations, and hence of zwitterions, would be decreased below that necessary for complex formation.



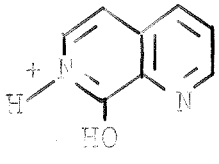
I.



II.



III.



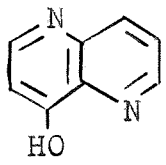
IV.

They therefore postulate that the more basic centres are not those nitrogen atoms involved in chelation. Now the physical properties of these reagents (see Section 3a) indicate that the neutral molecules exist predominantly in the zwitterion forms; if these species formed complexes with metal ions, a decrease in the amount of complex formation would only be expected when $pH > (pK_{OH} - 2)$. It was found that the complexes decomposed in the region $(pK_{NH} - 2) < pH < (pK_{NH} + 2)$, both in water [38], and in 50% aqueous dioxan. Moreover, the absorption spectra of the complexes formed by the species (I) and (III), which contain the same functional group as oxine, might be expected to resemble the spectra of the corresponding oxines. It was found that these reagents formed

blue complexes with copper and green complexes with nickel, although copper and nickel oxinates are yellowish. It is therefore felt that the complexes formed in acid solution are not chelates derived from the species (I) and (III).

The absorption spectra of both reagents indicate that the basic centres may in each case be the nitrogen atom in the chelating group; this is compatible with the electron-withdrawing properties of the hydroxyl group. If the basic centres of 4-hydroxy-1:5-naphthyridine and 8-hydroxy-1:7-naphthyridine were N_1 and N_7 respectively, the cations of these reagents would be unable to tautomerise, and hence would be considerably less stable than the corresponding neutral molecules, whose keto-tautomers would be stabilised by resonance with the zwitterion forms (see page 46) These reagents would then be expected to have very low values of pK_{NH}. If, however, the more basic nitrogen atom were the one in the functional group, the cation could tautomerise, and the keto-form would be somewhat stabilised by resonance. Although this would occur less in the charged cation than in the uncharged species, very low values of pK_{NH} would not be expected. The values of pK_{NH} for both reagents are found to be of the same order as that for 8-hydroxycinnoline, and might indicate that the basic centres of these hydroxynaphthyridines are those nitrogen atoms involved in chelation; but such a conclusion must be tentative in the absence of further evidence.

The titration curves for 4-hydroxy-1:5-naphthyridine (Graph 29) show that, in acid solution, the degree of formation of the acid, $\bar{n}^H$, is 2 in the absence of metal ions, but is only 1 in the presence of nickel and copper. The ligand species must therefore be the neutral molecule (V), or a zwitterion derived from it. If the neutral species (V) could co-ordinate to a metal ion



V.

through N_1, the resultant complex might be more stable than the cation of the reagent, but would doubtless be much less stable than the keto-zwitterion form of the neutral molecule. The complex could then exist in acid solution, but would be decomposed in the region where $pH \backsim pK_{NH}$. The similar phenomena observed for 8-hydroxy-1:7-naphthyridine could be explained in an analogous way.

The fact that no stable complexes are formed by the anions of 4-hydroxy-1:5-naphthyridine and of 8-hydroxy-1:7-naphthyridine, in spite of the high values of pK_{OH} of the reagents, may be attributed to the high stability of the keto-form of the neutral molecules, relative to the anions, or to the metal complexes derived from them.

(ii) Metal Complexes of 8-Hydroxy-1:6-naphthyridine.

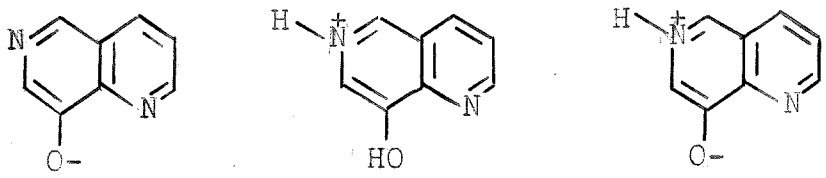
The formation curve of the zinc complex of 8-hydroxy-1:6-naphthyridine (calculated on the assumption that (VI) is the complexing species) in 50% aqueous dioxan, is plotted in Graph 31. It is seen that as pL is decreased, the value of $\bar{n}$ successively passes through a maximum and a minimum and then rises sharply. At low values of pH, the position of the formation curve depends on the total metal concentration. Somewhat similar curves are obtained for the copper complex (Graph 31), and also for the ferrous complex in water [38]. These curves obviously cannot be represented by the equation

$$\bar{n} + (\bar{n}-1)\,{}^{c}K_1[L] + (\bar{n}-2)\,{}^{c}K_1\,{}^{c}K_2[L]^2 = 0 \qquad \ldots.(38a)$$

and it is probable that more than one type of complex formation occurs (see page 34), and that values of 'pL' calculated from equation (23a) do not refer to the actual species involved in complex formation over the whole range of pH considered.

Albert and Hampton [38] suggest that the cation (VII) ionises to give the zwitterion (VIII), which takes part in complex formation.

VI. VII. VIII.



At very low values of pH (i.e. at high values of 'pl') an increase on pH results in increased ionisation of the cation, and hence in an increase in $\bar{n}$; as the pH is further raised, an increase in pH would lead to a decrease in the concentration of the cation, and hence of the zwitterion, and would therefore result in a decrease in $\bar{n}$; at still higher values of pH, $\bar{n}$ is again increased on account of complex formation by the anion (VI).

This type of behaviour would only be expected for reagents in which the more basic nitrogen atom is not that one involved in chelation, and in which the inductive effects acting on the more basic nitrogen atom, and on the hydroxylic oxygen atom are such that a zwitterion can exist. Albert and Hampton [38] have found that the value of pK_{OH} for 8-hydroxy-1:6-naphthyridine-6-methiodide (4.31) is only slightly greater than the value of pK_{NH} for the parent 8-hydroxy-1:6-naphthyridine (4.08). As the values of pK_{OH} would probably be little changed by the replacement of a hydrogen atom by a methyl group in the position meta- to the hydroxyl group, it is very probable that the zwitterion (VIII) can exist. Unlike the zwitterions of 4-hydroxy-1:5-naphthyridine (I) and 8-hydroxy-1:7-naphthyridine (III), it could not be stabilised by resonance with the amido-form. As the values of pK_{OH}

for the methiodides of 8-hydroxyquinazoline and 5-hydroxyquinoxaline are considerably higher than those of pK_{NH} for the parent reagents, zwitterions analogous to (VIII) would be unlikely to exist. The value of pK_{OH} of the methiodide of 8-hydroxycinnoline is not known.

The assignment of the position of the more basic nitrogen atom to N_6 in 8-hydroxy-1:6-naphthyridine is compatible with the results of absorption spectrum measurements, (see page 51).

3(d). THE INFLUENCE OF THE SOLVENT ON STABILITY.

As many organic chelating agents and their metal complexes are considerably more soluble in polar organic solvents than in pure water, stability constants have often been determined in aqueous dioxan and in aqueous ethanol. Only qualitatime inter-comparison of the results obtained in different solvent mixtures is as yet possible, as the influence of the solvent on the stability of a metal complex is very imperfectly understood. As there would seem to be some quantitative correlation between the dissociation constants of a reagent and the stabilities of its metal complexes (see pages 58, 69), the problem of relating complex stability to the nature of the solvent might be somewhat elucidated by a study of the variation of acid dissociation constants with change of solvent.

(i). The Variation of pK_{OH} with Solvent.

Values of pK_{OH} refer to dissociation of the type

$$HL \longrightarrow H^+ + L^-$$

which formally resembles the dissociation of an ion pair,

$$H^+L^- \longrightarrow H^+ + L^-$$

This was first treated by Niels Bjerrum [82], who related the dissociation constant, K, of an ion pair to a complex function of the interionic distance, a, and the dielectric constant, D, of the medium. The nature of the variation of K with D depends on the charge and radius of each ion, and on the values of a and D considered, but is always such that K decreases as D decreases. Thus Bjerrum's equation predicts that logK is a linear function of D for silver acetate [83], but is a linear function of -1/D for lanthanum ferricyanide [84,85]. The treatment deals only

with the electrostatic interaction between two charged particles and is based on the following simplifying assumptions:—

(a) No covalent forces are involved,

(b) The ions are rigid spheres, with the charge situated at the centre,

(c) The medium and solute form a continuous dielectric,

(d) No solute-solvent interaction occurs.

The best agreement with the Bjerrum treatment is observed with 1:1 electrolytes such as lanthanum ferricyanide [84,85] and tetraisoamyl ammonium nitrate [86], which give rise to large, symmetrical ions. Covalent bonding and ionic solvation are reduced to a minimum in these cases, and the ions behave as unpolarisable spheres. The dissociation of such compounds as lead chloride, zinc and copper sulphates, zinc malonate , and formic acid [84,87] is not adequately described by the Bjerrum equation.

The treatment has been modified by Kirkwood and Westheimer [88] who allow for the 'internal dielectric constant' of the solute, and the ellipsoidal shape of some of the species, but do not consider solvent-solute interaction [89]. The importance of this factor is shown by the fact that values of the interionic distances in some bromates and iodates, as calculated using the Kirkwood-Westheimer equation, appear to depend on the nature of the solvent, rather than of the salt, [90].The effect of solvent-solute interaction is greatly complicated if mixed solvents are used. It has been observed that values of pK for some substituted benzoic acids vary with the nature of the solvent, even when the dielectric constant is the same [91], and that the dissociation of metal picrates in pyridine is greatly increased by the addition of very small amounts of water [92]. It has been suggested [91] that preferential solvation of organic molecules

by dioxan may occur in water-dioxan mixtures, and result in the lowering of the dielectric constant in the neighbourhood of the solute. The large increase in conductivity [93-96] and decrease in catalytic properties [97,98] caused by the addition of very small amounts of water to solutions of hydrogen chloride in organic solvents indicate that the hydrogen ion is preferentially solvated by water. The degree of hydration may, however, differ appreciably in different mixed solvents [99,100].

The internal structure of the solvent is another difficulty which arises in any treatment of mixed solvents. Organic liquids probably approach the ideal 'continuous dielectric' to a greater extent than does water, which has a relatively ordered structure [101]. Very considerable changes in molecular arrangement must occur if a miscible organic solvent is added to the quasi-crystalline pure water. Further changes in order are produced by the addition of ions to a solvent [102-104] and would be of considerable importance in solutions with a high concentration of 'salt background'. These changes would affect both the dielectric constant of the solution and the entropy changes accompanying a reaction [105]. Other important factors which vary throughout a series of mixed solvents are the activity, and the ionic product, of water [46,106].

The above disscussion indicates that there are too many complicating factors to allow of any quantitative correlation between pK_{OH} and the physical proerties of the solvent. Some qualititive predictions are, however, possible. It has been seen on page 57 that the partial molar free energies of some species in solutions of binary mixed solvents are linearily related to the molar fraction, n_x, of the organic component, at low values of n_x.

If this were also true for the species H^+, L^- and HL, the dissociation constants of HL in water and in a mixed solvent are given by equations (62) and (63) respectively,

$$\ln K_{HL} = (\bar{F}^o_H + \bar{F}^o_L - \bar{F}^o_{HL})/RT \quad \ldots.(62)$$

$$\ln K'_{HL} = (\bar{F}^o_H + \bar{F}^o_L - \bar{F}^o_{HL}) + n_X(a_H + a_L - a_{HL})/RT \quad ..(63)$$

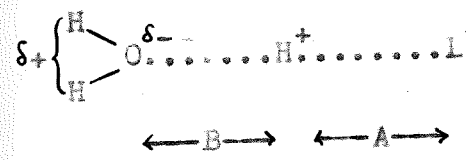
where the symbols are defined on page 56. Then from these equations,

$$pK'_{HL} = pK_{HL} + n_X(a_H + a_L - a_{HL})/2.303RT \quad \ldots.(64)$$

and a plot of pK' against n_X will be a straight line of slope $(a_H + a_L - a_{HL})/2.303RT$, and of intercept pK. Linear plots of pK_{OH} against molar fraction of dioxan have been reported for acetic and propionic acids [46], for β-diketones [47] and for 8-hydroxycinnoline [107]. Similar results have been obtained in this work for oxine-5-sulphonic acid in a series of water-dioxan mixtures. Values of $^c pK_{OH}$ are given in Table 16 (page 85) and are plotted in Graph 42. Similar plots for benzoic acid, and for o- and m-chlorobenzoic acids [91, 108, 109] are shown in Graph 42, and it is seen that for all these systems pK' is a linear function of the molar fraction of dioxan if $n_X < 0.2$ (i.e. if the % weight dioxan is less than 55). It is found in all the cases investigated that the term $(a_H + a_L - a_{HL})$ is positive, i.e. that pK_{OH} increases with increasing organic content of the solvent [110-113]. Similar observations have been made for the derivatives of oxine studied in this work (see Table 11).

Now the values of a_H, a_L and a_{HL} depend on the interaction of the species H^+, L^- and HL with each other, and with molecules of the solvent (or with other solute species). Izmaĭlov [114] has emphasised the importance of solvation of the neutral species HL by molecules of the organic component of the solvent. As the fraction of the organic solvent increases, the decrease in

in the hydration of H^+ and L^-, caused by the decreased activity of the water, will be offset by the increase in the electrostatic forces between the solute ions and the water dipoles. It is also possible that L^- may be solvated by the organic component of the solvent, L^- is itself organic. Perhaps the most important factor in determining a_H and a_L is the increased interaction between H^+ and L^-. As the organic content of the solvent is increased, the dielectric constant is decreased, and this results in increased electrostatic interaction between charged bodies.



The ionic forces both between H^+ and L^-, and between H^+ and water, will therefore be increased, but the ion-ion interaction (A) will be strengthed to a greater extent than the ion-dipole interaction(B) between H^+ and water. This may account for the positive sign of the term $(a_H+a_L-a_{HL})$, indicating that an overall increase in stability of an O—H bond accompanies an increase in the organic content of the solvent mixture.

TABLE 16. Some Dissociation Constants in Mixed Solvents.

Dioxan/Water.		Oxine-5-sulphonic Acid.		Pyridine.
%v.X	n_X	$^cpK_{OH}$	$^cpK_{NH}$	$^cpK_{NH}$
0	0.00	8.50	3.90	5.25
25	0.06	8.83	3.63	4.83
50	0.175	9.25	3.45	4.40
62.5	0.26	9.86	3.31	4.23

Constants valid in 0.3M sodium perchlorate at 20.0 ±0.2°C.

Values of n_X as a function of 1/D for water-dioxan mixtures are plotted in Graph 49, and it is seen that, if $n_x \lesssim 0.125$

(i.e. in solutions containing 40% w/w dioxan), the following relationship exists

$$n_X = 12.5/D - 0.15 \qquad .....(65)$$

Then from equations (64) and (65),

$$pK' = pK + (a_H+a_L-a_{HL})(12.5/D - 0.15) / 2.303RT \quad ..(66)$$

Thus, for water-dioxan mixtures with low values of 1/D, a plot of pK' against 1/D should be a straight line of slope 5.44/RT x $(a_H+a_L-a_{HL})$ and of intercept $pK - (a_H+a_L-a_{HL})/15.3RT$. Relationships similar to equation (65) may also exist for other solvent mixtures.

Elliot and Kilpatrick [91] have reported that linear relationships exist between pK' and 1/D for many substituted benzoic acids in water-dioxan mixtures, if the dioxan content of the solvent is not too high. Similar results were obtained for 8-hydroxycinnoline, and , in this work, for oxine-5-sulphonic acid.

(ii) The Variation of pK_{NH} with Solvent.

Values of pK_{NH} refer to dissociation of the type

$$HL^+ \rightarrow H^+ + L,$$

which has received much less attention than dissociation of the ion-pair type,

$$HL \rightarrow H^+ + L^-.$$

If the partial molar free energies of the species in a series of mixed solvents were linear functions of the molar fraction of the organic component of the solvent, the variation of pK'_{NH} with solvent would be described by equation (64), page 84, and a plot of pK'_{NH} against n_X would be a straight line of slope $(a_H+a_L-a_{HL})/2.303RT$, and of intercept pK_{NH}. Values of pK'_{NH} obtained in this work for oxine-5-sulphonic acid and pyridine are given in Table 16, and are plotted against the molar fraction

of dioxan in Graph 42. Plots of pK'_{NH} against n_X for aniline in aqueous dioxan [116] and for piperidine in aquoues methanol [115] are also shown, and it is seen that approximately linear plots are obtained at low values of n_X, and that the term $(a_H+a_L-a_{HL})$ is negative, i.e. pK'_{NH} decreases with increased organic content of the solvent. This decrease has also been observed for all the oxine derivatives studied in this work, and for a large number of amines of different types [110-111]. A report [117] that the value of pK_{NH} of some primary and secondary amines is increased by the addition of alcohol to the solvent has not been confirmed.

The sign of the term $(a_H+a_L-a_{HL})$ is probably primarily determined by the interaction between H^+ and L (see page 85). As the organic content of the solvent is increased, its dielectric constant is decreased, and the electrostatic forces between H^+ and L, and between H^+ and water, are strengthened. Both these forces are of the ion-dipole type, but as oxygen is more electronegative than nitrogen, the fractional charge on the water molecule may be greater than that on L, and the H^+—water bond will be strengthened to a greater extent than the H^+—L bond. The term $(a_H+a_L-a_{HL})$ will then be negative.

(iii) The Variation of Stability Constants with Solvent.

It has been seen that O—H are strengthened, and N—H bonds weakened, by an increase in the organic content of a mixed solvent. Analogous behaviour might be expected for O-metal and N-metal bonds, but no quantitative treatment has been proposed. Now if the partial molar free energies of the species in solution are linear functions of the molar fraction of the organic component of the solvent (see page 56), then

$$\ln K'_{ML} = \ln K_{ML} + n_X(a_M+a_L-a_{ML})/RT \quad \ldots.(67)$$

and $\log K'_{ML}$ will be a linear function of the molar fraction of the organic component of the solvent mixture. If, for a series of similar metals with a given ligand, the term $(a_M - a_{ML})$ is either constant, or negligible compared with the other terms, then a plot of $\log K'_{ML}$ against $\log K_{ML}$ for this series should be a straight line of unit slope. The intercepts of plots for different solvent mixtures should be proportional to n_X. Furthermore, from equations (55) and (56),

$$\ln K'_{ML} = \ln K'_{HL} + \ln \frac{K_{ML}}{K_{HL}} + n_X(a_M - a_{ML} + a_{HL} - a_H)/RT \qquad \ldots.(68)$$

and if $(a_M + a_{HL}) \backsim (a_H + a_{ML})$, the last term in the equation becomes negligible. A plot of $\log K'_{ML}$ against $\log K'_{HL}$ for values obtained in a series of solvent mixtures should then be a straight line of unit slope and of intercept $\log(K_{ML}/K_{HL})$; similarily, a plot of $\log K'_{ML}$ against $\log K_{ML}$ would be a straight line of unit slope and of intercept $\log(K'_{HL}/K_{HL})$.

Unfortunately, there are few suitable data on which to test these relationships, but some systems which have been studied will be discussed below.

(a). Chelate Complexes containing O-Metal Bonds.

James [87] has found that the overall dissociation constant (= $1/\beta_2$, see page 4) of zinc malonate was decreased by increasing the organic content of several mixed solvents. In aqueous dioxan, $\log 1/\beta_2$, is a linear function of 1/D in the range where $1/D < 0.0168$. As a linear relationship exists between n_X and 1/D in this region (see page 86), $\log 1/\beta_2$, and hence $\log \beta_2$, is a linear function of n_X. The dissociation constants of malonic acid were not determined in these solvent mixtures.

The stability constants of complexes of nickel with acetylacetone, and of magnesium with salicylaldehyde were determined in three water-dioxan mixtures by Maley and Mellor [19]. It is seen in Graph 44 that values of $\log K'_{ML}$ and of $\log K'_{HL}$ for both

systems, but while the value of $(a_H+a_L-a_{HL})$ is similar for the two reagents, the value of $(a_M+a_L-a_{ML})$ for nickel and acetylacetone is much larger than that for magnesium and salicylaldehyde. Values of $\log K'_{ML}$ against those of $\log K'_{HL}$ are plotted in Graph 44b, and it is seen that a straight line of unit slope is obtained for nickel acetylacetonate, indicating that $(a_M+a_{HL}) \sim (a_H+a_{ML})$. This is not the case for the magnesium-salicylaldehyde system, for which a straight line of slope 0.45 is obtained.

The stabilities of complexes of a series of metal ions with acetylacetone have been studied by Van Uitert and Fernelius [118], who have shown that $\log K'_{ML}$ increases linearily with the molar fraction of dioxan in the solvent. Straight lines were not obtained of $\log K'_{ML}$ were plotted against $\log K'_{HL}$ (equation (68)), doubtless because these authors found no exactly linear relationship $\log K'_{HL}$ and the molar fraction of dioxan in the solvent [47]. In Graph 45, $\log K'_{ML}$ is now plotted against $\log K_{ML}$ for a series of metal complexes of acetylacetone in both 50% and 75% v/v aqueous dioxan. The points for the complexes of Mg^{++}, Mn^{++}, Zn^{++}, Co^{++}, Fe^{++}, and Ni^{++} lie on straight lines of unit slope, showing that the term (a_M-a_{ML}) is either constant for these systems, or is negligible compared with the other terms in equation (68). The intercepts of the lines are approximately proportional to the corresponding values of n_X. The increase in the stability of the copper complex is greater than predicted. In all three solvent mixtures, the observed stability order is $Mg^{++} < Mn^{++} < Zn^{++} < Co^{++} < Fe^{++} < Ni^{++} < Cu^{++}$. Although the relative positions of Fe^{++} and Co^{++} are not those predicted by Irving and Williams [75], (see page 63), the stability order $Fe^{++} > Co^{++}$ has also been reported for complexes of riboflavin and of some purines [119] and may be due to 3d orbital staoilisation in the ferrous complexes [75].

(b) Complexes containing N-Metal Bonds.

It appears that the stabilities of O—H and O—metal bonds are increased by an increase in the organic content of the solvent and that, in may case, values of $\log K'_{ML}$ and of $\log K'_{ML}$ are linear functions of the molar fraction, n_x, of the organic component of the solvent. It is also seen that, for N—H bonds, $\log K'_{HL}$ decreases linearily as n_x increases; but no analogous relationship would seem to exist between $\log K'_{ML}$ and n_x for complexes containing N—metal bonds.

In 1934, Larrson [120] reported values of $\log \beta_2$ for the silver complexes of ammonia and of some aniline derivatives in 50% aqueous ethanol, and commented that the values differed by only ±0.6 log unit from those obtained in water [121,122]. Recently, Van Uitert and Fernelius [123] have found that the stability constants of the copper and nickel complexes of ammonia and of ethylenediamine in 75% aqueous dioxan were only slightly higher than the corresponding values obtained in water [12, 124-126].

As no one author appears to have studied the stability of a metal ammine in a series of mixed solvents, the formation curves for the copper and nickel complexes of pyridine were determined in water, and in 25% and 50% aqueous dioxan. The experimental pH titration curves are plotted in Graphs 47-49, together with the formation curves. As it was not possible to obtain complete formation curves by this method, accurate values of the stability constants could not be calculated, but the affect of the solvent on the stability may be assessed by comparing the values of pL at various values of $\bar{n}$. These are given in Table 17. It is seen that the stability of the nickel complexes is somewhat increased dioxan content of the solvent; the copper complexes appear to be almost equally stable in water and in 25% dioxan, but the stability is slightly greater in 50% dioxan. The results are compatible with thsoe for the complexes of ammonia and of ethylenediamine.

TABLE 17. Pyridine Complexes of Copper and Nickel.

		Nickel Complex.				Copper Complex.				
%v Dioxan.	$\bar{n}$	0.5	1.0	1.5	2.0	0.5	1.0	1.5	2.0	2.5
0	pL	1.87	1.41	1.07	0.80	2.64	2.19	1.80	1.52	1.27
25	pL	2.05	1.58	1.23	0.94	2.51	2.14	1.81	1.51	1.23
50	pL	2.29	1.82	1.44	1.13	2.80	2.34	2.00	1.68	1.41

This unexpected type of variation of the stability of metal ammines with change of solvent emphasises the inadequacy of any purely electrostatic treatment of dissociation, and may indicate that covalent forces are more important in $N \rightarrow M^{++}$ than in $N \rightarrow H^{+}$ bonding. The small observed changes in stability may also be related to the variation of entropy of complex formation with change of solvent.

(c) Chelate Complexes containing both O-Metal and N-Metal Bonds.

It is seen that the stabilities of some metal chelates containing O-metal bonds increase linearily with the molar fraction of the organic component of the solvent, and that the stabilities of some metal ammines are almost independent of the nature of the solvent. No one author seems to have investigated the effect of solvent composition on the stabilities of complexes which contain both O-metal and N-metal bonds, although stability constants of metal oxinates have been obtained in different solvents by various authors. Values of $\log K'_{ML}$ in some water-dioxan mixtures [19, 70, 78, 123, and this work] are plotted in Graph 55 against values of $\log K_{ML}$ determined in water by Näsänen et al. [14, 127-129]. It is seen that, (apart from the approximate values obtain-in water by Albert [78]), the experimental points lie very approx-

imately on a straight line of unit slope and of intercept pK'-pK (see page 88). This would imply that $(a_M - a_{HL}) \backsim (a_H - a_{ML})$ and that the stability of the metal oxinates is determined predominantly by the stability of the O-metal bond; thus the variation of $\log K'_{ML}$ with solvent merely reflects the variation of $\log K'_{HL}$.

In this work, the stabilities of some metal complexes of oxine-5-sulphonic acid have been determined in water, and in 25% and 50% aqueous dioxan. The titration and formation curves are plotted in Graphs 50-52, and the stoichiometric stability constants are given in Table 18.

TABLE 18. Stabilities of Complexes of Oxine-5-sulphonic acid.

%v. Dioxan.	Mg^{++}		Zn^{++}		Ni^{++}	
	$\log {}^cK_1$	$\log {}^cK_2$	$\log {}^cK_1$	$\log {}^cK_2$	$\log {}^cK_1$	$\log {}^cK_2$
0	4.03	3.46	7.96	6.95	9.26	8.34
25	4.44	3.58	8.17	7.16	9.26	8.35
50	4.82	4.23	8.08	7.66	9.50	8.34

	UO_2^{++}		
	$\log {}^cK_1$	$\log {}^cK_2$	
0	8.09	7.37	The stability constant of the copper complex could not be accurately determined.
25	9.26	8.00	
50	9.90	8.39	

Although the values obtained in water show only fair agreement with thermodynamic constants obtained spectrophotometrically by Näsänen and Uusitalo [130], they are reproduceable by the technique used in this work.

Now $${}^TK_n = {}^cK_n \left(f_{ML_n} / f_{ML_{n-1}} . f_L\right)$$

and activity coeffients of metal complexes of ligands such as oxine-5-sulphonic acid are not available in aqueous dioxan solutions. As the magnitude of the activity correction may be very sensitive to change of solvent, it is not strictly permissible

to substitute values of $^{c}K_1$ for those of $^{T}K_1$ in equations (67) and (68); but as the values of the correction in a given solvent might be expected to be almost constant for a series of complexes of divalent metal ions, some qualitative comparison of the behaviour of different metals is possible.

It is seen that, while the stabilities of the magnesium and uranyl complexes are appreciably increased by increased dioxan content of the solvent, the stabilities of the zinc and nickel complexes are only slightly increased. Thus, the complex of nickel is more stable than that of uranyl in water, but the reverse is true in 50% aqueous dioxan. The stability of the copper complex also appears to be only slightly increased. This behaviour seems to indicate that O-metal bonds, which are stronger in more organic solvent mixtures, play a more important part in the complexes of magnesium and uranyl than in those of zinc, nickel and copper.

The tendency to form N-metal bonds may be discussed with reference to Graph 46, which shows curves for the pH titration of acidic solutions of these ions with pyridine. The order of displacement of thecurves, relative to that for acid alone, is $Cu^{++} > UO_2^{++} > Ni^{++} > Zn^{++} > Mg.^{++}$ The colour changes, and values of pH of incipient displacement and precipitation, for the uranyl solution are identical to those obtained when titrating with alkali, and may be attributed to hydrolysis. No such behaviour was observed for the other cations, for which the magnitude of the displacement of the titration curves may be taken as a qualitative measure of the stability of the corresponding pyridine complex. The fact that the uranyl ion is appreciably hydrolysed in the presence of pyridine indicated that it forms O-metal bonds preferentially to N-metal bonds. The reverse is true for nickel and copper which form strong bonds with ligands containing polarisable nitrogen atoms (c.f[75]) ; these bonds would be little affected by the nature of the solvent.

The difference in the response of the complexes of oxine and those of oxine-5-sulphonic acid to change of solvent is unexpected. Indeed, the complexes of oxine-5-sulphonic acid are also anomalous in that their stabilities are similar to those of the corresponding oxinates, although the values of pK_{OH} and pK_{NH} for oxine-5-sulphonic acid are much lower than for oxine. Plots of $\log K_{ML(\text{oxine-5-sulphonic acid})}$ against $\log K_{ML(\text{oxine})}$ both in water [127-129], and in 50% aqueous dioxan are shown in Graph 53, and it is seen that in neither case do the points lie on the expected straight line of unit slope and of intercept ΔpK. It is not clear how the substitution of a charged $-SO_3^-$ group into the 5-position of oxine could give rise to amomalous behaviour of this type.

SECTION 4.

EXPERIMENTAL DETAILS.

4(e). MATERIALS.

As this work was concerned with organic compounds expected or known to be capable of forming complexes with metal ions, great care was taken to exclude traces of metallic impurities. Solutions were kept in stoppered Pyrex flasks, and the stoppers covered with small beakers to prevent dust from collecting round the rim of the flask. Pipettes were labelled, and used for solutions of one metal only.

(i) Organic Reagents.

'AnalaR' grade oxine was available, and pure specimens of methyl substituted oxines and of 1:2:3:4-tetrahydro-10-hydroxyacridine had previously been prepared in this laboratory [10]. Oxine-5-sulphonic acid was prepared by the method of Matsumara [131] and recrystallised three times from 5% hydrochloric acid, m.p.320°C (yield 80% theorectical).5-Fluror-oxine was a gift from Mr. R. Hollingshead of British Drug Houses, Ltd. The cinnoline and quinazoline derivatives were gifts from Dr.K.Schofield, of the University College of the South West of England, and the derivatives of quinoxaline and the naphthyridines were gifts from Professor A.Albert and Dr. A.Hampton, of the Australian National University.

The above reagents were used without further purification.

'AnalaR' pyridine was freed from carbon dioxide by redistillation over solid potassium hydroxide.

(ii) Solvents.

'AnalaR' dioxan was available and was used without further treatment. Water, and all other solvents, were redistilled before use from an all-Pyrex apparatus.

(iii) Other Materials.

Pure anhydrous sodium perchlorate was prepared from the hydrated commercial salt by repeated recrystallisation from water

at 90°C, tested for the absence of chloride and chlorate ions, and dried to constant weight at 120°c.[32].

Carbonate-free sodium hydroxide solution was prepared from the 'AnalaR' solid by the method described by Vogel [132], and was standardised against 'AnalaR' potassium hydrogen phthalate, dried to constant weight at 115°C.

All other chemicals were of 'AnalaR' grade, unless otherwise stated. The nickel sulphate solutions were analysed gravimetrically, using dimethylglyoxime.

4(b). SPECTROPHOTOMETRIC MEASUREMENTS.

Absorption spectra were measured with a Beckman DU spectrophotometer, with matched 1.00 cm. silica cells. Minimum slit widths were used, and the effective wave-band never exceeded 2 mμ.

(i) Absorption Spectra of Reagents.

The absorption spectra of oxine, and of some aza-derivatives of it were measured in acidic, neutral, and alkaline solution, and are shown in Graphs 11 to 15, in which $\log_{10}\varepsilon$ is plotted against the wavelength. From equation (6), page 6,

$\log\varepsilon$ = log (absorbancy / molar concentration)

in cells of length 1 cm.

Spectra of the cationic species were obtained in solutions where pH $<(pK_{NH} - 2)$; 5N hydrochloric acid was used for 5-hydroxyquinoxaline, 0.2N hydrochloric acid for 8-hydroxy-4-methyl-2-phenylquinazoline, 4-hydroxy-1:5-naphthyridine and 8-hydroxy-1:7-naphthyridine, and 0.01N hydrochloric acid for other reagents. Spectra of the neutral molecules were measured in '95%' methanol, prepared by adding 5 ml. water to 95 ml. methanol, previously tested for transparency in the region 230-250 mu. The spectra of the anions were obtained in solutions where pH $>(pK_{OH} + 2)$; 0.2N Sodium hydroxide was used for 4-hydroxy-1:5-naphthyridine and 8-hydroxy-1:7-naphthyridine, and 0.01N sodium hydroxide for other reagents.. Concentrations of the reagents were varied from 10^{-5}M to 10^{-3}M, depending on the part of the spectrum under investigation. All the reagents were shown to obey Beer's Law in this concentration range in the three solvents. Some typical Beer's Law plots are shown in Graph 10.

(ii). Spectrophotometric Determination of Dissociation Constants.

The change of absorbancy with pH for 8-hydroxycinnoline (and its 4-methyl derivative), 8-hydroxyquinazoline (and its

2:4-dimethyl derivative), and 5-hydroxyquinoxaline, are shown in Graph 5 to9. A solution of each reagent in 0.01N sodium hydroxide was diluted 50-fold with a series of buffer solutions, to which sufficient sodium chloride had been added to give a final ionic strength of 0.3M. The following buffer solutions were prepared as described by Britton [133] :—

pH Range	Author	Components.
2.0 - 5.2	Walpole.	Acetic acid, sodium acetate.
6.0 - 7.3	Sørensen.	Potssium hydrogen phosphate, potassium dihydrogen phosphate.
7.3 - 9.2	Sørensen.	Borax, hydrochloric acid.
9.6 -11.3	Kolthoff.	Sodium carbonate, hydrochloric acid.

The final concentrations of the reagents, and the wavelengths at which measurements were taken, are shown on the relevant graphs. Measurements of pH were made using a Morton glass electrode and calomel electrode system, with a Cambridge pH meter, standardised as described in Section 4(c). Brønsted dissociation constants were obtained from the graphs, using equations (8b),(8c),(13a) and (13b) (see page 10), and were converted to thermodynamic constants as described on page 13. These constants, which are tabulated on page 44, were obtained at room temperature, 14 $\pm 3^{\circ}$C.

(iii) Absorbancy Measurements in Water and in Amyl Alcohol.

Absorbabancy measurements for oxine and the aza-oxines in water and in amyl alcohol (each containing 2% v/v methanol) are shown in Graph 16. The concentration of the reagent was 1.66 x 10^{-4}M in each case. The condition that at least 99% of a reagent is in the form of its neutral molecule is given by $(pK_{NH}+2) < pH < (pK_{OH}-2)$. The pH of the aqueous solution was therefore measured and the condition was found to hold for all the reagents except 8-Hydroxy-1:-6naphthyridine. In this case the pH was adjusted to a suitable value (6.10) by the addition of a phosphate buffer,

which was also added to the appropriate 'blank' solution.

Measurements could not be made at wavelengths lower than 290 mμ, as amyl alcohol absorbs strongly in this region.

4(c). pH TITRATIONS.

(i) APPARATUS.

The titration apparatus was designed and built with a view to using only small volumes of solutions of the reagents, some of which were only available in small quantities ($\sim$ 0.2 gm.) Titrations were carried out at 20.0 ± 0.2°C in a double-walled Pyrex cell, A, (see Fig. 10) of total capacity 25 ml. Water from a thermostat circulated through the outer jacket. The contents of the cell were stirred by a stream of nitrogen, freed from carbon dioxide with soda lime, and presaturated with solvent. The pH was measured to 0.01 unit with a Cambridge bench type pH meter, standardised before, and checked after, each titration with buffer solutions of pH 4.01 and 9.20 at 20°C, prepared from 'Soloid' tablets.(Messrs. Boroughs Wellcome, Ltd.). A Doran 'Alkacid' sealed glass electrode, B, and a Pye dip-type microcalomel electrode, with fibre liquid junction, C, were used.

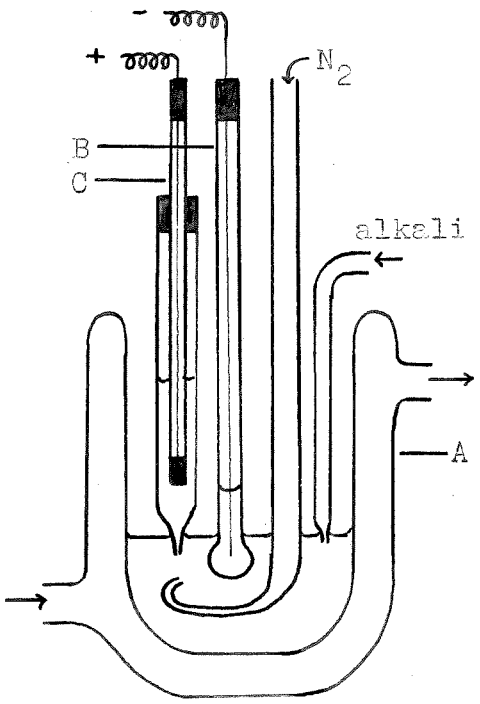


Fig. 10

The Microburette.

In order to titrate small quantities (6 x 10^{-5} gm.mol.) of reagents, a good microburette was required for the addition of small volumes of alkali. As no instrument reading to less than 0.02 ml. was initially available, several models were constructed

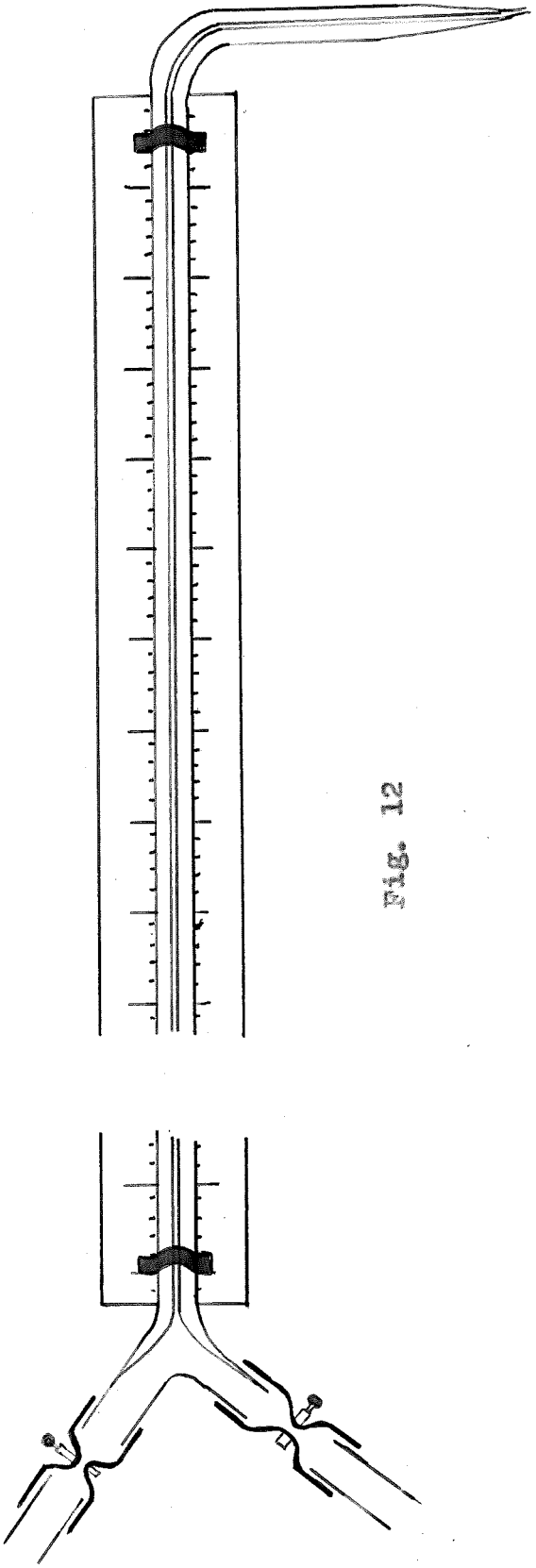


Fig. 12

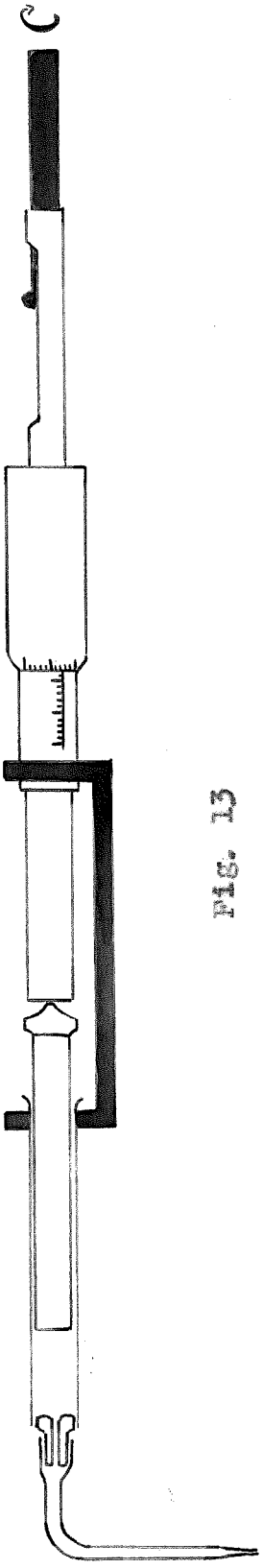


Fig. 13

and are descibed in outline below. All burettes were calibrated using mercury. The results quoted in this thesis were all obtained using Mark III, but Marks I and II were successfully used in preliminary work.

Mark I.(See Fig. 12). A tapless microburette was made out of a length of capillary tubing, bent at right angles to form a long arm, which was mounted on a meter rule, and a short arm, which was drawn out to a jet. The long arm was connected, through a T-pieee, both to a vacuum pump, and to the compressed air supply; by suitable adjustment of the pressure, liquid could be drawn up the tube, kept stationary, or discharged. The burette could be read to 0.004 ml., but was clumsy, and tiring to use for long periods.

Mark II.(See Fig.11). A commercial glass syringe was mounted horizontally, and fitted with a glass capillary nozzle, bent

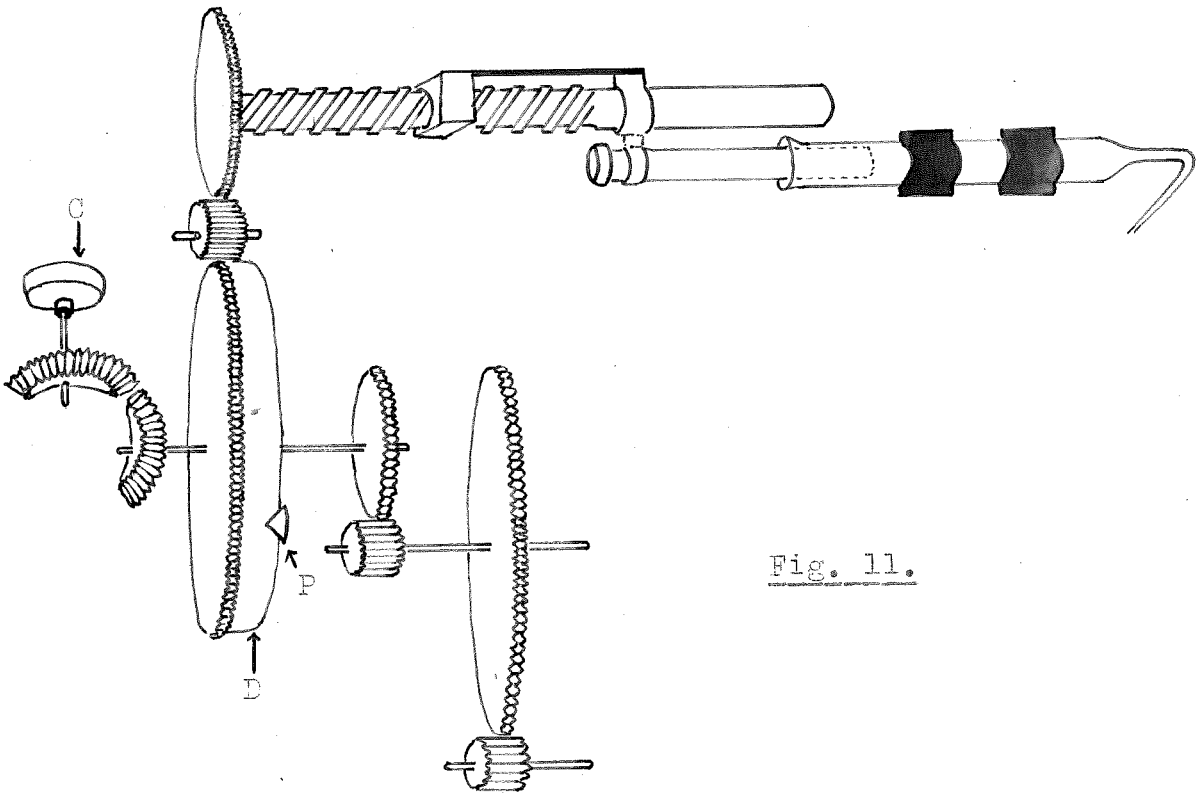


Fig. 11.

through 90° and drawn out to a jet. The plunger was mounted on a platform which was advanced by a screw thread connected, through a 'Meccano' gearing system, to an electric motor. The number of complete revolutions of the screw was indicated by a counter, C, incorporated in the gearing system, and the fractions of a revolution were shown by the position of a rotating drum, D, inder a stationary pointer, P. The main disadvantage of this type of instrument is that only a few of the syringes investigated were of uniform barrel cross-section.

Mark III.(see Fig. 13). The instrument finally used in this work was an 'Agla' micrometer syringe, of capacity 0.5 ml., fitted with a glass capillary nozzle bent at right angles to the barrel, which was mounted horizontally. The micrometer screw was connected to an electric motor through a 'Meccano' gearing system, and could be advanced to deliver 0.08ml./min., and reversed for refilling at ten times that speed. As the pH meter was sometimes sensitive to electric interference from the thermostat stirrer and water circulator, the syringe motor could be controlled by a master switch operating all nearby A.C. equiptment (except the lamps illuminating the scales of the Ph meter and the micrometer) as well as by an individual switch. One large scale division, which was subdivided one hundred-fold, was found to represent 0.01992 ± 0.00014 ml.

(ii). THE DETERMINATION OF STABILITY CONSTANTS IN 50% V/V AQUEOUS DIOXAN.

Solutions for the titration of metal complexes were prepared by pipetting 5.00ml. of 0.0394N perchloric acid containing 0.6M sodium perchlorate and 0.006M metal sulphate (or uranyl nitrate) into the titration cell, and adding 5.00 ml. of dioxan containing 0.012M reagent. (As 4-hydroxy-1:5-naphthyridine and 8-hydroxy-1;7-naphthyridine are insoluble in pure dioxan, all solutions for the titration of these reagents were made up in 50% v/v aqueous

dioxan, to give the concentrations stated above). Titrations of the reagent alone were carried out using similar solutions, but omitting the metal salt, and of the acid alone by omitting both metal and reagent. Curves showing the hydrolysis of metal ions in this solvent were obtained by titration in the absence of reagent. The titrant was ~1.1N sodium hydroxide in each case. Duplicate titrations were carried out in cases where the reagent was in good supply, and in some systems, titrations were also carried out with 0.003M metal, but the stability constants so obtained did not differ by more than 0.02 unit from those obtained at higher metal concentration (except in the case of 8-hydroxy-1:6-naphthyridine, see page 78). The titration curves are shown in Graphs 17 to 31.

The 5:7-dichloro-, 5:7-dibromo-, 5;7-dibromo-2-methyl-, 5-nitroso-, and 5-nitroso-2-methyl- derivatives of oxine, which were prepared in this laboratory, all proved to be too insoluble to be titrated under these conditions.

The change in volume on mixing water and dioxan was determined by measuring the densities of the pure liquids, ρ_W and ρ_D, and of the mixture ρ_M. The volume of the liquid obtained from mixing volumes V_W and V_D of water and dioxan respectively, is given by

$$V_M = (V_W\rho_W + V_D\rho_D)/\rho_M$$

When $V_D = V_W = 5.00$ ml., V_M was found to be 9.85 ml. The concentrations of the reactants were calculated allowing for this contraction, and also for the volume changes due to the addition of alkali during titration (see Section 2(b)).

'Practical' stability constants of the ligand-proton complexes were calculated, and converted to stoichiometric constants, by the methods described in Sections 2(b) and 2(c). The stoichiometric constants are given in Table 12, page 46. The term

log fU_H^o was obtained as the intercept of the plot of the pH Meter reading, B, against the hydrogen ion concentration, [H], of standard solutions of hydrochloric acid in 50% v/v aqueous dioxan, to which sufficient sodium chloride had been added to give a final ionic strength of 0.3M (see Graph 54). Values of of logU_H^o were calculated using the relevant values of f obtained from the data of Harned and Owen [46]. Values of log U_H^o were also determined in other water-dioxan mixtures, and a plot of log U_H^o against the molar fraction of dioxan (Graph 54) seems to agree well with the small diagram in the literature [28].

Sets of corresponding values of $\bar{n}$ and pL for metal-ligand complexes were obtained using equations (23a), (28) and (32) (see Section 2(b)), and the resultant formation curves are plotted in Graphs 17 to 31. The stoichiometric stability constants, which are tabulated on page 68, were obtained from these curves by the 'correction term' method. (see page 31).

(iii) pH TITRATIONS IN SERIES OF SOLVENT MIXTURES.

Oxine-5-sulphonic Acid.

Solutions for the titration of metal complexes were prepared by mixing 5.00 ml. 0.2N aqueous sodium hydroxide containing 4.8×10^{-2}M reagent, 5.00 ml. 0.388N aqueous perchloric acid containing 2.4M sodium perchlorate and 2.4×10^{-2}M metal ion, and a total of 30.00ml. of water or dioxan to give solutions of 0, 25, 50, and in some cases, 62.5% v/v dioxan. 10.00 ml. of this solution were titrated with ~1.1N sodium hydroxide.

The methods for determining values of 'practical' and stoichiometric stability constants of the ligand-proton complexes and values of the stoichiometric constants for the metal-ligand complexes, are those described in the previous section. The

titration and formation curves are plotted in Graphs 50-53, and the constants are tabulated on pages 85 and 92. The values of pK_{OH} and pK_{NH} in water are in good agreement with those obtained by Näsänen at a similar ionic strength [130].

Pyridine.

The dissociation constant of pyridine was determined by titrating 10.00ml. of a solution containing 0.0197M pyridine, 0.320M sodium perchlorate and 0.030N perchloric acid in water, 25%, 50% and 62.5% v/v aqueous dioxan, with 1.15N sodium hydroxide. The acid alone was titrated using similar solutions with the pyridine omitted. The titration curves are plotted in Graph . Values of pK_{NH} were calculated as described above, and are given in Table 16. The value obtained in water is in good agreement with that previously reported [67].

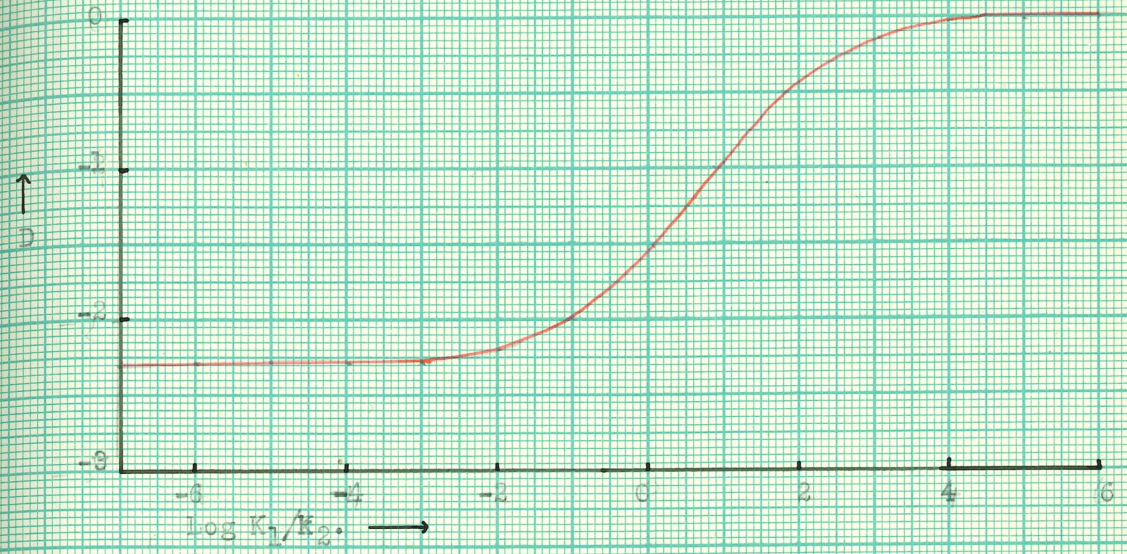
Formation curves for the copper and nickel complexes of pyridine were obtained by titrating solutions of 0.1M copper nitrate or nickel chloride and 0.05N nitric acid with 12.1N pyridine, standardised against hydrochoric acid. Titrations were carried out in water, and in 25% and 50% v/v aqueous dioxan, and similar titrations were carried out in the absence of copper and nickel, the ionic strength then being made up to 0.35M with potassium nitrate. Aqueous solutions of 0.1M magensium sulphate, 0.1M zinc sulphate, and 0.1M uranyl nitrate (not at uniform ionic strength) were also titrated with pyridine solution

The formation curves for the complexes of copper and nickel were calculated using equations (23a), (35) and (37) (see Section 2(b)), and are summarised in Table 17. The titration and formation curves are plotted in Graphs 46-49.

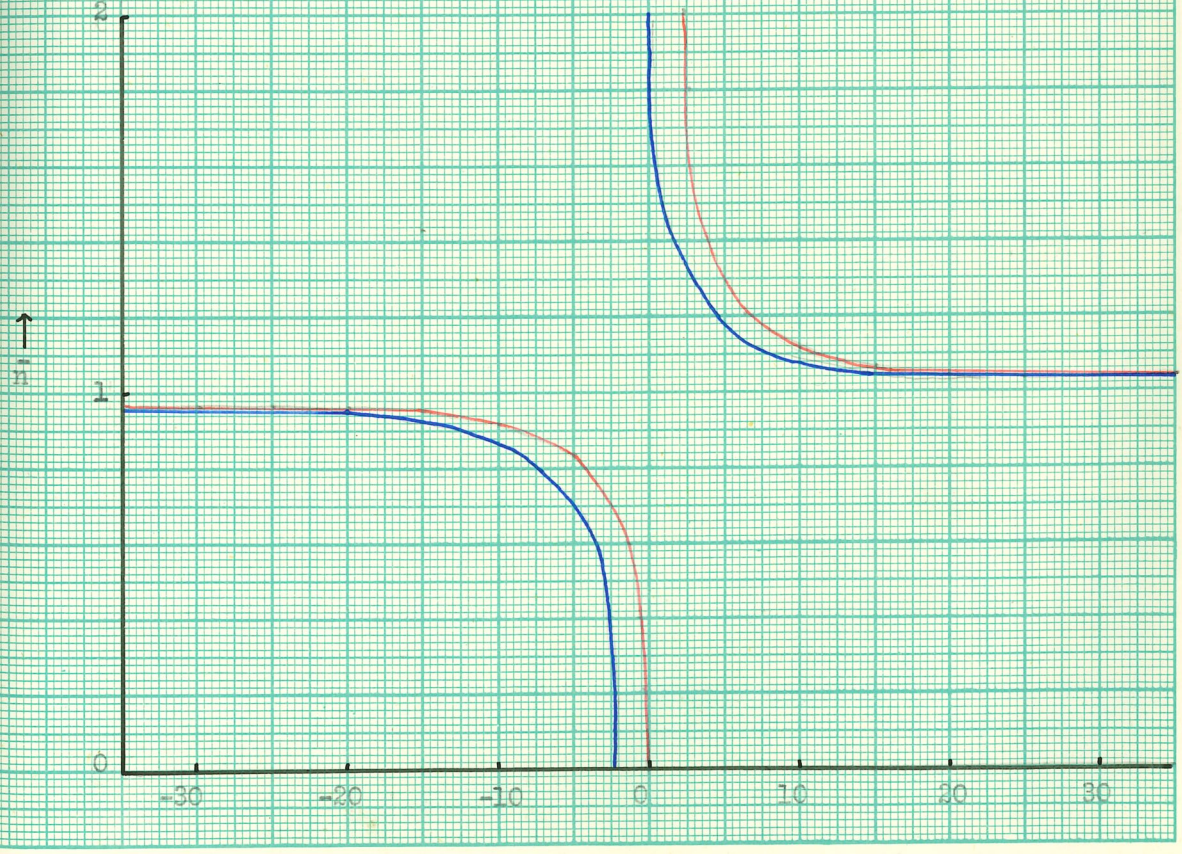
Values for the dielectric constant of various water-dioxan mixtures are taken from Critchfield, Gibson and Hall [134].

GRAPHS.

Graph 1a. The Midpoint Slope, D, for Systems in which N = 2.

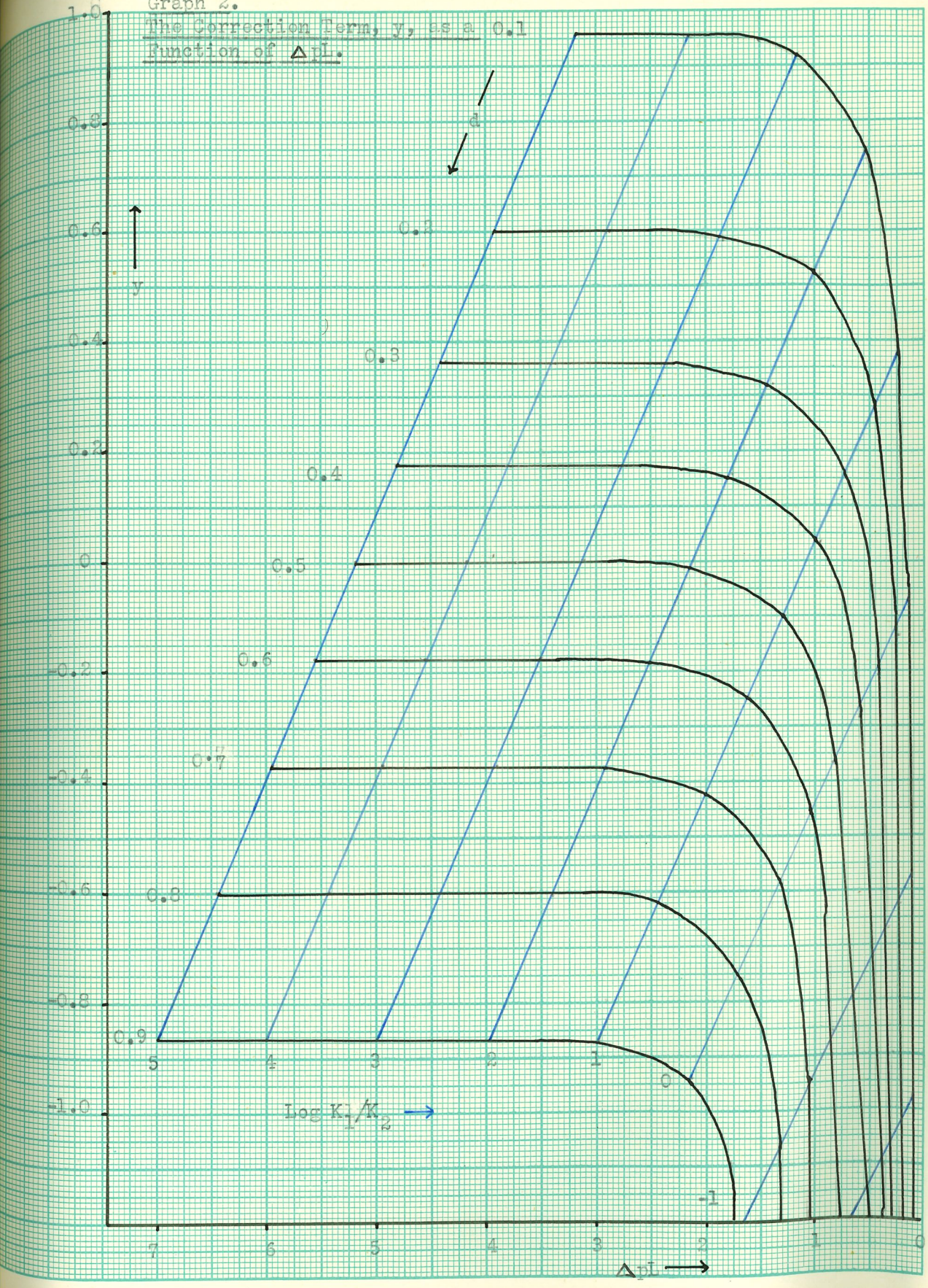


Graph 1b. The Functions $\bar{n}/(\bar{n}-1)$ —— , and $(2-\bar{n})/(\bar{n}-1)$ ——



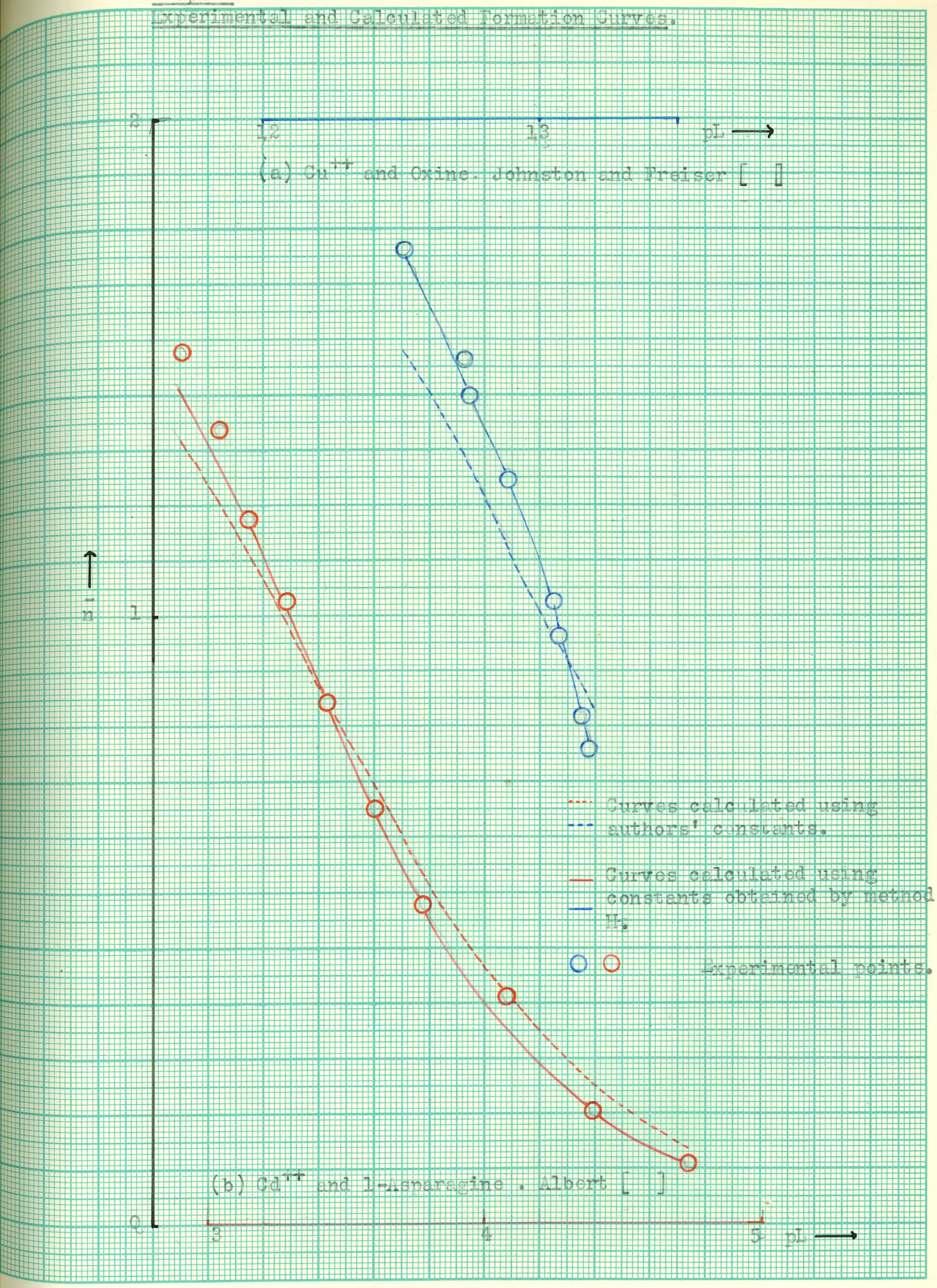
Graph 2.

The Correction Term, y, as a Function of ΔpL.



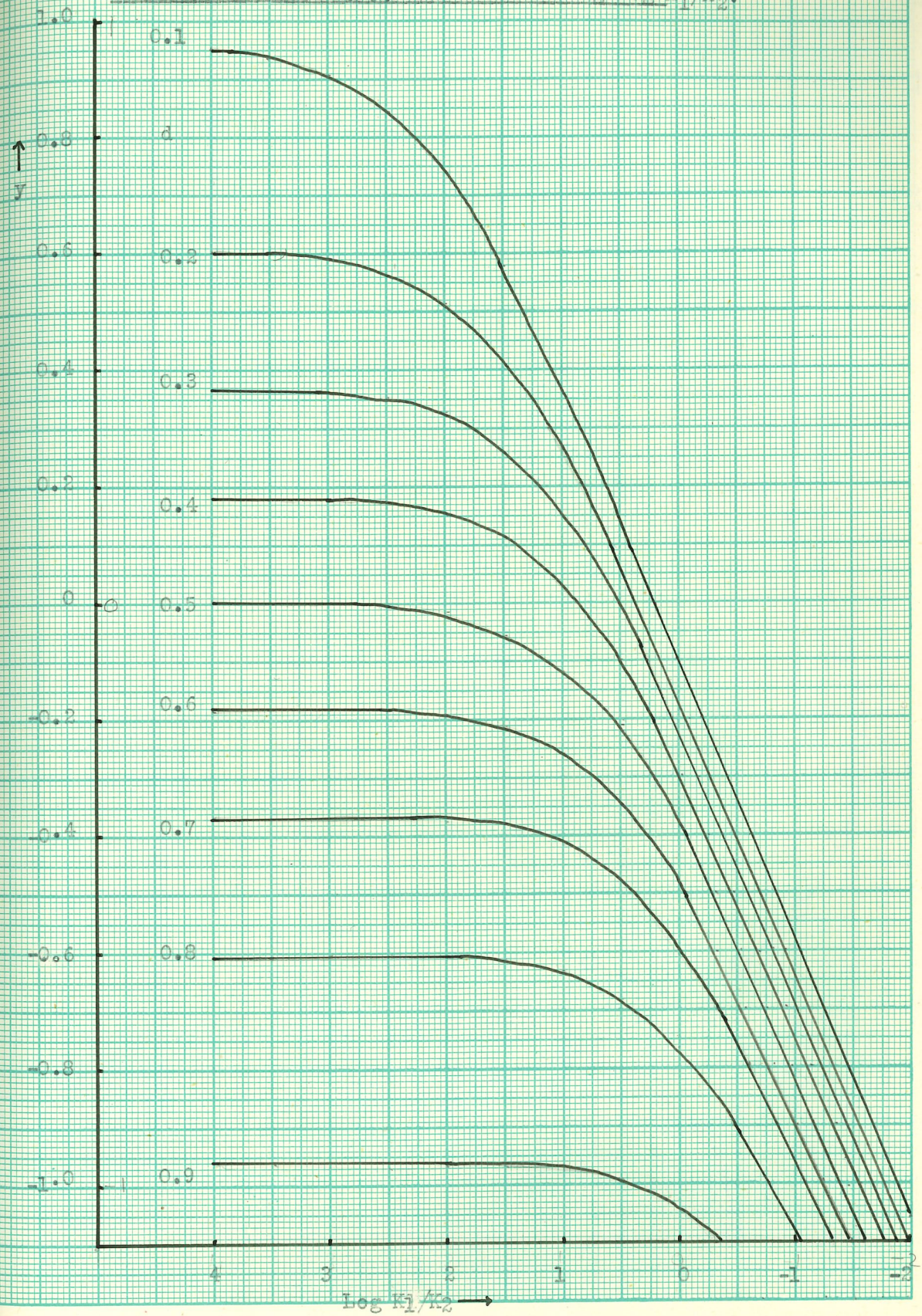
Graph 3.

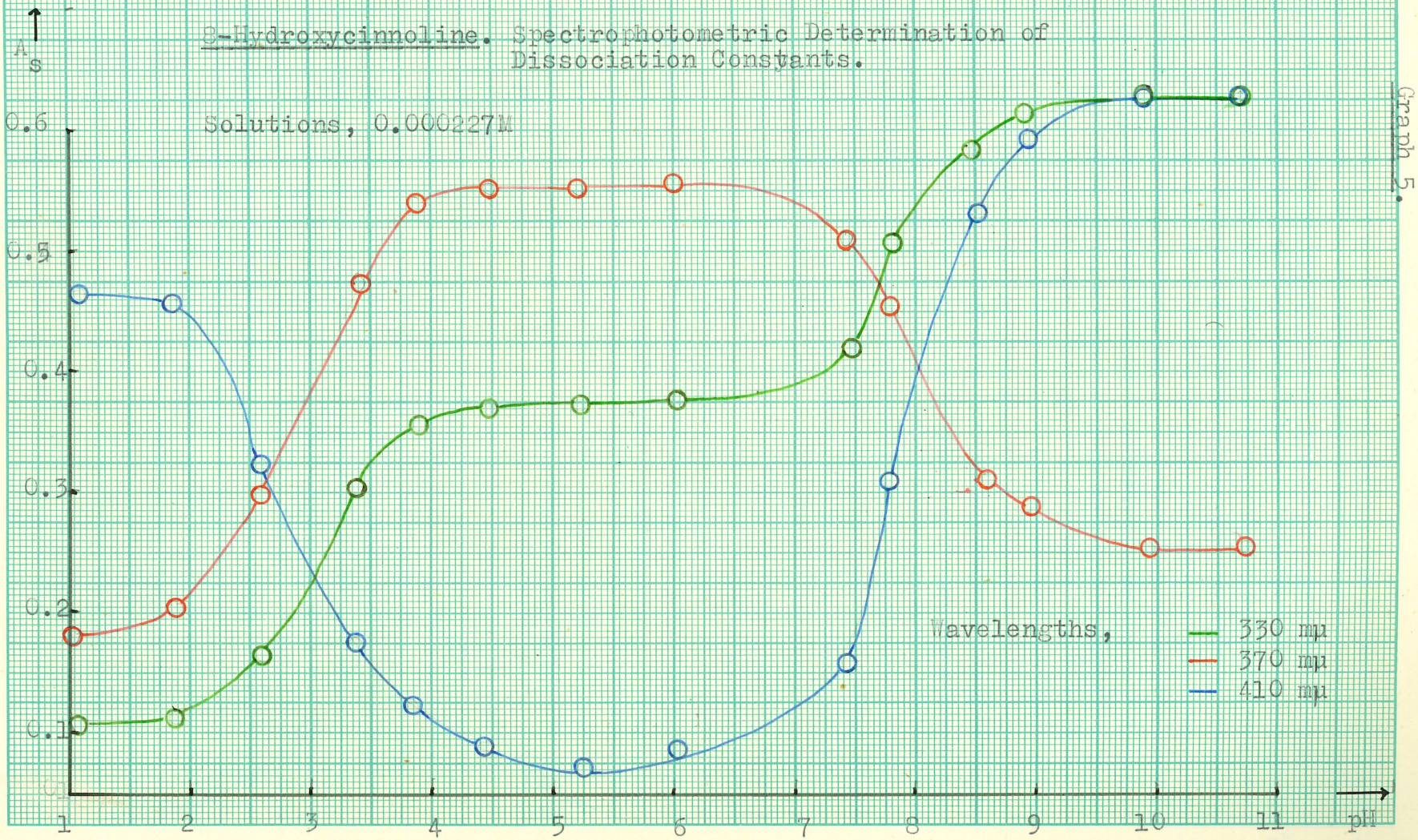
Experimental and Calculated Formation Curves.



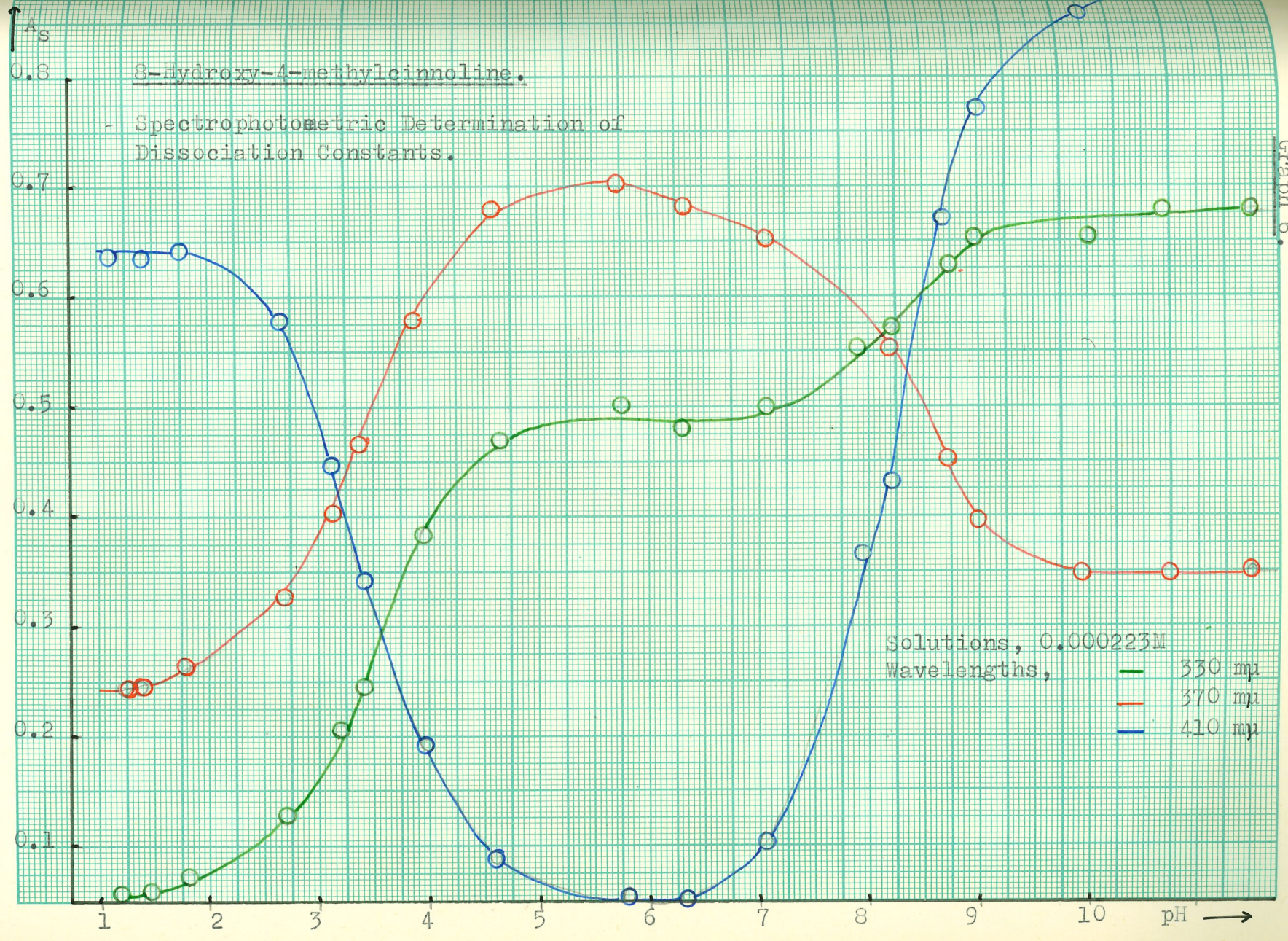
Graph 4.

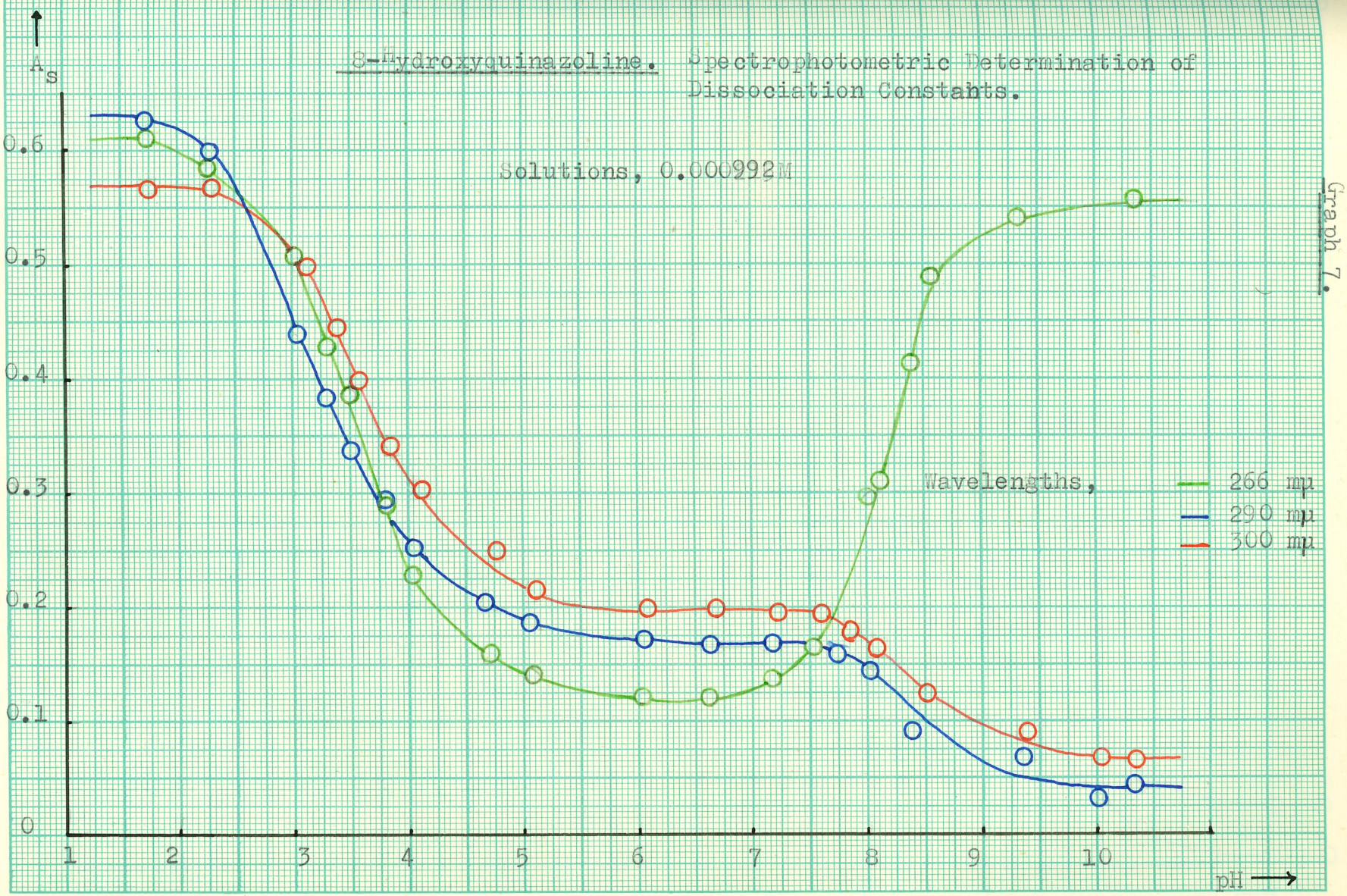
The Correction Term, y, as a Function of Log K_1/K_2.

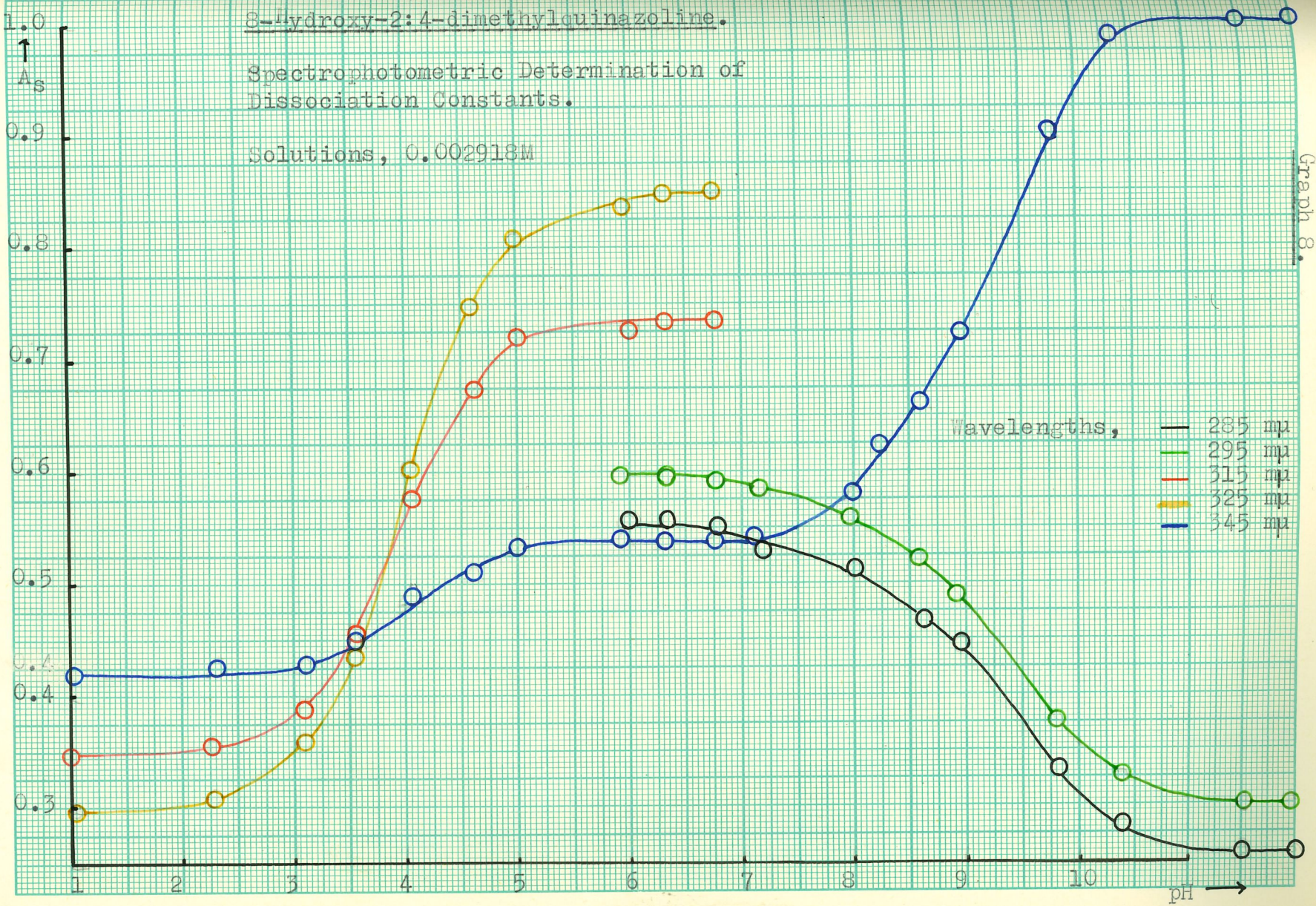



8-Hydroxycinnoline. Spectrophotometric Determination of Dissociation Constants.
Solutions, 0.000227M
As
0.6
0.5
0.4
0.3
0.2
0.1
1
2
3
4
5
6
7
8
9
10
11
pH
Wavelengths,
330 mμ
370 mμ
410 mμ

Graph 5.

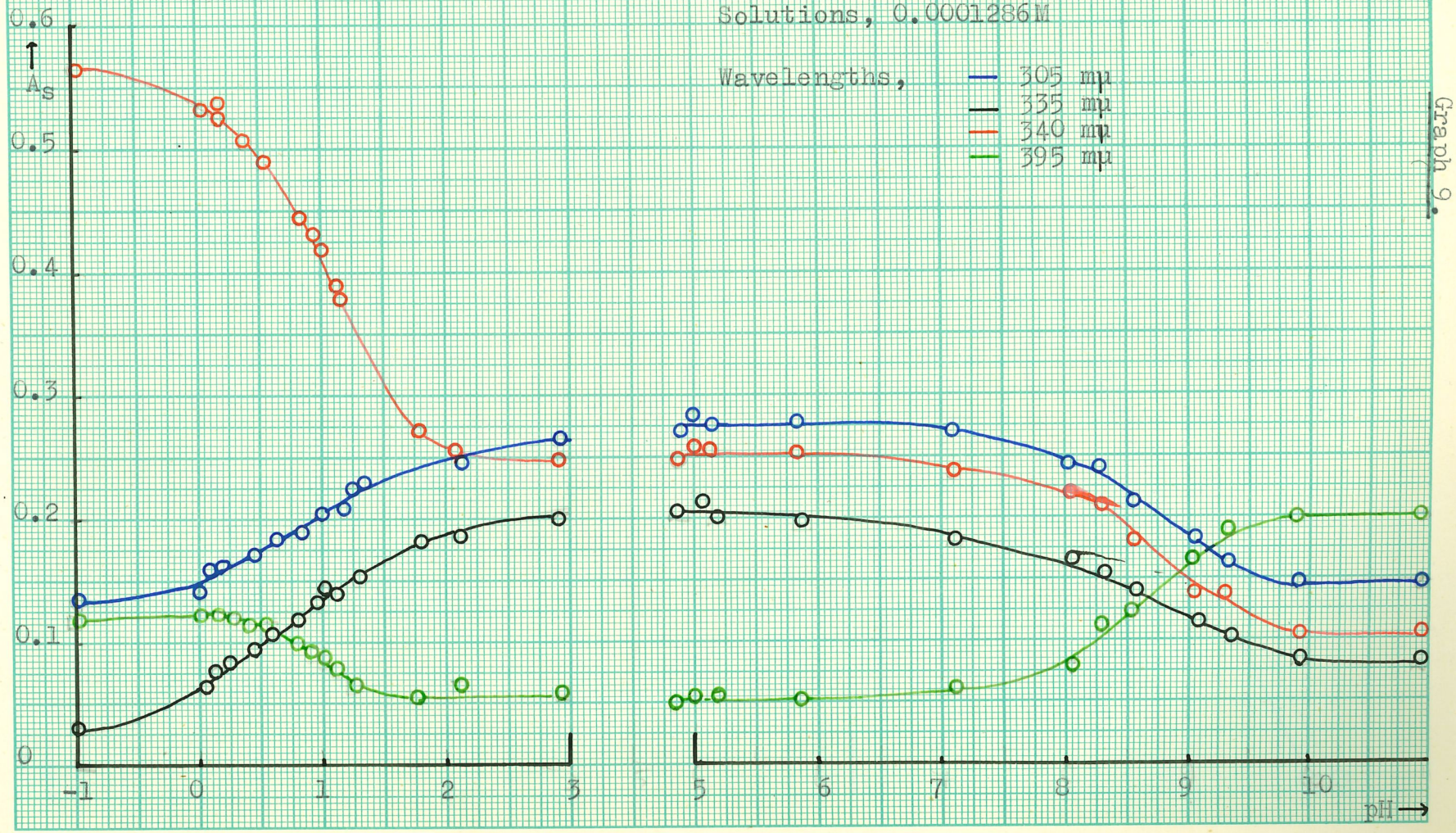

As
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
1
2
3
4
5
6
7
8
9
10
pH
8-Hydroxy-4-methylcinnoline.
Spectrophotometric Determination of Dissociation Constants.
Graph 6.
Solutions, 0.000223M
Wavelengths,
330 mμ
370 mμ
410 mμ


8-Hydroxyquinazoline. Spectrophotometric Determination of Dissociation Constants.
Solutions, 0.000992M
Graph 7.
A_s
0.6
0.5
0.4
0.3
0.2
0.1
0
1
2
3
4
5
6
7
8
9
10
pH
Wavelengths,
266 mμ
290 mμ
300 mμ


8-Hydroxy-2:4-dimethylquinazoline.
Spectrophotometric Determination of Dissociation Constants.
Solutions, 0.002918M
Graph 8.
A_s
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
1
2
3
4
5
6
7
8
9
10
pH
Wavelengths,
285 mμ
295 mμ
315 mμ
325 mμ
345 mμ

5-Hydroxyquinoxaline. Spectrophotometric Determination of Dissociation Constants.

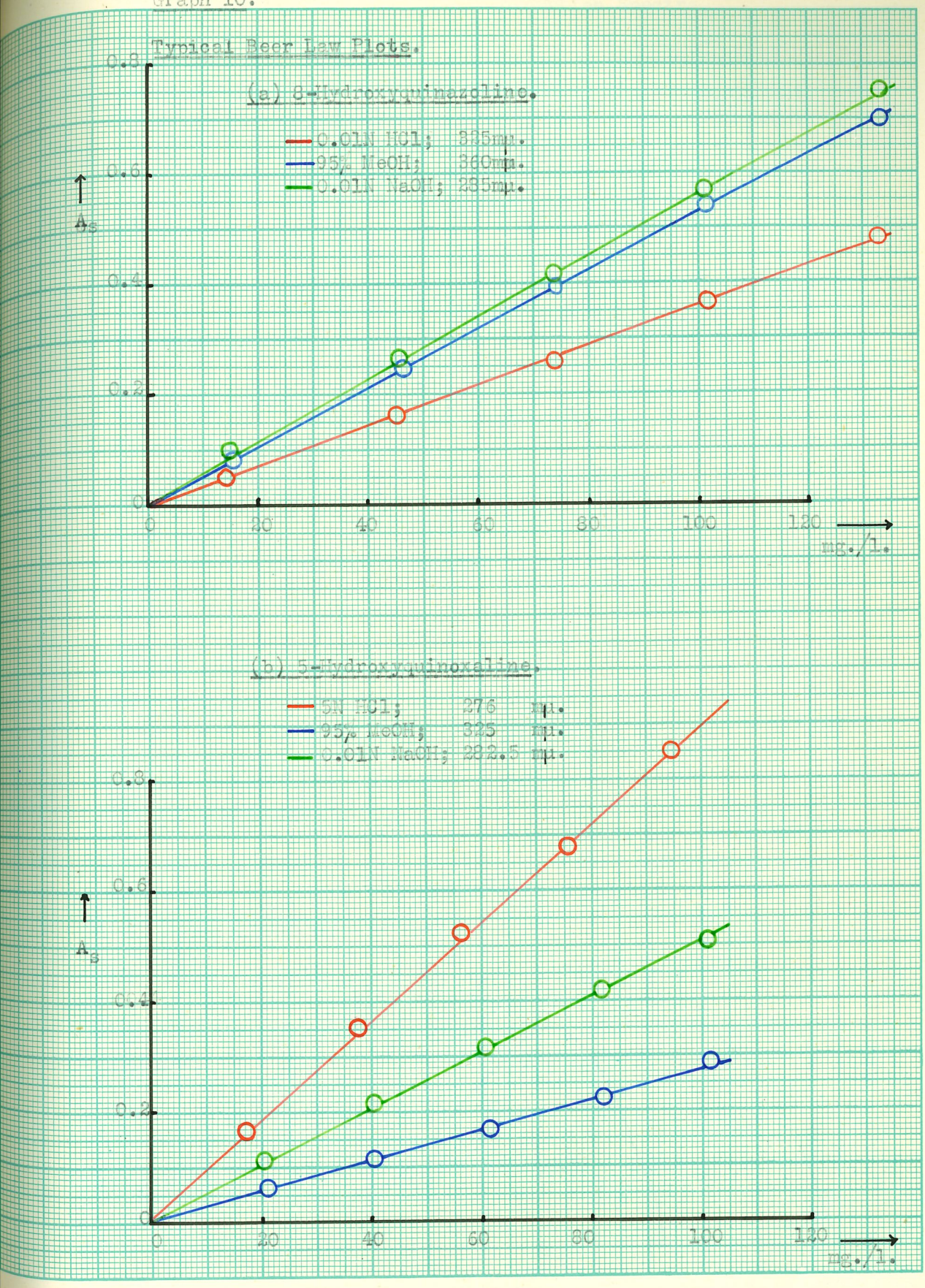
Solutions, 0.0001286M



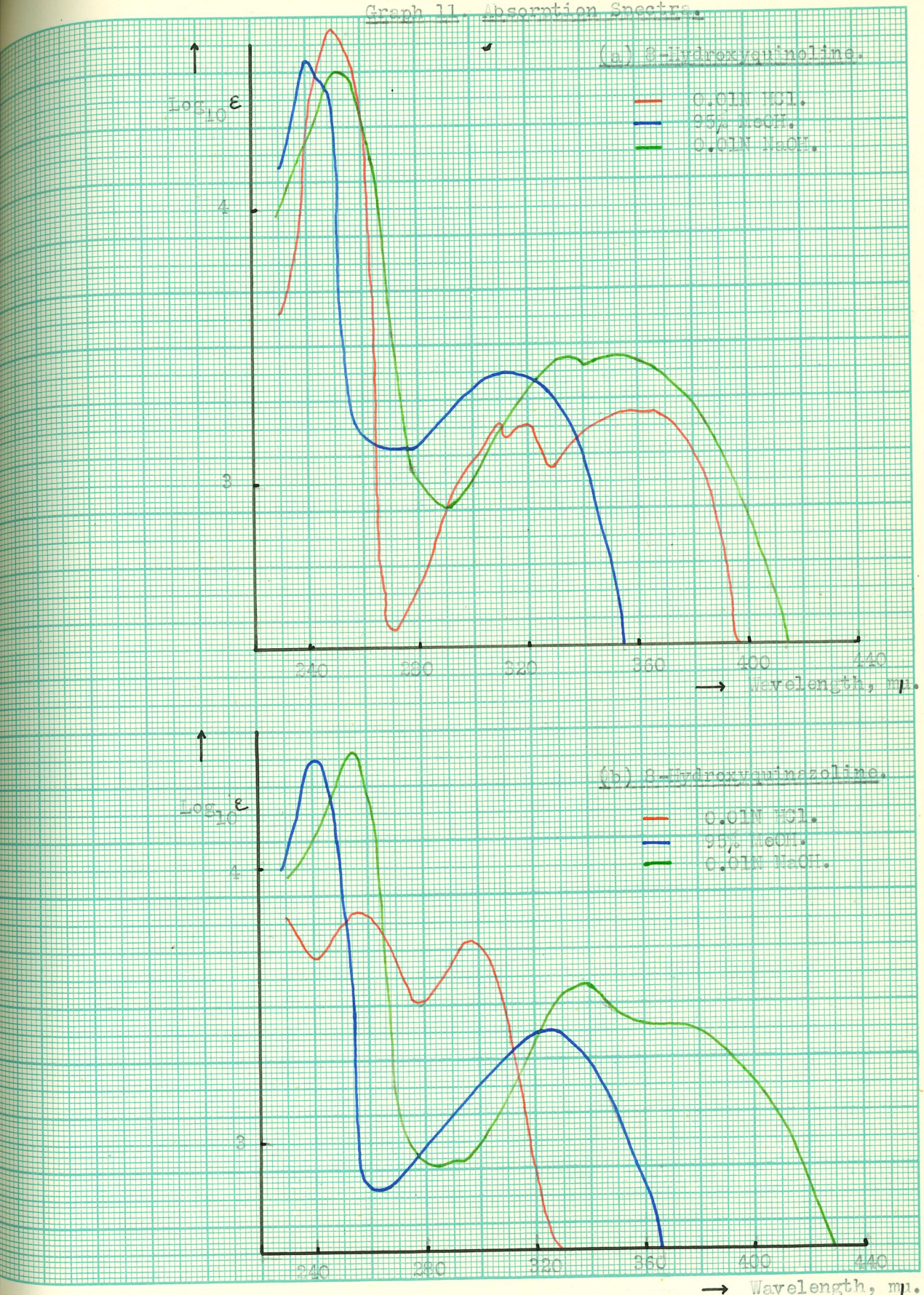
Graph 9.

Graph 10.

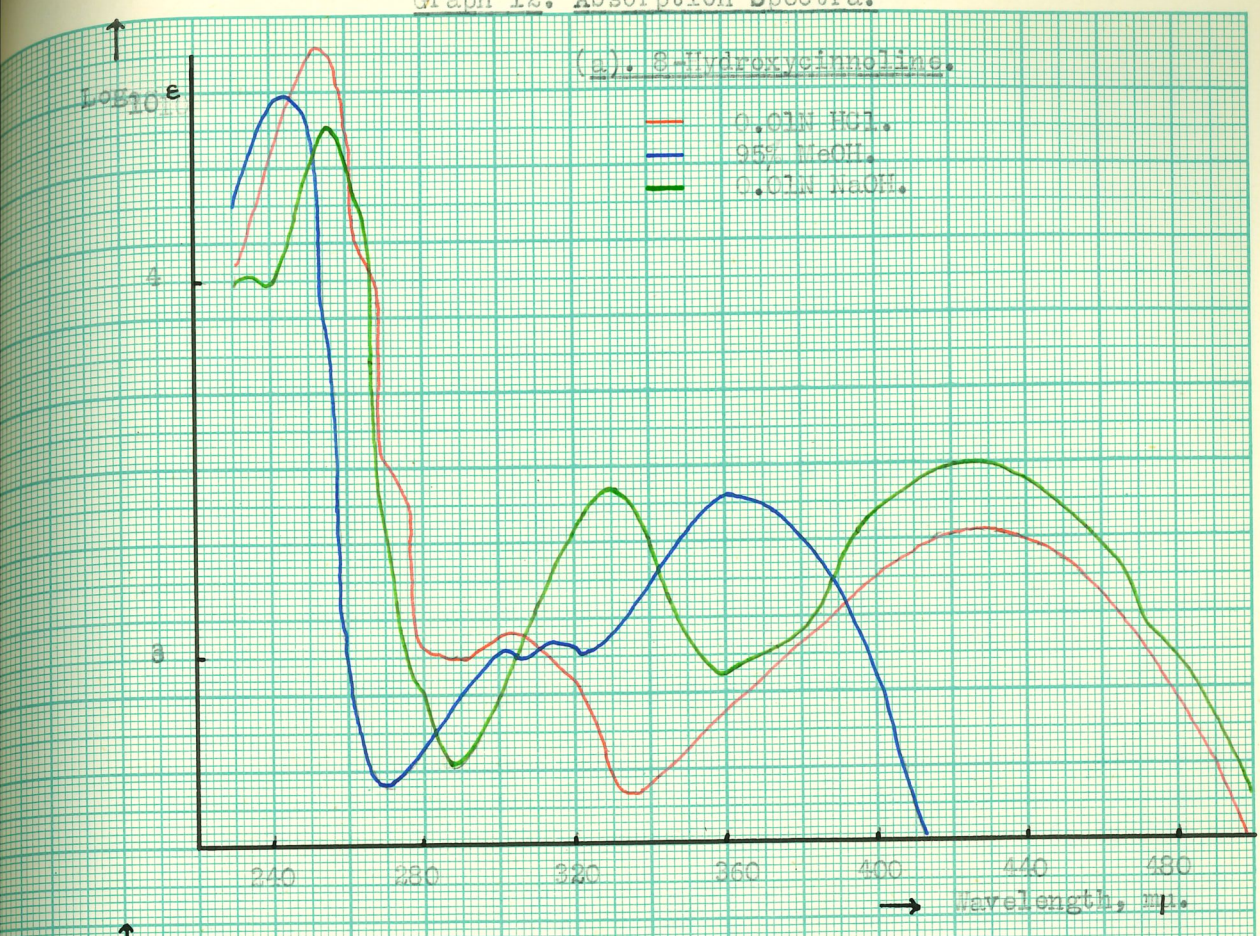
Typical Beer law Plots.

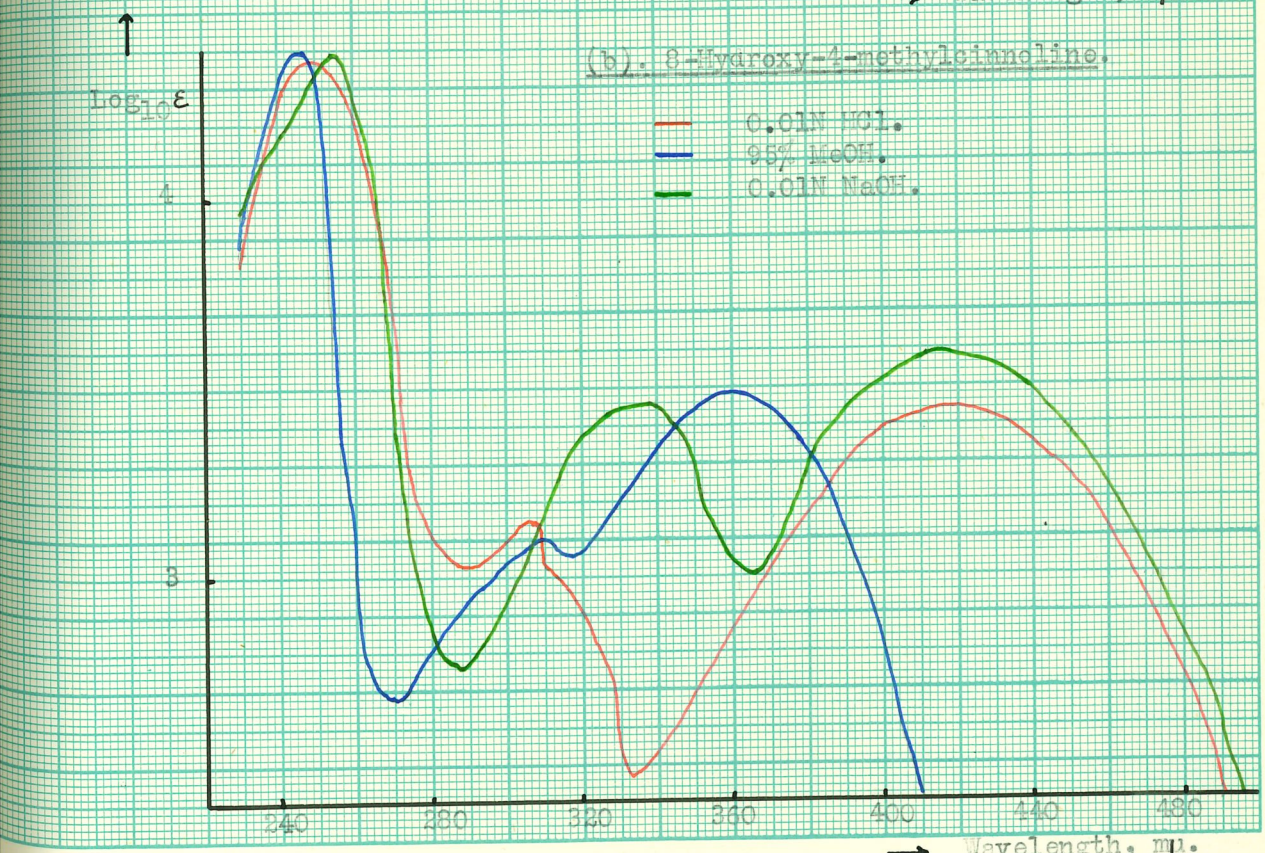


Graph 11. Absorption Spectra.

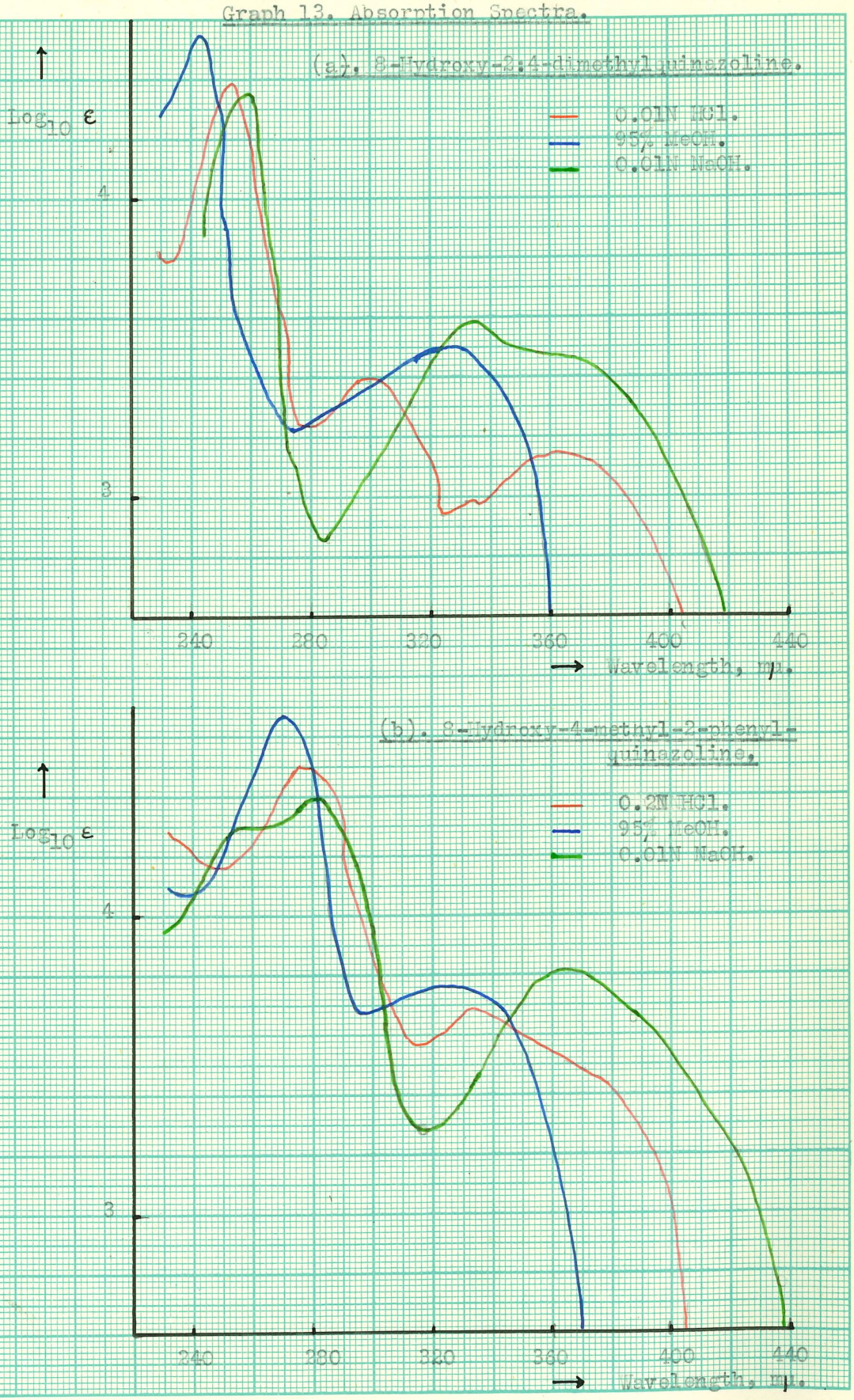


Graph 12. Absorption Spectra.

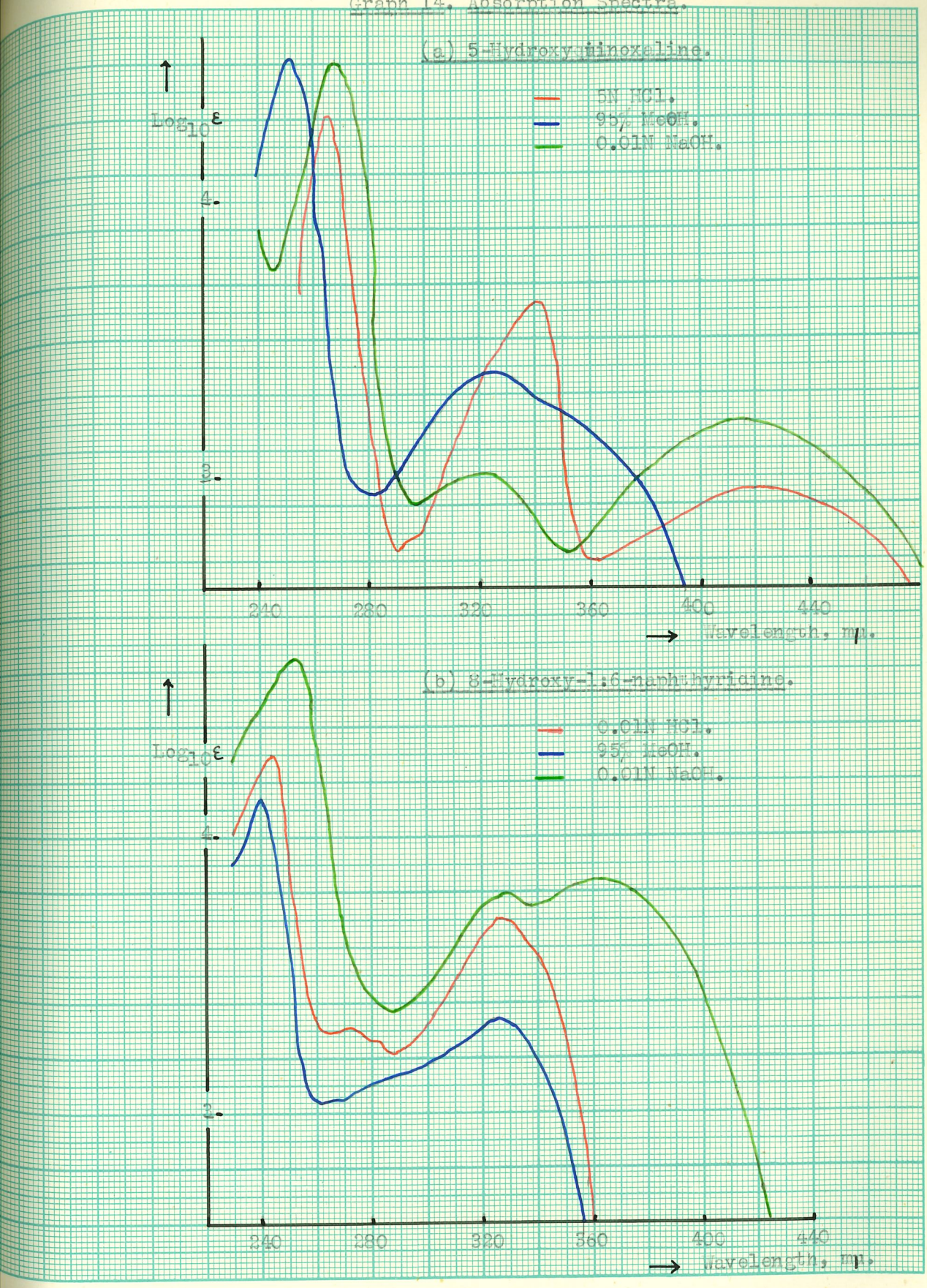




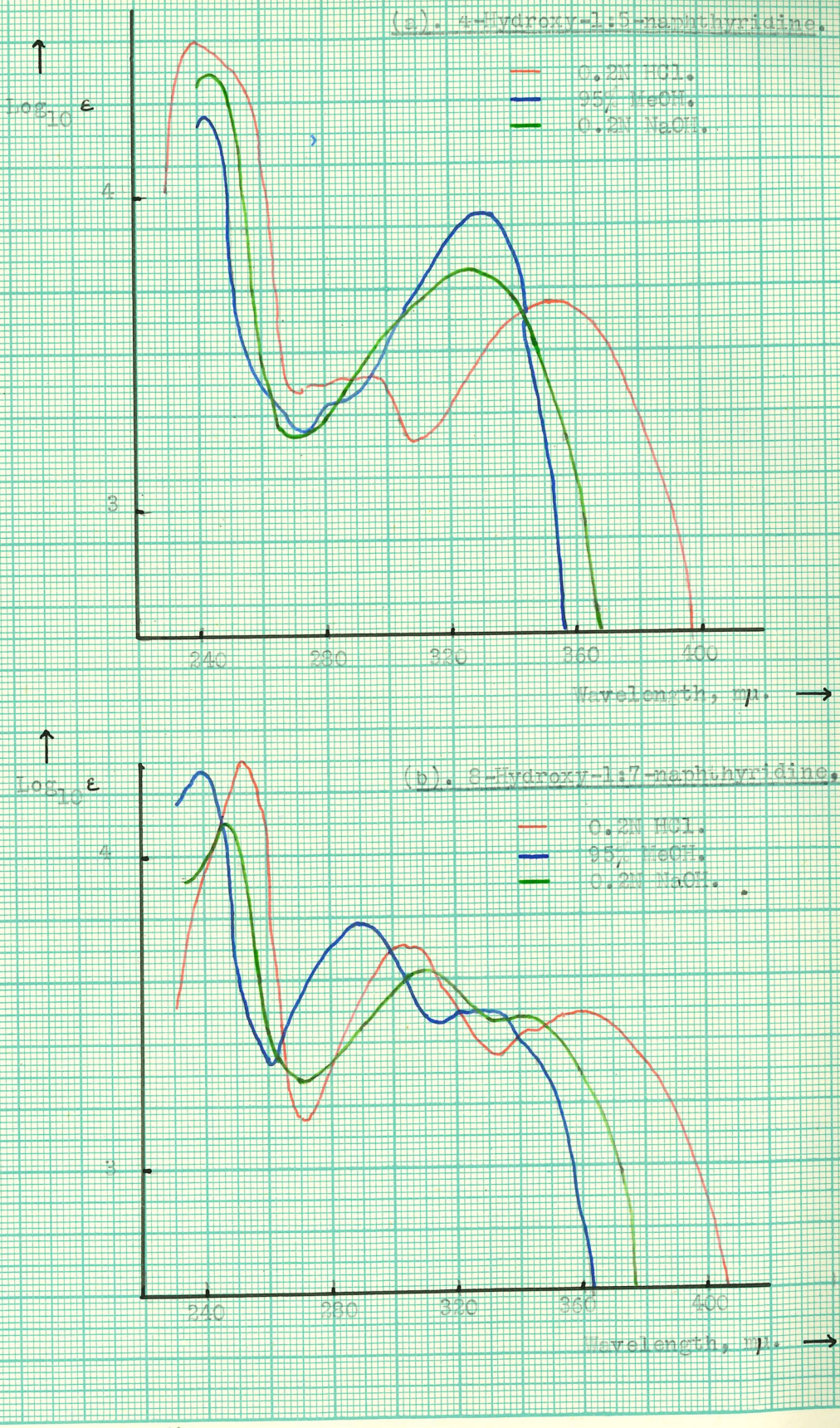
Graph 13. Absorption Spectra.



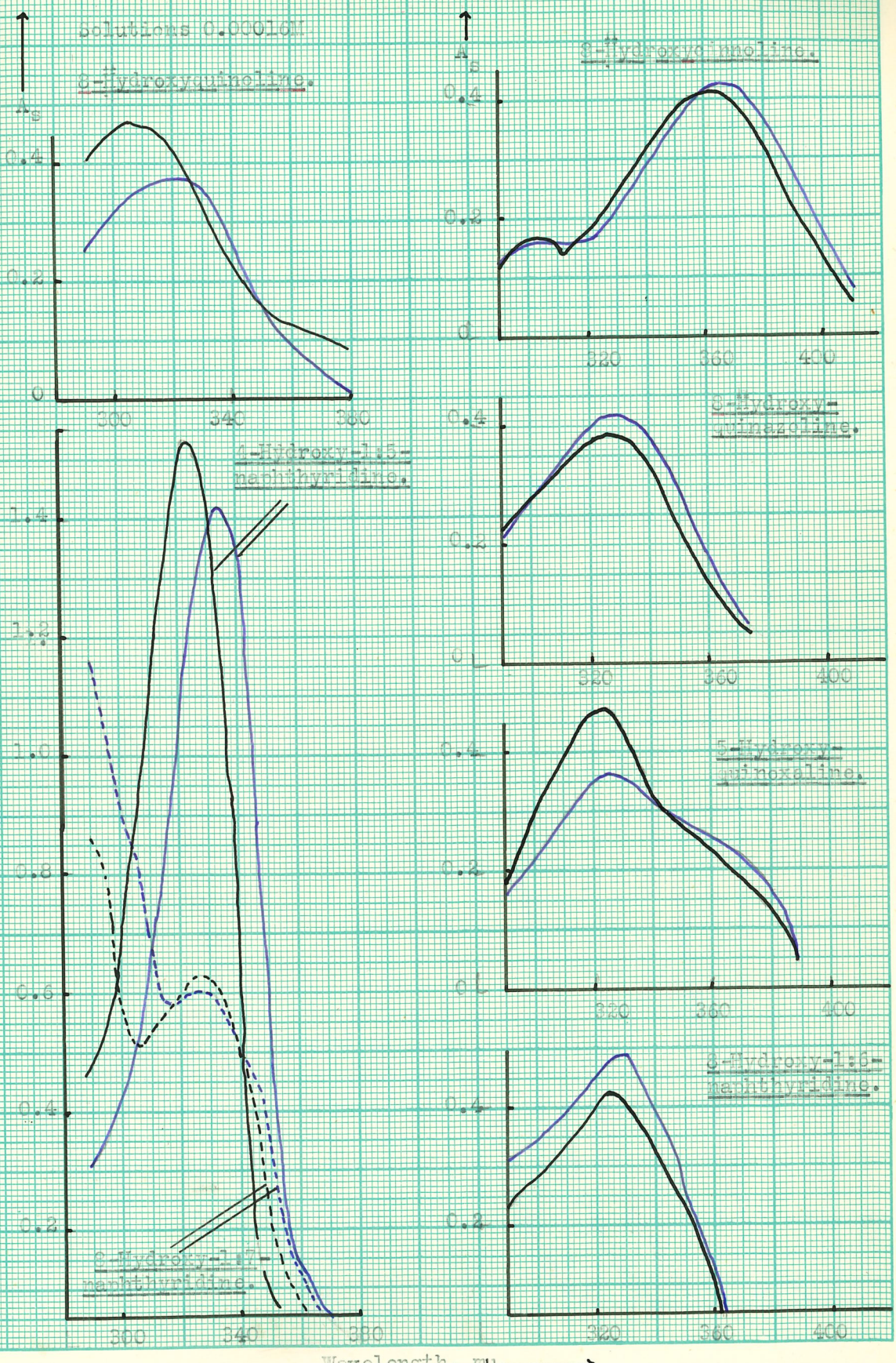
Graph 14. Absorption Spectra.



Graph 15. Absorption Spectra.

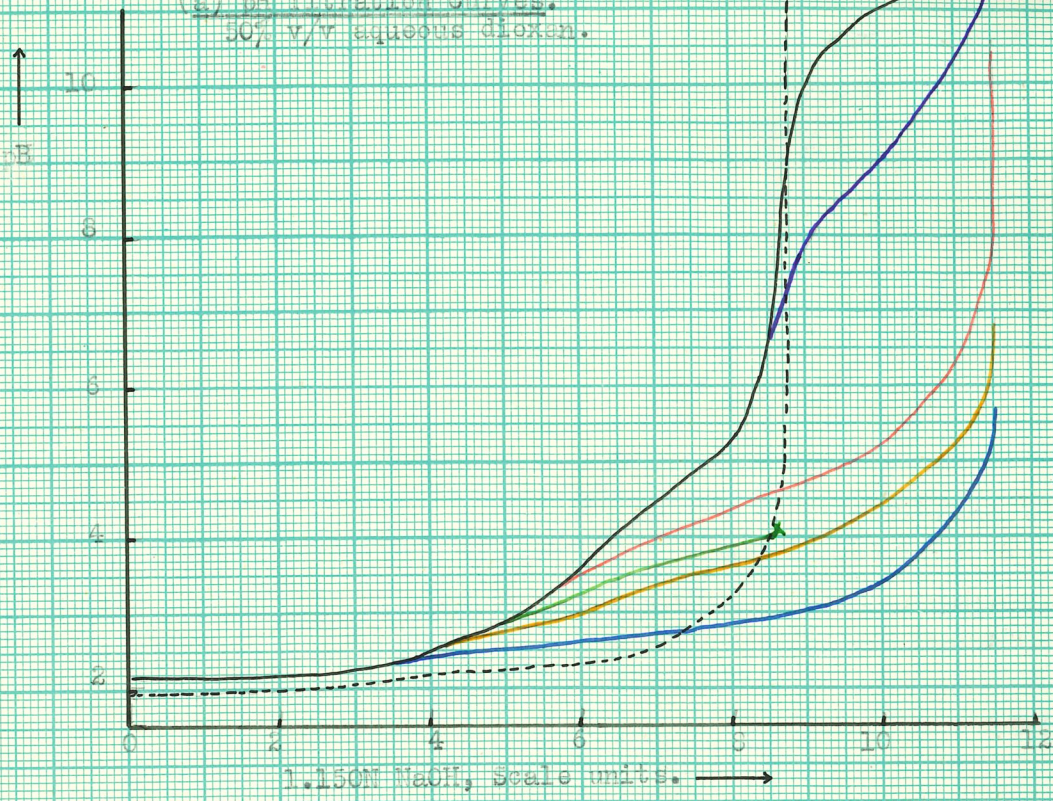


Graph 16. Absorbancies in Water, —— and in Amyl Alcohol, ——— .
solutions 0.00010M

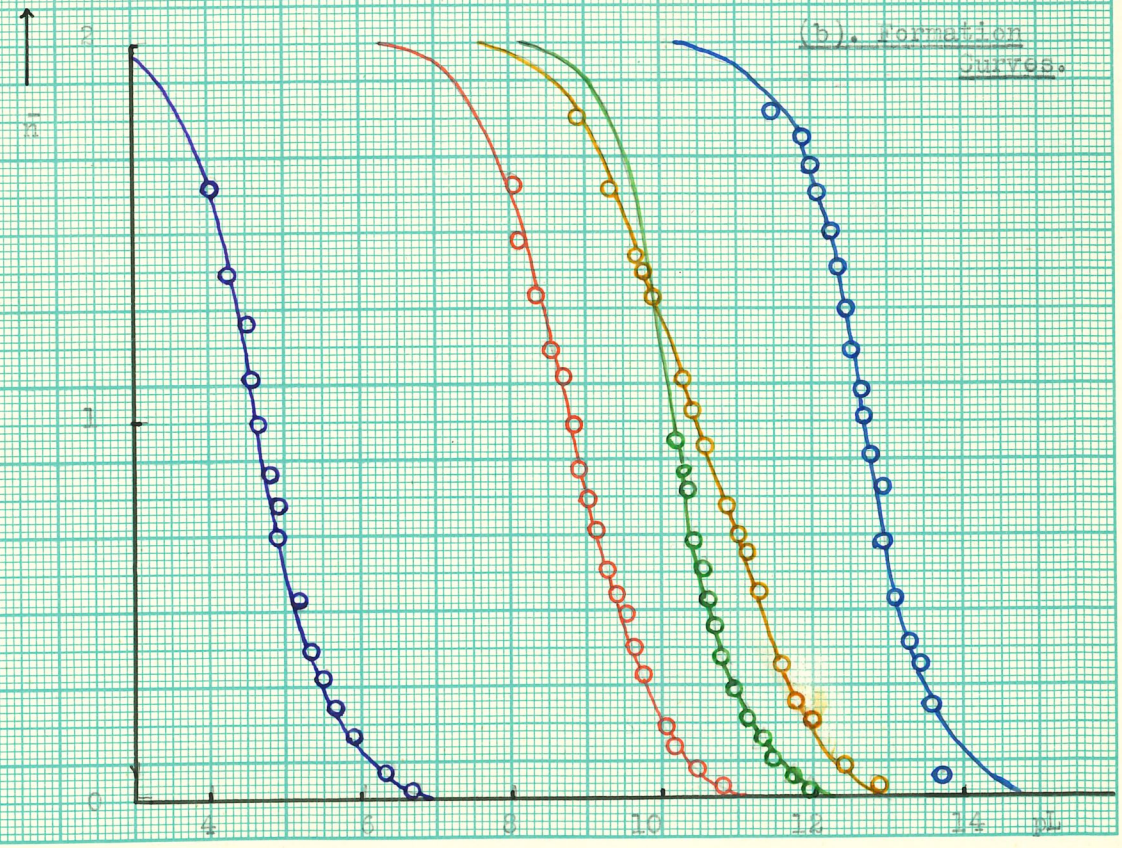


Graph 17. 8-Hydroxyquinoline. Metal Complexes.

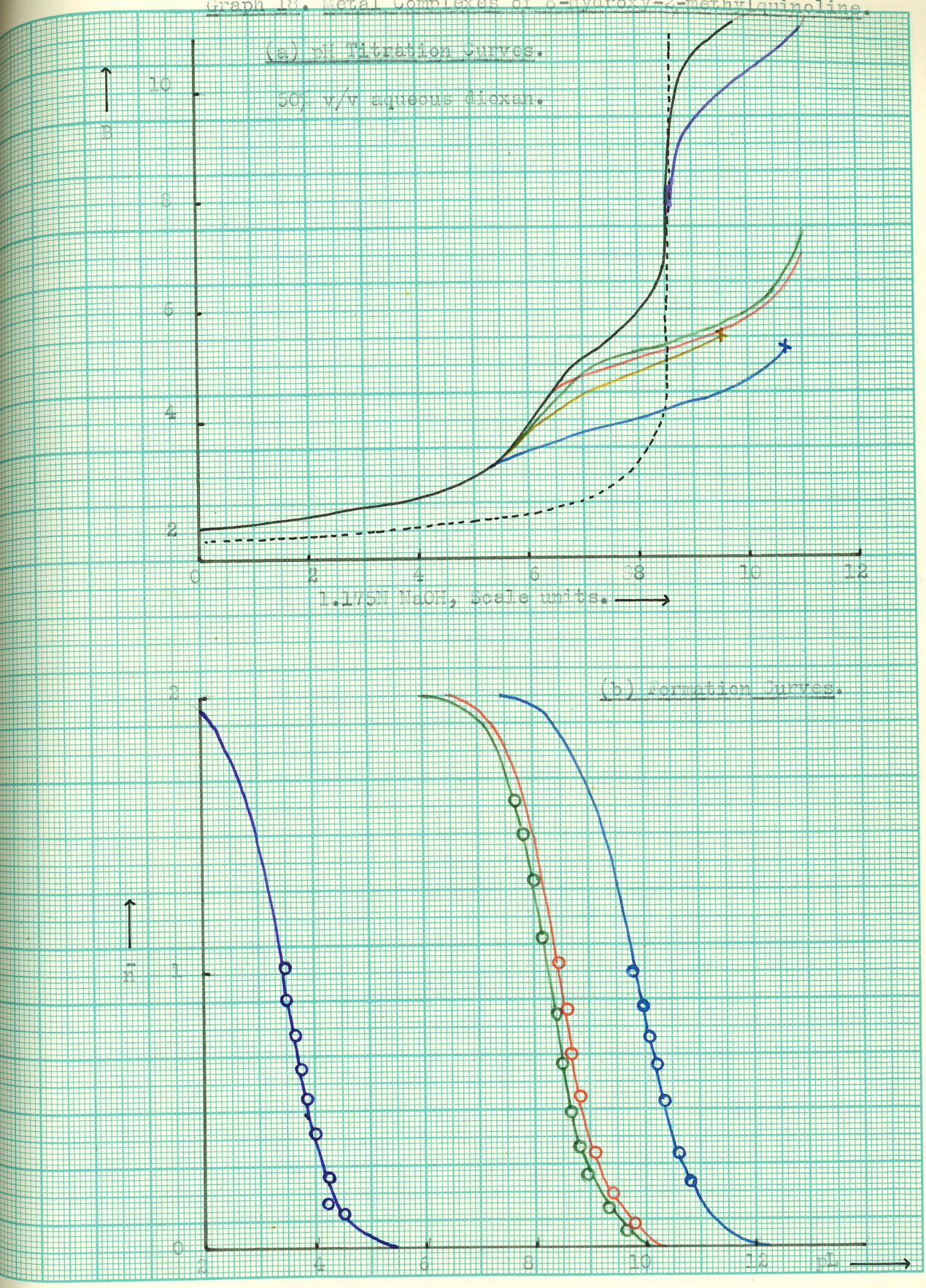
(a) pH titration Curves.
50% v/v aqueous dioxan.



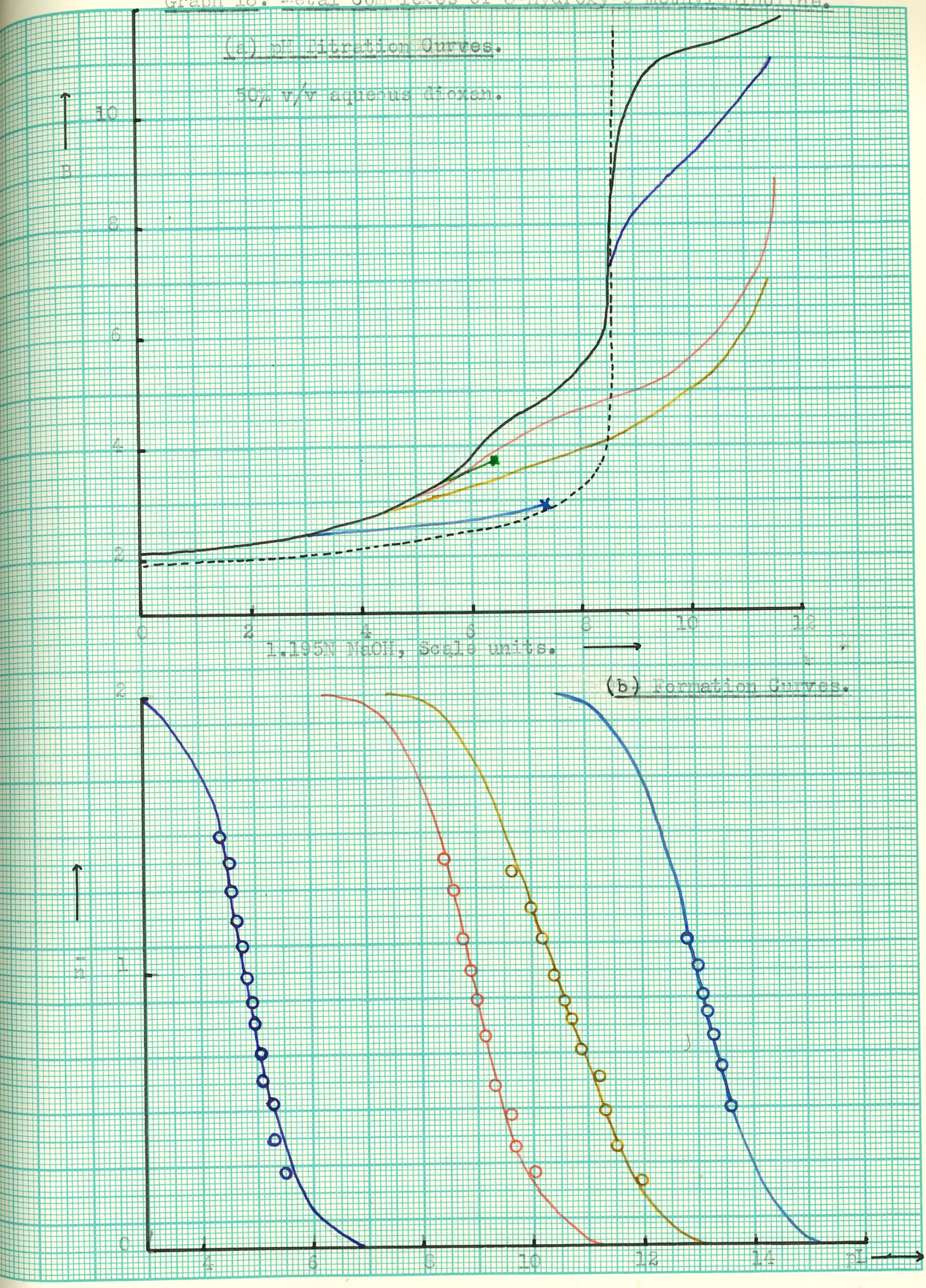
(b). Formation Curves.



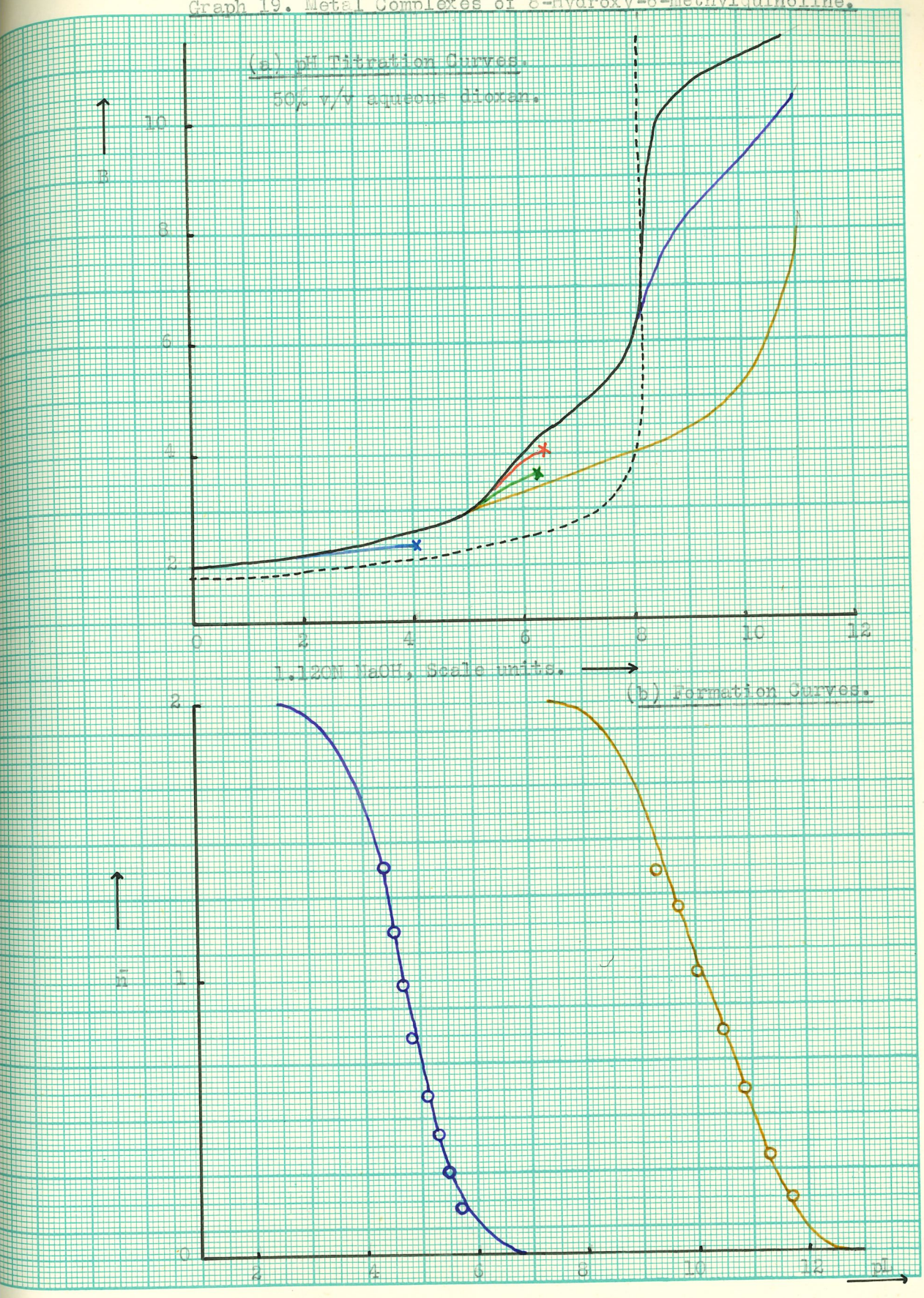
Graph 18. Metal Complexes of 8-Hydroxy-2-methylquinoline.



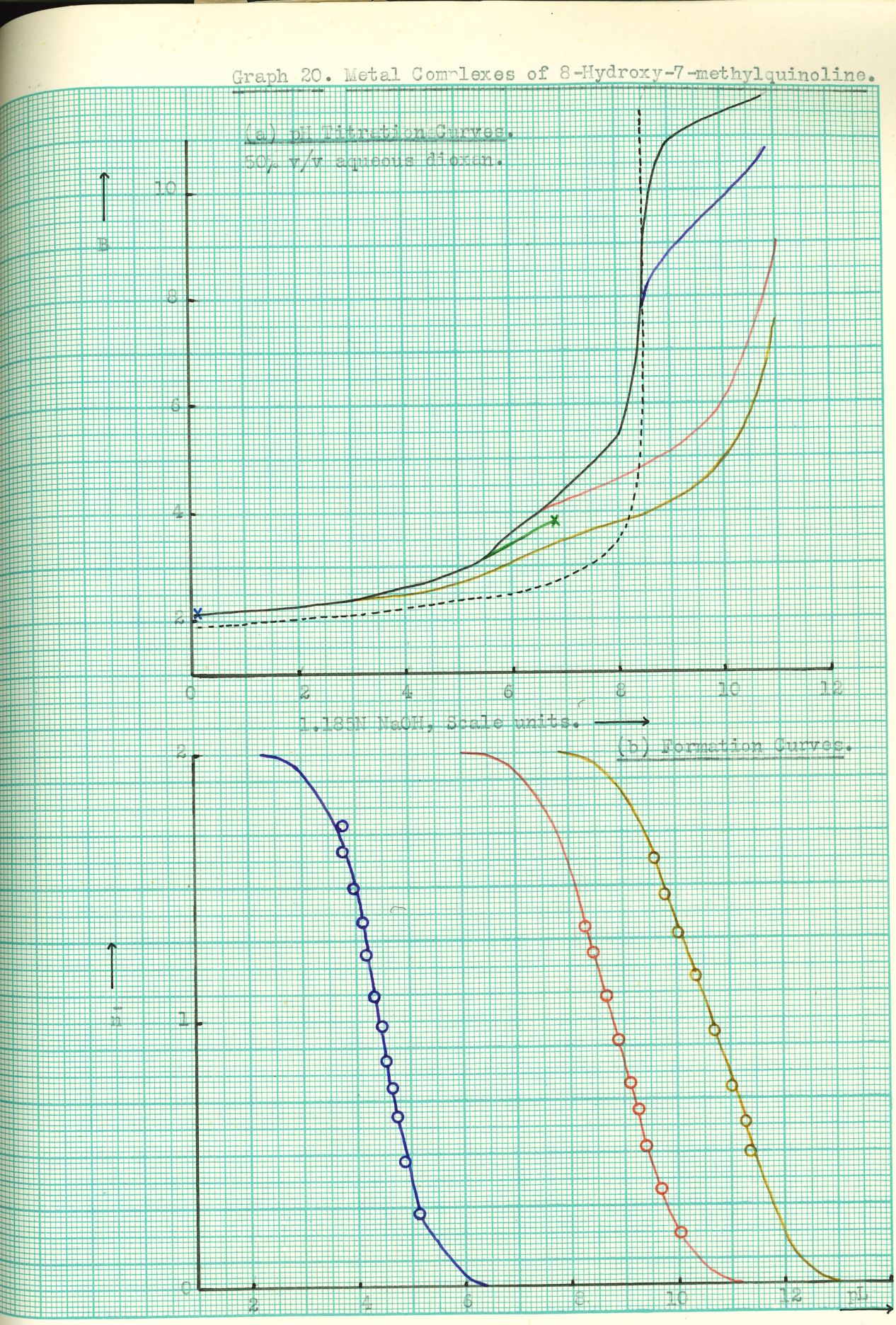
Graph 18. Metal Complexes of 8-Hydroxy-5-methylquinoline.



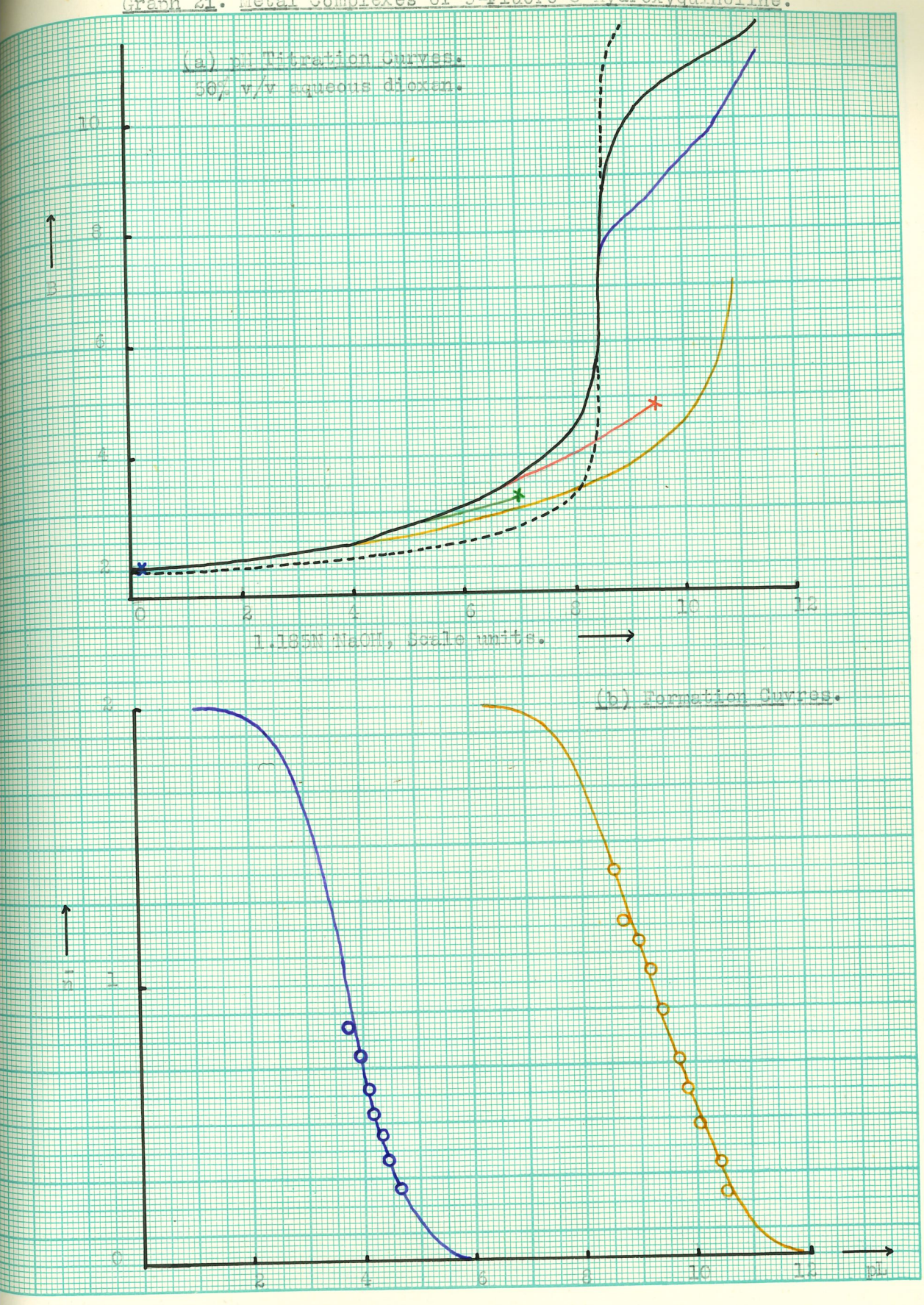
Graph 19. Metal Complexes of 8-Hydroxy-6-methylquinoline.



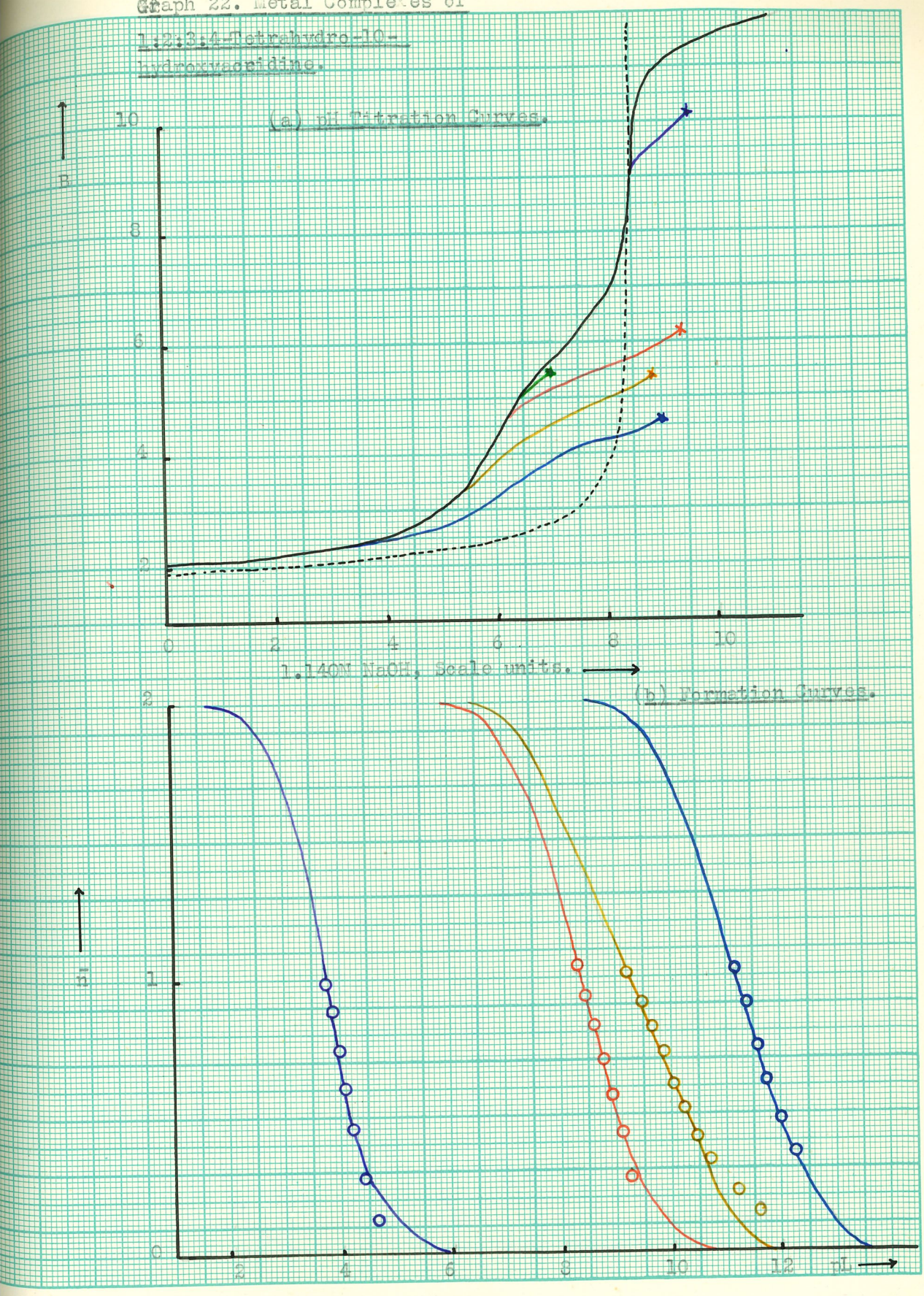
Graph 20. Metal Complexes of 8-Hydroxy-7-methylquinoline.



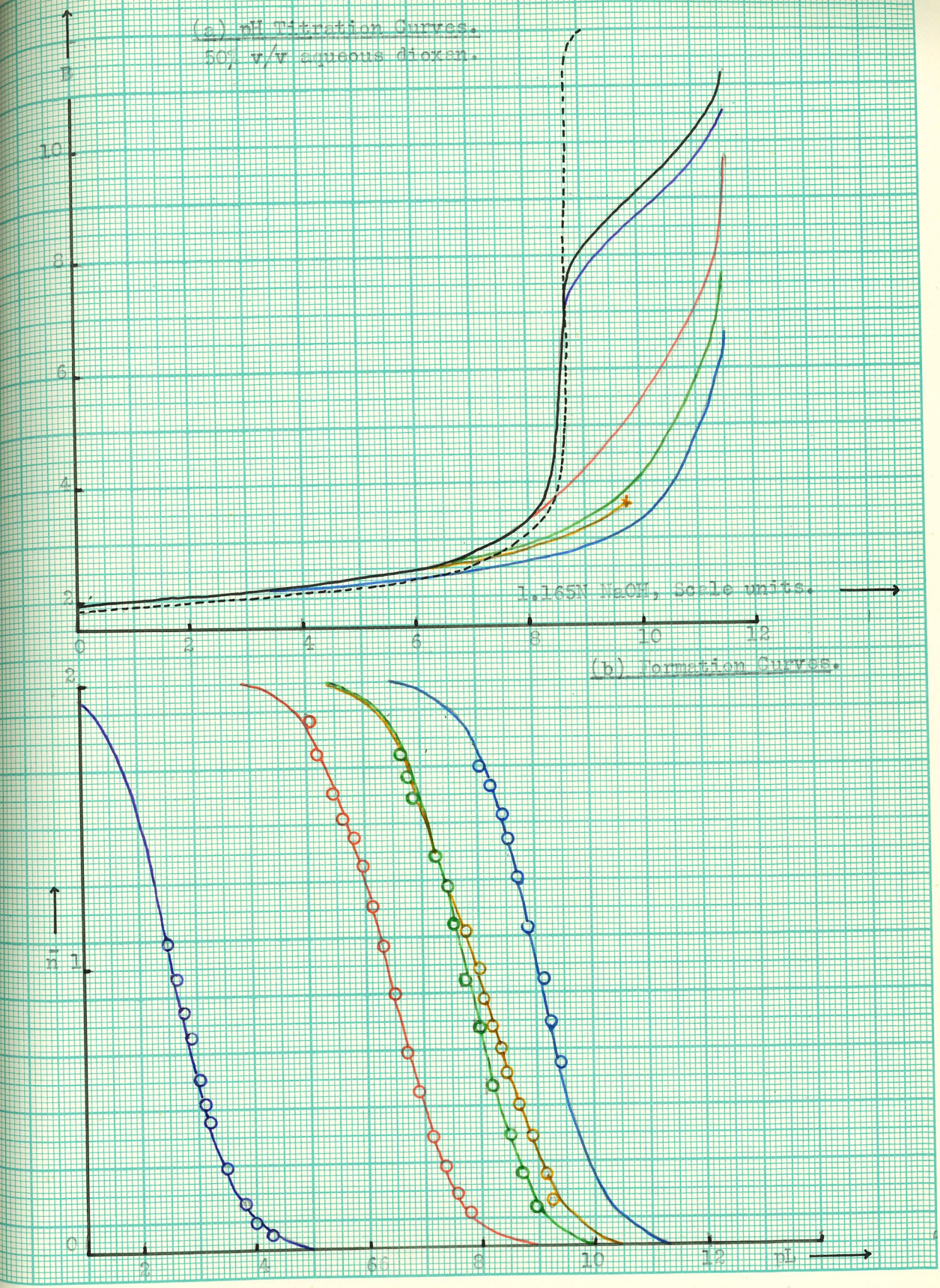
Graph 21. Metal Complexes of 5-Fluoro-8-hydroxyquinoline.



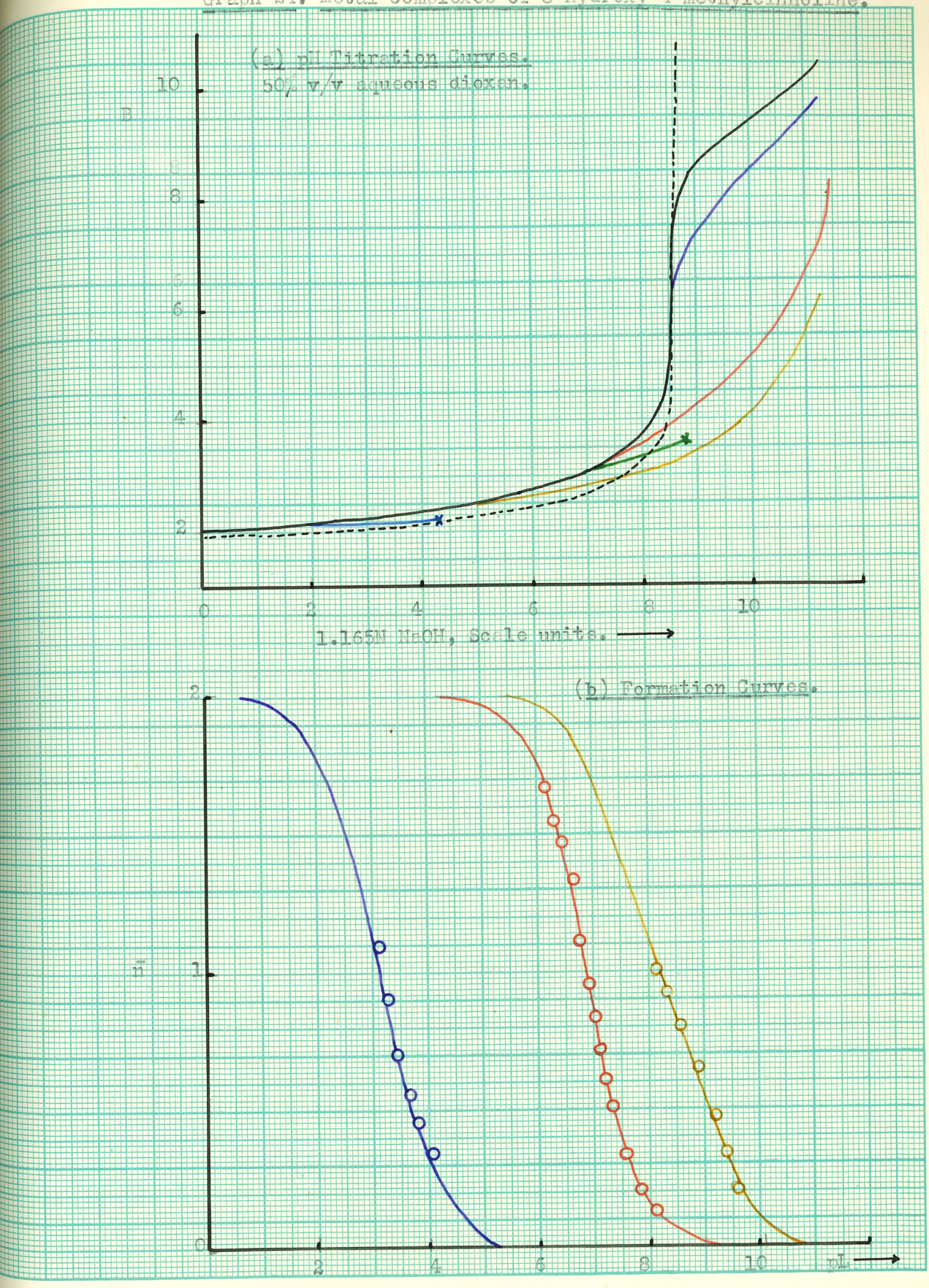
Graph 22. Metal Complexes of 1:2:3:4-Tetrahydro-10-hydroxycoeridine.



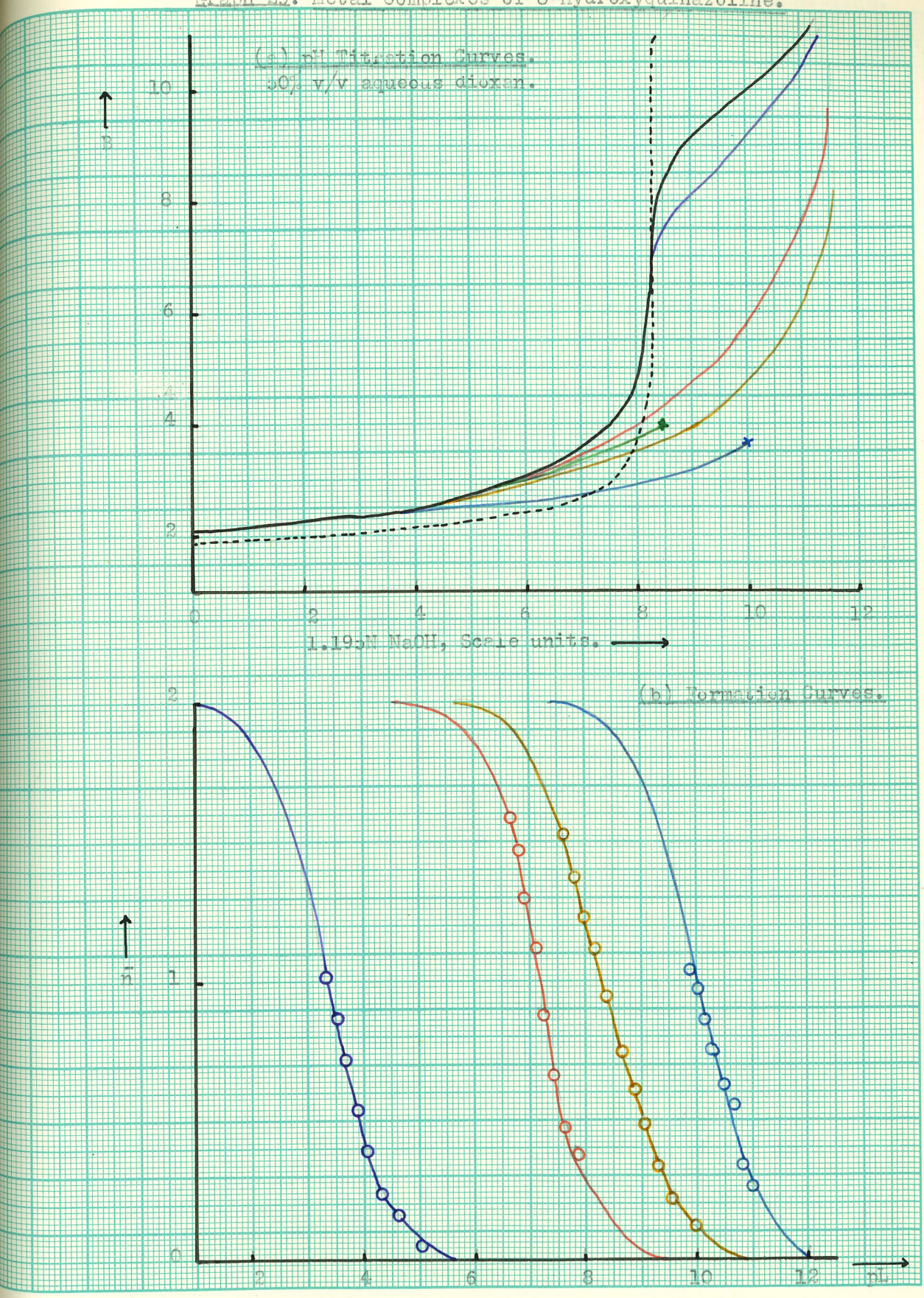
Graph 23. Metal Complexes of 8-Hydroxycinnoline.



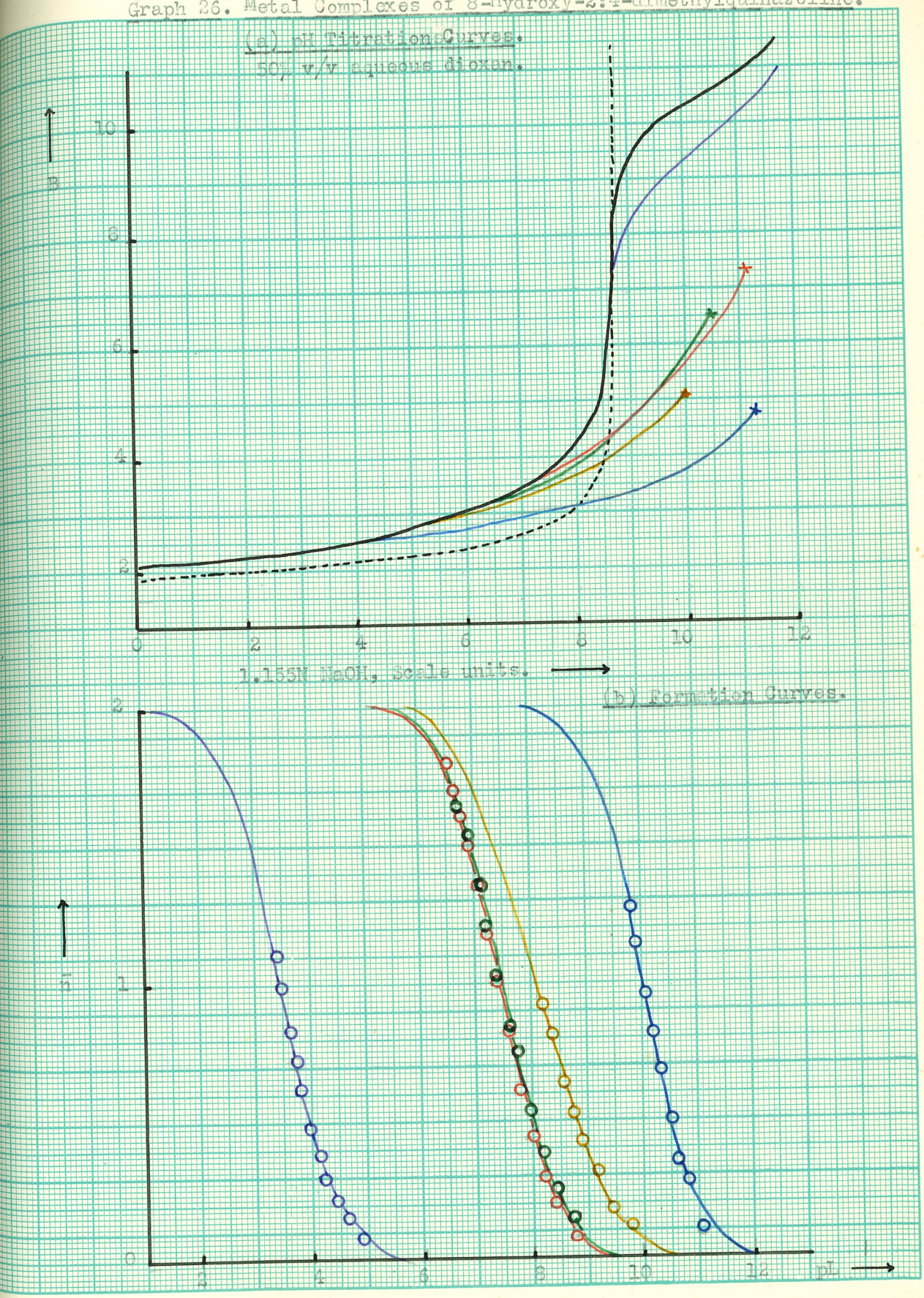
Graph 24. Metal Complexes of 8-Hydroxy-4-methylcinnoline.



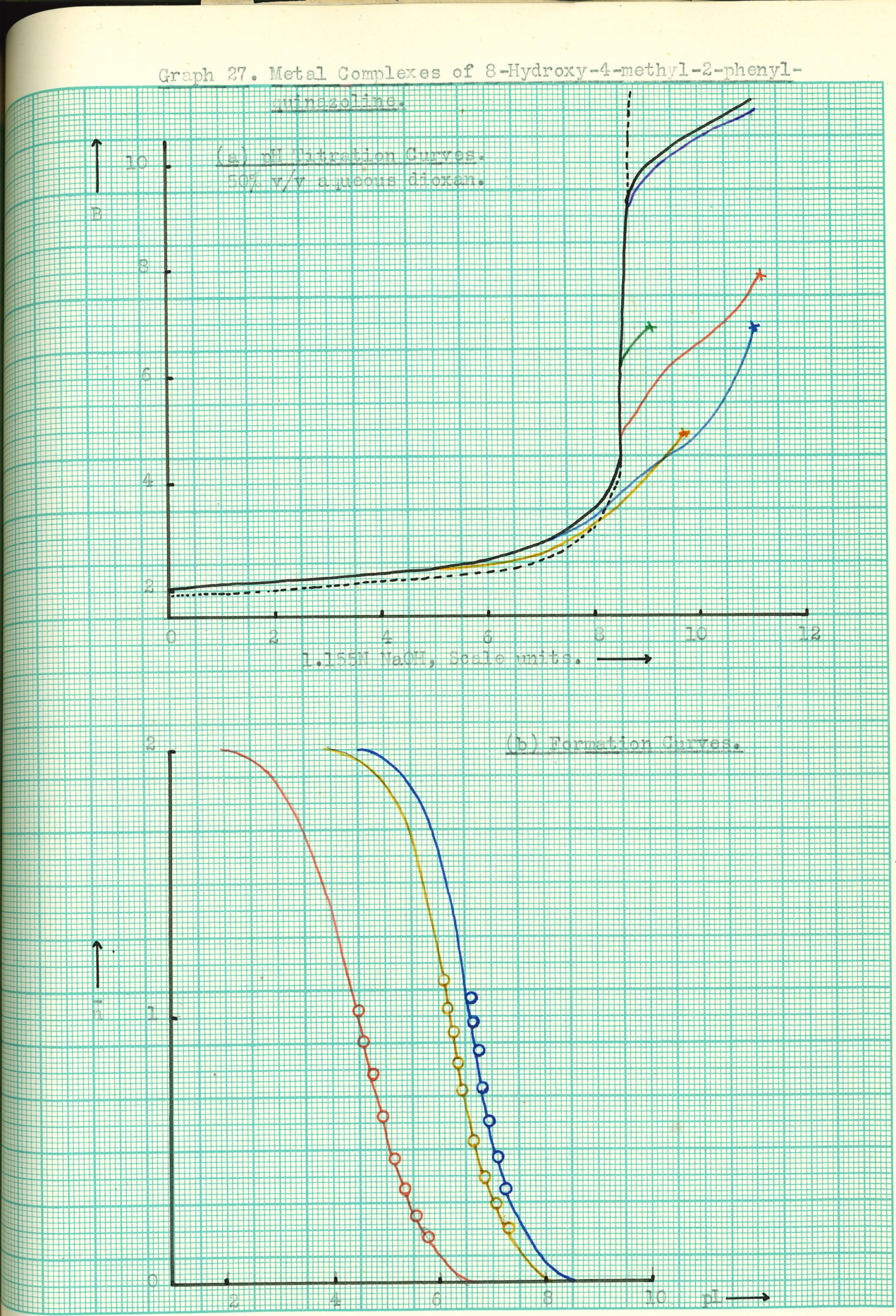
Graph 25. Metal Complexes of 8-Hydroxyquinazoline.



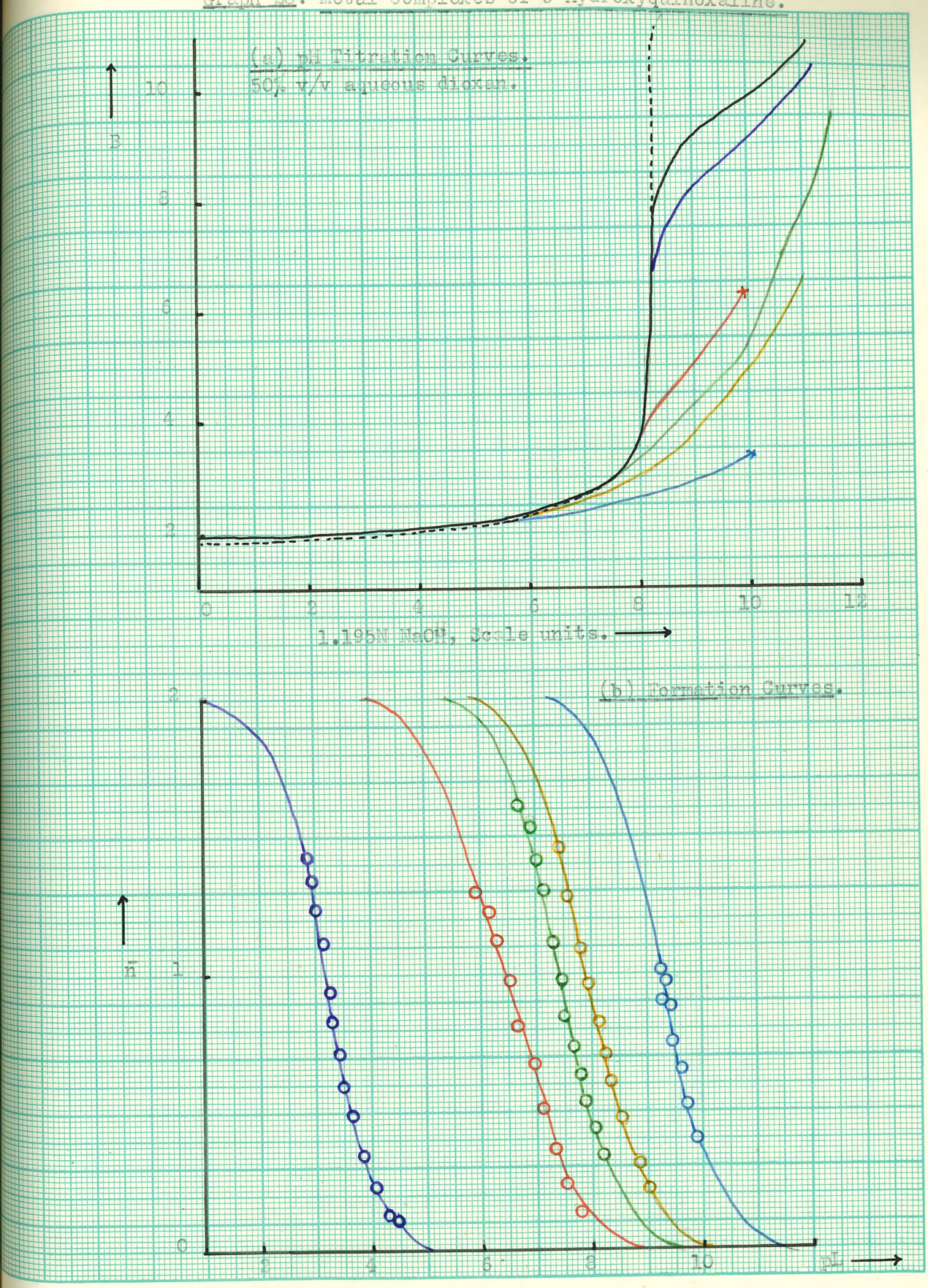
Graph 26. Metal Complexes of 8-Hydroxy-2:4-dimethylquinazoline.



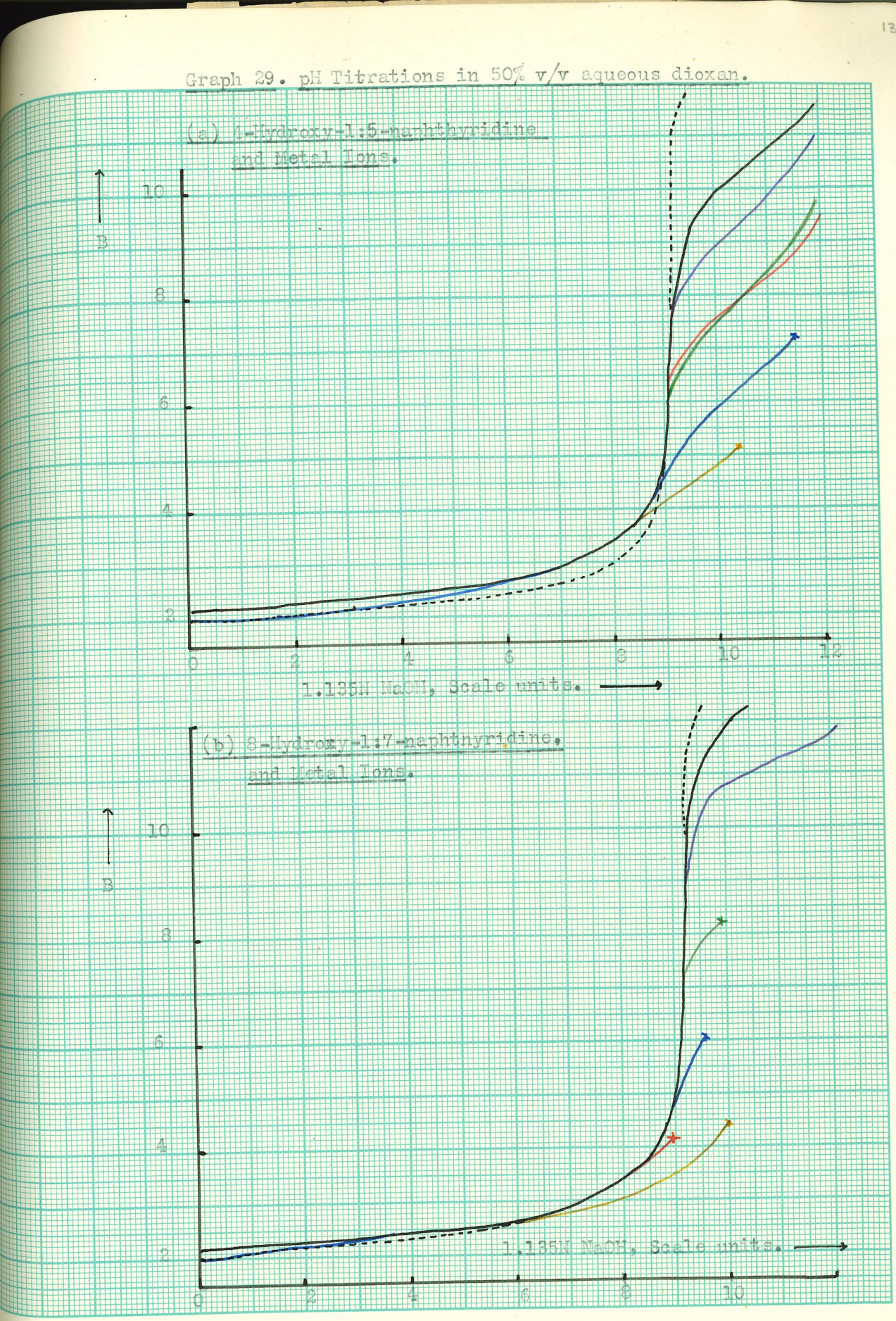
Graph 27. Metal Complexes of 8-Hydroxy-4-methyl-2-phenyl-quinazoline.



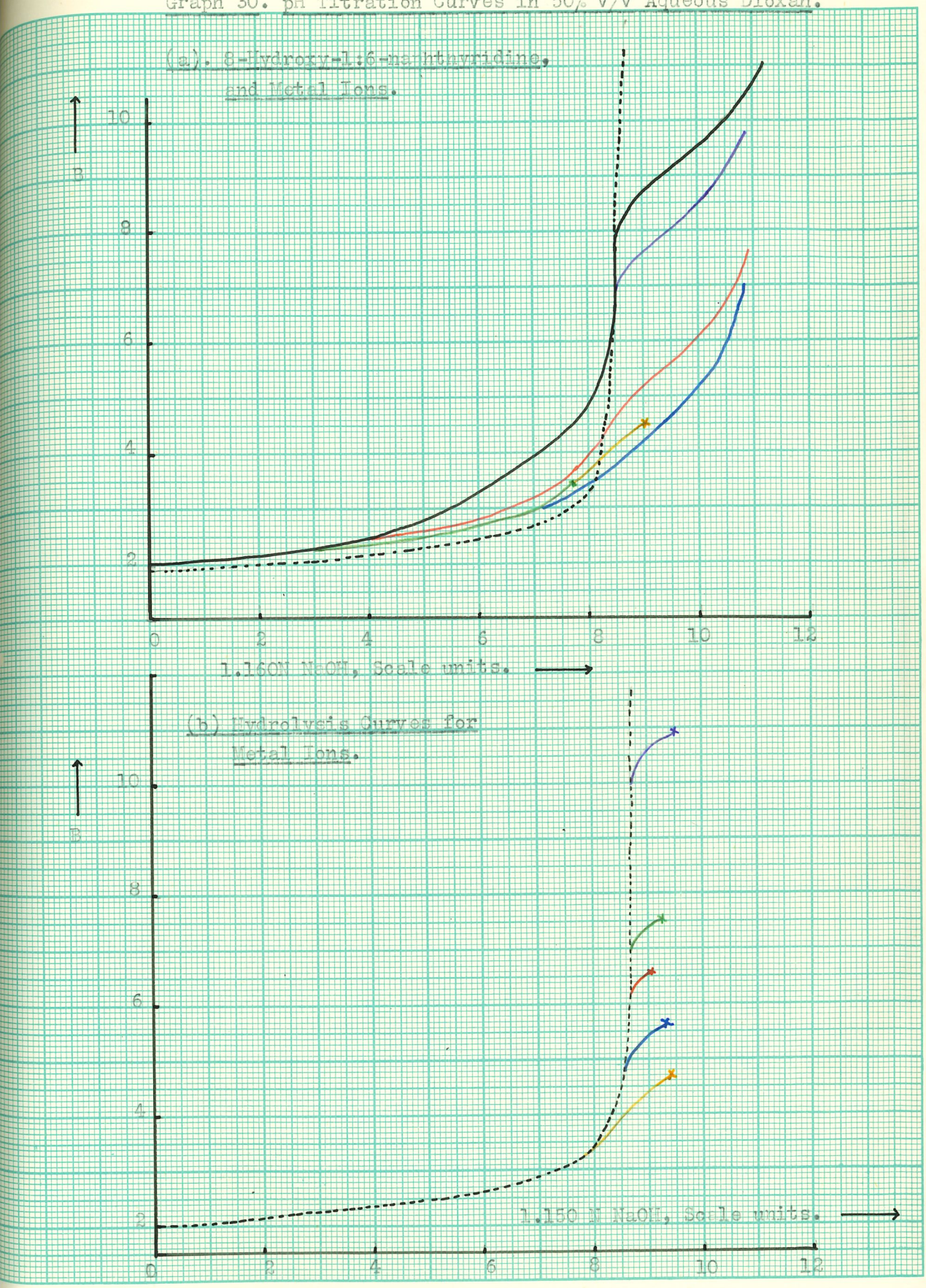
Graph 28. Metal Complexes of 5-Hydroxyquinoxaline.



Graph 29. pH Titrations in 50% v/v aqueous dioxan.



Graph 30. pH Titration Curves in 50% v/v Aqueous Dioxan.



GRAPHS 17 - 30.

pH Titration Curves.

------ 0.0197N $HClO_4$ + 0.3M $NaClO_4$ — 'A'.

——— 'A' + 0.006M Reagent.

——— " " + 0.003M $MgSO_4$.

——— " " + 0.003M $ZnSO_4$.

——— " " + 0.003M $NiSO_4$.

——— " " + 0.003M $CuSO_4$.

——— " " + 0.003M $UO_2(NO_3)_2$.

Formation Curves.

o Experimental Points.

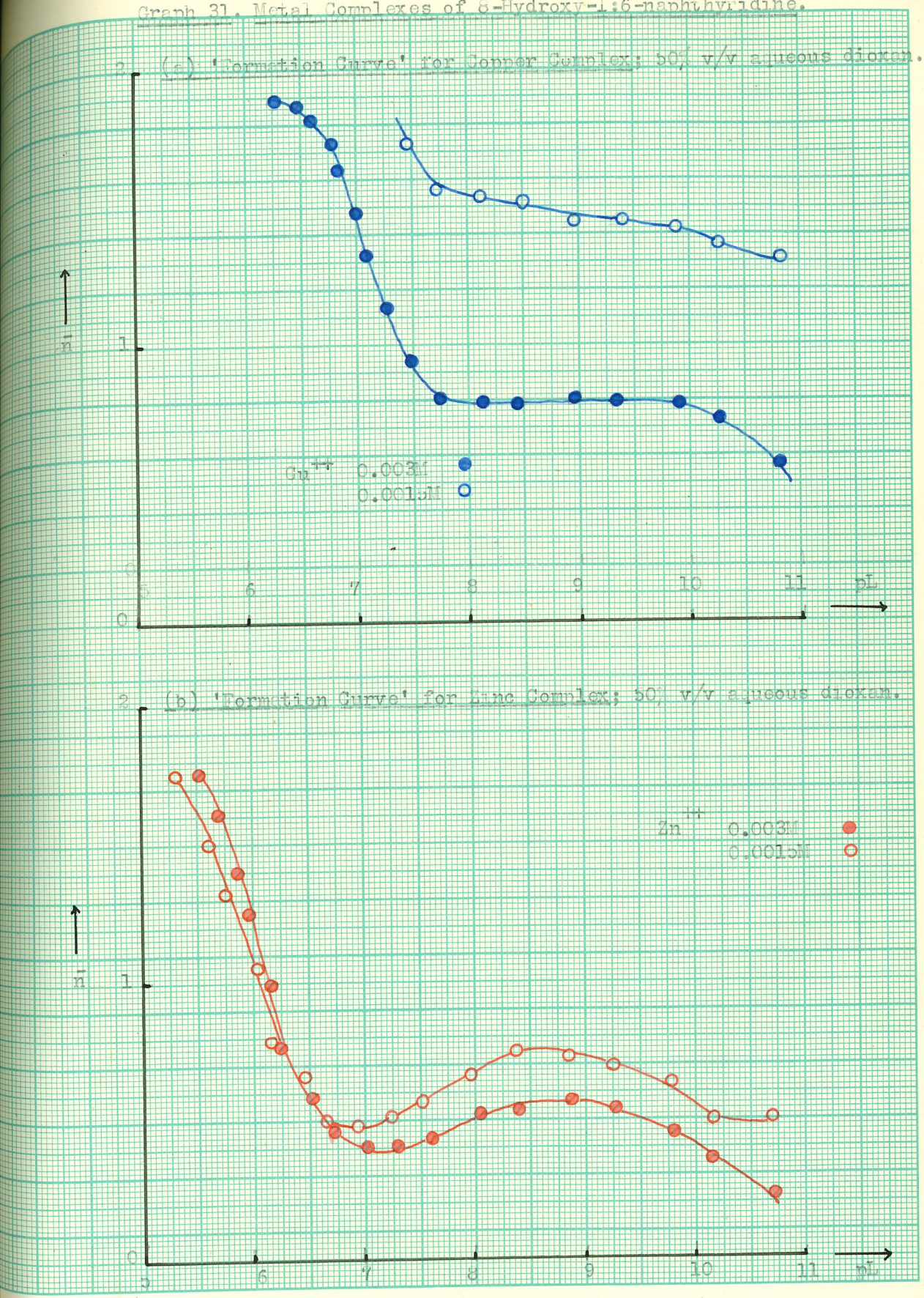
——— Formation Curves, calculated using stability constants given in Table 15.

The colours correspond to those metals shown above.

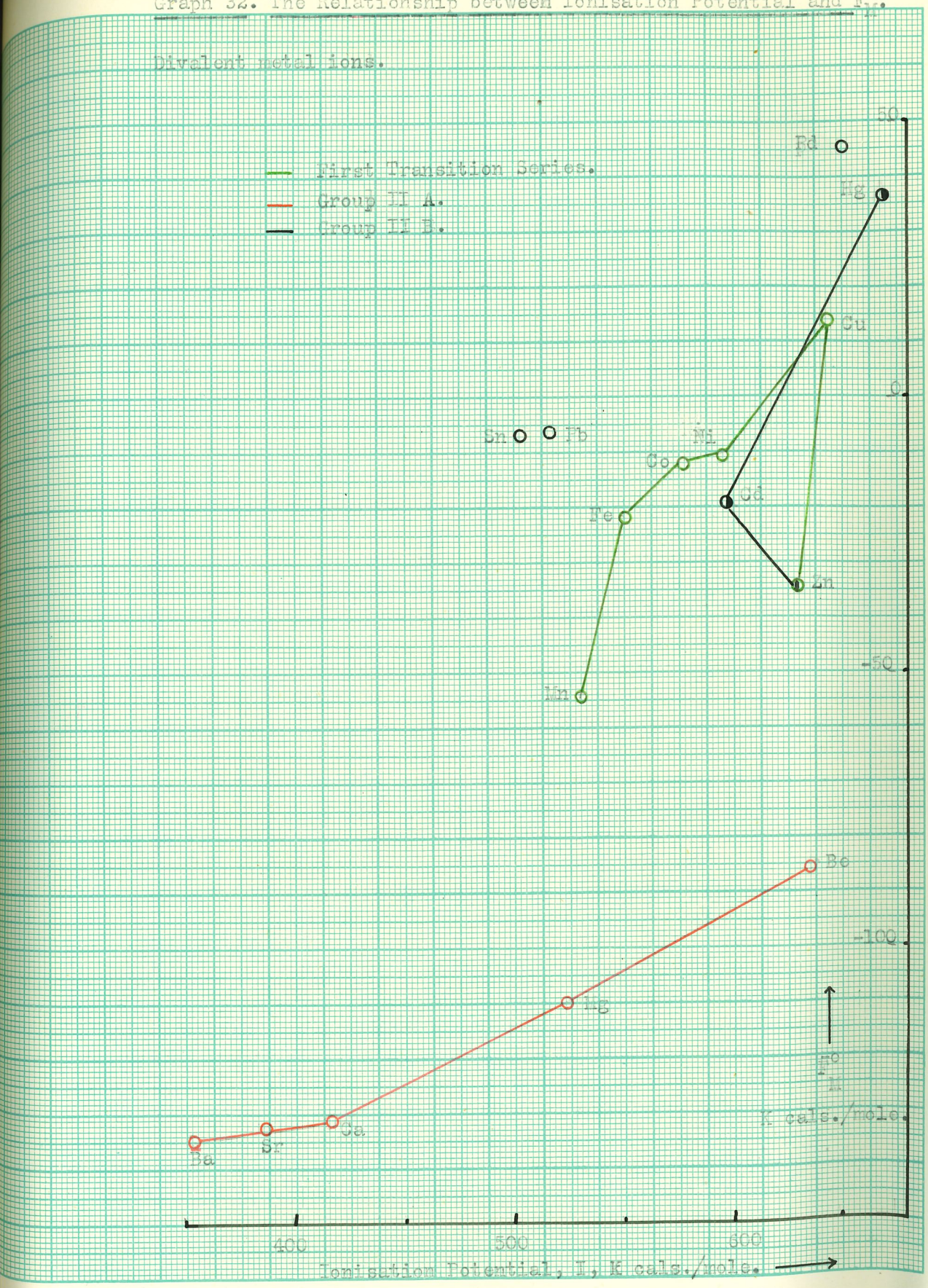
Volume of titration solution = 9.85 ml.

1 Scale unit = 0.01992 ± 0.00014 ml.

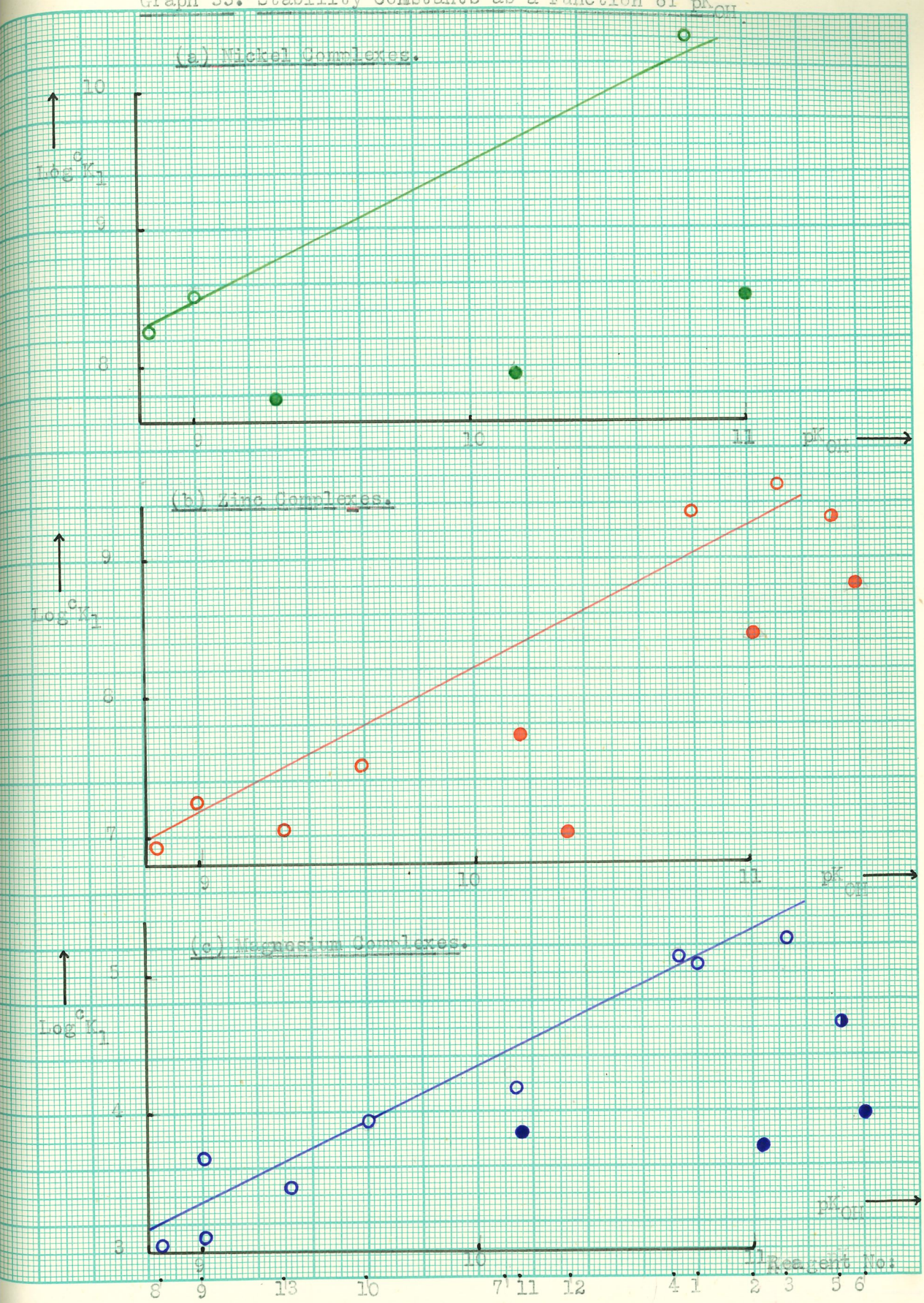
Graph 31. Metal Complexes of 8-Hydroxy-1:6-naphthyridine.



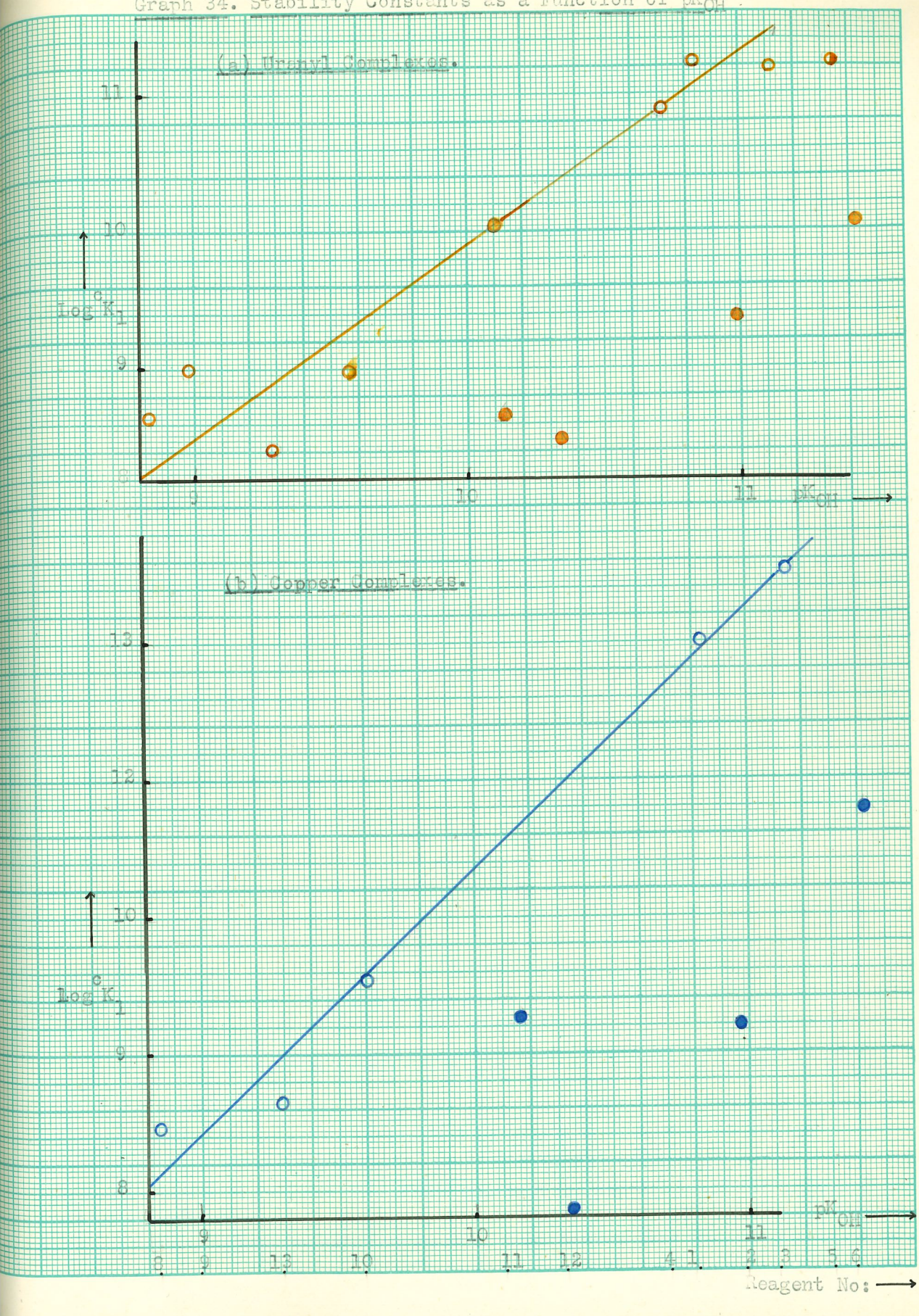
Graph 32. The Relationship between Ionisation Potential and $\bar{F}^{o}_{M^{2+}}$.



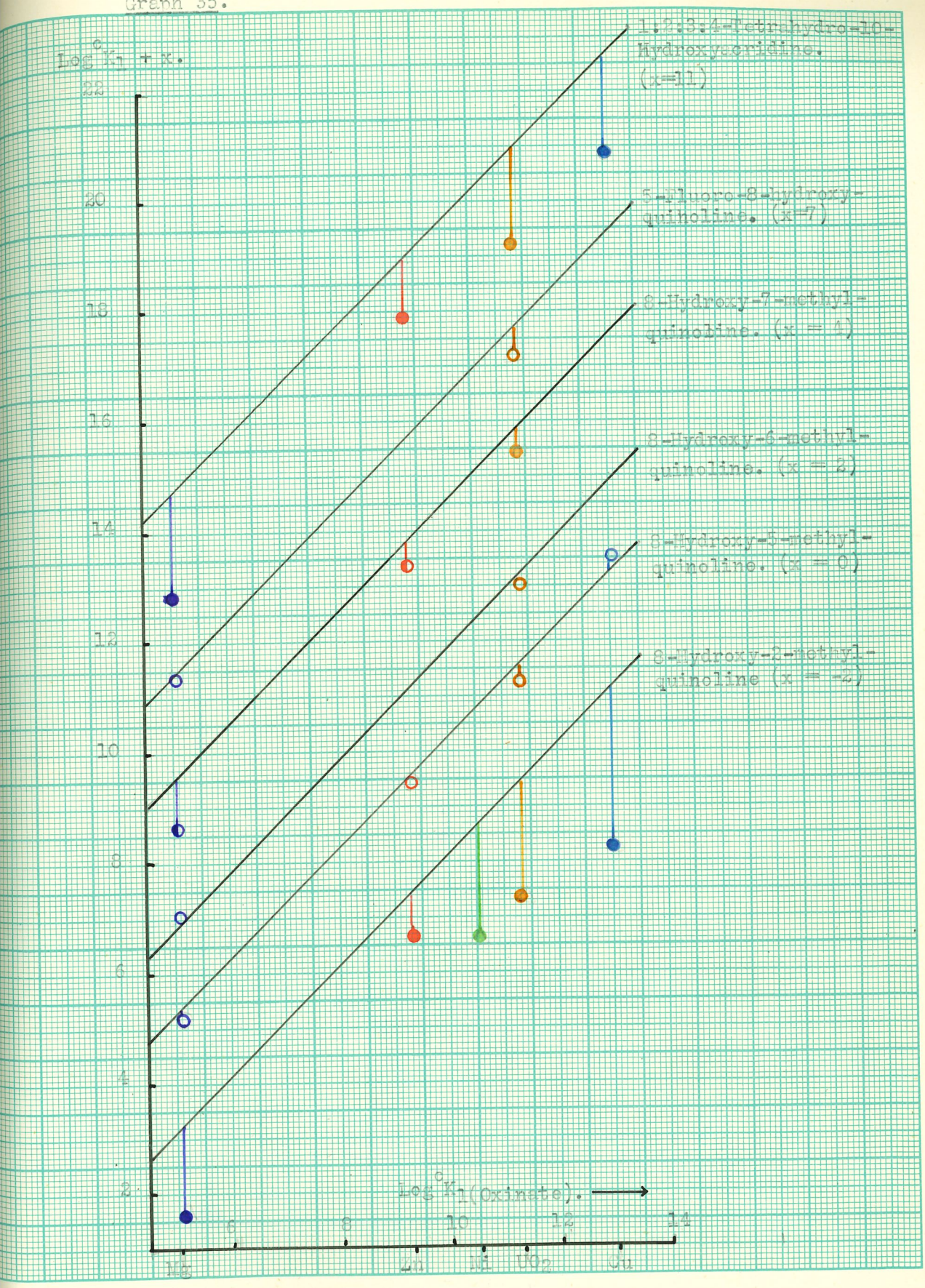
Graph 33. Stability Constants as a Function of pK_{OH}.



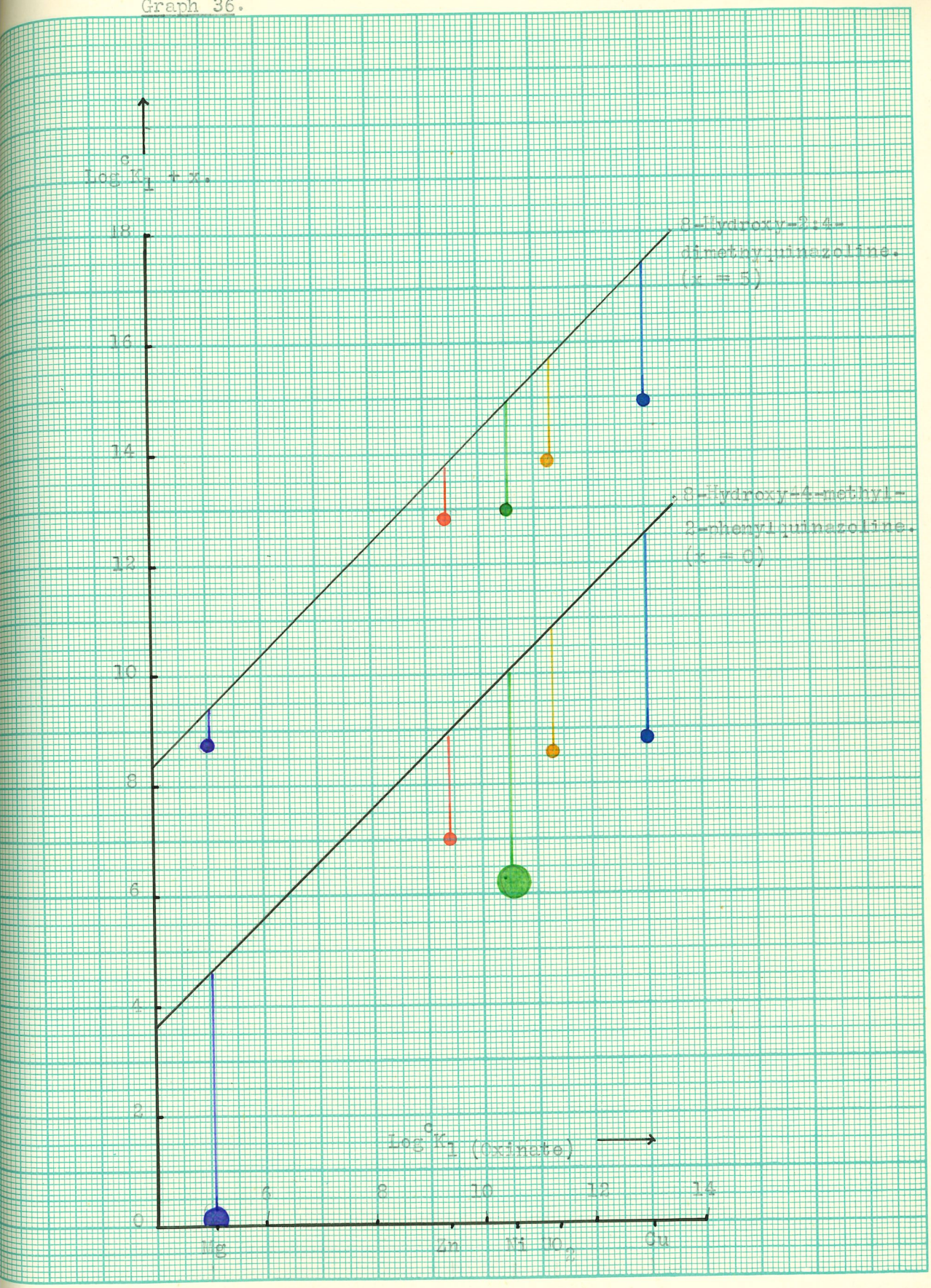
Graph 34. Stability Constants as a Function of pK_{OH}.



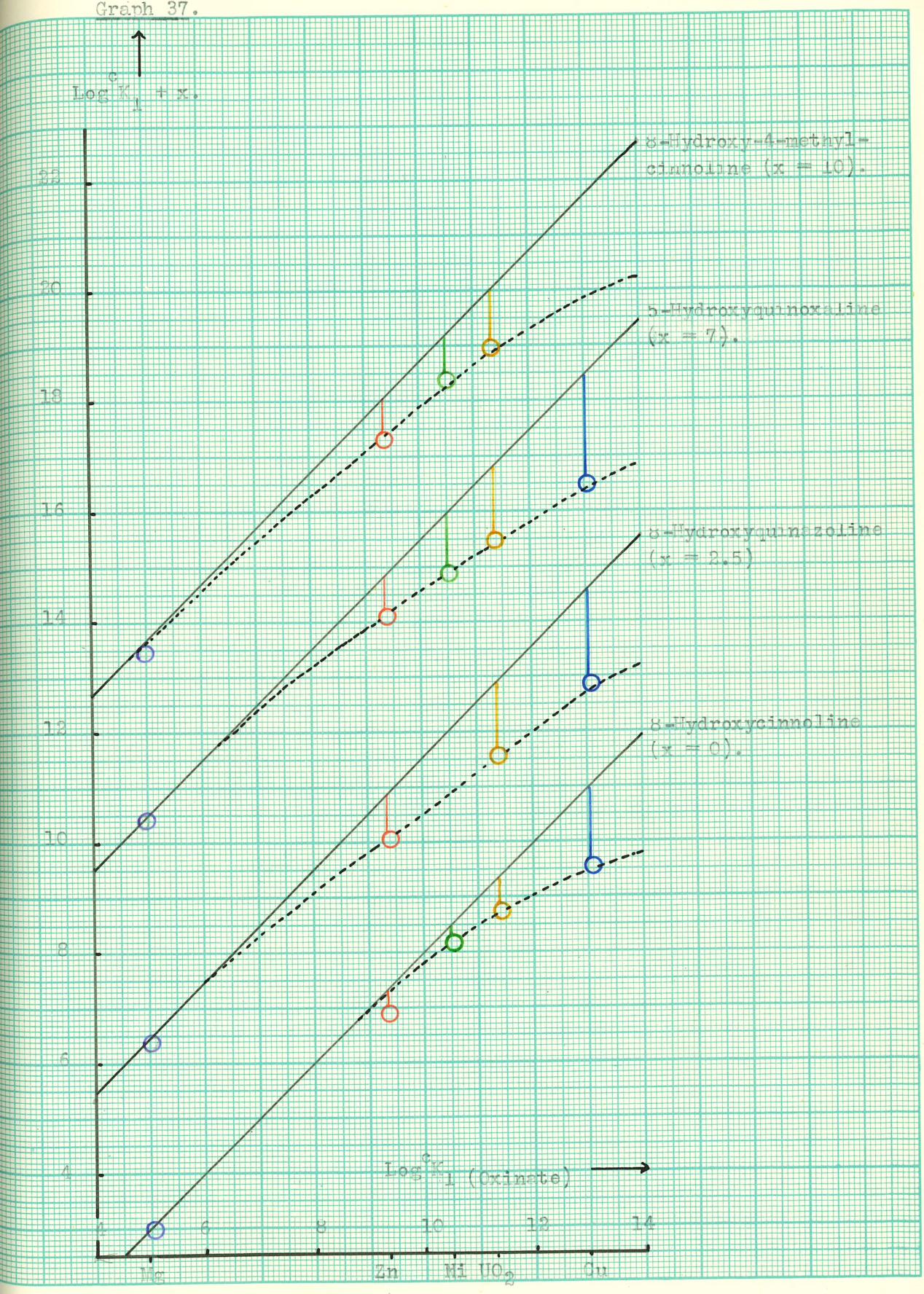
Graph 35.


Log $^{c}K_1$ + x.
22
20
18
16
14
12
10
8
6
4
2
1.2.3.4-Tetrahydro-10-Hydroxyveridine. (x=11)
5-Fluoro-8-hydroxy-quinoline. (x=7)
8-Hydroxy-7-methyl-quinoline. (x = 4)
8-Hydroxy-6-methyl-quinoline. (x = 2)
8-Hydroxy-5-methyl-quinoline. (x = 0)
8-Hydroxy-2-methyl-quinoline (x = -2)
Log $^{c}K_1$(Oxinate). ⟶
6
8
10
12
14

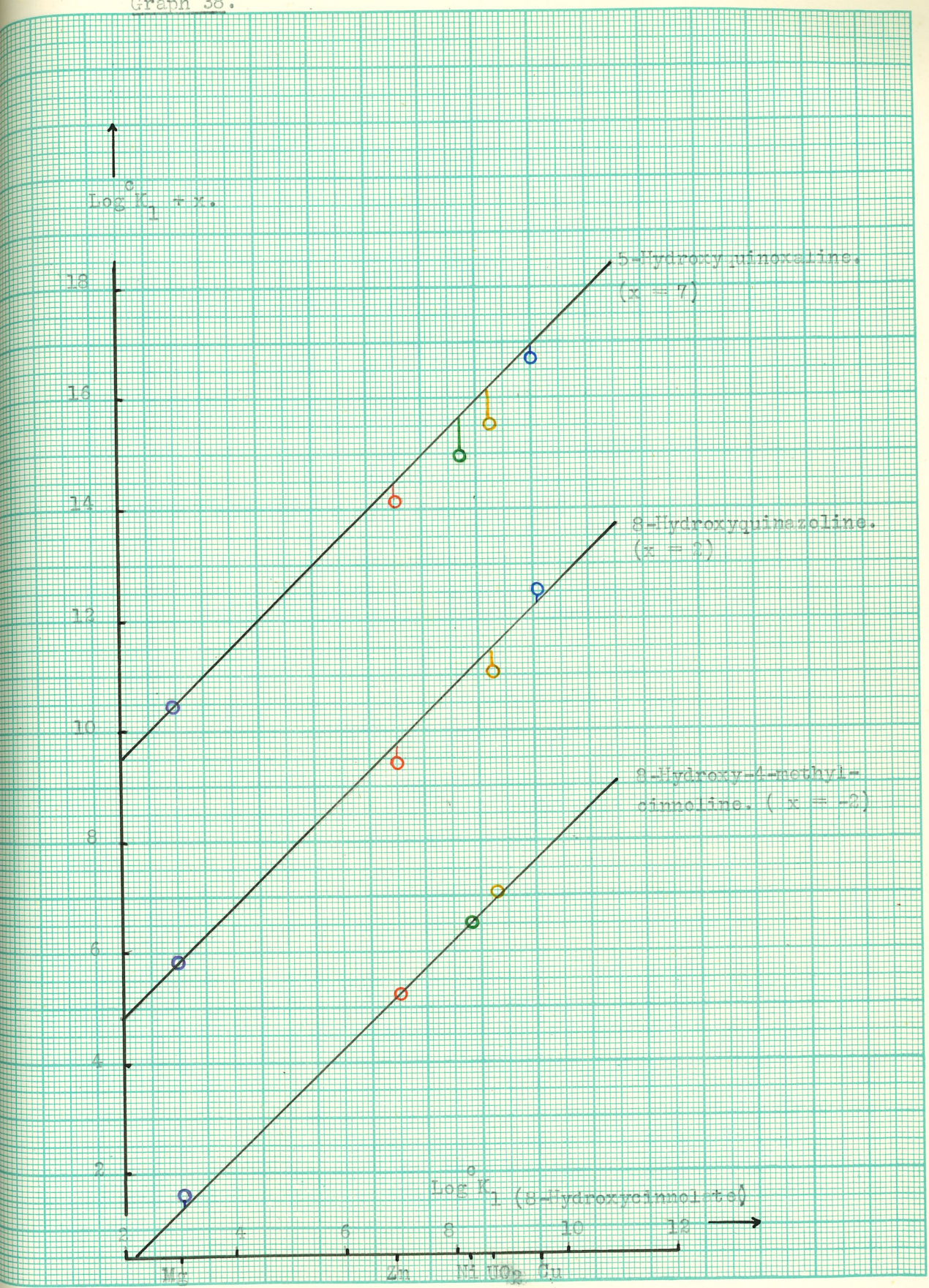
Graph 36.


log K1 + x.
18
16
14
12
10
8
6
4
2
0
8-Hydroxy-2:4-dimethylquinazoline. (x = 5)
8-Hydroxy-4-methyl-2-phenylquinazoline. (x = 0)
log K1 (oxinate)
6
8
10
12
14
Mg
Zn
Ni
Cu

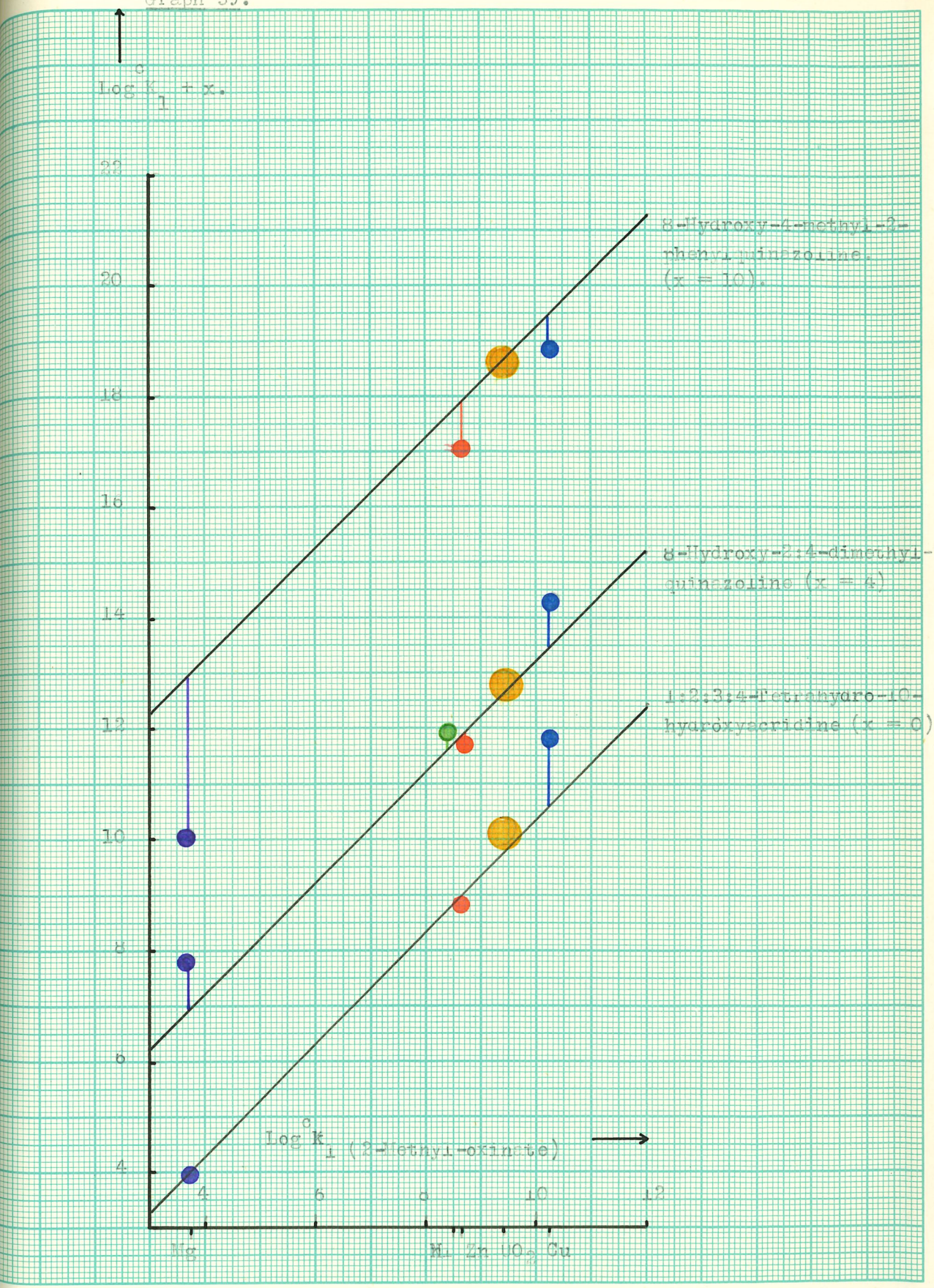
Graph 37.


Log $^{c}K_{1}$ + x.
22
20
18
16
14
12
10
8
6
4
8-Hydroxy-4-methyl-cinnoline (x = 10).
5-Hydroxyquinoxaline (x = 7).
8-Hydroxyquinazoline (x = 2.5)
8-Hydroxycinnoline (x = 0).
Log $^{c}K_{1}$ (Oxinate)
6
8
10
12
14
Mg
Zn
Mi UO_2
Cu

Graph 38.


Log °K1 + x.
18
16
14
12
10
8
6
4
2
5-Hydroxy quinoxaline. (x = 7)
8-Hydroxyquinazoline. (x = 2)
8-Hydroxy-4-methyl-cinnoline. (x = -2)
2
4
6
8
10
12
Log °K1 (8-Hydroxycinnoline)
Mg
Zn
Ni
UO2
Cu

Graph 39.


Log c K1 + x.
22
20
18
16
14
12
10
8
6
4
8-Hydroxy-4-methyl-2-phenylquinazoline. (x = 10).
8-Hydroxy-2:4-dimethylquinazoline (x = 4)
1:2:3:4-Tetrahydro-10-hydroxyacridine (x = 0)
Log c K1 (2-Methyl-oxinate)
4
6
8
10
12
Mg
Zn UO2 Cu

GRAPHS 33 - 39.

Numbers of reagents are those given in Table 11.

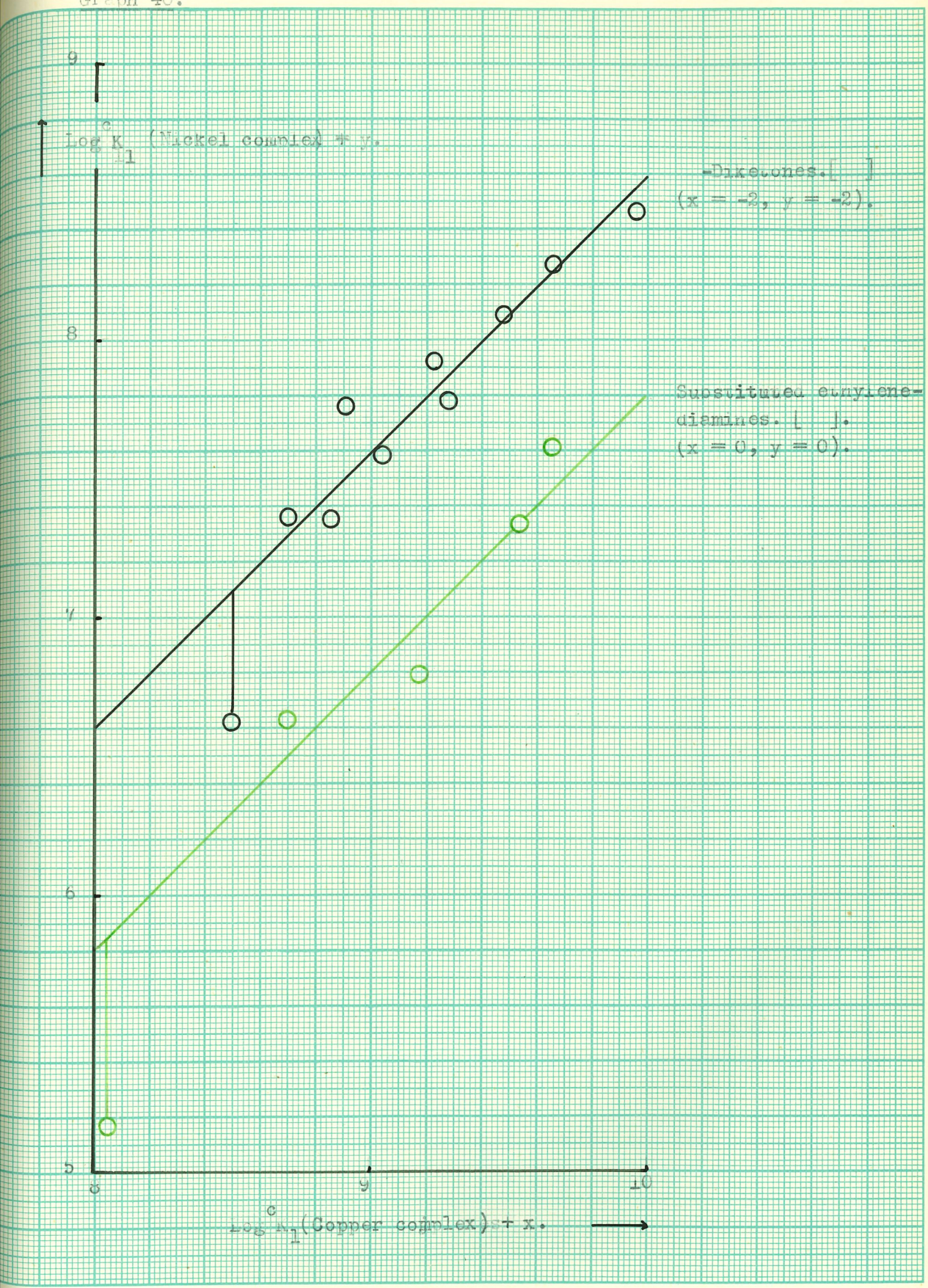
● Refers to reagents with a substituent adjacent to the chelating nitrogen atom.

◑ Refers to 7-methyl oxine.

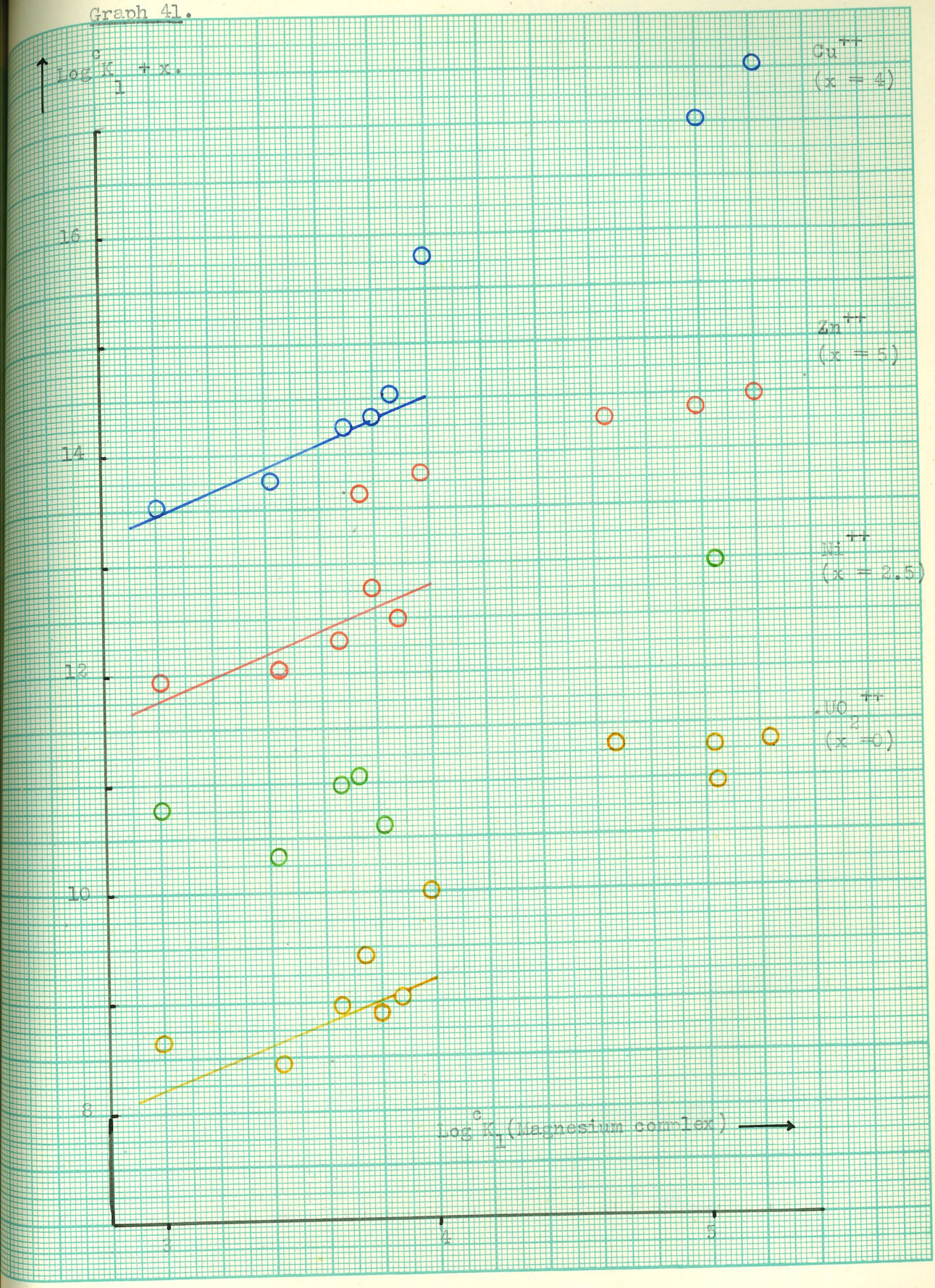
○ Refers to other reagents.

The full lines are of unit slope (except in Graph 34), and, in Graphs 35 - 39, are of intercept pK.

Graph 40.

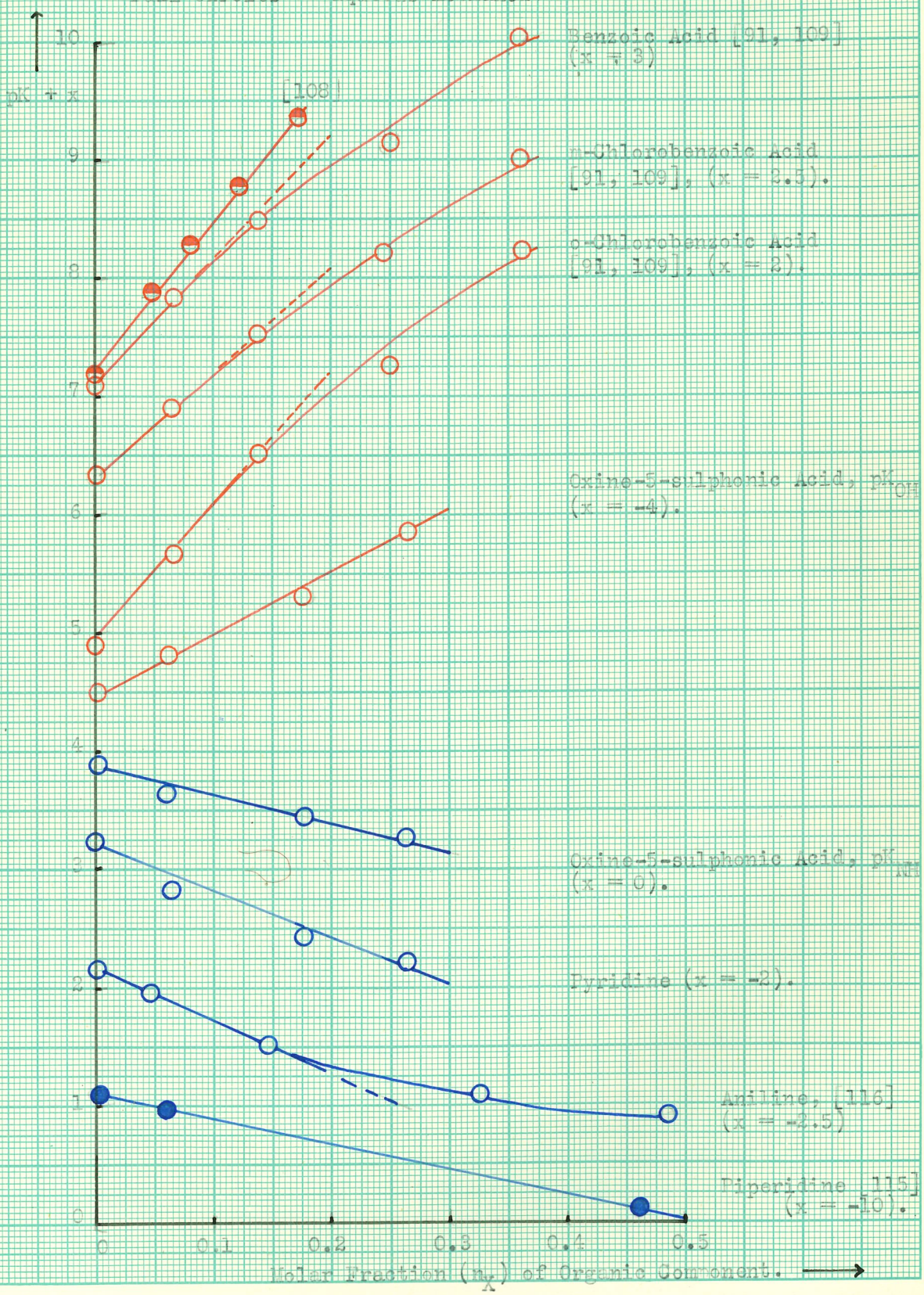

9
8
7
6
5
$\log \overset{c}{K}_{1}$ (Nickel complex) + y.
-Diketones. [ ]
(x = -2, y = -2).
Substituted ethylene-
diamines. [ ].
(x = 0, y = 0).
5
9
10
$\log \overset{c}{K}_{1}$ (Copper complex) + x.

Graph 41.

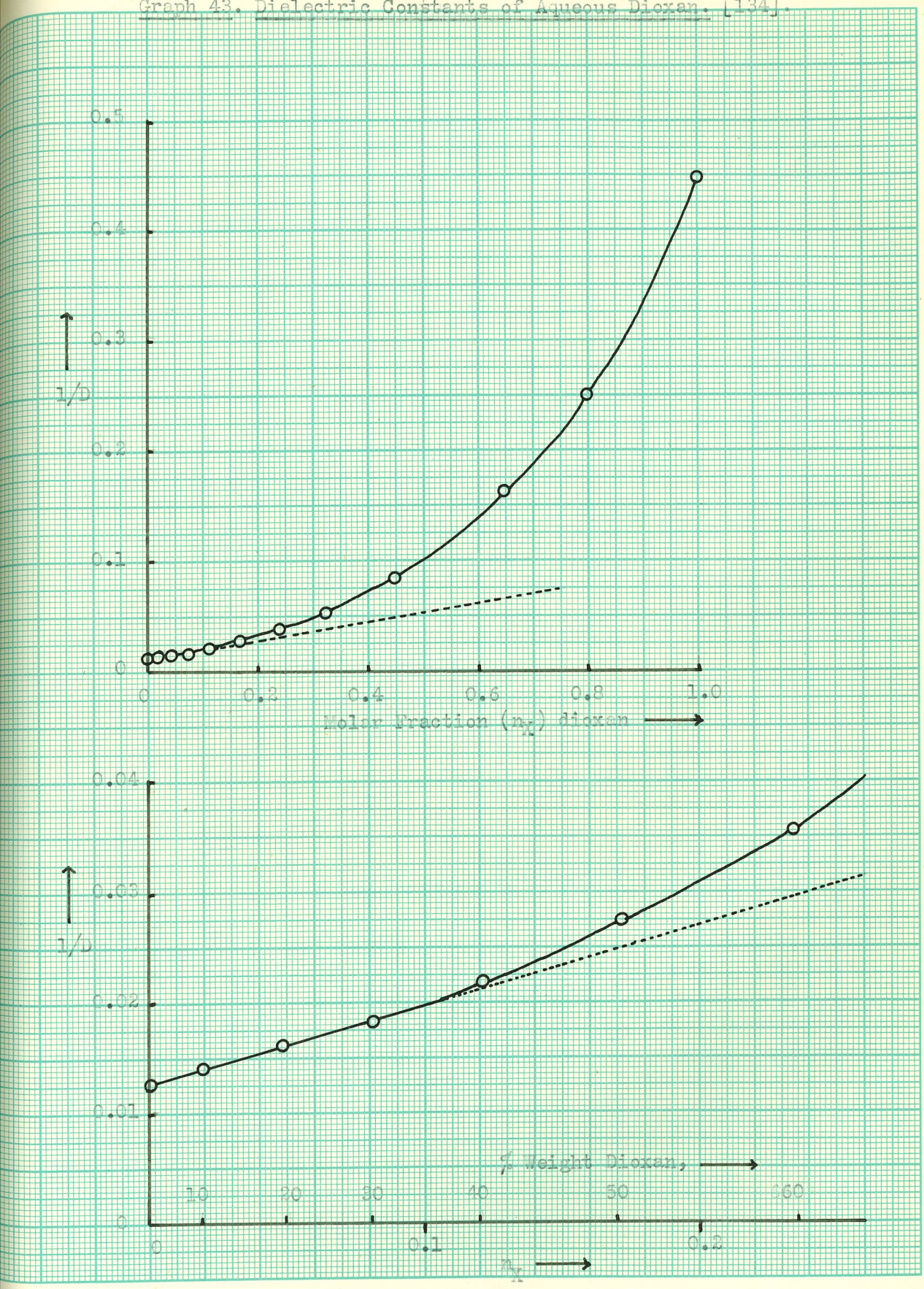

Log $^{c}K_{1} + x$.
16
14
12
10
8
3
4
5
Log $^{c}K_{1}$(Magnesium complex)
Cu^{++}
(x = 4)
Zn^{++}
(x = 5)
Ni^{++}
(x = 2.5)
UO_2^{++}
(x = 0)

Graph 42. The Variation of pK with Solvent.

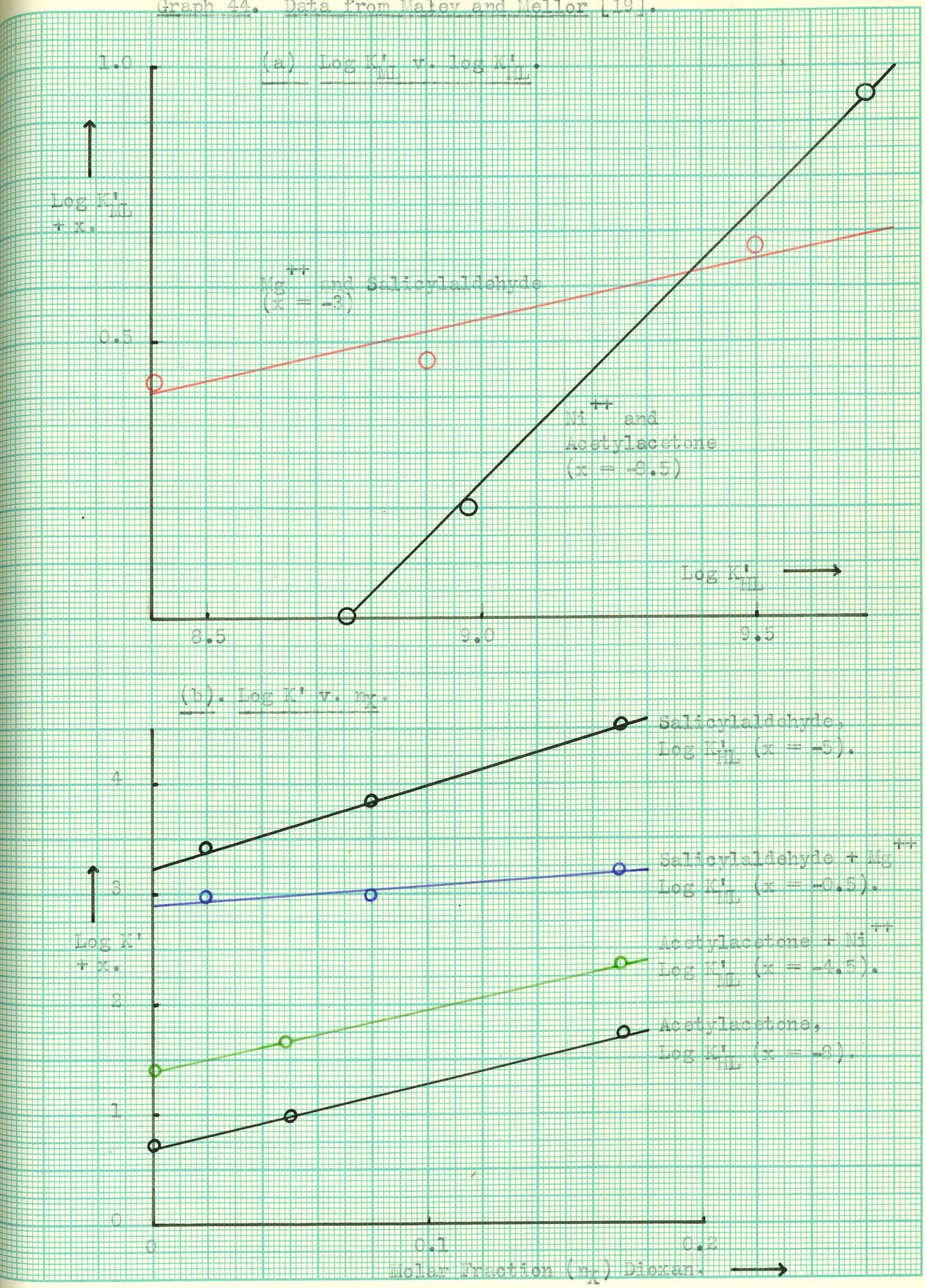
Open circles — aqueous dioxan.
Full circles — aqueous methanol.



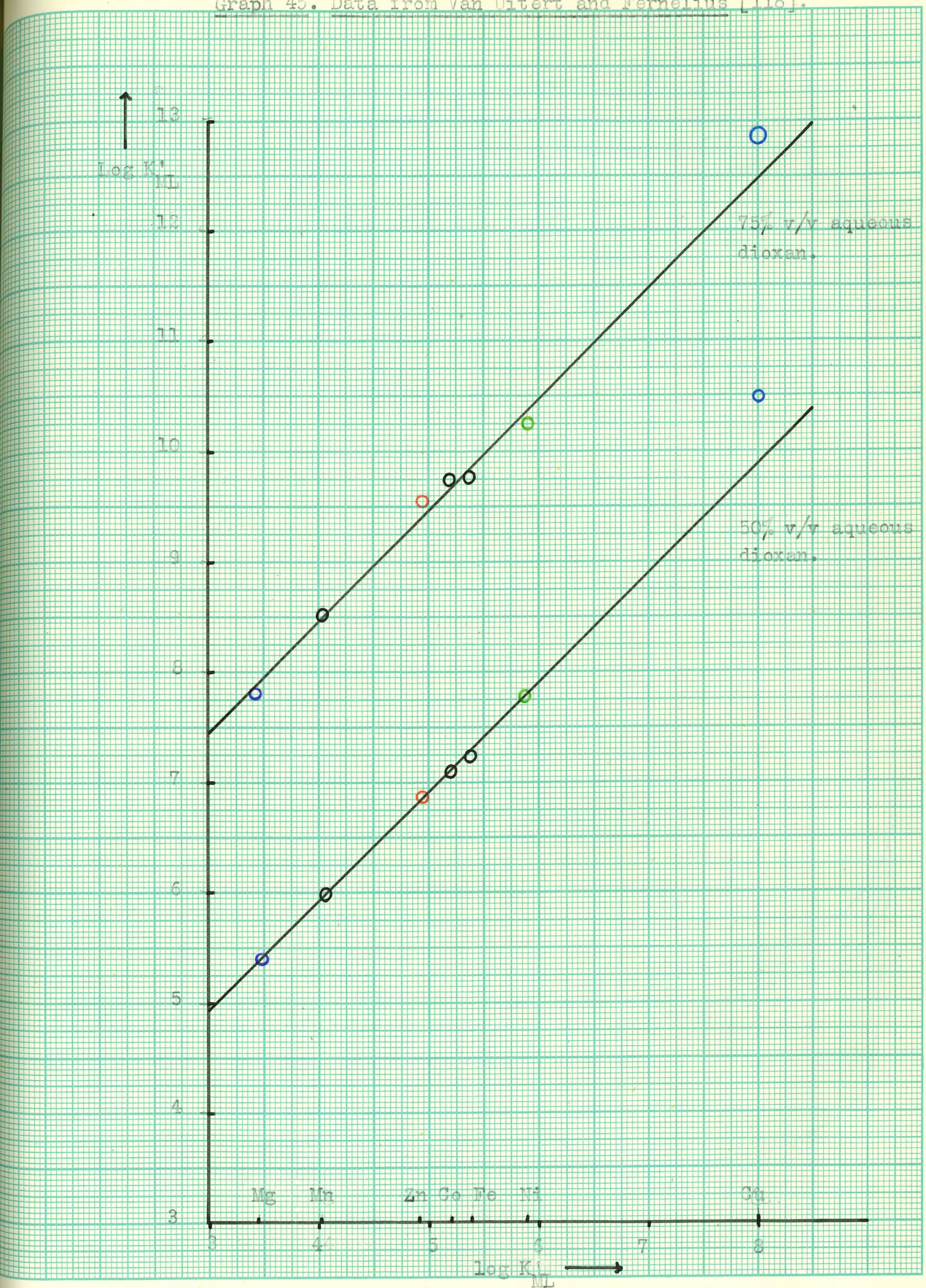
Graph 43. Dielectric Constants of Aqueous Dioxan. [134].



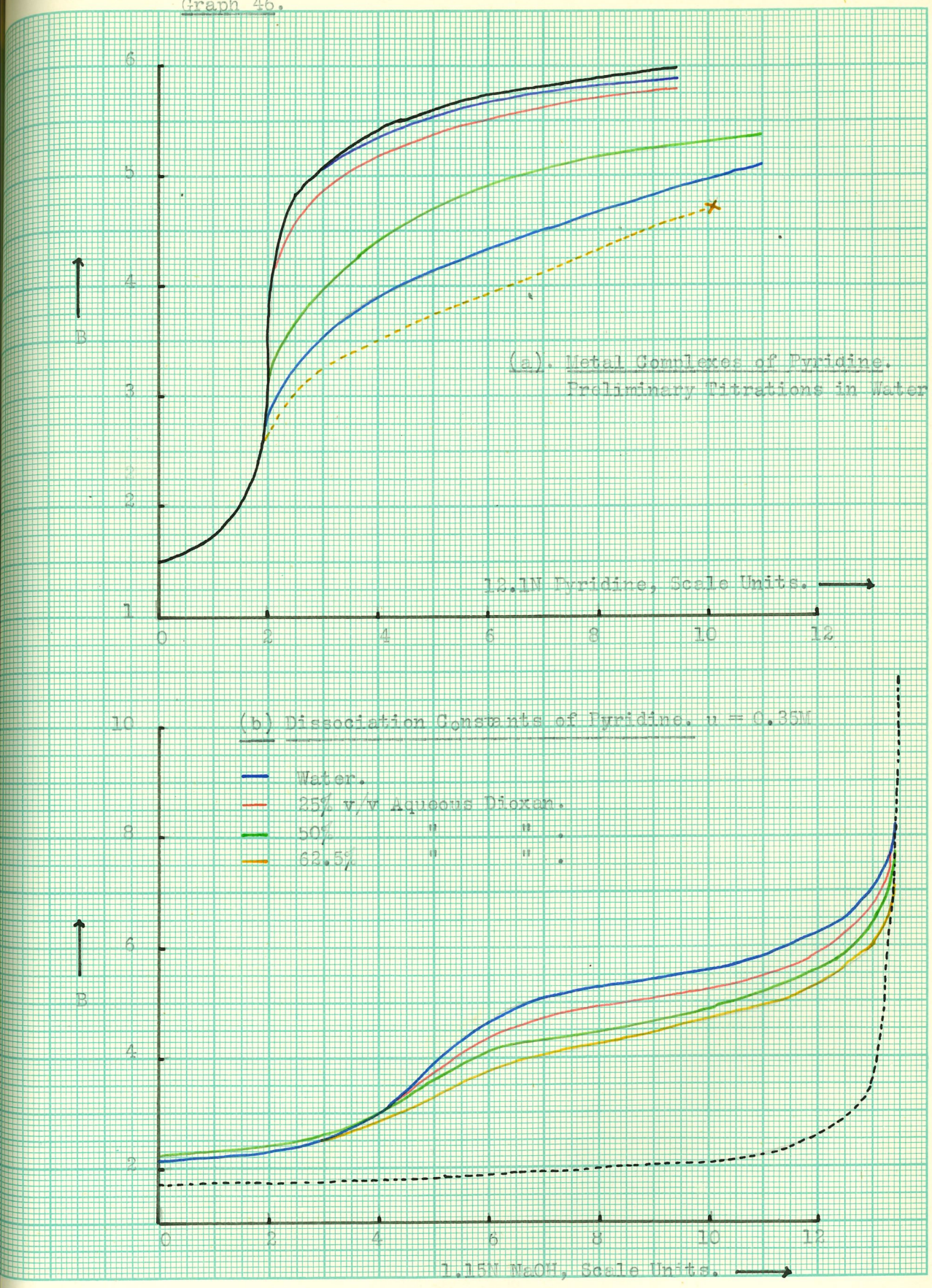
Graph 44. Data from Maley and Mellor [19].



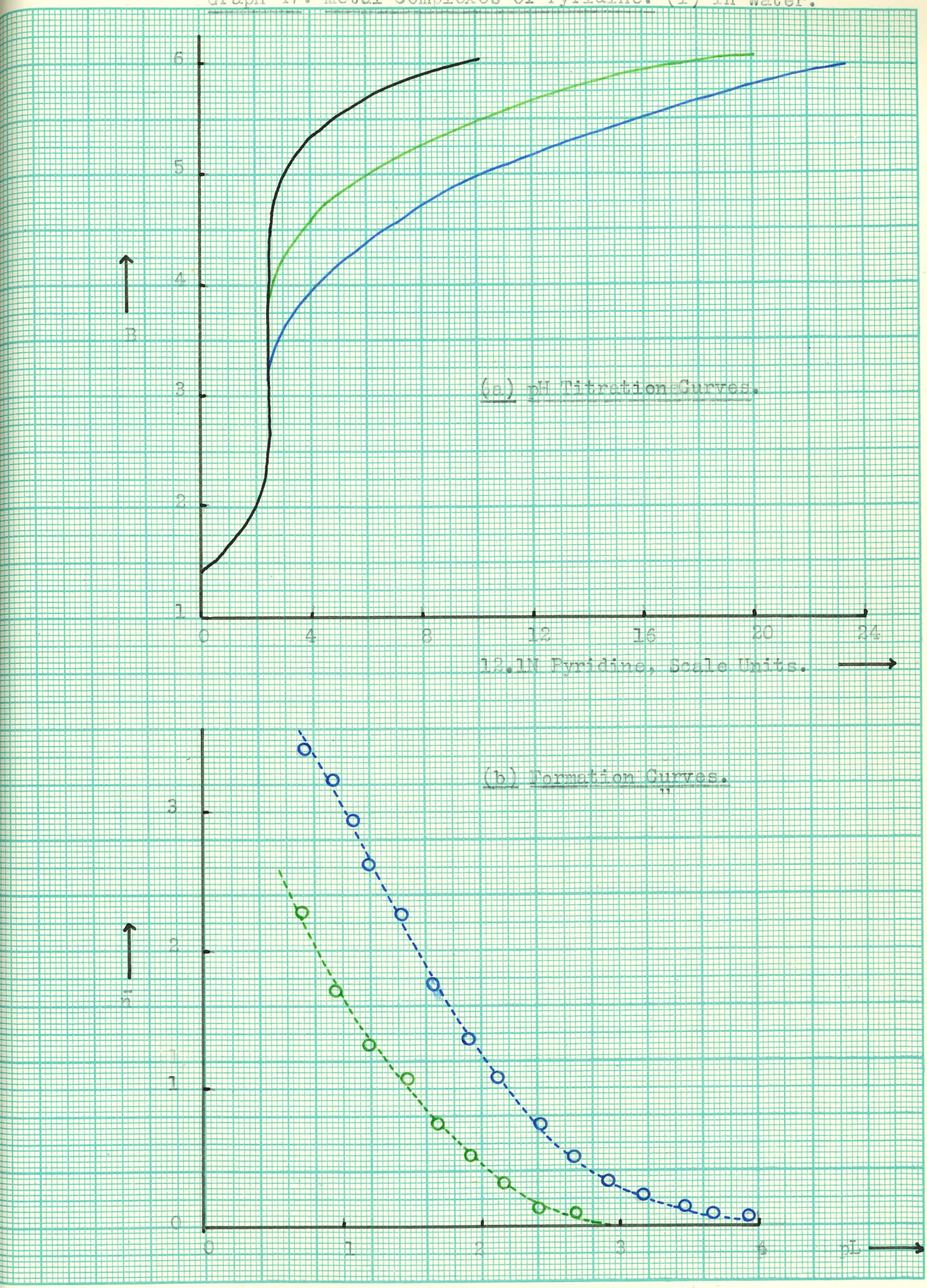
Graph 45. Data from Van Uitert and Fernelius [118].



Graph 46.

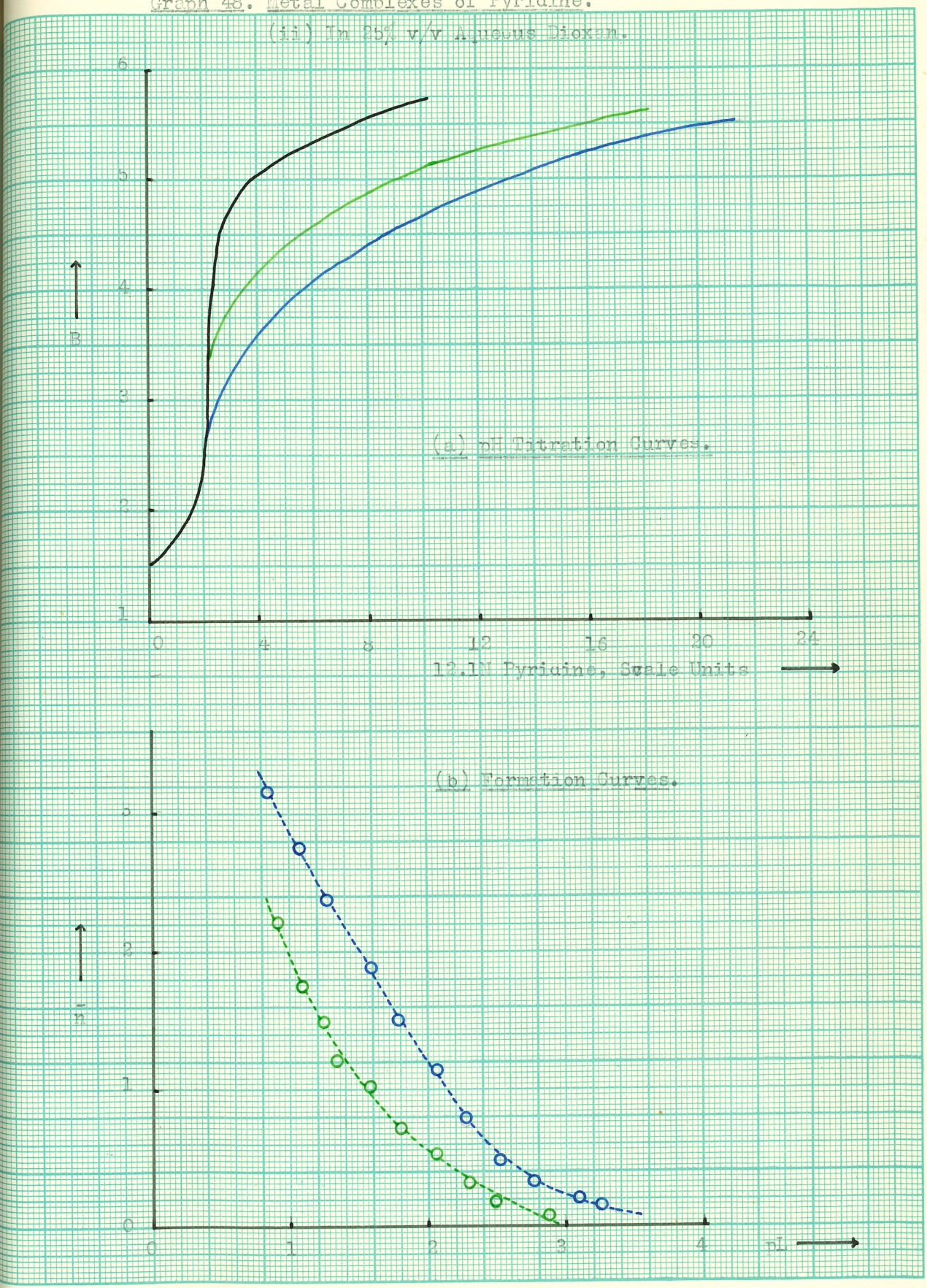

(a). Metal Complexes of Pyridine.
Preliminary Titrations in Water.
B
13.1N Pyridine, Scale Units.
(b) Dissociation Consmants of Pyridine. μ = 0.35M.
Water.
25% v/v Aqueous Dioxan.
50% " " .
62.5% " " .
B
1.15N NaOH, Scale Units.

Graph 47. Metal Complexes of Pyridine. (i) In Water.

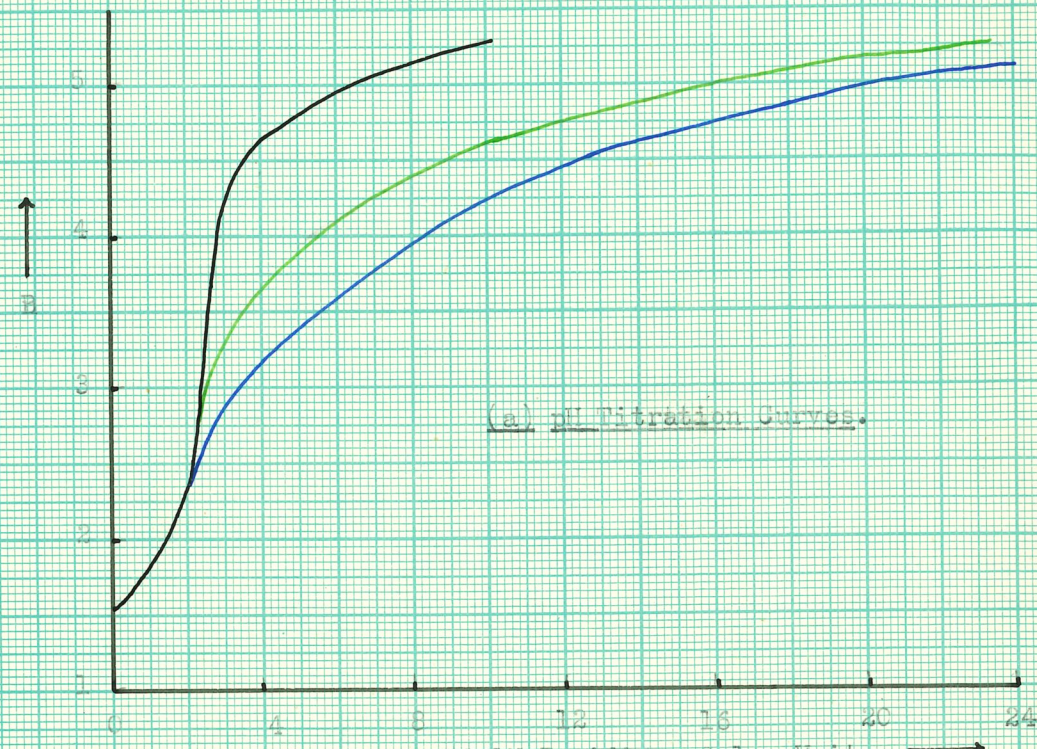


Graph 48. Metal Complexes of Pyridine.

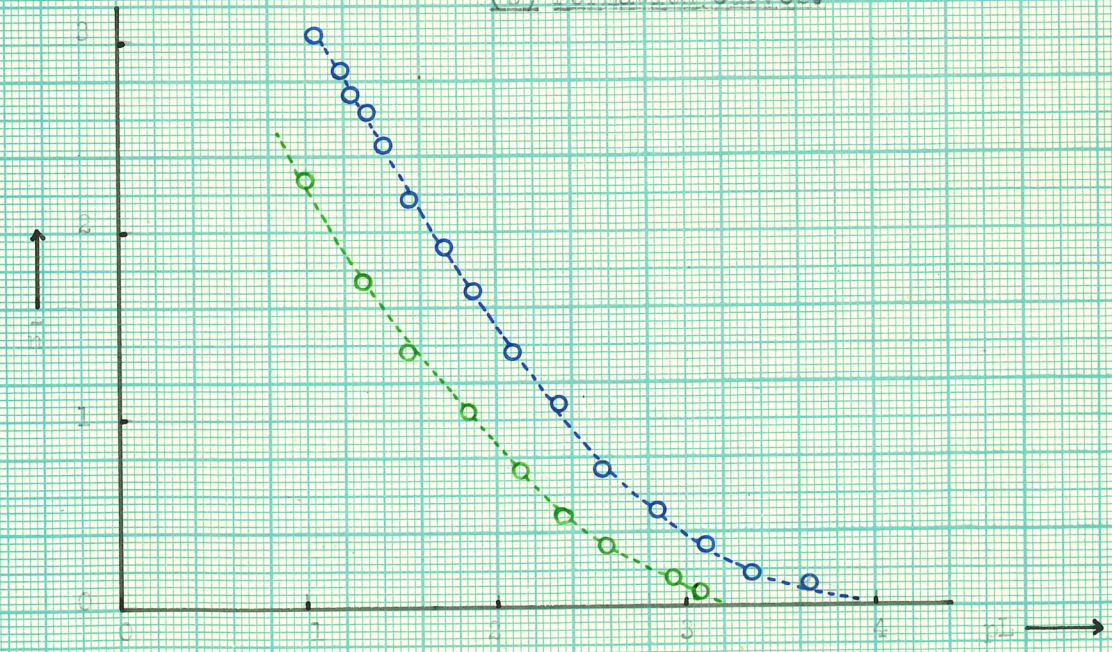
(iii) In 25% v/v Aqueous Dioxan.



Graph 49. Metal Complexes of Pyridine.
(1:1) In 50% v/v Aqueous Dioxan.



(a) pH Titration Curves.



(b) Formation Curves.

GRAPHS 47 - 49.

pH Titration Curves.

—— 0.05N HNO_3 + 0.35M KNO_3.
—— 0.05N HNO_3 + 0.1M $Cu(NO_3)_2$.
—— 0.05N HNO_3 + 0.1M $NiCl_2$.

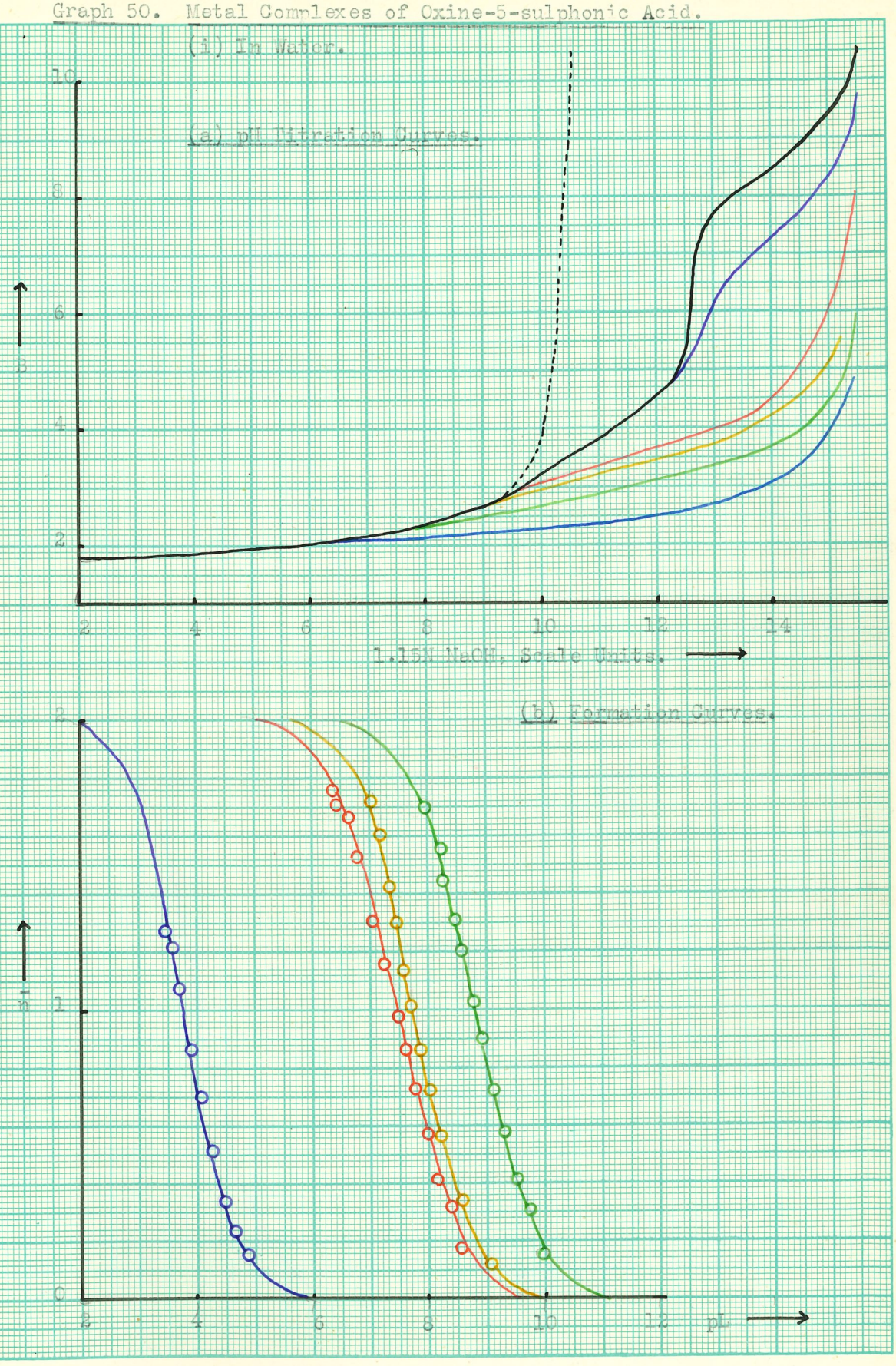
Volume of titration solution = 10.00ml.
1 Scale unit = 0.01992 ± 0.00014 ml.

Formation Curves.

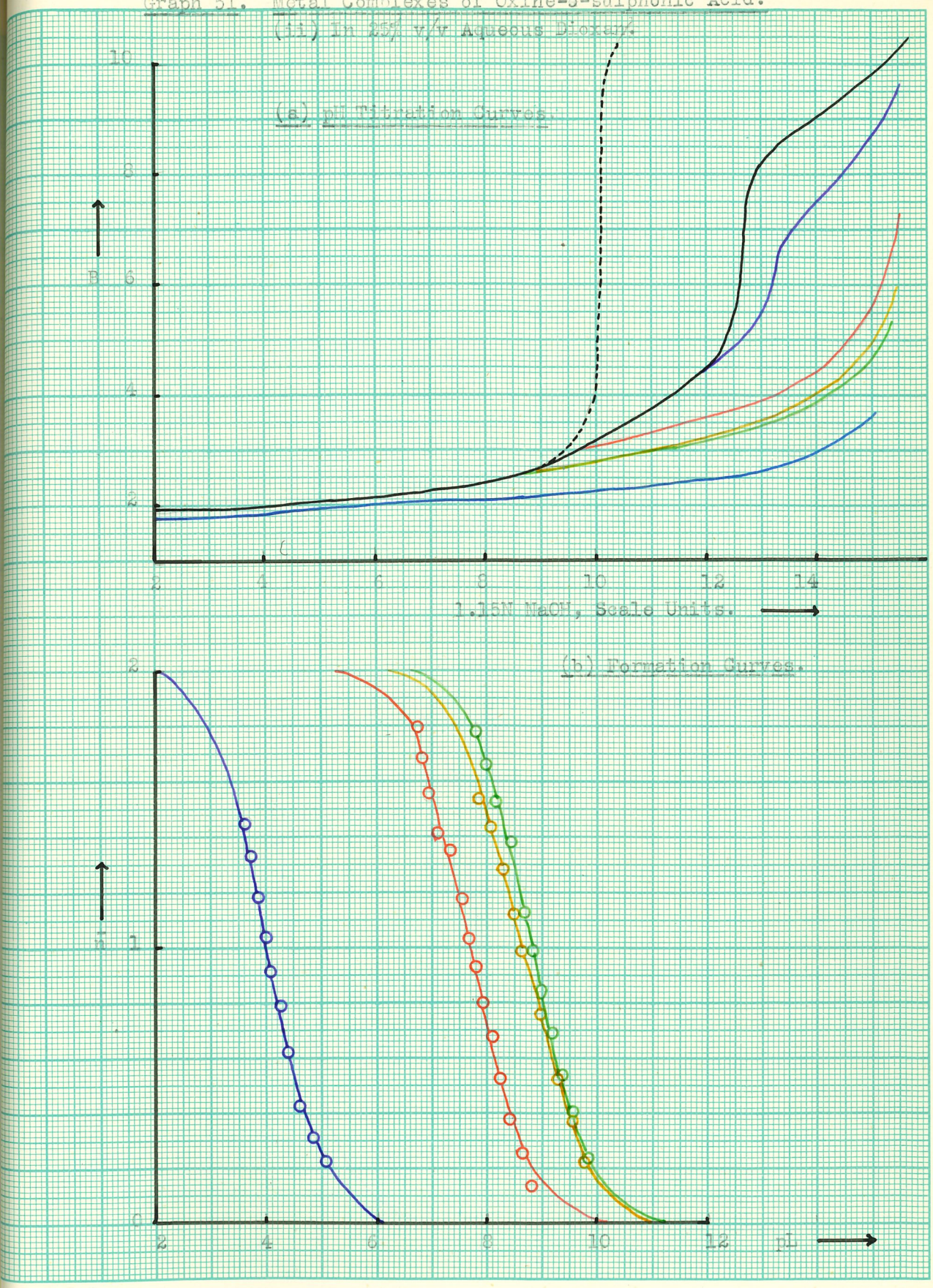
---o--- Experimental Curves for Nickel Complexes.
---o--- " " " Copper " .

Graph 50. Metal Complexes of Oxine-5-sulphonic Acid.

(1) In Water.



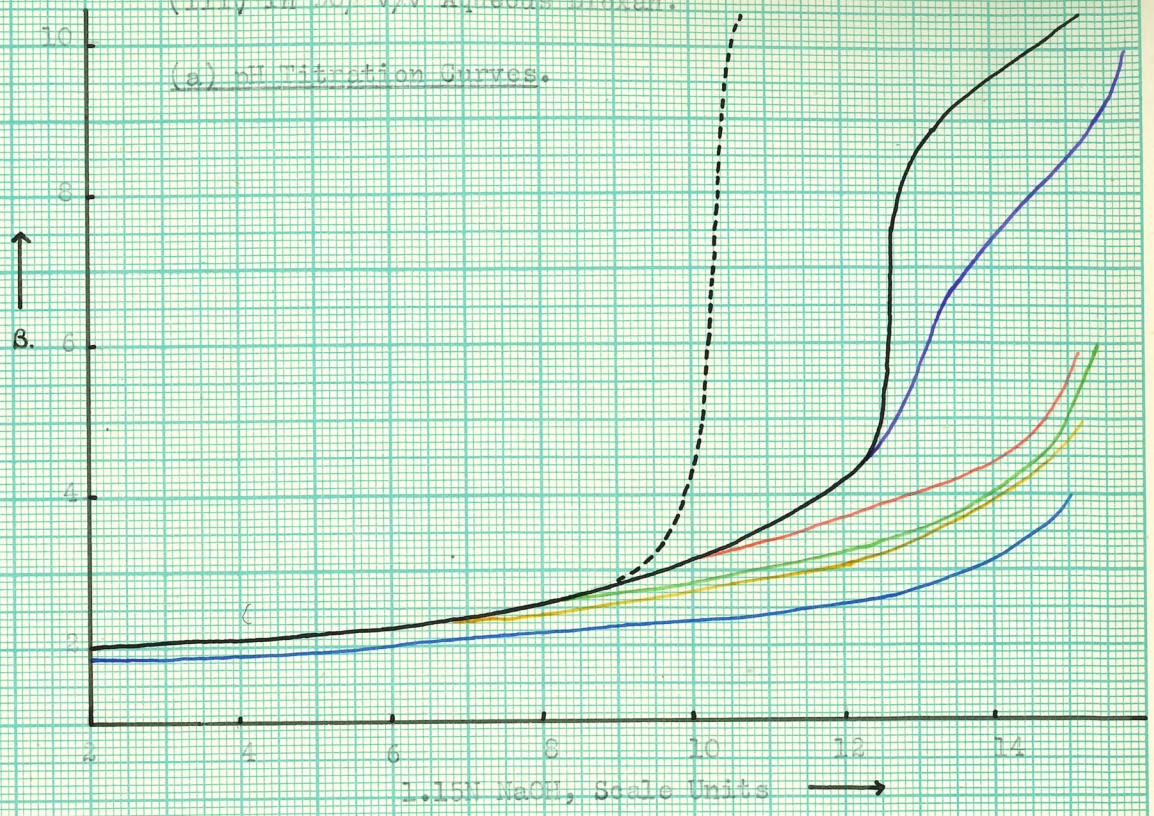
Graph 51. Metal Complexes of Oxine-5-sulphonic Acid.
(iii) In 25% v/v Aqueous Dioxan.



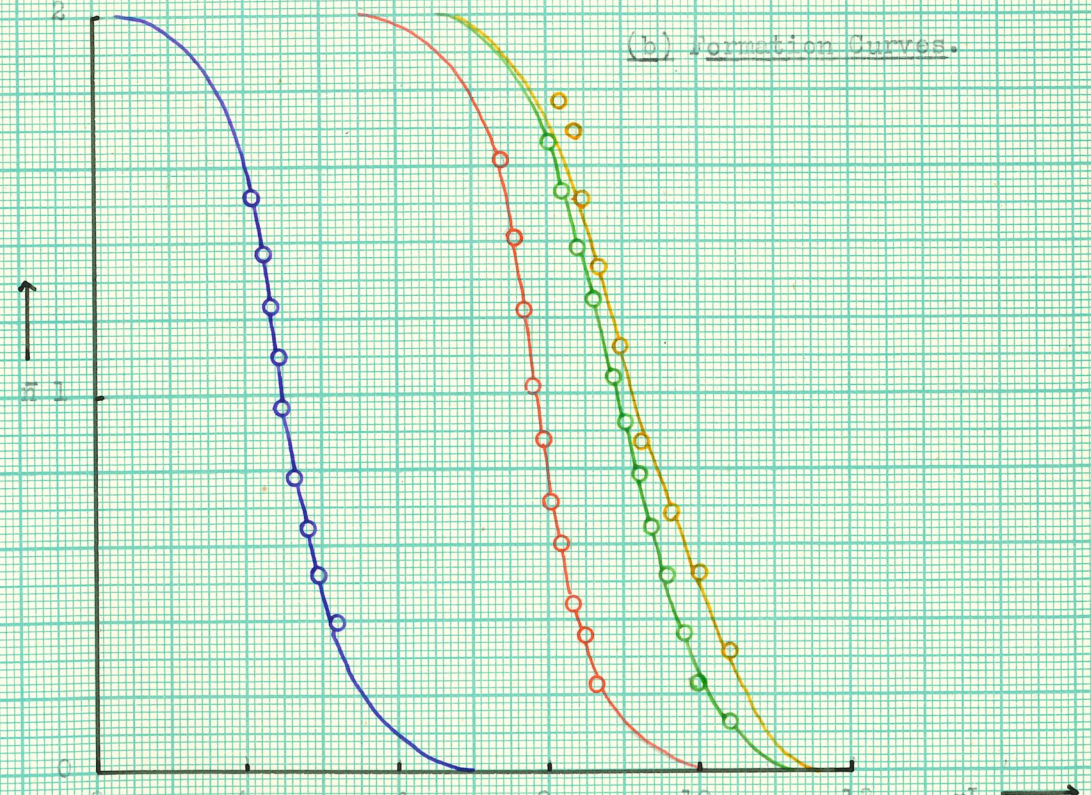
Graph 52. Metal Complexes of Oxine-5-sulphonic Acid.

(iii) In 50% v/v Aqueous Dioxan.

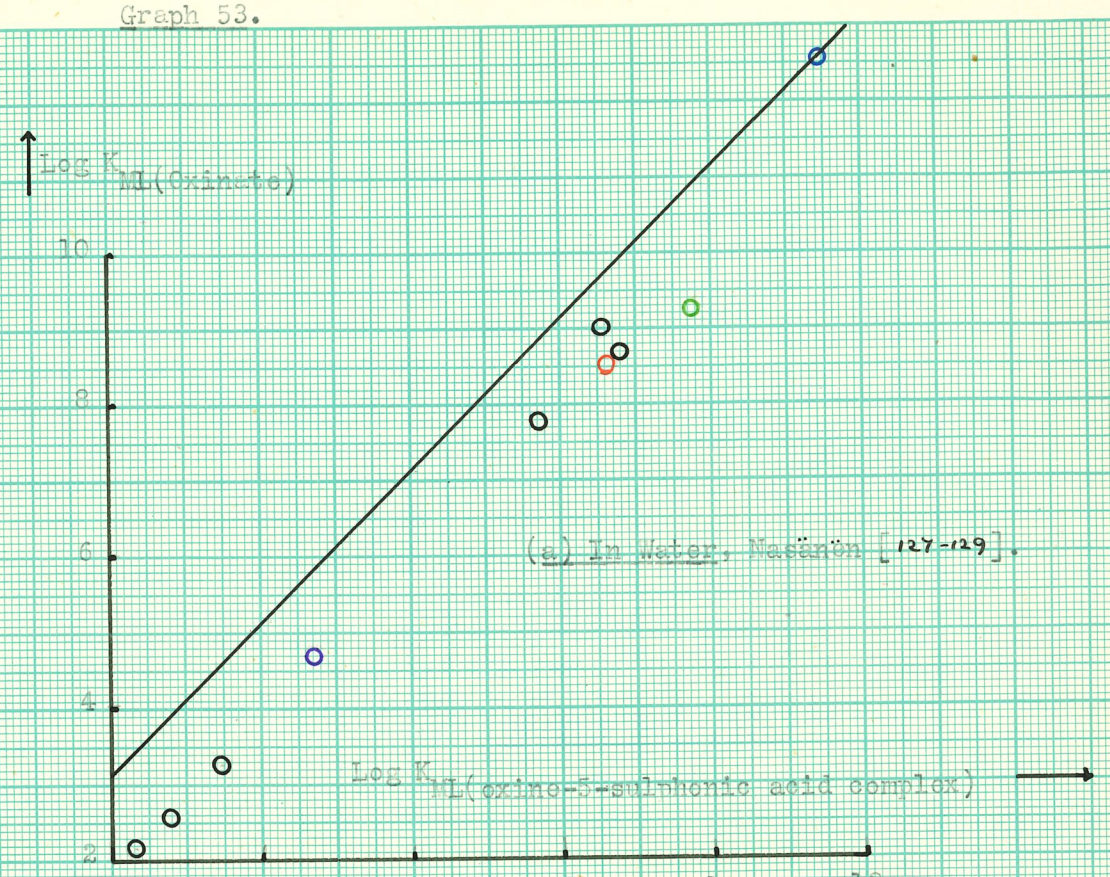
(a) pH Titration Curves.



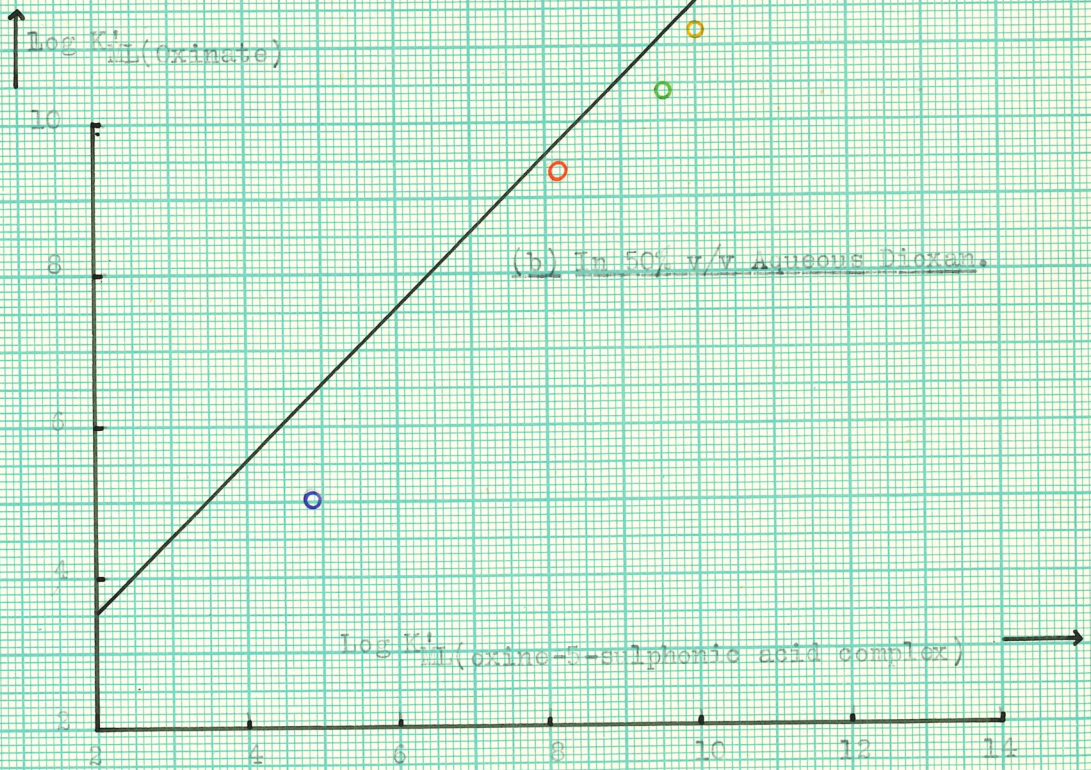
(b) Formation Curves.



Graph 53.



(a) In Water. Masäron [127-129].



(b) In 50% v/v Aqueous Dioxan.

GRAPHS 50 - 53.

pH Titration Curves.

------	0.047N $HClO_4$ + 0.3M $NaClO_4$ — 'A'.
———	'A' + 0.006M Reagent.
———	" " + 0.003M $MgSO_4$.
———	" " + 0.003M $ZnSO_4$.
———	" " + 0.003M $NiSO_4$.
———	" " + 0.003M $CuSO_4$.
———	" " + 0.003M $UO_2(NO_3)_2$.

Volume of titration solution = 10.00 ml.

1 Scale unit = 0.01992 ± 0.00014 ml.

Formation Curves.

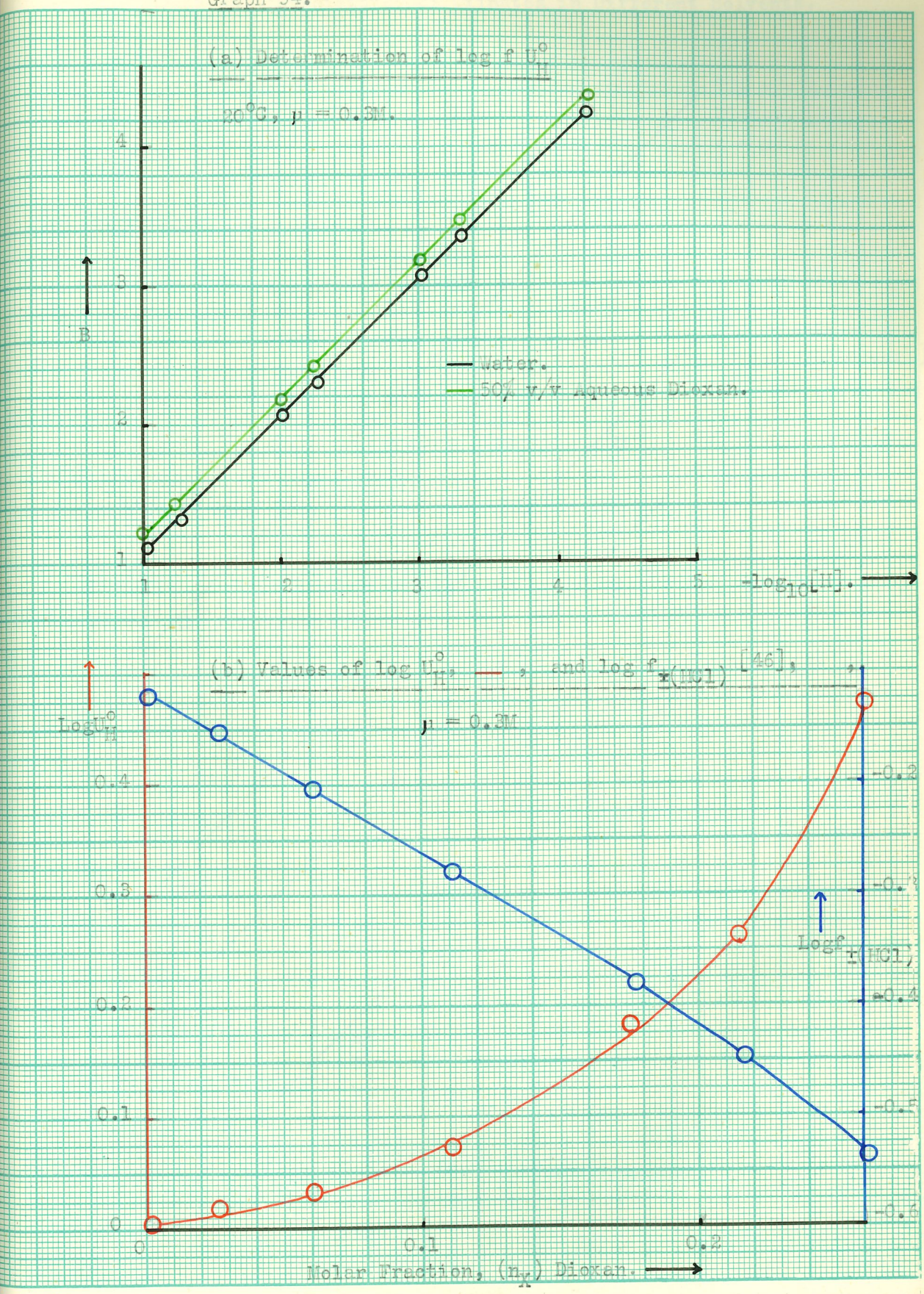
o	Experimental points.
———	Formation curves, claculated using stability constants given in Table 18.

The colours correspond to those metals shown above.

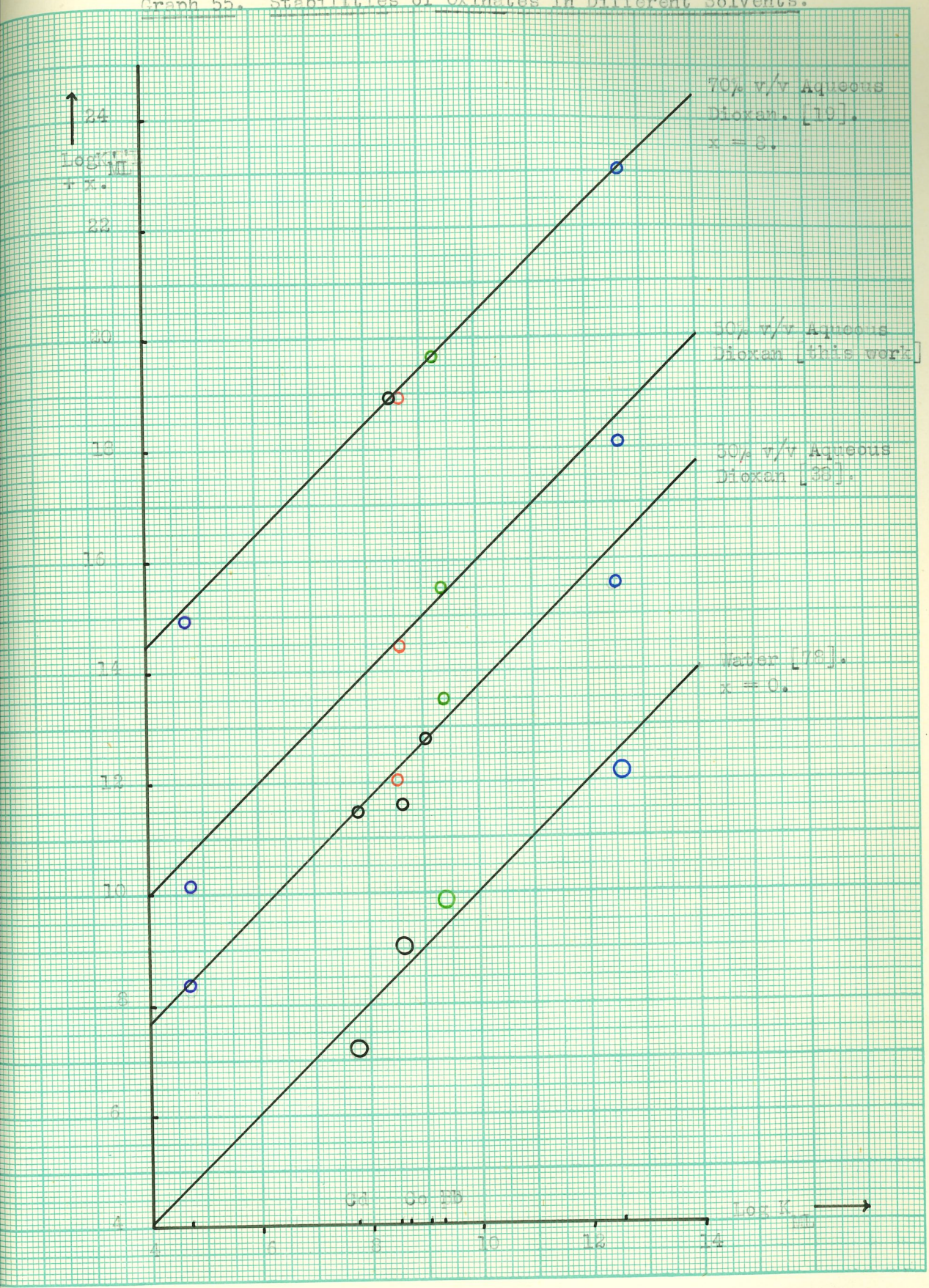
Graph 53.

Full lines of unit slope and of intercept pK.

Graph 54.


(a) Determination of log f U^{o}_{II}
20°C, μ = 0.3M.
B
4
3
2
1
— water.
— 50% w/w aqueous Dioxan.
1
2
3
4
5
$-\log_{10}[H]_{a}$.
(b) Values of log U^{o}_{II}, ——, and log $f_{x(HCl)}$ $[H]_{a}$, ——
μ = 0.3M
$\text{Log}U^{o}_{II}$
0.4
0.3
0.2
0.1
0
-0.2
-0.4
$\text{Log}f_{x(HCl)}$
0
0.1
0.2
Molar Fraction, (n_y) Dioxan.

Graph 22. Stabilities of Oxinates in Different Solvents.



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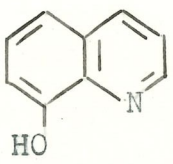
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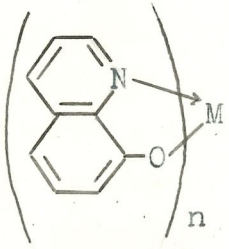
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ABSTRACT.

8-Hydroxyquinoline ('oxine', I) reacts with a wide variety of metal ions to give chelate complexes of the type II, which are commonly used in solvent extraction, and in gravimetric, chromatographic and colorimetric analysis; but the experimental conditions must be rigorously controlled if any degree of selectivity is to be obtained. Greater selectivity might be expected with reagents which form complexes of more varied stability than the corresponding oxinates, and some factors which influence the stability of such complexes are investigated in this work. The effects of substituents acting on the functional group in oxine have been modified by monoaza-substitution in all six possible positions, and by alkyl substitution in various positions of oxine and of some aza-oxines. Steric hindrance to complex formation was studied using reagents having substituents adjacent to the chelating nitrogen atom.



I.



II.

SECTION 1. INTRODUCTION.

Section 1 describes the purpose and scope of this work, and outlines Bjerrum's Treatment of Step Equilibria [1], on which the calculation of stability constants is based. The stoichiometric stability constant ${}^{c}K_{n}$, and the overall stability constant, ${}^{c}\beta_{n}$, of the species ML_n, are defined,

$$ {}^{c}K_{n} = [ML_n]/[ML_{n-1}][L] $$

$$ {}^{c}\beta_{n} = \prod_{1}^{n} {}^{c}K_{n} = [ML_n]/[M][L]^n $$

where charges are omitted for clarity. The degree of formation of the system, $\bar{n}$, is defined as the average number of ligands, L, attached to one central group, M. Thus

$$ \bar{n} = \sum_{n=1}^{n=N} n\,{}^{c}\beta_{n}[L]^n \Big/ \sum_{n=0}^{n=N} {}^{c}\beta_{n}[L]^n $$

where N is the maximum value of n, and ${}^{c}\beta_{o} = 1$. Values of ${}^{c}K_{n}$ may be calculated from the 'formation curve' which represents experimental values of $\bar{n}$ plotted against those of pL = -log[L].

SECTION 2. NEW METHODS OF COMPUTATION.

(a) Spectrophotometric Determination of Dissociation Constants.

A new treatment of the variation of optical absorbancy with pH is described for solutions of a weak acid. It may be used to find the dissociation constants of oxine derivatives in water. If the dissociation constants of a dibasic acid are of similar magnitude, a simple graphical method, derived from this treatment, may be used at any wavelnegth where the molecular extinction coefficient of the dibasic acid H_2L^+ is the same as that of the corresponding base, L^-. Similar treatments, relating pH with other physical properties, are suggested.

(b). The Determination of Experimental Formation Curves in Aqueous or in Mixed Solvents.

A new general method is described for determining formation curves of metal-ligand systems from the relative positions of the pH curves obtained when solutions containing acid alone, acid and reagent, and acid, reagent and metal, are titrated with alkali. A similar method is proposed if a solution of the ligand is used as titrant. The treatment is applicable to all ligands which are conjugate bases of weak acids, and may be used in aqueous or mixed solvents, as values of $\bar{n}$ and pL are calculated from the readings, B, of the pH meter, and no knowledge of the hydrogen ion concentration [H], or activity, is required. The terms B and [H] have been related [2] by an expression of the type

$$\log [H] = \log B + X$$

where X depends of the composition and ionic strength of the solvent, and may be determined experimentally. If the value of X is known, the stoichiometric dissociation constants of the reagents may also be determined from the relative positions of the titrat-

ion curves.

(c) Methods of Computing Successive Stability Constants from Experimental Formation Curves.

The approximations implicit in existing methods for computing stability constants from the experimental formation curve are discussed, and a new 'correction term' method is described. This makes use of the symmetry properties of the formation curve for the particular case N = 2.

The problem of computing the 'best' set of stability constants from inconsistent experimental data is shwon to be soluble by a least squares treatment after an algebraic transformation. The method is applicable to systems of higher complexity. The effect of improved methods of computation is illustrated by examples taken from the literature.

SECTION 3. RESULTS AND DISCUSSION.

(a) Some Physical Properties of the Reagents.

The dissociation constants of the reagents have been determined as some quantitative correlation might be expected between the stabilities of metal-ligand and proton-ligand bonds. Values of the thermodynamic constants were obtained spectrophotometrically in water for 8-hydroxycinnoline (and its 4-methyl derivative), 8-hydroxyquinazoline (and its 2:4-dimethyl derivative) and 5-hydroxyquinoxaline, and values of stoichiometric constants were obtained by pH titration in 50% v/v aqueous dioxan for these reagents, together with 8-hydroxyquinoline (and its 2-,5-,6-, and 7-methyl, and 5-fluoro derivatives), 1:2:3:4-tetrahydro-10-hydroxyacridine, 8-hydroxy-4-methyl-2-phenylquinazoline, and 4-hydroxy-1:5-, 8-hydroxy-1:6- and 8-hydroxy-1:7- naphthyridine. The observed changes in pK_{OH} and pK_{NH} , due to alkyl substitution, may be explained by the inductive effect. Aza-substitution causes a lower-

ing of pK_{NH}, and of pK_{OH} except in reagents where the nitrogen atom is α- or γ- to the hydroxyl group, and tautomerism with the amido-form can occur. Anomalously low values of pK_{NH} for 7-methyl-oxine and 8-hydroxy-4-methyl-2-phenylquinazoline may be due to steric factors.

As values of pK_{NH} for the aza-oxine derivatives do not necessarily to the nitrogen atom in the chelating group, the absorption spectra of the cationic, neutral and anionic species of these compounds, and of oxine, were measured to provide evidence for the position of the more basic centre. This appears to be N_1 in the cinnoline derivatives and in 8-hydroxy-2:4-dimethylquinazoline and 8-hydroxy-4-methyl-2-phenylquinazoline, N_3 in 8-hydroxyquinazoline, and N_6 in 8-hydroxy-1:6-naphthyridine ; the position of the basic centres of the other aza-oxines is uncertain.

Values of wet and dry melting points of the reagents indicate that considerable intramolecular hydrogen bonding occurs in oxine and its alkyl derivatives, and provide further evidence for the position of the basic centres in the aza-oxines. The high dry melting points of 4-hydroxy-1:5-naphthyridine and 8-hydroxy-1:7-naphthyridine, and the large deviation caused by the presence of water, indicate that these compounds exist predominantly as amido-zwitterions. These observations are compatible with values of the oleylol-water partition coefficients, calculated from the data of Albert and Hampton [3]. Further evidence for tautomerism in 4-hydroxy-1:5-naphthyridine and 8-hydroxy-1:7-naphthyridine is afforded by the appreciable differences between the spectra of the neutral species in water and in amyl alcohol; only slight variations are observed for oxine and the other aza-oxines.

(b) Some Factors influencing the Stability of Metal Complexes.

If K'_{ML}, K'_{HL}, are the thermodynamic stability constants of the species ML and HL respectively, measured in a binary mixed solvent, it is shown that

$$\ln K'_{ML} = \ln K'_{HL} + \{(\bar{F}^{o}_{M} - \bar{F}^{o}_{ML} + \bar{F}^{o}_{HL}) + n_X(a_M - a_{ML} + a_{HL} - a_H)\}/RT \quad \ldots(1)$$

where charges are omitted for clarity. $\bar{F}^{o}_{S}$ is the standard partial molar free energy of the species S, and n_X is the molar fraction of the organic component of the solvent. It is assumed that, for each species, a_S is a constant, such that

$$\bar{F}^{t}_{S} = a_S . n_X \quad \ldots(2)$$

where $\bar{F}^{t}_{S}$ is the free energy of transfer of the species S from the standard state in water to the same concentration in a mixed solvent.

Subject to certain assumptions, equation (1) serves as a basis for discussion of factors influencing the stability of metal complexes, and may be used to predict the following relationships :—

(i) If a given metal forms complexes with a series of closely related reagents, $\ln K'_{ML}$ will be a linear function of $\ln K'_{HL}$.

(ii) If two very similar ligands, P and Q, react with a series of metals, a plot of $\ln K'_{MP}$ will be a straight line of unit slope and of intercept $\ln K'_{HP}/K'_{HQ}$.

(iii) If two very similar metals, M and N, react with a series of closely related ligands, a plot of $\ln K'_{ML}$ against $\ln K'_{NL}$ will be a straight line of unit slope.

Large deviations from the predicted lines would indicate that some specific factor, such as steric hindrance, were operative. Some empirical plots of these types in the literature are discussed with reference to equation (1).

For some short series of metals, the term $\bar{F}^{o}_{M}$ is found to be

an approximately linear function of the second ionisation potential, I; if this were also the case for the term $\bar{F}^{o}_{ML}$, a linear relationship between $\ln K'_{ML}$ and I might be expected. This may account for the linear plots reported for a few metals with given ligands, but, although points for other metals may lie fortuitously on these lines, no general relationship between stability and ionisation potential is to be expected.

Irving and Williams [4] predict a universal 'stability order' for any series of metals in which the ionisation potential, I and the inverse ionic radius, 1/r, increase in the same order, provided that entropy changes be neglected. It is now shown that the terms I, 1/r and $\bar{F}^{o}_{M}$ should all increase in the same order. The importance of the term $\bar{F}^{o}_{M}$ is illustrated with reference to the stability of the complexes of zinc and of the first transition series, and the possibility of stability orders for other groups of metals is discussed.

(c) The Stability of Some Metal Complexes in 50% v/v Aqueous Dioxan.

Values of stoichiometric stability constants in 50% v/v aqueous dioxan are reported for the complexes of Mg^{++}, Zn^{++}, Ni^{++}, Cu^{++} and UO_2^{++} ions with the reagents listed on page A3, and are discussed with reference to plots of the type (i),(ii) and (iii) described above. Large deviations from the predicted lines are obtained with sterically hindered reagents, while smaller deviations, which are more marked for copper than for magnesium, are attributed to differences in the co-ordinating power of the chelating nitrogen atoms in the various reagents. Anomalous behaviour may also be due to strong bonding between a metal ion and one of the chelating atoms, with resultant modification of the co-ordinating power of the other. The effect of the nature of the metal

on the value of the ratio $^{c}K_1/^{c}K_2$, and on the extent of steric hindrance, is discussed.

It is found that 4-hydroxy-1:5-naphthyridine and 8-hydroxy-1:7-naphthyridine react with Cu^{++} and Ni^{++} ions in acid solution to give complexes which decompose as the pH is raised, and that 8-hydroxy-1:6-naphthyridine forms more than one type of complex with Zn^{++} and Cu^{++}. Explanations of these phenomona are suggested.

(d) The Influence of the Solvent on Stability.

Intercomparison of results obtained in different solvents demands an understanding of the effect of the solvent on stability. Many factors govern the stability of H—L bonds, but if equation (2) is valid for the species H, L and HL, a linear relationship between $\ln K'_{HL}$ and n_X would be expected; it is found that an increase in the molar fraction of the organic component results in a linear increase in the stability of O—H bonds, and a linear decrease in the stability of N— H bonds. An explanation of this behaviour is suggested. At low values of n_X for water-dioxan mixtures, the observed linear dependence of the inverse dielectric constant, 1/D, upon n_X accoubts for the linear relationships between $\ln K'_{HL}$ and 1/D which have been reported.

The stabilities of many complexes containing O—M bonds also increase linearily with n_X, and obey certain relationships predicted from equation (1). Results obtained in this work confirm preliminary reports that, in contrast to N—H bonds, N—M bondsare slightly stabilised by an increase in the organic content of the solvent. Stability constants of Mg^{++}, Zn^{++}, Ni^{++} and UO_2^{++} complexes of oxine-5-sulphonic acid are reported for water-dioxan mixtures, and the effect of the solvent on stability is correlated with the relative importance of O—M and N—M bonds in these complexes. Stability constants of metal oxinates have been measured

in various solvents by different workers, are also discussed.

SECTION 4. EXPERIMENTAL DETAILS.

The thesis ends with a description of the titration apparatus and experimental conditions.

References.

[1]. J. Bjerrum, "Metal Ammine Formation in Aqueous Solution", P.Haase and Son, Copenhagen, 1941.

[2]. Van Uitert and Haas, J. Amer. Chem. Soc.1953, 75, 451.

[3]. Albert and Hampton, J., 1954, 505.

[4]. Irving and Williams, J., 1953, 3192.

vii + 179 leaves
really vii + 183 leaves
as 1, 6, 43 + 95
have 2parts each.