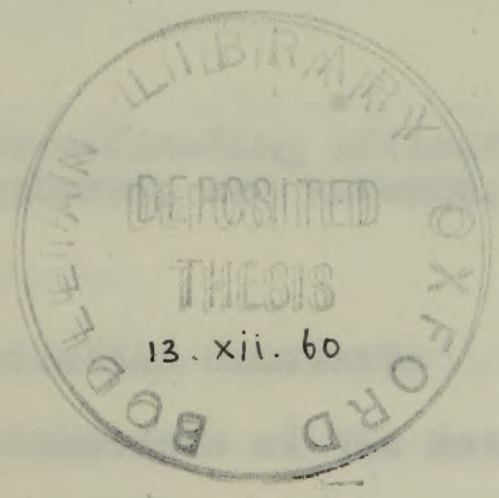
THE STABILITY OF METAL COMPLEXES.

A thesis submitted by

L. D. PETTIT.

in supplication for the degree of

Doctor of Philosophy.



Keble College

OXFORD.

Trinity Term, 1960.

CONTENTS.

page

Acknowledgements

Notes on Symbolism 1.

SECTION I. INTRODUCTION. . . . . 3.

The Scope of the Present Work 3.

The Experimental Approach 8.

SECTION II. RESULTS AND DISCUSSION. . . . . 11.

PART I.

The Amino-acids 11.

The Acid Dissociation Constants

The Glycine Derivatives 12.

PIPDA and PIPMA 18.

The Chelate Stability Constants

The Glycine Derivatives 27.

PIPDA and PIPMA 41.

PART II.

The Relative Co-ordinating Affinities of Nitrogen,, Phosphorus, and Arsenic. 51.

Introduction 51.

The Acid Dissociation Constants 53.

The Stability Constants of the Metal Complexes

The Metals Chosen and the Methods Used 59.

Some Individual Complexes

(a) The Complex of PHENASDA with Copper 64.

(b) The Silver Complexes 66.

page

(c) The Mercury^{II} Complexes 70.

The Complexes of PHENASDA and chlor-PHENASDPA

(a) With Class (a) Metals 74.

(b) With Class (b) Metals 76.

The Complexes of Diphenylaminepropionic acid and its Phosphorus and Arsenic analogues 83.

SECTION III. EXPERIMENTAL DETAILS . . . . . 86.

Introduction

Proton Displacement and Stepwise Equilibria 86.

Use of Concentrations in lieu of Activities 89.

The Hydrogen Electrode Titration Apparatus 91.

The Preparation of Electrodes 93.

The Measurement of E^{o} 97.

The Glass Electrode Titration Apparatus 99.

Titrations in the presence of Silver Ions 102.

The Measurement of Stability Constants of Mercury(II) complexes 105.

The Preparation of Carbonate-free Alkali 108.

SECTION IV. ORGANIC PREPARATIONS. . . . . 111.

CC-dimethylglycine 111.

cyclo-Hexane-1-amino-1-carboxylic acid 113.

cyclo-Heptane-1-amino-1-carboxylic acid 114.

Phenyliminodiacetic Acid 114.

Piperazine-NN'-diacetic Acid (PIPDA) 116.

Piperidine-N-acetic Acid (PIPMA) 117.

page

Diphenylamine-N-propionic Acid 118.

The Copper - PIPDA Complex 121.

The Copper - PHENASDA Complex 122.

SECTION V. METHODS OF CALCULATION . . . . . 124.

The Amino-acids

The Acid Dissociation Constants 124.

The Chelate Stability Constants 125.

Other Ligands

The Acid Dissociation Constants 127.

The Chelate Stability Constants 128.

The Stability Constants of Silver Complexes 131.

The Stability Constants of Mercury^{II} Complexes 133.

SECTION VI. THE EXPERIMENTAL RESULTS . . . . . 136.

The Experimental Results

The Amino-acids 136.

PIPDA and PIPMA 147.

Other Ligands 150.

Graphs 156.

REFERENCES . . . . . 177.

APPENDIX - An Automatic Recording Titrimeter. 181.

ABSTRACT.

ACKNOWLEDGEMENTS.

The Author wishes to express his thanks to the following:

Dr. H. Irving for his continued advice and encouragement during this research;

The Department of Scientific and Industrial Research for a maintenance grant;

Dr. F.G. Mann of the University of Cambridge and Prof. W.C. Fernelius of Pennsylvania State University for gifts of samples.

NOTES ON SYMBOLISM.

In this work the symbols used by the Chemical Society Special Publication 'Stability Constants' have been generally used. For example, K_n refers to the stability constant of the complex ML_n relative to ML_{n-1} and so corresponds to the symbol K_{ML_n} used by Schwarzenbach.

i.e. $$K_n = \frac{[ML_n]}{[ML_{n-1}][L]} = K^L_{ML_n}.$$

The overall stability constant of the species ML_n will be written β_n. Thus $\beta_n = K_1 K_2 \ldots K_n$.

The constants normally refered to are stoichiometric constants. When thermodynamic, or true, constants are used the left-hand superscript T is added,

e.g. $$^T K_2 = \frac{(ML_2)}{(ML)(L)} .$$

When it is considered necessary to make it clear which of several possible constants is referred to a right-hand superscript showing one of the species taking part is inserted, together with a subscript showing the species resulting from the reaction.

e.g. $$K^M_{MHL} = \frac{[MHL]}{[M][HL]} \qquad \text{while} \quad K^H_{MHL} = \frac{[MHL]}{[H][ML]} .$$

When referring to acid dissociation constants the

reciprocal of the logarithm of the constant of the dissociation reaction is used and is signified by pK_n where n is the n^{th} hydrogen ion to dissociate from the ligand. e.g., considering the acid H_2L,

$$K_1 = \frac{[H][HL]}{[H_2L]} \quad \text{and} \quad K_2 = \frac{[H][L]}{[HL]} .$$

The degree of formation of proton complexes is signified by $\bar{n}_A$ while for metal complexes the subscript is omitted.

SECTION ONE.

INTRODUCTION.

THE SCOPE OF THE PRESENT WORK.

For several years it has been noticed that metals which can act as acceptors to ligand atoms could be divided into two types: those which form their most stable complexes with the first atoms of each group of the periodic table, i.e. nitrogen, oxygen, and fluorine (class (a) metal ions), and those forming more stable complexes with the second or a subsequent atom of any particular group (class (b)) (1,2).

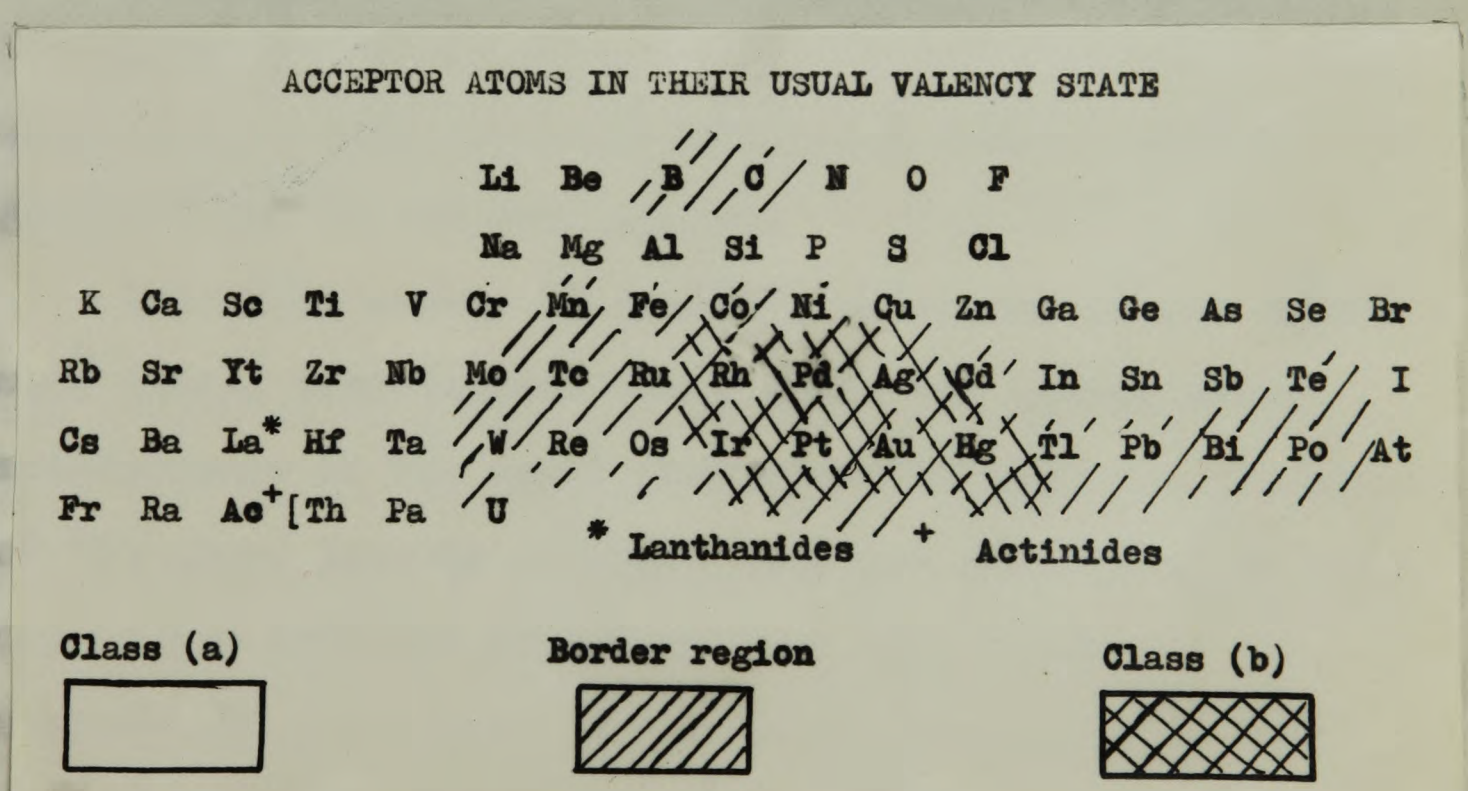


Fig. 1.

The majority of metals tend to belong to class (a). This class also contains the hydrogen ion so the affinities of ligands for class (a) acceptors tend to run approximately parallel to their basicities. Hence the relative stabilities of the complexes formed are what would be expected were the complex formation essentially electrostatic. The acceptors from class (b) are few in number and all lie in a central position of the periodic table. (see fig. I.) There is, however, no rigid boundary between the elements of these two classes and although much is known about the co-ordinating tendencies of all the ligand atoms in Group VII of the periodic table, (3) quantitative data relating to heavier donor atoms of groups V and VI are very sparse.

The first member of group V, nitrogen, is one of the most widely investigated donor atoms but quantitative measurements of the donor properties of subsequent members of the group towards acceptor ions are restricted to only one or two detailed investigations (4). There are two reasons for this. Most of the metals of class (b) form inert complexes which, in general, cannot be studied by equilibrium methods. Hence often only qualitative comparisons of their stabilities can be made. In addition to this, molecules containing trivalent phosphorus or arsenic as

donor atoms tend to be readily oxidised. If this valence state is stabilised by substitution of suitable aromatic groups on the donor atoms, the solubility in water generally becomes impracticably low.

In this work the acid dissociation constants and metal stability constants of phenylarsine-As-diacetic acid (i) have been measured. This acid is directly comparable with phenyliminodiacetic acid (ii) and similar to cyclo-hexylamine-NN-diacetic acid (iii), which was also fully investigated.

$\emptyset$-As.$(CH_2COOH)_2$ (i)

$\emptyset$-N.$(CH_2COOH)_2$ (ii)

$C_6H_{10}N.(CH_2COOH)_2$ (iii)

p-Cl.C_6H_4.As.$(CH_2CH_2COOH)_2$ (iv)

The complexes of p-chlorophenylenearsine-As- dipropionic acid (iv) were also studied. From the results obtained direct comparison of the donating abilities of nitrogen and arsenic with a series of metals can be made. Two class (b) metals were selected, silver and mercury, while class (a) metals were represented by copper^{II}, nickel and zinc.

Further qualitative comparisons can be made from results obtained by a study of the complexes of

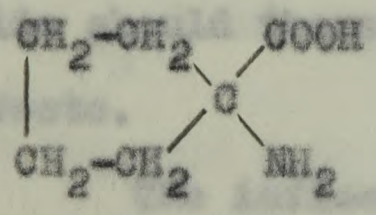
diphenylamine-N-propionic acid ($\emptyset_2N.CH_2CH_2COOH$) and its phosphorus and arsenic analogues. However on account of the low solubility of these compounds in water, 20% aqueous dioxan had to be used as solvent. Conditions, therefore, were not identical with those of previous determinations so that a rigid quantitative comparison with other data is not possible.

Results from all of these investigations are tabulated and discussed in section II, Part II, of this thesis.

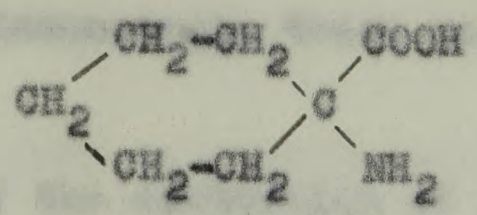
Before turning to the investigation of the donor properties of phosphorus and arsenic as ligand atoms, a series of C-substituted glycines was examined. The compounds studied are enumerated below:-

$NH_2-CH.CH_3-COOH$ (v)

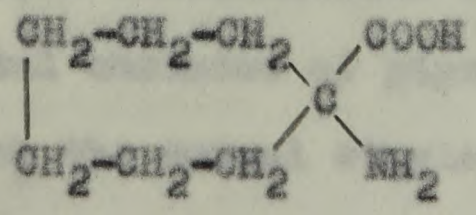
$NH_2-C(CH_3)_2-COOH$ (vi)



(vii)



(viii)



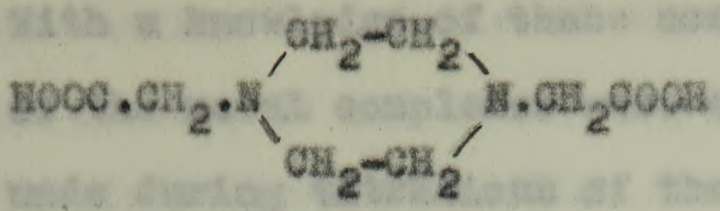
(ix)

On account of the close structural similarity between these ligands only small differences in acidity

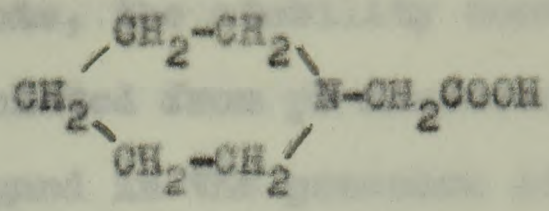
and chelating ability were to be expected. However, these ligands lend themselves to accurate investigation since they form stable, water-soluble chelates with both copper and nickel. Hence small differences in affinity for both protons and these metals can be detected quantitatively.

The methyl substituted glycines were studied to determine the influence of the substitution of groups with a positive inductive effect (+I) into the glycine molecule. The amino-acids containing cyclic substituents (vii-ix), while not expected to show large inductive effects, are interesting from a conformational point of view. The cyclo-hexane ring, unlike the cyclo-pentane and cyclo-heptane rings, can adopt strain-free conformations and any tendency to increase the ring angles will result in an energy increase (5). A study of the acid dissociation constants and chelate stability constants of these amino-acids should therefore demonstrate these conformational effects.

The influence of the distortion of chelate rings from their prefered conformations was investigated by a study of the metal chelates of piperazine-NN'-diacetic acid (x) in which the normal ethylenediamine chelate rings are held in an unfavourable conformation. For purposes of comparison piperidine-N-acetic acid (xi), two molecules of which correspond approximately to one



(x)



(xi)

molecule of (x), was prepared and its metal chelates studied. The results of these investigations are found in Part I of section II.

The Experimental Approach

All of the ligands investigated were weak acids and hence only partly dissociated in aqueous solution. Since metals form complexes more readily with the unprotonated ligand than with protonated species there is a tendency for proton displacement to take place when metal ions are added to a solution of the acid. This reaction may be represented by equations of the type:-

$$H_nL^{(p-n)-} + M^{m+} = ML^{(p-m)-} + nH^+$$

for the acid H_pL. The degree of proton displacement is therefore a measure of the affinity of the ligand for the metal and hence a measure of the stability of the complex formed. For a quantitative treatment of this equilibrium the proton dissociation constants must be known. In this work these were, in all cases, calculated from pH measurements made during titrations of the ligand with alkali.

With a knowledge of these constants, the stability constants of the metal complexes were calculated from pH measurements made during titrations of the ligand in the presence of metal ions and a salt background to maintain a constant ionic strength.

Silver, unlike many other metals, tends to form protonated complexes of high stability with amino-acids. Calculations, based on pH titration curve data alone, considering all of the complexes present are extremely lengthy and tedious and can lead to erroneous conclusions. In this work a silver-silver iodide indicator electrode, which measures the activity of free silver ions, was included in all titrations with this element to improve the accuracy and facilitate the calculation of stability constants.

Mercury complexes are generally both very stable and often very inert in that equilibrium is reached only slowly. Attempts have been made to measure quantitatively the complexation tendencies of this metal by a titration procedure (32) but in this work such an approach proved impractical. Stability constants of mercury complexes were calculated, however, using a mercury electrode in a 'pHg method' similar to that used by Schwarzenbach (6).

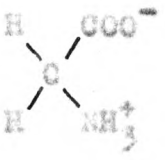
The experimental procedures are described in section III of this thesis and methods of calculation are outlined

in section V. Details of organic syntheses will be found in section IV and actual experimental results are tabulated in section VI.

SECTION TWO.

RESULTS AND DISCUSSION.

THE AMINO-ACIDS.



I

Glycine.



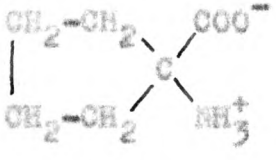
II

α-Alanine.



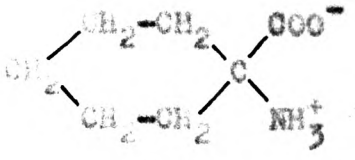
III

CC-Dimethylglycine.



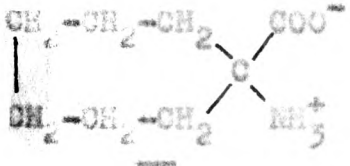
IV

cyclo-Pentane-1-amino-
-1-carboxylic acid.



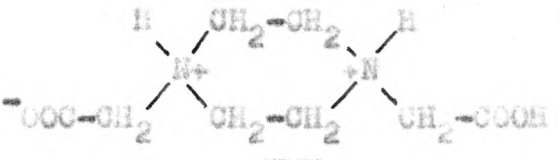
V

cyclo-Hexane-1-amino-
-1-carboxylic acid.



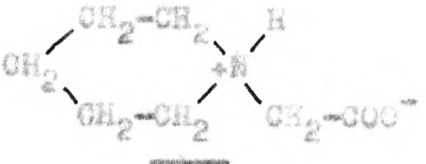
VI

cyclo-Heptane-1-amino-
-1-carboxylic acid.



VII

Piperazine-NN'-diacetic
acid monohydrochloride.
(PIPDA).



VIII

Piperidine-N-monoacetic acid. (PIPMA).

Section Two.

PART ONE.

The Amino-acids.

With the exception of piperazine-NN'-diacetic acid, PIPDA, (VII), and piperidine-N-monoacetic acid, PIPMA, (VIII), all the amino-acids investigated were structurally similar to glycine in being α-amino-acids with primary nitrogen atoms but with different substituents on the α-carbon atom. Apart from the acids VII and VIII they fall into two classes, one in which one and two methyl groups respectively are introduced into the glycine molecule (compounds II and III) and the other in which the substituents on the α-carbon atom are linked to form fully saturated alicyclic rings of five, six and seven carbon atoms respectively (compounds IV, V, and VI.).

In acid solution glycine takes up a proton to form the cationic species $H_3N^+.CH_2.COOH$ (H_2L^+) containing two ionizable hydrogen atoms. The most easily dissociated has been shown to be the proton of the carboxylic acid group leaving the zwitterion $H_3N^+.CH_2.COO^-$ ($HL^\pm$) which, at a higher pH value, looses a further proton to form the anion $NH_2.CH_2.COO^-$ (L^-) (7). The amino-acids II - VI would all be expected to behave similarly.

The Acid Dissociation Constants.

Acid dissociation constants were calculated from potentiometric titrations by using a glass electrode with a saturated calomel reference electrode, and no further salt bridges, in the cell :-

Hg_2Cl_2/Hg | Sat. KCl ‖ Amino-acid soln., KCl. (μ=0.1) | Glass Electrode.

Both the automatic recording apparatus (see appendix) and the manual apparatus (page 99) incorporating a 'Radiometer PHM4b' pH meter were used, the latter being preferred on account of its higher accuracy. The glass electrode was checked for linearity by means of a series of standard buffers and the pH meter calibrated at pH 4.00 with 0.05 potassium hydrogen phthalate before and after each titration. 20.0ml. of amino-acid solution (about 0.05 molar in 0.05 molar HCl) were used and titrated with standardised, carbonate-free alkali (5molar approx.). The temperature was maintained at 20.0°C. and the ionic strength of the solution at the commencement of a titration adjusted to 0.10M. with KCl. Dissociation constants were calculated by Irving and Rossotti's method (8) and are shown in Table I, where $K_1 = \frac{[H^+][HL^\pm]}{[H_2L^+]}$ and $K_2 = \frac{[H^+][L^-]}{[HL^\pm]}$.

The titration curves and formation curves are shown in graphs III to VIII.

Table I.

Acid Dissociation Constants at 20.0°C. and $\mu = 0.1$.

	I		II	III	IV	V	VI
	(9)	≡	≡	≡	≡	≡	≡
pK_1	2.24	2.27	2.30	2.35	2.40	2.41	2.59
pK_2	9.85	9.86	9.93	10.25	10.31	10.13	10.46

(≡ = this work)

The accuracy of the procedure was checked by determining the dissociation constants of glycine. The values found agreed well with those previously reported. (9). Complexes of α-alanine (II) had not been investigated previously at 20°C. so a complete range of measurements was made at this temperature. The reproducibility of the second constant (pK_2) in various determinations carried out with different solutions of amino-acid and alkali and on different occasions was about ±0.015 units. The precision in determination of pK_1 was, however, a little lower on account of the influence of even small errors in pH measurement on the value of this constant.

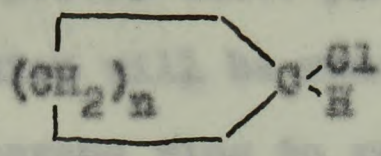
Replacement of the α-hydrogen atom in glycine is seen to produce small but regular increases in pK_1, the increases becoming larger as the substituents in the glycine molecule became larger. This is to be expected

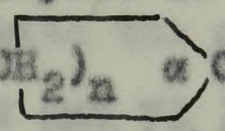
as a result of the inductive effect of the alkyl groups. The electron repelling nature of these groups (+I) will tend to make the α-carbon atom negatively charged; the effect will be transmitted to the nitrogen atom and the carboxylic acid group and thus increase the energy required to dissociate the attached protons. Further, changes in the solvation energies of the ions involved would cause slightly different dissociation constants. The effect of substituted alkyl groups on proton dissociation is best demonstrated in the simpler carboxylic acids where a large and progressive decrease in acidity is found as the size of the alkyl group is increased:-

Formic acid	pK = 3.77,
Acetic acid	4.76,
Propionic acid	4.88.

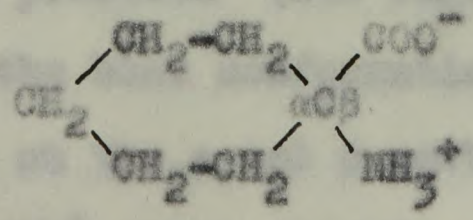
Cyclo-hexane-1-amino-1-carboxylic acid (V); pK_2= 10.13, appears to be an exception to the general trend found, the ammonium hydrogen being more acidic than expected to the extent of about 0.2pK units. The determination of its dissociation constants was repeated using different concentrations but the calculated constants differed by only 0.01pK units from the values first obtained. The value of the first dissociation constant, K_1, is also a little lower than might be expected, but since this could not be determined as accurately as pK_2,

the effect is not so definite. The increased acidity found finds an explanation in the work of H.C. Brown on the stabilities of aliphatic rings (5). While investigating the hydrolysis of cyclic compounds of the type:-



he found that the reaction proceeds at comparable rates with the cyclo-pentane and cyclo-heptane derivatives while chloro-cyclo-hexane was about 100 times more stable. He attributed this surprising difference to bond angle distortion. If the hydrolysis is a first order reaction an intermediate ion  will be formed in which the bond angle, α, will be 120°. This intermediate will stabilise cyclo-pentane and cyclo-heptane rings but decrease the stability of a strainless cyclo-hexane ring. Hence reactions requiring such intermediates will be far less likely in the case of cyclo-hexane rings. Numerous examples of such bond angle distortion effects, even when the distortion is small, are cited by Brown (10). In many cases the inflence is surprisingly large.

In the case of V the ion $HI^{\pm}$ has the structure



and the mutual attraction of the oppositeley charged

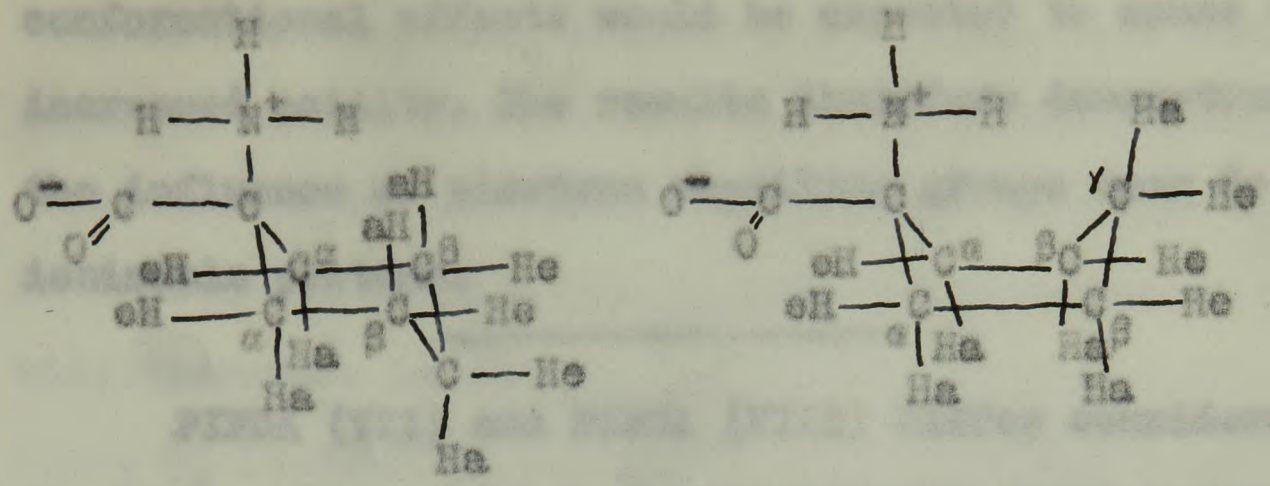
$-COO^-$ and $-NH_3^+$ groups will decrease the angle β. This will tend to increase the internal angle α so decreasing the stability of the cyclo-hexane ring. When ionisation of the second proton takes place to give the ion L^- this mutual attraction will be removed allowing the energy of the cyclo-hexane ring to return to its normal strain-free value. The result of this is that the reaction:-

$$HL^{\pm} \rightarrow H^+ + L^-$$

will be favoured. Hence the value of pK_2 will be depressed below that expected - as is, in fact, found. No similar effect will be noticed with the cyclo-pentane or cyclo-heptane derivatives (IV and VI).

A further factor which would promote a higher acidity is the energy difference between the 'boat' and 'chair' conformations of the cyclo-hexane ring system. In the chair conformation there will always be two axial hydrogen atoms which could cause steric interference, in the position β to the carbon atom to which the ammonium group is attached. Since the NH_3^+ group is smaller than the $-COO^-$ group the former would be expected to occupy the axial position (see Fig. II).

In the boat conformation, however, all axial hydrogens on the α and β carbon atoms are directed away from the NH_3^+ group assuming substitution to be on the carbon atom (1). The only interfering hydrogen atom is



(Ha = axial hydrogen atoms, He = equatorial hydrogen atoms).

Fig. II.

the axial hydrogen on the γ-carbon atom. The 'chair' conformation of <u>cyclo</u>-hexane has been shown to be more stable than the 'boat'conformation (11), and steric hindrance in the chair form of V would be reduced by ionisation of one of the protons attached to the nitrogen atom. Hence, if the chair conformation is to be maintained, the acidity would be higher than expected. No such effect would be expected with the <u>cyclo</u>-pentane derivative (IV) since the ring system in this case is virtually planar, and in the <u>cyclo</u>-heptane derivative (VI) ring conformations of comparatively high stability are possible without introducing noticeable steric hindrance. All of these effects may be clearly demonstrated by the use of scale atomic models when the possibilities of interference are more readily appreciated.

Hence it would appear that the acids behave as expected, apart from V when bond angle distortions and

conformational effects would be expected to cause the increased acidity. The results therefore demonstrate the influence of electron repelling groups near to ionisable protons.

PIPDA (VII) and PIPMA (VIII) differ considerably from the amino-acids so far considered, being more similar to ethylenediamine-NN'-diacetic acid (EDDA) or N-disubstituted glycines. The acid dissociation constants of PIPDA were determined by potentiometric titration of 0.001M solution of the acid in 0.1M KCl, the neutralisation being followed by the change in potential of the cell:-

$$\text{Ag/AgCl} \;\Big|\; \begin{matrix}\text{PIPDA}\\ \text{KCl}\end{matrix} \;\Big|\; \text{H}_2\text{/Pt}$$

in the apparatus (page 91) which incorporates this cell. For this cell

$$E = E^{\circ} + \frac{RT}{nF} \ln[H^+] = E^{\circ} - 0.05818\text{pH at } 20^{\circ}\text{C}$$

The value of E° was determined by carrying out a titration with perchloric acid as described on page 97 . Hence, from experimentally determined values of E and knowing E° hydrogen ion concentrations at each stage of the neutralisation could be calculated and the neutralisation curve of the acid plotted (graph I).

As a diamine, PIPDA VII, could take up two protons

to give two possible 'onium acids. Under the conditions employed in the present work only one extra proton is co-ordinated to give the tribasic acid VII which will be denoted as H_3L^+. The successive dissociation constants will therefore be:-

$$K_1 = \frac{[H_2L][H^+]}{[H_3L^+]} \quad \ldots(i), \qquad K_2 = \frac{[HL^-][H^+]}{[H_2L]} \quad \ldots(ii),$$

$$K_3 = \frac{[L^{2-}][H^+]}{[HL^-]} \ldots(iii).$$

From Graph I it is clear that pK_3 and pK_2 are well separated but that the stages of ionisation corresponding to pK_2 and pK_1 overlap to some extent. The second and third dissociation constants were readily calculated by means of the following equations, the derivation of which is outlined on page 127:-

$$K_2 = \frac{(R-1)[H^+]}{(R-3)} + \text{a correction term of } \frac{R[H^+]}{K_1(R-2)},$$

and $K_3 = \frac{(2-R)[H^+]}{(R-3)}$ where the correction terms are negligible.

($R = (aC_a + [H^+] - [OH^-])/C_a$ and C_a = total acid conc.). Values calculated are shown in Table II.

By using both a graphical method suitable for overlapping constants (page128) and the method of successive approximations a reliable value for pK_2 was found but

the valve of pK_1 could only be found very approximately from the present data (1.4 ± 0.4) owing to errors introduced by uncertainties in measurements of pH in the more acid solutions. A much stronger solution of PIPDA was therefore titrated using the glass electrode apparatus. Since the titration curve covered the region between pH two and three a more accurate value of pK_1 could be calculated. Values of pK_2 and pK_3 agreed reasonably with those already found (see Table II).

Table II.

Acid Dissociation Constants at 20.0°C. and μ = 0.10.

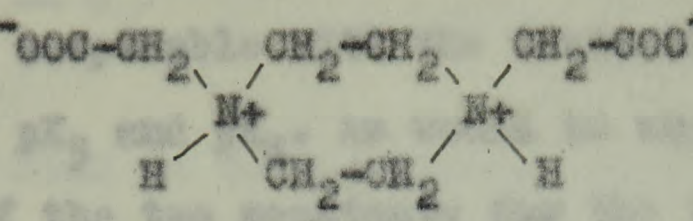
	PIPDA 0.001M.	PIPDA 0.01M.	EDDA (12)	EDDMEA (13)	EDTA (14)	N-DIMGLY (15)
pK_{COOH}	1.4	1.78				2.08
$pK_{NH(1)}$	4.46	4.40	6.42	6.69	6.16	9.80
$pK_{NH(11)}$	8.70	8.68	9.46	9.58	10.26	

EDDA = $^-OOC.CH_2.\overset{+}{N}H_2.CH_2.CH_2.\overset{+}{N}H_2.CH_2.COO^-$,

EDDMEA = $^-OOC.CH(CH_3).\overset{+}{N}H_2.CH_2.CH_2.\overset{+}{N}H_2.CH(CH_3).COO^-$,

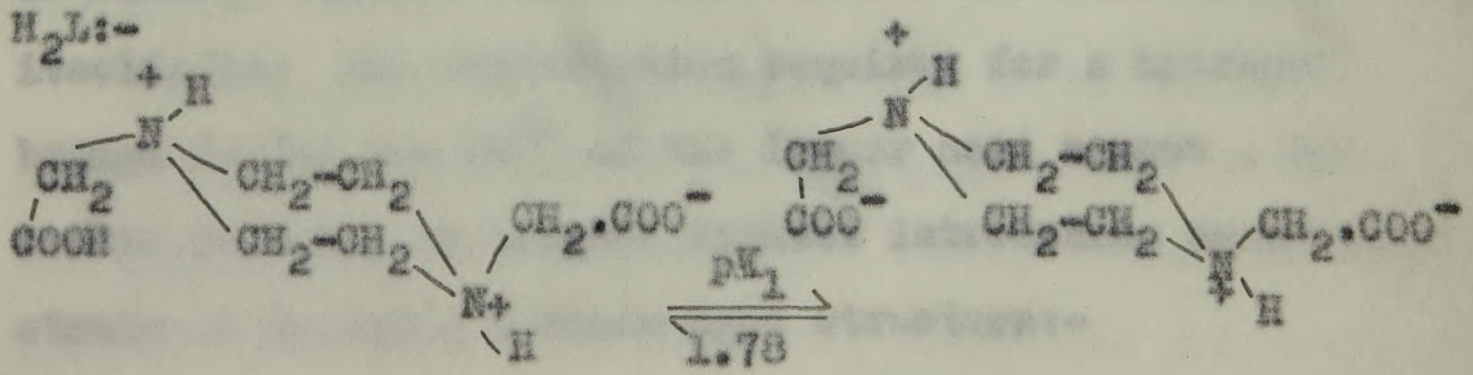
EDTA = $HOOC.CH_2.\overset{+}{N}H.CH_2.CH_2.\overset{+}{N}H.CH_2.COOH$
$\quad\quad\quad

That the neutral species of PIPDA should be represented by the zwitterion structure:-



is indicated by the fact that the pKs are comparable with the pKs of species of similar structures and which, by analogy with glycine, are thought to exist as zwitterions. (7). Evidence for this is provided by Raman spectra of aqueous solutions of amino-acids and their properties typical of ionic compounds.

There are two possible conformations for the piperazine ring - the 'boat' and the 'chair' conformations. If they exist as zwitterions, the species H_3L^+ and H_2L would both have two positively charged nitrogen atoms which, in the boat conformation, would be extremely close together. Hence electrostatically, as well as sterically, the chair conformation will be preferred - giving the following probable structures for H_3L^+ and H_2L:-



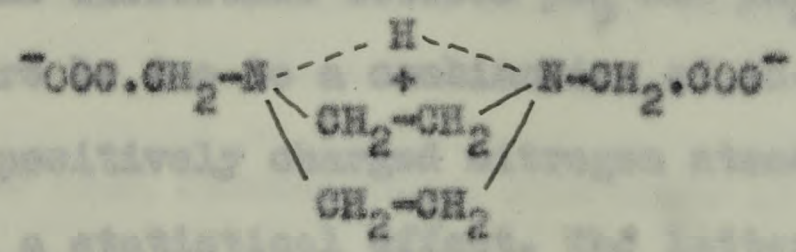
Both pK_2 and pK_3 represent ionisation of protons from nitrogen atoms in a similar environment and are directly comparable with the ionisations of EDTA represented by pK_3 and pK_4. As would be expected the relative values of the two constants for the two ligands are almost identical.

Table III

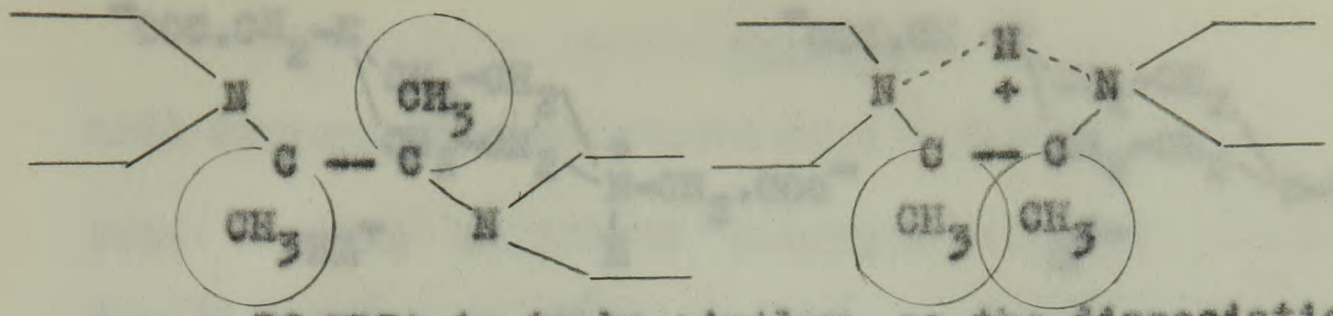
PIPDA	pK_2=4.46	pK_3=8.70	pK_3-pK_2=4.2
EDTA (14)	pK_3=6.16	pK_4=10.26	pK_4-pK_3=4.1
DIMEDTA (17)	pK_3=6.32	pK_4=10.55	pK_4-pK_3=4.2

DIMEDTA = meso-1:2-dimethylethylenediaminetetraacetic acid

This comparatively large difference has been attributed by Schwarzenbach (16) to a hydrogen bridge of the type:-



This is unlikely since the dissociation constants of DIMEDTA (quoted above) are similar to those of EDTA itself.(14) The conformation required for a hydrogen bridge in the ion HL^{3-} of the former acid cannot , for steric reasons, be adopted without introducing considerable strain so implying a chair-type structure:-



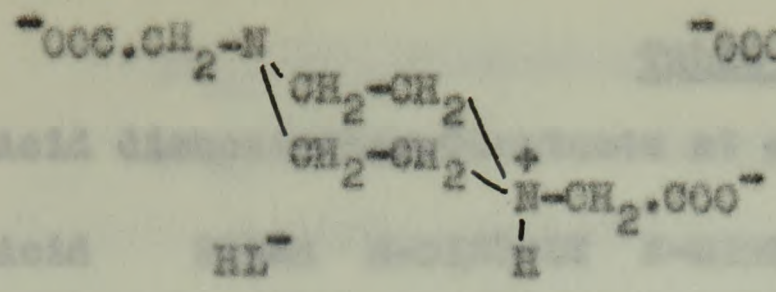
If EDTA is to be similar, as the dissociation constants imply, no hydrogen bridge can be present. The decrease in the stability constants of the metal chelates of DIMEDTA compared with EDTA also supports this view since boat-type conformations must be present in those.

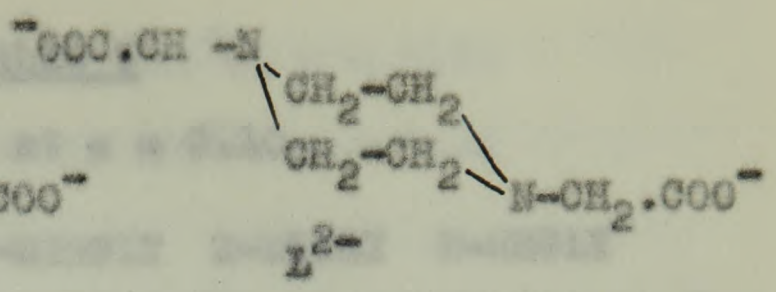
Table IV

	Log K_{Ca}	Log K_{Sr}	Log K_{Ba}
EDTA (14)	10.70	8.63	7.76
DIMEDTA (17)	9.09	7.09	5.92

The difference between pK_3 and pK_2 in PIPDA will therefore be due to a combination of the inductive effect of the positively charged nitrogen atoms in the species H_2L and a statistical effect. The latter will account for 0.6 units (i.e. $Log_{10}4$) leaving an inductive effect of 3.6 units.

The species L^{2-} will definitely be in the chair conformation on account of the lone-pair repulsion between the electron pairs on the nitrogen atoms; the acetic acid radicals will presumably be in the equatorial positions.





The values of the acid dissociation constants given in Table II show that the protons are more labile in PIPDA than in comparable acids. This increased acidity is due to the fact that, in long chain molecules such as EDTA, the maximum separation of the nitrogen atoms is greater than the comparable distance in the chair conformation of PIPDA. (when the nitrogen atoms are part of a fixed ring system). As a result of electrostatic repulsion between these charged nitrogen atoms, the protons attached to them in PIPDA will be more labile than in EDDA - so causing the increased acidity found.

The acid dissociation constants of PIPMA (VIII) were determined by titration of a 0.01M solution of the ligand using a glass electrode and a saturated calomel reference electrode to detect changes in the pH of the solution. Dissociation constants were determined by using equations similar to those used to calculate the constants for PIPDA. The titration curve is shown in Graph II and the results in Table V together with the dissociation constants of comparable acids.

Table V

Acid dissociation Constants at $\mu = 0.10$

Acid	PIPMA	N-DIETGLY	N-DIMGLY	N-ETGLY	N-MEGLY	
Temp°C	20°	25°	25°	25°	25°	20°
pK_1	2.13	2.08	2.04	2.30	2.24	2.07
pK_2	10.25	9.80	10.47	10.10	10.01	10.21
Ref:		(15)	(15)	(15)	(15)	(15b)

N-DIETGLY = NN-diethylglycine

N-DIMEGLY = NN-dimethylglycine

N-ETGLY = N-ethylglycine

N-MEGLY = N-methylglycine

As a result of the structural similarity between PIPMA and N-disubstituted glycines, acid dissociation constants would be expected to be similar to those of N-dimethylglycine or N-diethylglycine. That this is so is demonstrated in Table V but, since values for these comparable acids were determined at a different temperature, direct comparison is not possible. It is interesting to note, however, that the relative increase in the acidity of piperidine on substitution of an N-acetic acid group is of the same order as the increase resulting from the substitution of a similar group in piperazine:-

pK_{MH} (piperidine) = 11.28 ($25^{\circ}C$, $\mu = 0.5$)

pK_{MH} (PIPMA) = 10.25 ($20^{\circ}C$, $\mu = 0.1$)

ΔpK_{MH} = 1.03

pK_{MH} (piperazine) = 9.82 ($20^{\circ}C$, $\mu = 0.1$)

pK_{MH} (PIPDA) = 8.70 ($20^{\circ}C$, $\mu = 0.1$)

ΔpK_{MH} = 1.12

The Amino-acid Chelate Stability Constants

Titration curves for the amino-acids II - VI in the presence of metal ions were determined by titrating mixtures of the appropriate acid and metal ions, in the ratio 2:1, with alkali in the apparatus that had been used for the determination of the acid dissociation constants. The temperature was 20.0°C and the ionic strength of the solutions employed was adjusted to 0.1 with KCl. The concentration ratio [Ligand]:[Metal] = 2:1, favoured the formation of the complexes of formula ML_2. The titration curves are shown in graphs IV - VIII.

From these curves and the curve for the acid alone, values for the free ligand exponent, pL, and the degree of formation, $\bar{n}$, were calculated by Irving and Rossotti's method (8). These are plotted on graphs IX - XIV. Chelate stability constants for the complexes ML and ML_2 were calculated from these by Irving and Rossotti's 'correction term' method (18) provided the curves extended beyond $\bar{n} = 1.5$; otherwise a least squares treatment of the following equation, derived on page 125, was employed.

$$\frac{\bar{n}}{(2-\bar{n})[L]^2} = \frac{(1-\bar{n})}{(2-\bar{n})[L]} K_1 + K_1K_2 \quad \ldots\ldots (i)$$

Stability constants calculated are shown in Table VI (page 40).

In all titrations apart from those with the cyclo-heptane derivative (VI) deep blue solutions were produced with copper, due to the formation of soluble complexes. With VI a blue precipitate was formed at about pH 4.3. The titration was repeated at a lower copper concentration (Ligand:copper = 2.5:1) but the precipitate still formed. This was found to be an organic copper compound and was assumed to be the insoluble di-chelate since, with such a large aliphatic group in the amino-acid, the uncharged chelate CuL_2 would not be expected to be very soluble. However, before precipitation, the degree of formation of the complexes reached 1.4 so that accurate stability constants could be calculated. The formation curves obtained from the two copper titrations at different copper concentrations are in excellent agreement (graph XIV) and the constants calculated were identical over the range, $\bar{n} = 0.2$ to precipitation.

In titrations with metals other than copper, particularly with zinc and cobalt, precipitation of the metal hydroxide often occured at a comparatively early stage of the titration. An accurate calculation of K_1 was usually possible but the value of K_2 was far less certain since the degree of formation often failed to reach one.

In some cases cobaltous hydroxide did not precipitate

but the solution became violet at higher pH values and a faint brown precipitate sometimes formed. This was clearly due to oxidation of cobalt^{II} to cobalt^{III} and could be detected by deviations from the straight line expected from equation (i). For the calculation of stability constants only $\bar{n}$ and pL values before deviations started were used.

Equilibrium was reached slowly in all the titrations involving nickel ions whereas with all other metals it was almost instantaneous. The stirring technique was the same in all cases. At high $\bar{n}$ values the formation curve of nickel chelates ceased to be symmetrical about the point $\bar{n} = 1$. This probably indicates formation of chelates of the formula NiL_3. The value of Log K_3 could not be calculated accurately from the titration curves of 2:1 ligand to metal ratio but appears to be of the order of 3.

The inductive effect of the alkyl groups would be expected to cause an increased stability in the metal chelates in the same way as it increased the stability of the proton complexes. This increase is immediately apparent in the copper chelates but not with the other metals. A more quantitative comparison is afforded by comparing the constants for the reactions:-

$$M^{2+} + HL \rightleftharpoons ML^{+} + H^{+}$$

which represents the competition between the metal ions and protons for bonding with the ligand. These constants are defined as:-

$$K' = \frac{[ML^+][H^+]}{[M^{2+}][HL]} = \frac{K_1}{K^H_{HL}}$$

where K^H_{HL} is the stability constant of the acid HL and equal to $1/K^H_2$. Hence $pK' = pK^H_2 - \text{Log } K_1$

Similarly $pK'' = pK^H_2 - \text{Log } K_2$ from a consideration of the reaction:-

$$ML^+ + HL \rightleftharpoons ML_2 + H^+$$

where

$$K'' = \frac{[ML_2][H^+]}{[ML^+][HL]}$$

Values for these constants are shown in Table VII and plotted on graph XV.

Table VII

Ligand		I	II	III	IV	V	VI	
pK^H_2-Log K_1,	Cu	1.73	1.78	1.99	1.68	1.54	1.84	pK'
'' ,	Ni	4.12	4.53	5.09	4.71	4.63	5.13	
'' ,	Zn	4.69	5.38	5.70	5.55	5.35	5.85	
'' ,	Co	-	5.61	6.14	5.85	5.66	6.29	
pK^H_2-Log K_2,	Cu	2.94	3.15	3.41	2.98	2.87	3.09	pK''
'' ,	Ni	5.09	5.43	6.02	5.68	5.58	5.98	

Any increase in values of pK' or pK'' indicates a decrease in metal-ligand stability relative to that of the proton-ligand complex as compared with glycine. Alternatively such a decrease may be demonstrated by a plot of Log K_1 against pK_2^H (Graph XVI) (20). Such a plot should show a straight line relationship of unit gradient for ligands of similar structure and without different steric effects. Points falling below such a line passing through the glycine point indicate a decreased chelate stability relative to glycine.

Such a decrease in stability may result from three causes:- (i) Steric factors due to the groups substituted in the glycine molecule interfering spatially with the metal ions, so tending to distort or lengthen the metal-ligand bonds. In other cases the ring systems attached to the glycine skeleton may be forced into unfavourable conformations.

(ii) Differences in the co-ordinating power of the oxygen atoms since pK_2 refers only to the N-H bond energy. In a series such as the one considered in which the ligands are very similar the influence of this factor would be expected to be small.

(iii) When considering the formation of the chelate ML_2 (as measured by pK_2^H-LogK_2) a third possibility presents itself. Chelate ring-formation with one molecule

of ligand may sterically prevent or impede addition of a further molecule of ligand. This third effect would show itself in the ratio K_1/K_2 (the logarithm of which corresponds to Log K_1 - Log K_2) which would be approximately constant in the absence of such influence. Table VIII shows values for Log K_1 - Log K_2. These, apart from the zinc chelates with VI where measurements of Log K_2 were the least reliable, are generally constant indicating the absence of contributions from (iii):-

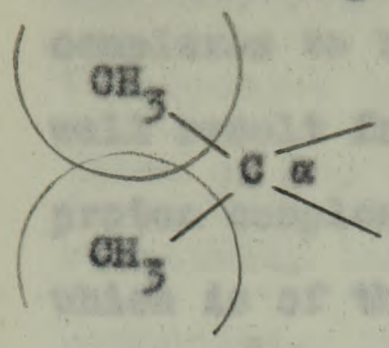
Table VIII

Metal \ Ligand	I	II	III	IV	V	VI
Cu	1.21	1.37	1.42	1.30	1.33	1.25
Ni	0.97	0.90	0.93	0.97	0.95	0.85
Co	-	0.7	0.7	0.8	0.8	0.5
Zn	0.8	0.5	0.5	0.4	0.4	~0

Hence it would appear that the increases in the values of pK' and pK'' shown in Table VII are due to the first possible cause.

The amino-acids II and III, i.e. without cyclic substitution groups, show decreasing stability compared with glycine itself. This could not easily arise through steric hindrance between the methyl groups and the metal ions, but the effect of substituents on the α-carbon atom of the glycine chelate ring (particularly the

gem-dimethyl groups in III) would be expected to distort the bond angle between the other two carbon bonds (21):-

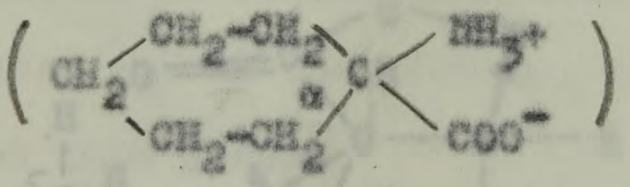


Bailar has shown that the amino-acid chelate ring, unlike that formed by ethylenediamine, is virtually planar (22). Hence further ring flattening cannot occur so that any decrease in the angle α must result in decreased chelate stability since change in bond direction would prevent the co-ordinating centres from satisfying the spatial requirements of the metal as effectively as they would if part of an unsubstituted ring.

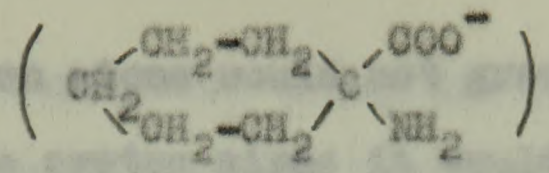
The chelates of the amino-acids containing cyclic substituents (IV,V,VI) show much smaller deviations from the stabilities expected. This would be anticipated from the fact that, while free rotation round the C-CH_3 bond in the methyl substituted glycines is possible, the methylene groups of the cyclic acids are locked in one of two possible conformations. A freely rotating methyl group would naturally sweep out a larger volume than that required by a fixed methylene group so that distortion of the bonds of the α-carbon atom would be expected to be only small.

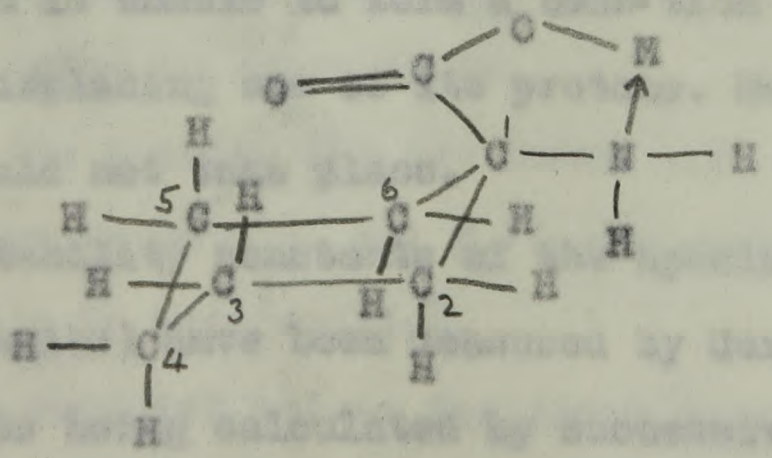
The chelated complexes of the cyclo-hexane derivative

(V) are exceptional in being relatively more stable than those of glycine assuming the stability of the proton complexes to be comparable. This apparent anomaly may well result from the comparatively low stability of its proton complex as demonstrated in the low value of pK_2, which is of the order of 0.2 pK units lower than expected. If this value (i.e. 0.2 pK units) is added to the values of pK' and pK'' (yielding the figures shown in parentheses in Table VI) the anomaly is removed and the results demonstrate a progressive decrease in chelate stability (relative to that of the proton complex) as the size of the cyclo-paraffin group is increased. This is demonstrated in Graphs XV and XVI.

The implication of adding 0.2pK units to the values of pK' and pK'' is that the proton complex is less stable than the metal chelate relative to the complexes of glycine. This is conceivable for two reasons. Firstly, in the ion $HL^{\pm}$  the charges will

attract one another so decreasing the bond angle between the COO^- and NH_3^+ groups. This will tend to increase the angle between the other two bonds of the α-carbon atom and would cause the increased acidity found as explained on page 15 . Such an increase in bond angle will not be found

in the ion L^-  since the electrostatic attraction is now absent. Since this is the species taking part in chelate formation the stabilities of the metal chelates would be expected to be relatively larger than those of the corresponding glycine compounds. Secondly, in the proton complexes, free rotation round the C—NH_3^+ and C—COO^- bonds is possible and, through steric hindrance, could contribute towards the decrease in the proton stability constant found in the case of V. Once chelate formation has taken place the conformations of both the $-NH_2\rightarrow$ and the -CO-O- groups are 'locked' in the planar ring. If the carboxylate ion is axial to the cyclo-hexane ring, which would be expected to be in the chair conformation, the carbonyl oxygen atom would lie between the two axial hydrogen atoms on carbon atoms 3 and 5 (see diagram).



Were rotation of the carboxyl group allowed, interference would take place; but since the group is fixed, the nearness

of axial hydrogen atoms would not greatly affect the stability of the system since it would not increase its entropy.

The influence of substitution on the α-carbon atom of glycine on the stability of its metal chelates may therefore be explained in terms of distortion of bond angle and the effect of the restriction of movement on the entropy, and hence the free energy, of the system.

Since the zwitterion $HL^{\pm}$ has a large range of existence (approximately pH 2 - 10) there is the possibility that, at high hydrogen-ion concentrations, the species MHL^{++} may exist. Such a species would be most likely with copper where proton displacement is noticeable as low as pH 2.8. Such a complex would not be expected to be very stable since in the ion $HL^{\pm}$ ($NH_3^+-CH_2-COO^-$) the nitrogen is unable to form a bond with a metal ion without first displacing one of its protons. Hence chelate formation could not take place.

Stability constants of the species $CuHL^{++}$ (where L is α-alanine) have been measured by Curchod (23), the constants being calculated by successive approximations. In this work the stability constants of the protonated complexes of III, IV, VI have also been calculated by

successive approximations using the computing facilities of the University 'Mercury' electronic computor. Values of K^{M}_{MLH} obtained agree with those found by Curchod for α-alanine, being very small in comparison with K_{ML} and K_{ML_2}.

Table IX

Stability Constants of the Protonated Complexes of α-amino-acids.

Conditions:	25°, μ=0.375	20°, μ = 0.1		
Ligand	II (23)	III	IV	VI
Log K^{Cu}_{CuHL}	1.37 0.72	1.22	1.86	1.09
Log K_1		8.29	8.72	8.74
Log K_2		6.81	7.35	7.26

On account of their much smaller order of magnitude, the values of K^{M}_{MHL} quoted in Table IX can only be taken as approximate.

If the species MHL are taken into consideration the values of both K_1 and K_2 (previously shown in Table VI) should be recalculated.

The modified values for these constants are shown in Table IX but are unreliable since they tended to vary by up to 0.1 Log units from one approximation to another, mainly because the relevant experimental data is for very acidic solutions in which proton

displacement is small and the accuracy of measurement lowest.

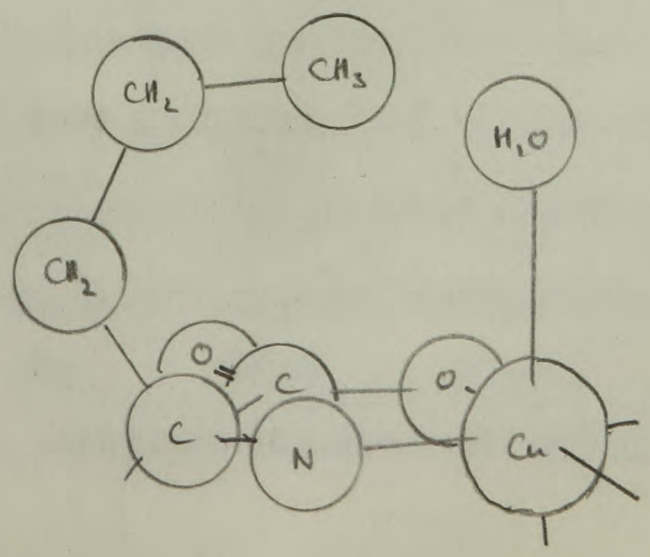
Basolo has reported that the nickel chelates of C-methyl substituted ethylenediamines show a transition from violet-blue paramagnetic to yellow diamagnetic compounds as substitution in the ligand increases from two methyl groups to four (24). The reason suggested for this change was that the increase in size of the organic ligand in the paramagnetic octahedral complex $[Ni(X\text{-}X)_2(H_2O)_2]^{++}$ forced the water molecules away from the nickel ion leaving the diamagnetic square planar complex. An alternative, or at least an additional, explanation is that the inductive effect of the methyl groups (+I) increases the ligand field of the nitrogen atoms until a point is reached when spin-pairing of the nickel d_γ-electrons takes place. This could cause the change from paramagnetism to diamagnetism found by Basolo. No such changes in magnetic properties would be expected in the amino-acid series considered since three methyl groups in the ethylenediamine skeleton were required to produce any diamagnetism in the nickel whereas no more than two substituents are ever present in the amino-acids. Further the ligand field of the nitrogen atom is stronger than that of the oxygen atom and, in amino-

acid chelates, there is only one N-M bond compared with two in ethylenediamine chelates. Hence substitution of groups with far stronger inductive effects would be required to bring about spin-pairing. However to test this the absorption spectra of the nickel-cyclo-hexane and nickel-cyclo-heptane amino-acid derivatives (V and VI) were determined. Both showed peaks in the region of 625mμ corresponding to the paramagnetic octahedral nickel with no indication of any absorbancy in the region of 440mμ which would correspond to diamagnetic square planar nickel.

While investigating the copper chelates of α-amino-acids Graddon and Munday noticed a sharp decrease in solubility in water as the length of the sidechain, R, in the glycine skeleton was increased (25):-

$$R\text{-}CH(NH_2).COOH$$

The explanation they suggested was that interference between the alkyl chain in molecules such as α-n-propyl-glycine and water molecules co-ordinated by the cupric



ion in positions normal to the plane of the chelate ring (along the z-axis) caused dehydration of the ion and hence a decrease in hydrophilic character and hence in solubility. They noted that water molecules would be only weakly held on account of the long bonds along the z-axis found in distorted octahedral copper complexes. Such an explanation of dehydration seems unlikely since, for the propyl group to interfere with co-ordinated water in the copper chelate, all the hydrogen atoms in the chain would have to be in eclipsed conformation. This is energetically unlikely.

The difference in solubility between the cupric chelates of the cyclo-hexane (V) and cyclo-heptane (VI) derivatives cannot be due to this cause since, sterically, it is quite impossible for the cyclo-heptane ring even to approach any water which may be co-ordinated along the z-axis of the cupric ion. What is more the nickel and the zinc chelates of VI were only sparingly soluble and the acid itself was soluble in water only to the extent of 0.05 moles per litre. Rather the effect is probably due to the influence of an increase in the size of the hydrophobic alkyl side-chain which would naturally tend to decrease the solubility of the compound containing it.

TABLE VI.

The Stability Constants of Amino-acid Chelates at 20.0° and μ = 0.1OM (KCl.).

Ligand		I.(9)	II.	III.	IV.	V.	VI.
	pK_1	2.24	2.30	2.35	2.40	2.41	2.59
	pK_2	9.85	9.93	10.25	10.31	10.13	10.46
Log. values- Cu	K_1	8.12	8.15	8.26	8.83	8.59	8.62
	K_2	6.91	6.78	6.84	7.33	7.26	7.57
	β_2	15.03	14.93	15.10	15.96	15.83	15.99
Ni	K_1	5.73	5.40	5.16	5.60	5.50	5.33
	K_2	4.76	4.50	4.23	4.63	4.55	4.5
	β_2	10.49	9.90	9.39	10.23	10.05	9.8
Zn	K_1	5.16	4.85	4.55	4.76	4.78	4.61
	K_2	4.34	4.1	4.0	4.4	4.4	4.6
	β_2	9.50	8.7	8.6	9.2	9.2	9.2
Co	K_1	5.1	4.32	4.11	4.46	4.47	4.17
	K_2	3.8(19)	3.6	3.4	3.7	3.7	3.7
	β_2	8.9	7.9	7.6	8.2	8.15	7.9
Ca	K_1	1.4				1.2	
pK_2-logK_1	Cu	1.73	1.78	1.99	1.68	1.54(1.74)	1.84
pK'	Ni	4.12	4.53	5.09	4.71	4.63(4.83)	5.13
	Zn	4.69	5.38	5.70	5.55	5.33(5.55)	5.85
	Co	4.7	5.61	6.14	5.85	5.66(5.86)	6.29

(Cobalt - glycine(I) results reported at μ=0.01M, 20°C.)

The Chelate Stability Constants of PIPDA (VII) and PIPMA (VIII).

The titration curves for PIPDA in the presence of metal ions were determined by titrating mixtures of the acid and metal ions in the same apparatus as that used for the determination of acid dissociation constants. i.e. the hydrogen electrode apparatus (page 91) for magnesium, calcium, strontium and barium, or the glass electrode apparatus for copper, nickel and zinc complexes. The latter apparatus was also used for titrations of PIPMA (VIII) with metals. Solutions used were 0.001 M or 0.01M and the ionic strength was adjusted to 0.1M with KCl. The temperature was maintained at 20°C.

In titrations of PIPDA in the presence of copper, nickel and zinc using the glass electrode apparatus the pH meter was standardised with solutions of perchloric acid of known concentrations, the ionic strengths being adjusted to 0.1M with KCl. By using this method the meter was standardised in terms of hydrogen ion concentrations . Hence measurements were truly comparable with measurements made in the cell, incorporating the hydrogen electrode, which was used to determine the acid dissociation constants of PIPDA. In all other cases 0.05M potassium hydrogen phthalate was used (pH = 4.00) so standardising the pH meter in terms of hydrogen ion activities. This was

permissible since both acid dissociation constants and metal complex stability constants were determined by the same method.

By employing mixtures of copper and PIPDA in different concentration ratios (viz. 5:1, 1:1, 1:2) it was found that only the 1:1 chelates could be obtained. This was shown by the facts that the calculated stability constants were the same for these mixtures and that the degree of formation, $\bar{n}$, tended towards one and no higher. Chelates of formula ML_2 were formed with PIPMA and copper although precipitation always occured well before $\bar{n} = 1$. The existence of the dichelate was demonstrated by plotting $\frac{\bar{n}}{(1-\bar{n})[L]}$ against $\frac{(2-\bar{n})[L]}{(1-\bar{n})}$ (see page 125). A straight line graph was obtained giving values of 6.33 for Log K_1 (the intercept) and 12.0 for Log β_2 (the gradient). With nickel the hydroxide precipitated before $\bar{n} = 0.5$ but an approximate value for Log K_1 was obtained. While investigating the chelates of NN-diethylglycine Basolo found a similar tendency for nickel hydroxide to precipitate at an early stage in the titration (15). Zinc hydroxide was precipitated before any measurable proton displacement could be detected making calculation of the metal stability constants impossible. Titration curves for PIPDA and PIPMA in the presence of metal ions are shown in Graphs XVII and XVIII.

In the titrations of PIPDA in the presence of copper a green-blue precipitate formed at pH = 5 using a 0.001M solution and at pH = 3.9 using a 0.01M solution. This could not be cupric hydroxide since this does not precipitate until above pH = 5. The precipitate was collected and its analysis proved it to be the 1:1 complex, CuL. With both zinc and nickel complex formation was observed in the more acid solutions but the metal hydroxides precipitated in more alkaline solutions.

Proton displacement was noticable by pH = 2.8 in the titration of PIPDA with copper and by pH = 3.7 with nickel indicating the possible existence of the species MHL^{+}. With copper this was further supported by the rapid increase in calculated values of K_{ML} as the hydrogen ion concentration increased, irrespective of the metal:ligand ratio. Attempts to calculate K^{M}_{MHL} by Schwarzenbach's method of temporary constants using a large excess of metal ions (26) indicated that this constant was large and of the order of 10,000. The figures obtained in the titration of the 1:1 mixture of PIPDA and copper ions were therefore used to calculate the constants K_{ML} and K^{M}_{MHL}, utilising the 'Mercury' electronic computor programme, which employed a method of successive approximations. The constants for nickel were calculated in a similar way.

Since there was no indication of complexes of the type MHL in the solutions of PIPDA with zinc or the alkaline earth metals, the stability constants of chelates of the form ML were calculated by means of the equation derived on page 130.

Values obtained for the stability constants of complexes of both PIPDA and PIPMA are shown in Table X, where they are given with the values obtained by other workers for similar ligands.

Table X.

The Metal Chelate Stability Constants (μ = 0.1OM.).

Ligand	PIPDA	HEDDA (12)	HEDPBA (13)	EDTA (14)
Temperature, °C.	20	30	20	20
pK_1	4.46(pK_2)	6.42	6.69	6.16(pK_3)
pK_2	8.70(pK_3)	9.46	9.58	10.26(pK_4)
Log K				
Mg	1.5	3.9	2.8	8.69
Ca	2.5		1	10.70
Sr	2.2		n.m.	8.63
Ba	1.6		n.m.	7.76
Zn	3.05	11.1	10.1	16.26
Cu	7.37 $\log K_{MHL}^{M} = 4.09 - \log K_{ML}^{M}$	16.2	15.2	18.79
Ni	3.64 $\log K_{MHL}^{M} = 1.30 - \log K_{ML}^{M}$	13.5	12.2	18.56

(n.m. = not measurable).

In Table X, EDDA = ethylenediamine-NN'-diacetic acid.

EDDMBA = ethylenediamine-NN'-di(methylacetic) acid.

EDTA = ethylenediamine-NNN'N'-tetraacetic acid.

The values quoted in Table X show that there is only weak chelation between PIPDA and the alkaline earth metals, and that the stability order, viz. Mg〈Ca〉Sr〉Ba, is that commonly found. For the heavier alkaline earth metals PIPDA appears to give stronger complexes than EDDMBA but the position is reversed for the small magnesium ion which forms a relatively weak complex. Much weight however must not be attached to the numerical difference between the low stability constants. This is because, with weak complexes, the precision of the measurements becomes less reliable since the proton displacement caused by adding metal ions to the ligand solution is very small (see graph XVIIb). The results for copper, nickel and zinc show that the stabilities of the chelates of these metals with PIPDA are distinctly lower than the values of the corresponding EDDA chelates.

Other things being equal, the affinity of a ligand for metal ions should increase as its affinity for protons increases. Since pK_3 for PIPDA is less than the corresponding value for EDDA (8.70 as opposed to 9.46) a corresponding decrease in the stabilities of all its metal complexes would be expected. However, other factors

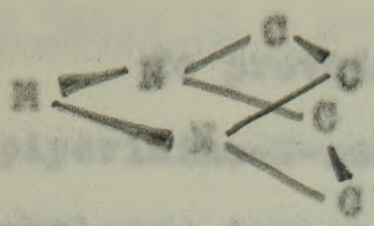
must contribute to the disproportionately small values for the stabilities of the complexes with copper, nickel, zinc and possibly magnesium.

In order to form metal chelates PIPDA and HEDDA must both be in a 'boat'-type conformation. This has been shown by X-ray studies of the NN'-dimethylpiperazine chelate with palladium (27). There is only one possible arrangement for the acetic acid groupings in such a PIPDA chelate, i.e. both equatorial to the piperazine boat, while there are three possible spatial arrangements for these groupings in HEDDA:- (i) Both equatorial with hydrogens axial.

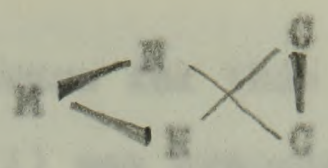
(ii) Both axial with hydrogens equatorial.

(iii) One equatorial and the other axial.

Hence the entropy contribution to the free energy of formation of PIPDA chelates would be less favourable than with the HEDDA chelates. Further the formation of the 'boat' conformation of PIPDA introduces the repulsion contributions of more eclipsed hydrogen atoms than the formation of the ethylenediamine-type chelate ring in EDDA. This will reduce the enthalpy change on chelate formation in the former case. Most important of all, the ethylenediamine chelate ring is puckered to reduce strain but in a different way to the only possible piperazine chelate ring shape:-

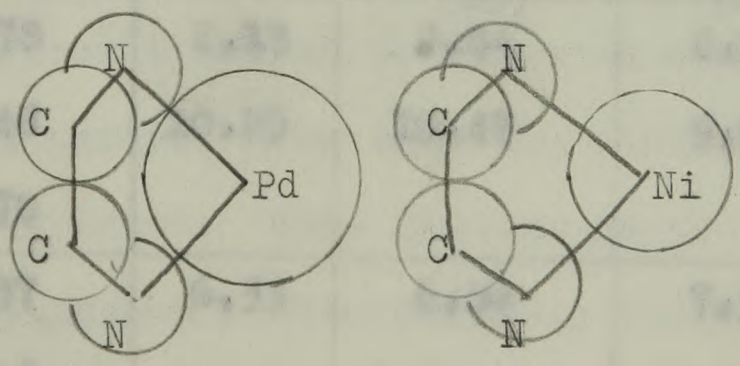


Piperazine chelate



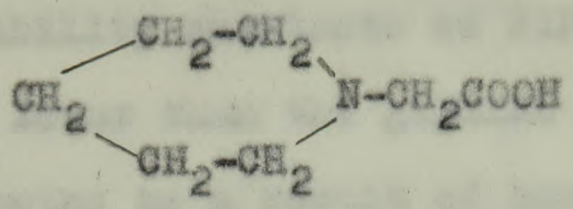
Ethylenediamine chelate

While investigating the chelates of NN'-dimethylpiperazine, Mann and Watson found that, while chelates with large ions such as platinum^{II} or palladium^{II} could be prepared readily, copper chelates were unstable and nickel chelates could not be made (28). They attributed this to the stereochemistry of the piperazine ring, the nitrogen atoms being sufficiently close for both to co-ordinate with larger ions but unable to co-ordinate effectively with smaller ones. Hence large ions such as calcium, strontium or barium should chelate reasonably easily with PIPDA while the chelates of magnesium, copper, zinc and nickel would be expected to be markedly unstable compared with the EDDA chelates.



The Piperazine Chelates of Palladium^{II} and Nickel.

To provide further evidence for this suggestion piperidine-N-acetic acid (VIII) was prepared and its chelates investigated.



PIPMA (VIII)

Structurally this ligand is similar to half of the PIPDA molecule so that chelates of formula M(PIPDA) would be expected to correspond approximately to the dichelates of PIPMA with metals. Hence K_{ML} for PIPDA chelates would be expected to be as large as or (as a result of the chelate effect) even larger than β_2 for the corresponding PIPMA chelates, if no steric factors interfere.

Chelate Stability Constants at 20°, μ = 0.1 Table XI

Ligand	PIPDA	PIPMA	N-DIETGLY (15)	N-DIMGLY (15)	GLYCINE (9)
pK_1	1.78	2.13	2.04	2.08	2.24
pK_2	4.46	10.25	10.47	9.80	9.76
pK_3	8.70				
Cu.Log K_{ML}	7.37	6.33	6.88	7.30	8.12
Log K^M_{MHL}	4.09				
Log β_2		12.0	12.86	13.65	15.03
Ni.Log K_{ML}	3.64	3.7	4.21	4.82	5.73
Log K^M_{MHL}	1.30				
Log β_2		7		8.60	10.49
Zn.Log K_{ML}	3.05	n.m.			

In Table XI : N-DIETGLY = NN-diethylglycine,

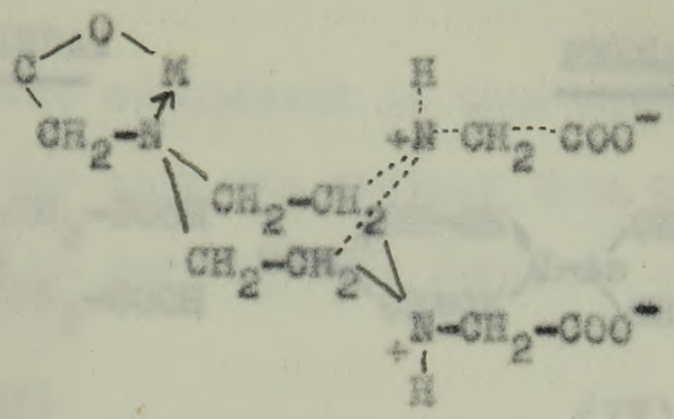
N-DIMGLY = NN-dimethylglycine.

n.m. = not measurable.

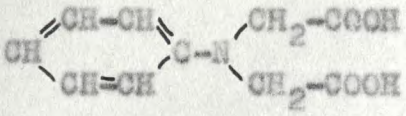
The stability constants of PIPMA (VIII) chelates are consistently lower than the glycine chelates. This would be expected as a result of the lower co-ordinating ability of tertiary aliphatic nitrogen atoms. Neglecting differences resulting from the differences in the temperatures of measurement, the chelate stabilities fall into the order : Glycine > N-DIMGLY > N-DIETGLY > PIPMA. The decrease in stability as the size of the substituents on the tertiary nitrogen atoms increases has been attributed by Basolo to increased steric hindrance affecting the stereochemistry of the nitrogen atom. The results for PIPMA are in agreement with this suggestion.

Comparison of the results for PIPMA with the results for PIPDA demonstrates a marked decrease in the stability of chelates of the latter, even when the different proton affinities are considered. This implies that, in agreement with Mann and Watson's observations, PIPDA is unable to bond effectively through both nitrogen atoms and both carboxyl groups. Further, K^{M}_{MHL} for PIPDA chelates is uncommonly large compared with the value for K_{MHL}. This would be expected if the piperazine ring was unable to

chelate effectively with smaller ions since co-ordination could take place between a carboxyl group and the metal with only one nitrogen-metal bond but the other nitrogen atom free to co-ordinate a proton.

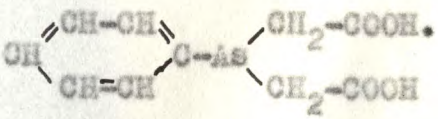


The stability constants found are in full agreement with Mann and Watson's observations and the differences in stability between chelates of PIPDA and PIPMA demonstrate clearly the influence of steric and conformational effects on the stabilities of metal chelates.



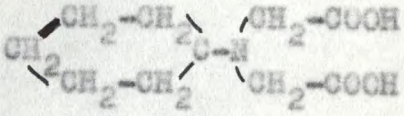
(I)

Phenyliminodiacetic acid. PHENIMDA.



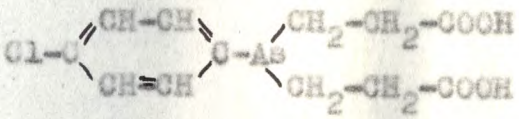
(II)

Phenylarsinediacetic acid. PHENASDA.



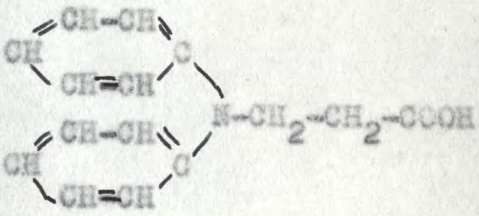
(III)

cyclo-Hexylaminediacetic acid. HEXDA.



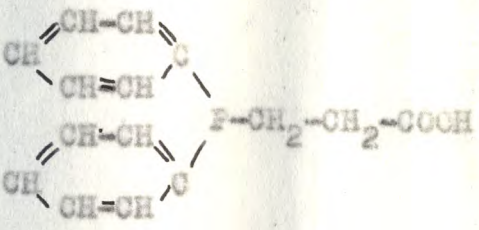
(IV)

p-Chlorophenylenediaminedipropionic acid. chlor-PHENASDPA



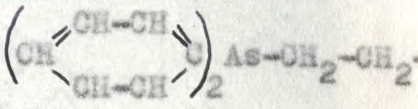
(V)

Diphenylaminepropionic acid. (DIPHENAMPA)



(VI)

Diphenylphosphinepropionic acid (DIPHENPHOSPA).



(VII)

Diphenylarsinepropionic acid. (DIPHENASPA).

PART TWO.

The Relative Co-ordinating Affinities of Nitrogen, Phosphorus and Arsenic.

Introduction :-

The compounds considered in this section are structurally less similar with one another than the amino-acids considered in Part I. The formulae will be found attached to page 50.

PHENIMDA (I) and PHENASDA (II) provide a direct comparison between the donor properties of nitrogen and arsenic. HEXDA (III) is a similar compound but metal complexes with this ligand would be expected to be generally more stable than the phenyl analogue, on account of the large -I inductive effect of the phenyl group.

In order to form a complex through both the carboxyl groups and the arsenic atom, chlor-PHENASDPA (IV) would have to form six-membered chelate rings. These are known to be less stable than five-membered chelate rings, as would be formed by PHENASDA (II) (29). Hence comparison of the stability constants of complexes of PHENASDA and chlor-PHENASDPA should throw light upon the strength of bonding through the carboxyl groups.

Diphenylaminepropionic acid, DIPHENAMPA, (V) and its phosphorus and arsenic analogues (VI and VII) would be

expected to form weaker complexes than the monophenyl derivatives, but the proton dissociation constants and metal complex stability constants should provide a comparison between the donor properties of nitrogen, phosphorus and arsenic.

Apart from the phenyl disubstituted compounds (V - VII) all the acids were sufficiently water-soluble to provide a 0.002M solution, having a salt background of 0.10M KNO_3. In solution they were resistant to oxidation and showed no tendency to decompose over periods of several weeks. Wherever possible, however, freshly prepared solutions were used and were stored in stoppered flasks.

Solutions of the diphenylamine, -phosphine and -arsine derivatives were prepared using 20% dioxan as solvent. In practice a 0.002M solution, with the ionic strength adjusted to 0.10 with KNO_3, was prepared in 40% dioxan. For titrations, 10 ml. of this stock solution were diluted with 10 ml. of an aqueous solution of either 0.10M KNO_3 or of metal ions of suitable concentration in 0.10M KNO_3. It was found that commercial AnalaR dioxan was weakly acidic and hence unsuitable for use. A little pure dioxan was available and a further quantity was purified by distillation from sodium and shaking with anion exchange resin (Amberlite IRA 400).

The Acid Dissociation Constants:-

Acid dissociation constants were all determined from titration data obtained by following the neutralisation of the acids with the cell :-

$$Hg/(HgCl)_2 \;\Big|\; \begin{matrix}\text{Sat}\\ KCl\end{matrix} \;\Big\|\; \begin{matrix}\text{Acid}\\ 0.1M\ KCl\end{matrix} \;\Big|\; \text{glass electrode}$$

Attempts were made to use the hydrogen electrode apparatus, following the neutralisation of PHENASDA (I) by the change in potential of the cell :-

$$Ag/AgCl \;\Big|\; \begin{matrix}\text{PHENASDA (0.001M)}\\ 0.1M\ KCl\end{matrix} \;\Big|\; H_2/Pt$$

However, it was found that the potential became unsteady above pH 7, presumably due to the poisoning of the hydrogen electrode by arsenic. Once poisoned, the electrode had to be completely resurfaced before it could be used again. Consequently a cell employing a glass electrode had to be used.

Acid dissociation constants were calculated from the titration curve data by employing equations of the form used for the calculation of the dissociation constants of PIPDA (p.19). A graphical method was used to determine the constants of PHENASDA (II) and chlor-PHENIMDA (IV) since the values of the dissociation constants for the acids were very similar in magnitude, causing the ranges of ionisation of the protons involved to overlap considerably.

An attempt was made to measure the dissociation constant of DIPHENASPA (VII) in water by preparing a saturated solution at 20°C. A titration curve was obtained but the maximum concentration of acid obtainable at 20°C was only 1.16×10^{-4}molar. This solution is rather too dilute for a quantitative treatment and consequently the value calculated for the dissociation constant showed a large deviation, i.e. $K_1 = 5.1 \pm 0.2$. A value accurate to within 0.02pK units was obtained using a 10^{-3}molar solution in 20% aqueous dioxan. This solvent was therefore used for the nitrogen and phosphorus analogues of the acid.

The titration curves are shown in graphs XIX - XXIV and the acid dissociation constants derived from these are shown in Table XII.

TABLE XII

Acid Dissociation Constants at 20°C and $\mu = 0.10(KNO_3)$.

Ligand	I	II	III	IV	V	VI	VII
Ref:-	(30)	*	(31)	*	*	*	*
pK_1	2.40	3.60	2.25	4.17	5.06	5.03	5.21
pK_2	4.96	5.03	10.61	5.08	20% aqueous dioxan		

* = this work.

It is probable that the second dissociation constant of PHENIMDA represents ionisation of a proton attached to the nitrogen atom. In general such protons dissociate far less readily (pK 8-11) but the aromatic ring stabilises the basic ion L^{2-} relative to the conjugate acid form, HL^{-}. Hence dissociation of the anilinium ion, ϕNH_3^+, occurs at a comparatively low pH (pK=4.6). In this case the dissociation must represent ionisation of an amino- proton. Arsenic, being larger and less electronegative than nitrogen, cannot combine with a proton to form the species R_3AsH^+; hence PHENIMDA(I)and PHENASDA (II) are not directly comparable. With both acids, however, pK_1 represents the ionisation of a proton attached to a carboxyl group so that comparison of these values is possible. Nitrogen, being more electronegative than arsenic, will exert a greater electron attracting effect. This effect will be transmitted through the methyl carboxy-groupings and so facilitate the ionisation of the protons. Hence the decrease in acid strength found for the arsenic analogue is to be expected. The difference between pK_2 and pK_1 for PHENASDA (1.43pK units) is greater than can be attributed to purely statistical factors; these would cause a difference of about 0.6 pK units. The negative charge on the ion HL^{-} would tend to overrule the weak electron attracting nature of the ø-As-

group causing a smaller decrease in the value of pK_2 than in pK_1 relative to that of the corresponding carbon acid (glutaric acid, pK_1=4.21, pK_2=5.06). Hence, compared with glutaric acid the decrease in pK_1 is 0.41 units while the decrease in pK_2 is negligible (0.03 units).

In chlor-PHENASDPA (IV) the carboxyl groups are further removed from the arsenic atom than in PHENASDA; hence they will be influenced to a smaller extent by inductive effects from this atom or the phenyl group. In fact, the dissociation constants found are similar to that of propionic acid itself (pK=4.88) and the difference between pK_2 and pK_1 is largely accounted for by statistical factors.

Diphenylaminepropionic Acid (V) and Its Phosphorus and Arsenic Analogues (VI, VII).

The acid dissociation constants were determined using 20% aqueous dioxan as solvent in each case. Hence, while detailed comparisons with dissociation constants determined using water as a solvent are not possible, the values are directly comparable between themselves.

Before titrations were carried out the purified dioxan was treated with alkali to ensure that it did not

contain any weak acids. Solutions containing equal concentrations of perchloric acid, using water as a solvent in one case and 20% dioxan in the other, were then titrated. The curves were superimposable indicating that, in 20% dioxan, the value of $\log(fU_H^o)$ in Van Uitert and Haas' equation :- $-\log[H^+] = B + \log(fU_H^o)$, where B is the pH meter reading, is zero.

The ionisable hydrogen atom of the nitrogen derivative (V) would certainly be bonded to the carboxyl group and not the nitrogen atom; this is demonstrated by the high acidity of the species $\phi_2NH_2^+$ (pK=0.87). Hence each dissociation represents the ionisation of a carboxyl group.

The dissociation constants of the nitrogen and phosphorus derivatives are almost identical while those of the arsenic analogue indicate that it is a slightly weaker acid. This is to be expected as a direct result of the electronegativity difference between nitrogen and arsenic. Since two methylene groups intervene between the group V atoms and the carboxyl groups, the influence of such electronegativity differences on the ionisation of the hydrogen of the carboxyls would be small.

It has been shown that the dissociation constants of carboxyl hydrogen atoms are decreased by the addition of dioxan to the solution (33). The decrease generally results in an increase in the pK value of about 0.3 units.

If, then, this value is subtracted from the dissociation constants calculated, the approximate values for these constants in water will be found.

TABLE XIII

	pK_1	$pK_1 - 0.3$
$\phi_2N.(CH_2)_2COOH$	5.06	4.76
$\phi_2P.(CH_2)_2COOH$	5.03	4.73
$\phi_2As.(CH_2)_2COOH$	5.21	4.91

These values are very similar to the dissociation constant of propionic acid (4.71, $\mu = 0.2$, $T = 20^{\circ}C$).

Stability Constants of the Metal Complexes.

The Metals Chosen and the Methods Used.

The reason for investigating the metal complexes of these ligands was to compare the acceptor properties of class (a) and class (b) metals (see Fig. 1, page 3) for donor atoms of the same group of the periodic table.

The complexes of many representative class (a) metals may be readily investigated in solution by a potentiometric titration technique similar to that used in the investigation of the complexes of the amino-acids described in Part I. In general equilibrium is rapidly established in solution and the complexes formed are comparatively resistant to oxidation or reduction. The most stable complex found is usually of the form $ML_n(H_2O)_m$ and, in the acidity range normally investigated (pH 3-10), there are usually only small contributions from protonated complexes or hydroxy complexes; these can usually be treated quantitatively by calculations involving successive approximations. Actual measurements made during the potentiometric titrations of the ligands in the presence of metal ions are shown in section VI and the titration curves in graphs XIX—XXIV. The stability constants calculated from these figures are found in Table XIV, page 65.

Metals with a strong class (b) character, however, are few and their complexes do not lend themselves readily to quantitative investigation. Many of the complexes formed are 'inert' in that equilibrium is established very slowly. Hence methods requiring the rapid establishment of successive equilibria (e.g. titration methods) cannot be used. A further complication is that many of the complexes, once formed, are insoluble in water and may not, in fact, be simple complexes but polynuclear species of high molecular weight. Quantitative treatment of these is, at the best, approximate and incomplete.

Of all the class (b) metals, silver is probably the most readily investigated. Univalency is the only common valence state so that problems of oxidation (which introduce difficulties when working with cuprous copper) are not encountered. Further, reduction to the metal does not normally take place with most organic ligands. Equilibrium is rapidly attained in solutions of silver ions and ligands, and although the complexes formed between the metal and ligand ions often tend to be insoluble in water, sufficiently high concentrations are usually obtainable.

With amino-polycarboxylic acids and similar ligands containing both oxygen and some other donor atom, protonated

silver complexes of high stability are often found (34). This is presumably a result of the very weak character of the silver-oxygen bonds which are readily broken, allowing a proton to bond with the oxygen atom. Such complexes of both hydrogen and metal may be investigated by potentiometric titration methods but present many difficulties if pH measurements only are made during the titration. Calculations based on such measurements are both involved and lengthy and the constants obtained are extremely sensitive to small uncertainties in measurements of pH. Fortunately reversible electrodes which respond both accurately and reproducibly to changes in silver ion activity can be made (e.g. the silver/silver iodide electrode) and, from simultaneous measurements of both pH and pAg (the free silver ion exponent) accurate values for the stability constants of both protonated and unprotonated complexes may be obtained. This method has therefore been used to determine the values for stability constants of complexes of silver with the ligands discussed in this section.

Changes in the pH of the solution under investigation were followed in all cases with a glass electrode and a saturated calomel reference electrode. In titrations in the presence of silver, electrical connection between

the solution and the reference electrode was made with a potassium nitrate salt-bridge (page 102). A total volume of 20 ml. of titration solution was used (usually of ligand concentration 0.001M, with a salt background of KNO_3 to maintain a constant ionic strength of 0.10M). Carbonate-free alkali was added from an 'Agla' micrometer syringe. Silver ion concentrations were determined as described on p.102, E° being determined for both aqueous solutions of ionic strength 0.1M and for 20% aqueous dioxan solutions of the same ionic strength. The values differed by only 1mV.

Titration curves obtained are shown in graphs XIX - XXIV and the stability constants found are shown in Table XIV. The actual experimental results are tabulated in Section VI.

Mercuric ions (Hg^{2+}) form very stable complexes with ligands of the type considered but equilibrium is established slowly, so that potentiometric titrations are not very practical. Mercuric ions also hydrolyse readily in all but strongly acid solutions so that neutral standard solutions cannot be prepared. Attempts were made to employ solutions containing a known amount of mineral acid, but the titration curves obtained were not accurately reproducible and stability constants

calculated from these showed very large drifts in magnitude. The experimental technique actually adopted was based on Schwarzenbach's 'pHg' method (6) and involved the measurement of both pH and pHg. It is described on pages 105 and 133. When the number of ligands coordinated to the metal ion is greater than one (e.g. ML_2) calculation of the stability constants becomes more difficult and values for the stepwise equilibrium constants are considerably less reliable than the values for the overall constant (β_n).

Since the mercury electrode is a reducing electrode there is a considerable excess of mercurous ions in the mercuric ion solution. The validity of the method used in this work depends upon the assumption that mercurous ions do not enter into the reactions of complex formation. This is a reasonable assumption when bonding is of a purely σ-type (as with nitrogen) but when there is a possibility of additional charge transfer between the metal and ligand donor atoms, the supposition is more dubious. No data are available to give even an indication of the magnitude of the stability constants of Hg_2^{2+} with any ligands containing heavier donor atoms.

Mercuric chloride does not hydrolyse in aqueous solution in which it is scarcely ionised. Attempts were

therefore made to titrate slowly the ligands considered in this section in the presence of a known concentration of mercuric chloride since, knowing the stability constants of the chloride complexes of mercury, corrections could be applied to the constants calculated from the titration curve to give the stability constants required. Fair agreement was found between constants calculated from the titration curve and by the 'pHg' method for PHENASDA (II), but in other cases the drift in the value for the constants was excessively large. Even with PHENASDA it amounted to more than a power of 10 between 'a' = 0.2 and 1.7.

Calculated stability constants are tabulated in Table XIV, shown on the following page.

Some Individual Complexes.

Complexes of PHENASDA (II) were considered in more detail since only very small quantities of the other ligands were available and PHENASDA is directly comparable to PHENIMDA (I), which, apart from the silver and mercury complexes, had been investigated by Schwarzenbach (30).

(a) The Complex of PHENASDA with Copper.

Mixtures of cupric copper and PHENASDA formed a

Table XIV.

Metal Complex Stability Constants at 20°C. and μ=0.10M(KNO_3)

Ligand	PHENIMDA I	PHENASDA II	HEXDA III	chlor-PHENASDPA IV	DIPHEN-AMPA V	DIPHEN-PHOSPA VI	DIPHEN-ASPA VII
					20% DIOXAN.		
pK_1	2.40 (30)	3.60	2.25 (31)	4.17	5.06	5.03	5.21
pK_2	4.96	5.03	10.61	5.08			
log values Cu K_1	6.57(30)	2.51	11.04	~1.5	n.m.	n.m.	n.m.
Ni K_1	3.53(30)	1.49	8.08	n.m.	n.m.	n.m.	-
Zn K_1	3.22(30)	1.4	7.60	n.m.	n.m.	-	-
Cd K_1	2.90(30)	~1	6.94	n.m.	-	n.m.	n.m.
Ag_M		4.02	-	3.98		2.7~	2.3~
K_{MHL}							
K_1	~1	5.37	4.60	5.00	n.m.	3.80	3.87
β_2						6.5~	
Hg^{II}							
K_1	8						
β_2	8.26 / 12.91	14.7 / 19.92	13.8 / 22.8	24.4	(20.9	16.9	22.5)
Cu^{I} K_1		5.7(35)					

n.m. = not measurable.

Hg^{II}- PHENASDA complex; from a titration in the presence of $HgCl_2$ - log K_1 = 13.4, log β_2 = 19.2.

light green precipitate in the region of pH 4.6. This precipitate formed with several different concentration ratios of ligand to metal so a sample was prepared and analysed. The results for carbon, hydrogen, and copper indicated a complex of formula CuL (see page 122). This formula for the complex was later confirmed using Job's method of continuous variations and following the formation of the complex by its absorbancy at 327 and 350mμ. (35). Even using a large excess of ligand (5:1) in potentiometric titrations, $\bar{n}$ values greater than 0.6 were never obtained before precipitation occurred.

The value given for the stability constant of the complex of chloro-PHENASDPA with copper is very approximate because, in every titration that was attempted, a light green precipitate formed almost immediately.

(b) <u>The Stability Constants of Silver Complexes</u>

Various procedures were followed to obtain values for the stability constants of silver with PHENASDA. Potentiometric titrations during which pH only was measured were carried out using several different ratios of metal to ligand but, on account of the high stability of the species MHL, the constants found were unreliable. A large excess of metal was therefore used and Schwarzenbach's method of 'temporary constants' employed (26). Results of the same

order, but rather lower, than those calculated from the measurement of pH and pAg were obtained. Silver bromate has a limited solubility in water so that, if an excess of silver bromate is used the solution will always be saturated and, at a constant temperature and ionic strength, the silver ion concentration in solution will be constant. A titration was carried out under such conditions using an ionic background of 0.10M $KBrO_3$ to which a calculated amount of $AgNO_3$ was added to maintain always a faint precipitate. The value quoted by Schwarzenbach for the solubility product of $AgBrO_3$ under these conditions was used (36) and stability constants calculated. The constants found were again lower than those quoted in Table XIII (differing by 0.5 Log units). Since the silver ion concentration in the solution used was not itself measured in-dependently, a constant error may have been introduced from this source.

Measurements of stability constants of silver with analogous ligands have been made by Chatt using a version of the method of corresponding solutions (4). This method had to be used because the ligands he studied were all strong acids; hence proton displacement measurements could not be made. A similar technique was therefore used to examine the silver complexes of PHENASDA. Sodium acetate-

acetic acid buffer solutions were used to maintain a constant pH and corrections were applied during the calculations to allow for the incomplete dissociation of PHENASDA at the acidities used. Silver/silver iodide indicator electrodes were employed, prepared as described in section III, and the titrations were carried out at two different pH values (pH 5.92 and 4.48), each using three different metal ion concentrations. Stability constants were calculated by Leden's method, as modified by Fronaeus (4), employing graphical integration to determine free ligand concentrations.

Values for $\bar{n}$ tended to go a little beyond unity at high ligand concentrations but the predominant complex was clearly the mono-complex AgL. The calculated stability constant for AgL in the solution of lower pH was a little higher than that for the more alkaline buffer. This indicates the presence of protonated complexes. Assuming the only protonated form to be AgHL, stability constants for both AgL and AgHL were calculated. The values found were higher than those determined by potentiometric titration procedures but the ratio K_{ML}/K^{M}_{MHL} was almost exactly the same. Were the species AgH_2L also present the values of the constants would be somewhat lower.

Whenever a large excess of silver ions over ligand was used a white granular precipitate formed above pH 3.5. The results of an analysis on a sample of this precipitate showed that the composition approximated to that required for AgL.

Mixtures of chloro-PHENASDPA (IV) with silver in the concentration ratio of 0.001M ligand to 0.001M silver produced no visible precipitate over the pH range covered during titration with alkali. However, when the ratio was 0.001M ligand to 0.0005M silver a white precipitate formed. This precipitate redissolved on adding more silver solution to make the ratio 0.001:0.001M. This suggested that an insoluble complex of the formula AgH_xL_2, might have been formed. A similar observation was made during titrations of DIPHENPHOSPA (VI) in the presence of silver (using 20% dioxan as solvent.) Calculations using measurements made during a titration of this latter compound with an equal concentration of silver ions definitely indicated the formation of a complex species of formula AgL_2. However quantitative treatment of the equilibrium to take account of all the species, Ag, AgHL, AgL AgL_2 etc. is extremely difficult and only approximate values for the stability constants were obtainable.

(c) The Stability Constants of Mercury^{II} Complexes.

The procedure used is described fully in Section III and the basis of the method of calculation of stability constants is outlined in Section IV. In all cases it was found that a white precipitate formed when mercury^{II} ions were added to solutions of the ligands unless the mercury concentration was very small (below 10^{-4}M.) and there was a large excess of ligand. Precipitates, once formed, could often be redissolved by adjusting the pH of the solution. In other cases they did not appear to redissolve but instead they turned grey, indicating some sort of irreversible decomposition. When precipitates, however faint, formed on the surface of the mercury electrode, the potential of the cell became unsteady and irreproducible and the readings had to be rejected. Such incipient precipitation was often difficult to detect and may have led to the variations found in the calculated values of the constants.

When 20% dioxan had to be used as solvent the further complication of possible complex formation between mercury and dioxan arose. Normally mercury does not complex strongly with oxygen as a donor atom but solid compounds with dioxan have been prepared (37). Compound formation of this type, together with possible complex

formation between mercurous ions and phosphorus and arsenic, introduces uncertainties in the values quoted for stability constants.

Since the value for E° in aqueous solution (determination of which is described on page 105) would be different to that in 20% dioxan solution the appropriate value for use in this solvent was determined. A series of pairs of mercury solutions was prepared. Each pair contained the same concentration of mercury but differed in that one of the pair used 0.1M aqueous KNO_3 as a solvent while the other used 0.1M KNO_3 in 20% dioxan solution. Potentials of mercury electrodes in these solutions were then measured. The differences found between different pairs were not constant but varied from 2mV to 12mV, having a mean value of 4mV. This indicates that little complex formation takes place between mercury and dioxan. Mercury, however, formed very insoluble complexes with the ligands investigated in dioxan solution so that only very dilute and alkaline solutions could be studied. The potentials of the mercury electrodes often drifted considerably and were not reproducible, and stability constants calculated from the most reliable apparent potentials were not always self-consistent. Hence no great reliance can be placed upon the values for the mercury complex stability

constants found for ligands V-VII.

The Stability Constants of the Chelates of HEXDA.(III)

Table XV

Stability Constants at 20°, and μ = 0.10M (KCl)

	Me-IMDA (Ref:38)	HEXDA
pK_1	2.81	2.25
pK_2	10.18	10.61 (31)
Log K_1, Cu	11.09	11.04
'' K_2,	6.83	6.70
'' β_2,	17.92	17.74
Log K_1, Ni	8.73	8.08
'' K_2,	7.22	7.04
'' β_2,	15.95	15.12
Log K_1, Zn	7.66	7.60
'' K_2,	6.43	5.9
'' β_2,	14.09	13.5
Log K_1, Co	7.62	7.19
Log K_1, Cd	6.77	6.94

Me-IMDA = N-methyliminodiacetic acid.

Comparison of the stability constants of the chelates of HEXDA with the chelates of iminodiacetic acid is not

possible since the latter compounds have only been investigated at 30°C (39). However comparison with the results obtained for N-methyliminodiacetic acid (Me-IMDA) is possible.

The cyclo-hexyl group could influence the chelate stabilities in two ways. By the influence of its inductive effect it could tend to increase the stabilities while, being a large substituent, it could bring steric factors into play and tend to decrease the values. In fact the stability constants found are slightly lower than those found for the comparable Me-IMDA chelates which were investigated by Schwarzenbach (38). This indicates that the cyclo-hexyl ring sterically hinders the formation of complexes. Comparison of the results with those for the PHENIMDA chelates clearly demonstrates the marked decrease in stability of both proton and metal complexes caused by the replacement of the cyclo-hexyl ring with a phenyl ring. Although it forms very stable complexes with mercury^{II} and a comparatively stable complex with silver, HEXDA clearly bonds far more strongly with class (a) metals than with those of class (b): this is seen most clearly if its complexes are compared with those of PHENASDA.

The Stability Constants of the Chelates of PHENASDA (II) and chloro-PHENASDRA(IV)

(see Table XIV, page 65.)

Complex Formation with Class (a) Metals.

The complexing ability of arsenic with class (a) metals is shown clearly to be less than that of nitrogen in comparable compounds. PHENASDA is directly comparable with PHENIMDA, I, and, since the proton complexes of the arsenic acid tend to be more stable than those of the nitrogen analogue, co-ordination through the carboxylic acid group would be greater in the case of the arsenic acid than the comparable nitrogen compound. This means that co-ordination through the arsenic atom will be even weaker than is indicated by the stability constants quoted in Table XIV, page 65.

In the ion HL^-, the electronegativity effects of the Ø-N< and Ø-As< groupings are small since the values of the second acid dissociation constants (K_2) of both PHENASDA and PHENIMDA are similar to the second dissociation constant of glutaric acid, the analogous compound containing $-CH_2-$ in place of the Ø-N group. If the metal stability constants of the arsenic and nitrogen ligands are compared with the values for glutaric acid itself, any increase in the size of the constant will

indicate bonding through the nitrogen or arsenic atoms. Copper^{II}, while showing some class (b) characteristics, is a typical class (a) metal with respect to the donor atoms of Group V. Cadmium did not show any marked class (b) character in any of the complexes investigated in this work.

Table XVI

Ligand	Glutaric Acid (40)	PHENIMDA (30)	PHENASDA
Conditions:	25°, μ = 0.2	20°, μ = 0.1	
pK_2	5.08	4.96	5.03
Log K_{CuL}	2.40	6.57	2.51
Log K_{ZnL}	1.60	3.22	1.4

Table XVI shows that, in the case of PHENIMDA, bonding through the nitrogen atom contributes by far the greater part of the free energy of complex formation while, in PHENASDA, bonding through the arsenic atom appears to be negligible.

Since arsenic is a larger atom than nitrogen, it would not be expected to form as strong a sigma(σ)-bond with metals by lone-pair donation. Hence, considering single bond formation only, weaker complex formation is to be expected between PHENASDA and metals than with PHENIMDA.

The same argument applies to the complexes of chloro-PHENASDPA (IV) but, since data for the complexes

of pimelic acid are not available, further comparison is not possible. The stability of the copper complex is, however, of the order expected for such a dicarboxylic acid forming a chelated complex containing a large ring.

Complex Formation with Class (b) Metals.

(i) The Silver Complexes.

The argentous ion, Ag^+, has a completely filled 4d shell and low ionic charge; it tends to form predominately covalent complexes. The stabilities of complexes formed are increased considerably if the donor atom of the ligand has vacant orbitals of suitable energy and shape which allow an overlap of the metal's filled d-orbitals to take place. This would cause the metal-ligand bond to take on some double bond character. When this can occur the metal—donor atom distance is decreased and the free energy of the bond formation increases considerably, resulting in an increase in the stability of the complex found. Such dative π-bond formation can reasonably take place between silver and phosphorus or arsenic but not between silver and nitrogen, which has no available d-orbitals of the required energy.

PHENIMDA was synthesised and its silver complex investigated. As is usual in ligands of this type which

can readily chelate with class (a) metals through the carboxyl groups, it was found to have a low stability compared with the complexes with copper and nickel. If σ-bond formation only is considered, the stabilities of the silver complexes of PHENASDA and chloro-PHENASDPA would be expected to be very low since it is known that silver-carboxylate ion bonds are weak. Furthermore, on account of the larger size of the arsenic atom, silver-arsenic σ-bonds would be much weaker than silver-nitrogen bonds.

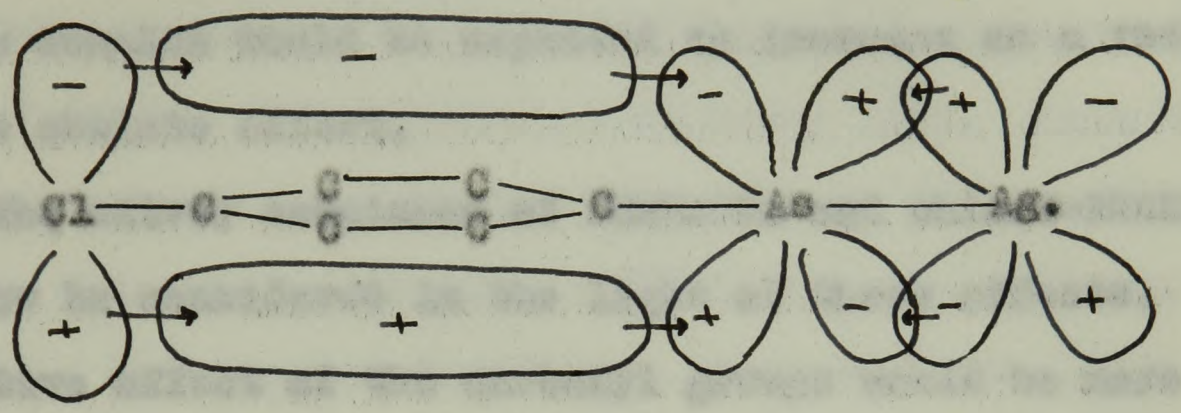
The high stabilities found for the silver complexes of these ligands definitely indicates additional silver-arsenic bonding, presumably of a π-type. The only comparable investigation has been made by Chatt and co-workers and they found the same marked effect in their study of the silver complexes of sulphonated aniline, triphenylphosphine, triphenylarsine.(4)

PHENASDA and chloro-PHENASDPA are both weak acids and hence may be studied by means of potentiometric titrations, which are more convenient than Leden's corresponding solution method, which was used by Chatt. As mentioned earlier, this latter method was used to determine the stability constant of PHENASDA-silver complex to make comparison more reliable, although the temperature

and ionic strength used in Chatt's experiments were different to those employed in this work. The value found for this constant was slightly larger than the value reported by Chatt for the stability constant of the silver-tri(g-sulphophenyl)arsine complex. This increase is to be expected since the presence of three g-sulphophenyl groups bonded to the arsenic atom would probably decrease the co-ordinating affinity of arsenic rather more than the groups attached to arsenic in PHENASDA or chloro-PHENASDPA.

The values of the stability constants of the silver complexes of PHENASDA and chloro-PHENASDPA are very similar, the PHENASDA complex being a little more stable. The effect of the para-chloro group in chloro-PHENASDPA would be two-fold. Being strongly electronegative it will tend to draw electrons away from the phenyl ring and arsenic atom so decreasing the donating ability of the latter. This would then weaken the As-Ag σ-bond. Further, the unshared p-electrons of the chlorine atom could conjugate with the electron system of the benzene ring. The result of this would be that any overlap between the 4d orbitals of the arsenic atom and the Π-orbitals of the ring would result in an increased transfer of charge to the arsenic atom. This would weaken π-bond formation between the full 4d

orbitals of the silver ion and vacant 4d obitals of the arsenic atom.



Chatt has shown unambiguously that mixing between d orbitals of large atoms bonded to a benzene ring and the π -orbitals of the ring does take place (41). The overall effect of the para-chlorine atom in chloro-PHENASDPA (IV) would therefore be expected to result in a decrease in complex stability.

Normally oxygen co-ordinates only weakly with silver, hence bonding through the carboxyl groups would not be expected to be strong. Chatt has shown that the co-ordination number of silver with ligands having a large d_π-bonding capacity is normally one (or possibly three). Hence bonding to silver through the carboxyl groups of PHENASDA and chloro-PHENASDPA would be even less than is normally found. The -I (electron attracting) inductive effect of -COO$^-$, and

especially -COOH, groups is large, hence they will tend to decrease the strength of the As-Ag σ-bond. If they do co-ordinate themselves with the silver then the stability of the complex would be expected to increase as a result of the chelate effect.

The silver complexes of PHENASDA and chloro-PHENASDPA may now be considered in the light of these effects. The inductive effect of the carboxyl groups would be more noticeable in PHENASDA since there is only one methylene group between these groups and the arsenic atom. In chloro-PHENASDPA two methylene groups intervene. However, if bonding through the carboxyl groups does take place it will increase the stability of the PHENASDA complex more than the comparable chloro-PHENASDPA complex, since, in the former case, the chelate ring formed is five membered while it is six membered in the latter. Since the stability constants found are of similar magnitude it is probable that in neither case does bonding through the carboxyl groups take place. Rather, the lowering of the stability of the chloro-PHENASDPA complex, resulting from the introduction of the p-chlorine atom, appears to be comparable to the lowering of the stability of the PHENASDA complex resulting from the -I inductive effect of the carboxyl groups β to the arsenic atom. Hence it appears that,

while class (a) metals tend to bond almost entirely through the carboxyl groups of these ligands, a typical class (b) metal bonds almost entirely through the arsenic atom.

This is further supported by investigations of the copper^{I} (class (b)) complex of PHENASDA (35). From the redox potential measurements James showed that noticeable complex formation took place well before the carboxyl groups ionised. The complex formed was found to have a high stability (Log K = 5.7) and to be a dibasic acid with acid dissociation constants of pK_1 = 2.70, pK_2 = 3.96.

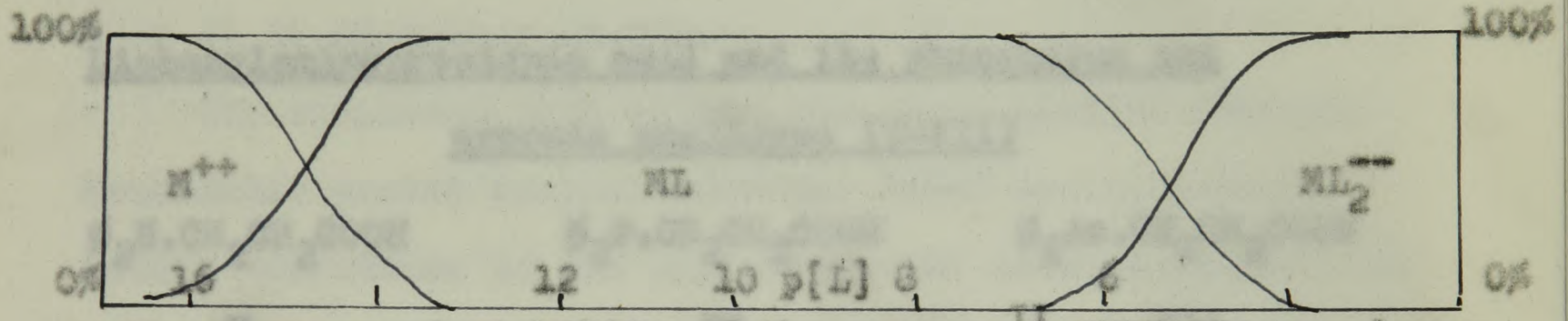
(ii) <u>The Mercury^{II} Complexes.</u>

Stability constants of complexes of mercury^{II} with phosphorus or nitrogen as donor atoms have not been previously determined. Mercury^{II}, however, shows distinct class (b) characteristics and would be expected to form very stable complexes. This has been shown to be the case.

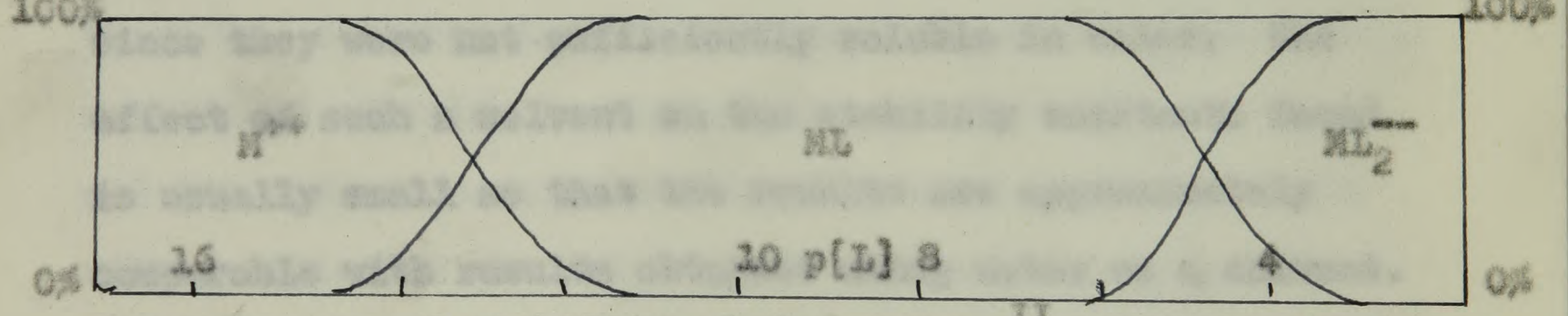
The complex with PHENIMDA has a high stability constant which is of the order expected from a comparison with other data relating to mercury^{II} complexes with nitrogen as donor atom. The species HgL_2 is certainly present but the calculation method did not consider the possibility of protonated complexes. Attempts to calculate the stabilities

of such complexes proved useless but showed that they were less than the stabilities of unprotonated species by at least four powers of ten.

As expected, the mercury^{II} complex of PHENAMDA is considerably more stable than the comparable complex with PHENIMDA. This is demonstrated in the graphs shown below.



The regions of stability of the mercury^{II}-PHENAMDA complexes.



The regions of stability of the mercury^{II}-PHENIMDA complexes.

The value found for β_2 was reproducible over a wide concentration and pH range and demonstrates clearly that mercury has a marked class (b) character. Bonding through the arsenic atom would be expected to be the major factor in the high stability found.

The stability constant of the mercury complex with chloro-PHENANDPA is known with much less certainty on account of its low solubility in water. The value found is rather higher than would be expected and it is difficult to see the cause of such an increase.

Diphenylaminepropionic acid and its phosphorus and arsenic analogues (V-VII)

$\phi_2N.CH_2CH_2COOH$ $\phi_2P.CH_2CH_2COOH$ $\phi_2As.CH_2CH_2COOH$

V. VI. VII.

These ligands were investigated in 20% dioxan solution since they were not sufficiently soluble in water. The effect of such a solvent on the stability constants found is usually small so that the results are approximately comparable with results obtained using water as a solvent.

In no cases could measurable proton displacement be detected in the presence of class (a) metals; this is in keeping with the weak donor properties normally found for tertiary nitrogen atoms, especially when two of the substituted groups are phenyl groups. Further, chelate formation through the carboxyl group would form a six membered chelate ring which is known to be considerably

less stable than five membered rings (29).

All the ligands appeared to form stable complexes with mercury but the low solubilities of these complexes prevented accurate investigation. The only comparatively reliable and reproducible results obtained were those for the diphenylarsine-propionic acid complex and these indicate that it is abnormally stable.

The complexes with silver were more readily studied. Measurable proton displacement was found during potentiometric titrations of the phosphorus and arsenic derivatives and the silver ion concentrations of the solutions dropped throughout the titrations. With the arsenic derivative there was evidence for the existence of an insoluble silver complex in addition to the soluble species AgHL and AgL, and the titration curve of the phosphorus derivative with silver indicated the existence of the species AgL_2 and allowed an approximate calculation of its stability constant.

The stability constants found are of the order expected. The high stabilities of the protonated complexes indicate little bonding through the carboxyl groups and since two methylene groups separate the carboxyls from the donor atoms, they would have little effect on their co-ordinating ability. The two phenyl groups attached to the phosphorus and arsenic

atoms would be expected to decrease their abilities to form either σ- or π-bonds with acceptor ions and account for the lower stability of the complex of the arsenic acid compared with the PHENASDA complex.

It is interesting to note that the stability constants of the silver complexes of both the phosphorus and the arsenic derivatives are almost identical. This result differs from Chatt's finding that, when phosphorus is the co-ordinating atom, the complexes formed are considerably more stable than the arsenic analogues. (4). However, the compounds studied in this work were considerably different from those examined by Chatt and, in his investigations, the substituents on the phosphorus and arsenic atoms were slightly different.

SECTION THREE.

EXPERIMENTAL DETAILS.

SECTION III.

Experimental Details.

Introduction:

(a) Proton Displacement and Stepwise Equilibria.

Polybasic acids dissociate by a series of steps, each representing the liberation of a proton and the formation of the conjugate base of the acid species involved :- $H_pL^{(m-p)-} = H^+ + H_{p-1}L^{(m-p-1)-}$,

$\ldots HL^{(m-1)-} = H^+ + L^{m-}$. . . .(i)

From a knowledge of the molar concentration of the acid, the fraction neutralized and the hydrogen ion concentration of the solution (all derived from the titration curve), the dissociation constants of each of these stepwise equilibria can be calculated.

In solution acidic ligands in the presence of metal ions establish the following equilibrium which represents competition between the protons and metal ions for bonding with the ligand :-

$$M^{q+} + H_pL^{(m-p)-} = ML^{(m-q)-} + pH^+ \quad \ldots\ldots(ii)$$

The magnitudes of the proton displacements caused by equimolar concentrations of different metals will clearly be measures of the relative stabilities of the metal complexes formed.

The stability of a metal complex is defined as the

mass action constant for the reaction of complex formation:- $M^{q+} + L^{m-} = ML^{(m-q)-}$ .....(iii)

Hence $^{T}K = \frac{[ML]}{(M)(L)}$ or, considering the stoichiometric constant, $^{C}K = \frac{[ML]}{[M][L]}$ ..... (iv)

When more than one ligand molecule can co-ordinate with the metal, co-ordination takes place in a stepwise fashion as in the formation of the proton complexes,

e.g. $M^{q+} + L^{m-} = ML^{(m-q)-}$,

$ML^{(m-q)-} + L^{m-} = ML_2^{(2m-q)-}$ .....(v)

The equilibrium constants for these consecutive reactions are known as the step-equilibrium constants of the species formed. The overall equilibrium constant of the species $ML_n^{(nm-q)-}$ will therefore be the product of the stepwise equilibrium constants,

i.e. $\beta_n = K_1K_2...K_n = \frac{[ML_n]}{[M][L]^n}$ .....(vi)

If no polynuclear species are present, the degree of formation of the system, $\bar{n}$, may be defined as the average number of ligand molecules attached to each metal ion. In the systems considered, species of complexity greater than ML_2 were not found. In such cases

$$\bar{n} = \frac{\Sigma(\text{bound ligand})}{\Sigma(\text{metal ions})} = \frac{[ML]+[2ML_2]}{[M]+[ML]+[ML_2]} = \frac{[L](K_{ML} + 2K_{ML}K_{ML_2}[L])}{1+[L](K_{ML} + K_{ML}K_{ML_2}[L])}$$

.....(vii)

From the preceding equation it is clear that stability constants can be calculated from a knowledge of sufficient $\bar{n}$ and pL values for the system. It is found convenient to express such values in the 'formation curve' of the system by plotting $\bar{n}$ against pL, the free ligand exponent.

Values for these quantities may be calculated from a knowledge of the acid dissociation constants of the ligand and the hydrogen ion concentrations of solutions of the ligand, at a known degree of neutralization, and in the presence of a known concentration of metal ions. To obtain a large number of experimental points for the formation curve it is convenient to titrate the ligand, in the presence of metal ions, with standardised, carbonate-free, alkali. By taking measurements of the pH at many points during the neutralisation, each representing the addition of a known amount of alkali, a titration curve may be plotted.

The apparatus and technique used to obtain titration curves is described in this section and the calculation of stability constants from such data is outlined in Section IV.

The Use of Concentrations in lieu of Activities.

The true, or thermodynamic, dissociation constants of an acid (or the stability constant of a metal complex) are difined in terms of activities rather than concentrations,

$$\text{e.g.,} \quad {}^{T}K_{HL} = \frac{a_{H^+}.a_{L^-}}{a_{HL}} ,$$

whereas the calculated conetants are defined in terms of concentrations,

$$\text{e.g.,} \quad {}^{C}K_{HL} = \frac{c_{H^+}.c_{L^-}}{c_{HL}} = \frac{[H^+][L^-]}{[HL]} .$$

It therefore follows that

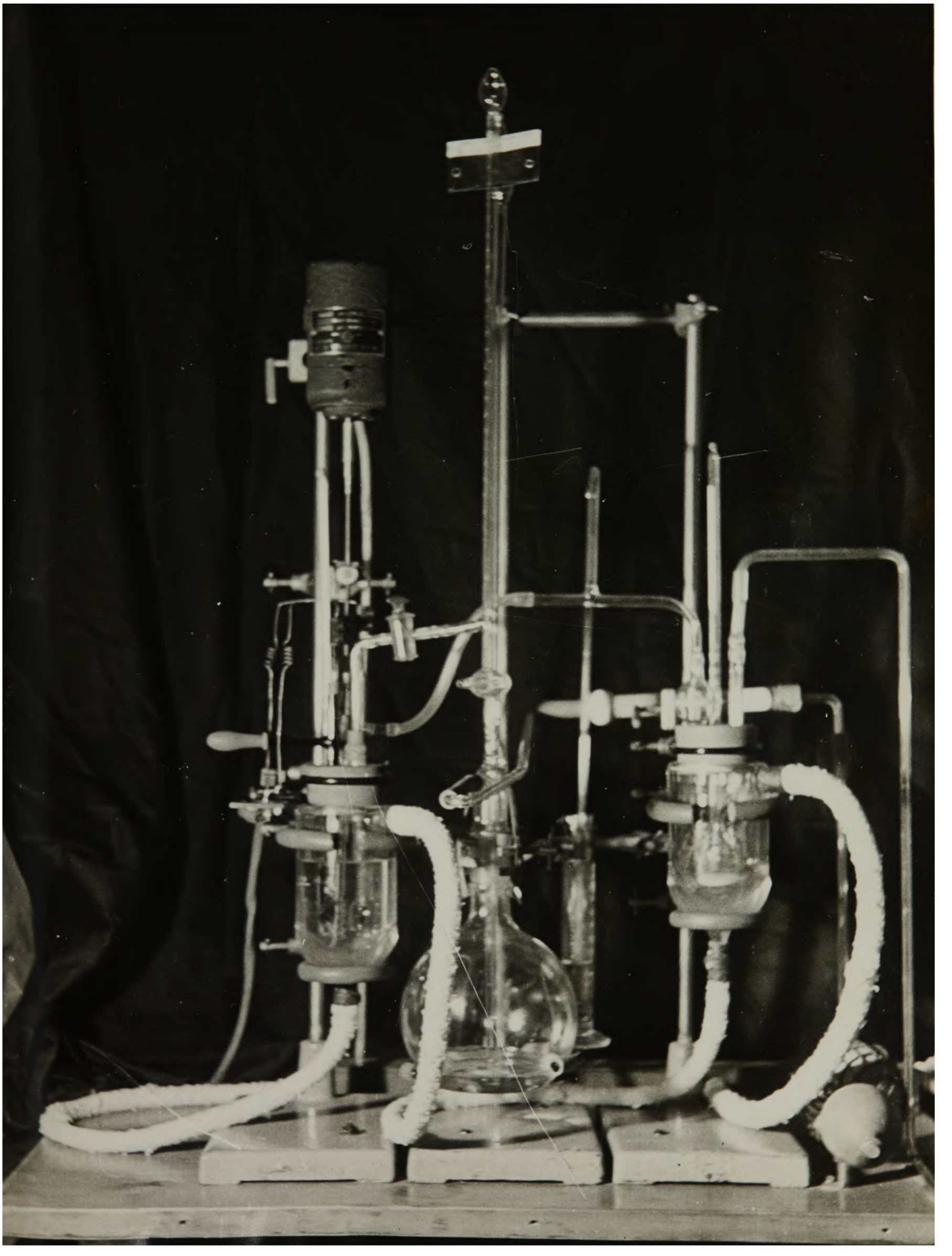
$${}^{T}K_{HL} = {}^{C}K_{HL}.\frac{f_{H^+}.f_{L^-}}{f_{HL}} , \text{ where } a_{HL} = c_{HL}f_{HL}.$$

The values of such calculated, or stoichiometric, constants will thus be constant if the relevant activity coefficients do not vary from one measurement to another. In this case ${}^{T}K_{ML} = {}^{C}K_{ML}$ x constant, or

$$\log {}^{T}K_{ML} = \log {}^{C}K_{ML} + \text{constant.}$$

In this work this has been secured by determining all constants in solutions containing an inert salt (KCl or KNO_3) of a strength such that the ionic strength of the solution, μ, is constant at 0.10M. (defining μ as $\frac{1}{2}\Sigma cz^2$, where c = concentration, and z = ionic charge, of each species in solution).

The stoichiometric constants so determined may differ considerably in magnitude from the thermodynamic values but it is accepted that, in solutions of constant ionic strength, activity coefficients are reasonably invariant. Hence values obtained in these investigations are directly comparable with those obtained by other workers using similar conditions.



The Hydrogen Electrode Titration Apparatus.

The titration apparatus was based on that used by Schwarzenbach (30) and gave similar quality results. In fact, to test it after a period of idleness, the titration curve of EDTA (Graph 28) was measured to ensure that it agreed with Schwarzenbach's and that constant performance was therefore maintained.

The indicator electrode was a hydrogen electrode of the Hildebrand type and the reference electrode was of electrolytically-prepared silver/silver chloride. The latter electrode was mounted inside a blackened glass tube whose lower end was drawn out into a tip of small diameter. The tube was dipped well into the liquid being titrated and adequate contact between the electrode and the liquid was arranged by squeezing a rubber bulb fitted on a side arm of the tube. The liquid in the tube was thereby expelled and fresh liquid drawn in. In this way hydrogen was prevented from making contact with the silver electrode, and at the same time junction potentials were avoided.

The titration vessel was of about 250 ml. capacity. It was double-walled, with water from a thermostat at 20°C circulating through the jacket.

The electrodes, a microburette, thermometer, a mechanical stirrer and an escape vent for hydrogen entered

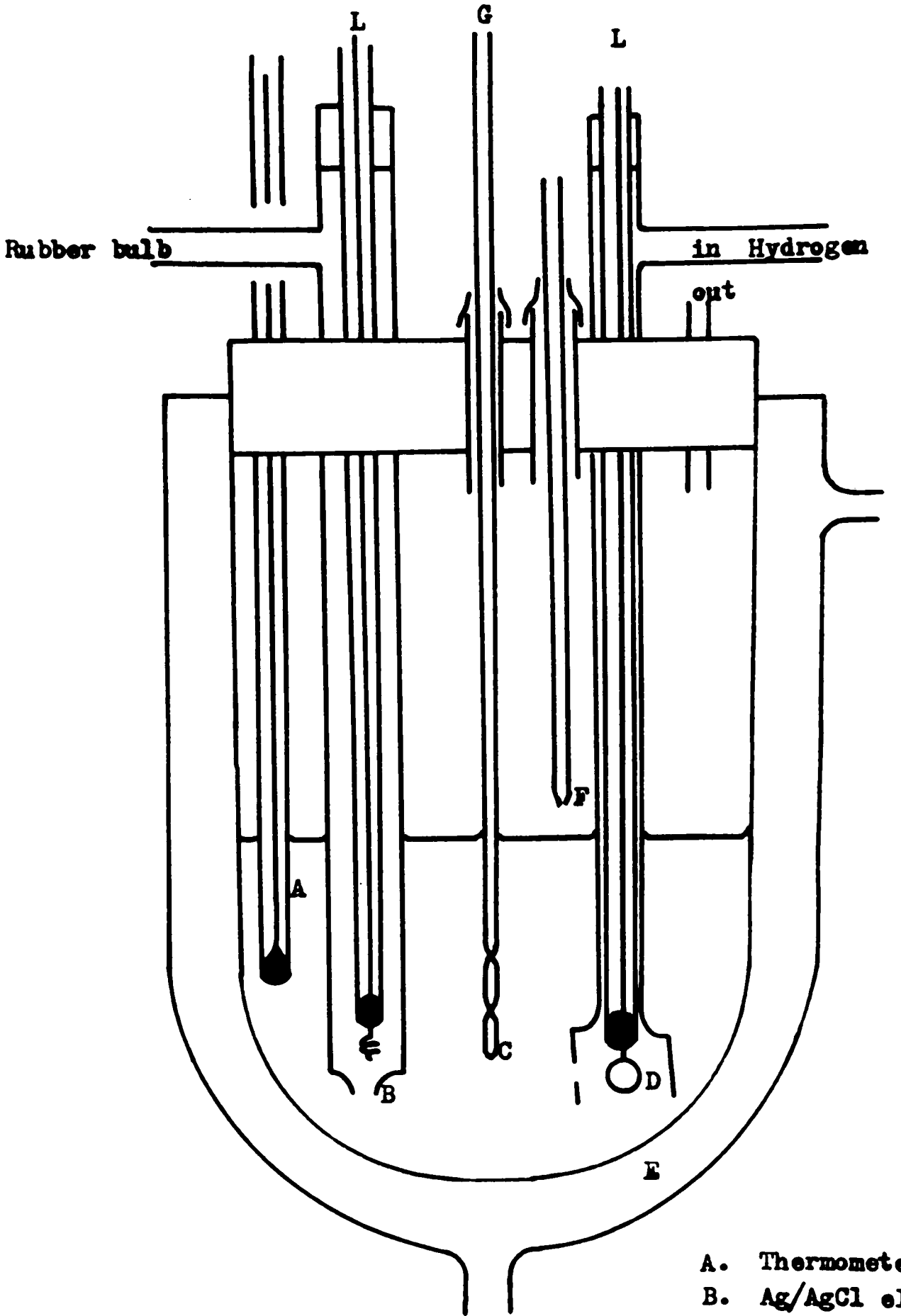


FIGURE 111

TITRATION CELL

A. Thermometer
B. Ag/AgCl electrode
C. Stirrer
D. H_2 electrode
E. Water jacket
F. Micro-burette
G. Flexible drive to motor
L. Leads to potentiometer

the vessel through a tight-fitting rubber stopper. An electric motor, remote from the electrodes, drove the stirrer through a flexible drive.

The delivery tube of the burette passed through the stopper inside a sleeve of glass tubing. This permitted the burette to be raised out of the solution between successive additions of titrant. This avoided troubles arising from diffusion of titrant from the capillary bore of the delivery tube into the main solution.

The hydrogen was electrolytic gas of the highest purity obtainable. Attached to the cylinder was a 'De-oxo' platinum catalyser to remove traces of oxygen. Hydrogen was led, through polythene tubing, to a saturator, a vessel identical with the titration flask containing titration liquid at the same temperature as in the main vessel. It was then led, via a glass sinter to remove droplets of liquid, to the electrode.

The silver/silver chloride electrode (conventionally positive) and the hydrogen electrode (conventionally negative) were connected to a Pye 'Universal' Slide Wire Potentiometer on which the cell E.M.F. could be read to one hundredth of a millivolt.

The Preparation of Electrodes.

a) Platinised Platinum Hydrogen Electrode.

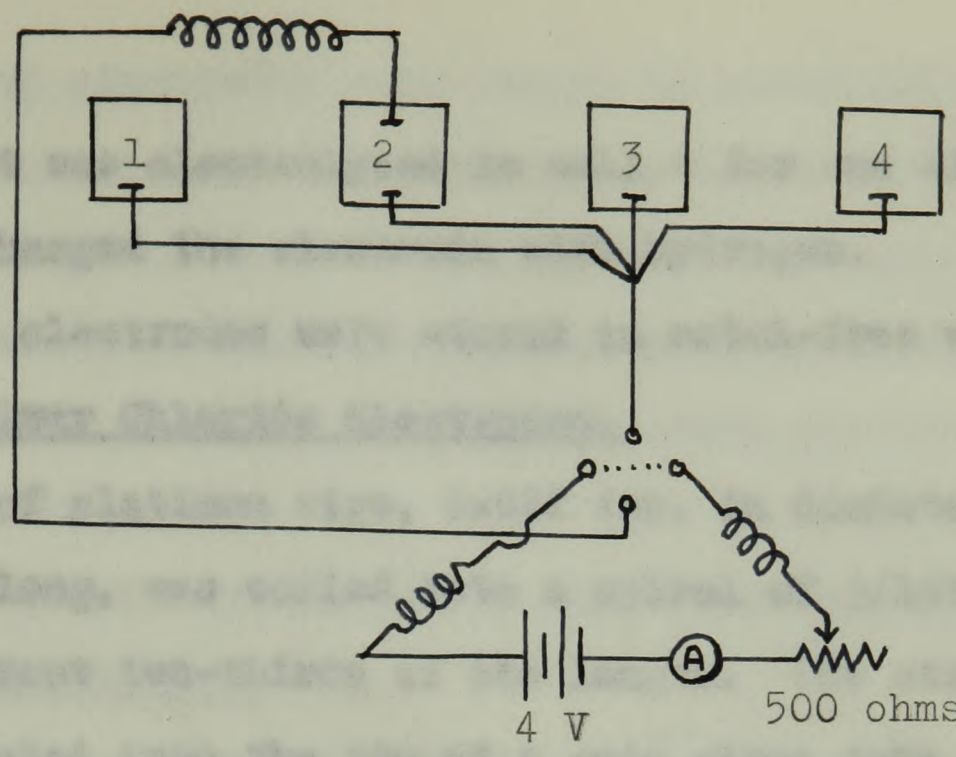
The electrodes were of the usual mercury contact type, and had a surface area of about 0.75 sq. cm.

The method of preparation was essentially similar to that recommended by Clarke (42) and Kunz (43).

Four cells of 2 cm. diameter and 5 cm. depth were mounted in a wooden rack, and an ordinary platinum wire electrode mounted in each. The latter were connected to a junction box in circuit with a fixed terminal of a double pole two throw switch. The opposite terminal was connected to the electrode being prepared by a flexible lead, so the latter could be moved from cell to cell as required. The centre terminals of the switch were in series with a milli-ammeter, 500 ohm variable resistance and a 4 volt battery. The circuit diagram is shown on the following page.

The cells contained the following solutions:-

1. Diluted (1:1) AnalaR hydrochloric acid.
2. 10% AnalaR sulphuric acid.
3. A 3% solution of chloroplatinic acid, made by dissolving platinum chloride in N/10 hydrochloric acid, and adding to every 100 ml. of this solution 0.5 ml. of N/10 lead acetate.
4. 10% AnalaR sulphuric acid.



APPARATUS FOR PREPARING PLATINUM ELECTRODES.

The procedure for platinising the electrodes was:-

1. The electrodes were cleaned by electrolysing as anode in the hydrochloric acid of cell 1. New electrodes were first polished with fine emery paper, following by immersion in boiling carbon tetrachloride, hot alkali and finally nitric acid.

2. The cleanliness of the electrodes was tested by electrolysis and counter-electrolysis in cell 2, and noting that gas was given off freely and evenly over the whole surface.

3. After washing, the electrodes were electrolysed as cathode in the chloroplatinic acid solution for 15 minutes at a current density of 1.35 amps. per sq. decimetre (about 12.0 milliamps. in this case), reversing the current every five minutes. The deposit was examined for completeness and

uniformity.

4. Finally it was electrolysed in cell 4 for one minute. This process charged the electrode with hydrogen.

Prepared electrodes were stored in metal-free water.

b) Silver/Silver Chloride Electrodes.

A piece of platinum wire, 0.022 ins. in diameter and about 1¼ ins. long, was coiled into a spiral of 3/16ths in. diameter for about two-thirds of its length. The straight portion was sealed into the tip of a soda glass tube, and made contact with a copper wire by means of a little mercury. Glass protrusions round the base of the tube prevented damage to the electrode when it was being inserted into the outer tube described previously.

New electrodes were first cleaned with carbon tetrachloride, strong alkali and nitric acid, and by washing in metal-free water. They were then plated with silver by electrolysis (as cathode) in a 10% solution of potassium silver cyanide, in an H-type cell. A current of 3 milliamps. was used, and the anode was a thick silver wire. The potassium silver cyanide was prepared as follows. 25 gms. of silver nitrate were dissolved in 250 ml. of metal-free water, and a solution of 25 gms. of potassium cyanide in 250ml. of water was slowly added, with shaking, until the precipitate (AgCN) had nearly redissolved. The solution was filtered, and in this way excess cyanide was avoided.

The plated electrodes were washed in metal-free water for 24 hours, and finally electrolyzed as anode in N/10 potassium chloride solution to which a few drops of hydrochloric acid had been added. A current of 5 milliamps was employed for 15-20 minutes, and the operation was carried out in a blackened cell.

The electrodes were generally light red in colour.

c) Check of Electrodes.

The hydrogen and silver halide electrodes were checked simultaneously by determining the E.M.F. of the cell:-

$$Ag/AgCl(s), HCl(N/10)/H_2(Pt)$$

The tests were performed in the actual titration vessel, using carefully standardised hydrochloric acid instead of titration liquid.

The E.M.F. of the cell was determined and compared with the data of Harned and Ehlers.(44).

The electrodes were examined before and after each titration, using the same hydrochloric acid. If the value of the E.M.F. differed from the correct one by more than 0·2 millivolts, the electrodes were discarded.

The Measurement of E°.

The value of E° was calculated from the titration curve of standard perchloric acid against standard potassium hydroxide. The latter had been standardized by potentiometric titration against potassium hydrogen phthalate, while the concentration of the former was calculated from the actual titration used to determine E°. The end-point was found by Gran's method (45).

E° is given by the equation:-

$$E = E^{\circ} + \frac{RT}{nF}\ln[H] \qquad 1.$$

or at $20^{\circ}C$,

$$E = E^{\circ} - 0{\cdot}05816pH \qquad 1a.$$

Assuming perchloric acid to be completely ionized in solution, and knowing the fraction of the alkali required for neutralization that has been added, the hydrogen ion concentration can be calculated.

E° may therefore be calculated from a number of points on the neutralisation curve of the perchloric acid by using equation 1a. In this work, its value varied between 291 and 293 millivolts, and was very sensitive to barometric pressure. It was determined by this method almost every day.

The Meaning of E°.

The E.M.F. of the cell :-

$$Ag/AgCl \;\Big|\; \begin{matrix} 0{\cdot}01M \text{ Ligand} \\ 0{\cdot}10M \text{ KCl} \end{matrix} \;\Big|\; H_2/Pt$$

is given by the equation :-

$$E = E^{\circ\prime} + \frac{RT}{nF}\ln a_{H^+}.a_{Cl^-}$$

where $E^{\circ\prime}$ is the standard potential of the cell and a_{H^+} and a_{Cl^-} the activities of the respective ions. If now f_{H^+} is the activity coefficient of the hydrogen ions, of molarity m_{H^+},

$$E = E^{\circ\prime} + \frac{RT}{F}\ln a_{Cl^-} + \frac{RT}{F}\ln f_{H^+} + \frac{RT}{F}\ln m_{H^+}$$

In this equation, $E^{\circ\prime}$ is constant by definition, a_{Cl^-} is maintained constant and, since there is no appreciable change in ionic strength during titrations, and from one measurement to another f_{H^+} may be considered invariable,

$$E = E^{\circ} + \frac{RT}{F}\ln m_{H^+},$$

$$= E^{\circ} + \frac{RT}{F}\,pH\,,$$

where $E^{\circ} = E^{\circ\prime} + \frac{RT}{F}\ln a_{Cl^-} + \frac{RT}{F}\ln f_{H^+}$,

and is constant under the conditions of the experiment and constant atmospheric pressure.

The Glass Electrode Titration Apparatus.

This apparatus consisted of a water jacket titration vessel similar to that used with the hydrogen electrode apparatus (p.91) with the electrodes mounted in a similar way. These consisted of a glass electrode (either an Electronic Instruments Ltd. type GHS 23, or a Radiometer type B electrode) and a saturated calomel reference electrode connected either to an electronic direct-reading pH meter (Electronic Instruments Ltd., model 23), or to the more accurate battery powered Radiometer 'PHM4b' pH meter. The latter could differentiate between solutions differing by as little as 0·003 pH units. The titration cell held 20 to 30 ml. of solution, which was stirred by a small glass paddle driven by a miniature electric motor. To prevent the entry of atmospheric carbon dioxide into the titration cell, presaturated nitrogen was passed through a jet just above the solution surface to maintain a pressure inside the cell slightly above that of the atmosphere. Alkali was added from an 'Agla' micrometer syringe, delivering up to 0·5 ml., mounted in the way outlined in the Appendix (p 181). This could be driven by an electric motor, as described, or operated manually. The pH meter was standardized before and after each titration, using 0·05M potassium hydrogen phthalate which has a pH of 4·00 at 20°C. The response of the glass electrode was checked for linearity before use by

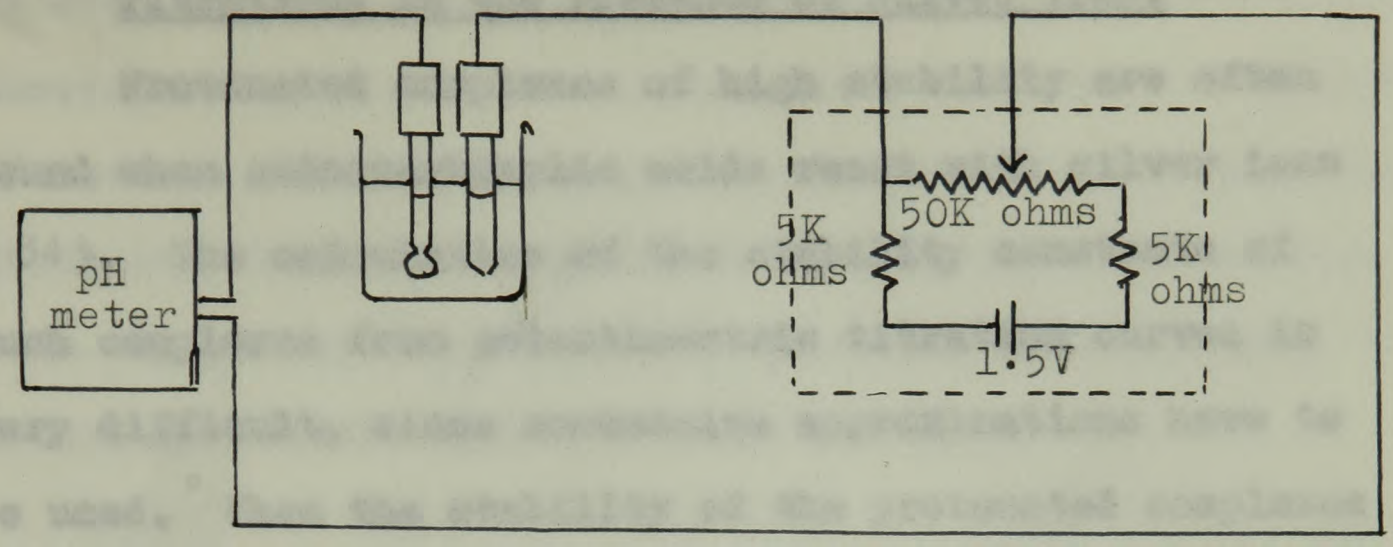
a series of standard buffer solutions.

Whenever possible, the saturated calomel reference electrode was used in direct contact with the solution being investigated. In titrations in the presence of silver ions this was not possible, so a salt bridge had to be incorporated. To minimise junction potentials, a saturated potassium nitrate bridge was used, connecting the titration solution with 0·1M KCl solution. The reference electrode was then inserted into the latter.

$$Hg_2Cl_2/Hg \;\Big|\; \begin{matrix}\text{Sat.}\\ KCl\end{matrix} \;\Big\|\; \frac{N}{10}\ KCl \;\Big\|\; \begin{matrix}\text{Sat.}\\ KNO_3\end{matrix} \;\Big\|\; \begin{matrix}\text{titration}\\ \text{solution}\end{matrix} \;\Big|\; \begin{matrix}\text{glass}\\ \text{electrode}\end{matrix}$$

With this arrangement it was found that junction potential errors never amounted to more than 0·02 pH units, using solutions with an ionic strength of 0·1M and standardizing with the pH 4·00 buffer.

It was found that the Radiometer pH meter required an electrode assembly which had a potential of zero at 6·3 ± 1·5 pH units; this limited the range of glass electrodes which could conveniently be used. This difficulty was overcome by incorporating an adjustable but constant source of potential in the circuit which enabled the potential of the electrode system to be corrected to that required by the pH meter. The circuit used is shown in the diagram on the following page.



The 'Flag' cell, potentiometer and resistances were all enclosed in a hermetically sealed metal canister, which was earthed, and the unit was inserted in series with the calomel electrode, since capacity effects were negligible between this electrode and the pH meter. The potentiometer was adjusted until the pH meter could be standardized to the value of the solution in the titration vessel. Since only a very small current indeed was taken from the 'Flag' cell, the potential was very steady and did not cause any detectable drift in standardization of the pH meter over periods of several days.

Titrations in the Presence of Silver Ions.

Protonated complexes of high stability are often found when aminocarboxylic acids react with silver ions (34). The calculation of the stability constants of such complexes from potentiometric titration curves is very difficult, since successive approximations have to be used. When the stability of the protonated complexes is comparable with that of the unprotonated complex, results from successive approximations converge only slowly, making calculation almost impossible. In such cases, measurement of the silver ion concentration simultaneously with the measurement of pH allows direct calculation of the various stability constants to be made (p.131).

Silver ion concentrations were measured by a silver/silver iodide electrode, with a saturated calomel reference electrode in the cell :-

reference electrode	$\frac{N}{10}$ KCl	Sat. KNO_3	titration solution	Ag/AgI glass electrode

The potential of the cell was measured by a Pye 'Universal' slide wire potentiometer and the silver ion concentrations were calculated by the following equation:-

$$E = E^{\circ} + 0.05618 \log_{10}[Ag] \quad (\text{at } 20^{\circ}C).$$

E° was determined by measuring the potentials of silver solutions of known concentrations and ionic strength

of 0·1M and extrapolating to zero silver ion concentration. Corresponding pH values were measured with the Radiometer pH meter. Silver/silver iodide electrodes were used, since Chatt has noted that ligands which form strong complexes with silver tend to dissolve both silver chloride and, to a smaller extent, silver bromide (4).

Preparation of Silver/Silver Iodide Electrodes.

Batches of six silver/silver iodide electrodes were prepared by a method similar to that described by Brown (46). Platinum wire, 0·5 mm. in diameter, was sealed into soft glass tubing leaving about 1 cm. outside the tube. The end of the wire was fused to remove any sharp edges and the wire cleaned in concentrated nitric acid. Electrical contact between the wire inside the tube and a stout copper wire was made by a small pool of mercury.

For electrolysis, the electrodes were supported by rubber stoppers inserted into holes drilled through a thin wooden disc, which formed a cover for the beaker used as an electrolysing bath. These formed the cathode and a platinum wire the anode. The silver plating solution used was a 10% solution of potassium silver cyanide, prepared as described on p. 95. Since hydrogen cyanide is generated, and silver cyanide precipitated, at the anode during electrolysis, contamination of the main body of the solution

was prevented by isolating the anode in a glass tube into which a sintered glass disc had been sealed. The group of electrodes was silver plated by electrolysis for a period of three hours at a total current of 1 milliampere.

After careful washing, the electrodes were iodized by electrolysis as anodes in a 0.1M. solution of potassium iodide for half an hour, using a total current of about 2 milliamperes. The electrodes were stored in distilled water in a dark cupboard, although they were not seriously affected by exposure to diffused daylight.

The Measurement of Stability Constants of Mercuric Mercury Complexes.

Since equilibrium between mercuric ions and ligands was reached very slowly, mixtures of various known concentrations of the two species were made up and allowed to equilibrate in a thermostat. Mercuric ions are readily hydrolysed in solution unless they are stabilised by complex formation (e.g. in $HgCl_2$ solution) or if the acidity is high. In this work basic mercuric nitrate, dissolved in nitric acid, was used as a source of mercuric ions.

Suitable mixtures of ligand and this solution of mercuric ions, with the pH's adjusted to approximately the desired values by the addition of alkali, were placed in 50 cc. test-tubes. These tubes were fitted with B-ground-glass joints and stoppers and each had a short length of platinum wire fused into its base. A quantity of mercury sufficient to cover the wire was added and the glass stoppers inserted. After the tubes had been vigorously shaken they were put into a thermostat at 20°C. This shaking procedure was repeated from time to time until equilibrium had been reached. The tube was then removed from the thermostat and a bung containing a glass electrode and a salt bridge was inserted. The platinum wire in the base of the tube was placed in a pool of mercury so that electrical contact could be made with the mercury inside the tube. The potential of

the mercury with respect to a saturated calomel reference electrode was measured with a Cambridge slide-wire potentiometer and the pH of the solution with a 'Radiometer' pH meter.

At values of pH below 3 the junction potential was appreciable, but it could be calculated approximately by Henderson's equation (47) or by the measurement of solutions of known pH. In practice, the latter procedure was followed.

The E.M.F. of the mercury electrode relative to the saturated calomel electrode is given by the equation:-

$$E = E^{o} + \frac{RT}{nF} \ln Hg^{++} + e_j$$

where e_j represents the junction potentials. In the cell used these junction potentials were approximately zero above pH 3, hence, in this region and at 20°C

$$E = E^{o} + \frac{0.05818}{2} \log Hg^{++} .$$

The value of E^{o} was found by measuring the potential of the cell for various mercury ion concentrations, making suitable corrections for junction potentials at low pH values. Such corrections were found from a graph in which the calculated pH values of solutions of known hydrogen ion concentrations, were plotted against the differences between these calculated pH values and the actual experimental values measured using the cell and pH meter calibrated against a buffer at pH 4.00.

The mercuric ion solution used for the determination of

E° was standardized by titration with E.D.T.A. using Eriochrome Black T as a metallochromic indicator. Solutions containing mercuric ions in the presence of metallic mercury are reduced according to the equation:-

$$Hg^{++} + Hg = Hg_2^{++} .$$

The equilibrium constant for this reaction, at 20°C and μ=0·1, is 87·5 ( ). Hence the concentration of free mercuric ions in a solution of the standardized mercury in the presence of mercury metal may be calculated. On account of the junction potential, appreciable at the pH values which had to be used to prevent hydrolysis, the calculated value of E° was dependent on pH. By plotting a graph of E° (measured) against the hydrogen ion concentration, the true value of E° was found as the intercept on the E° axis. As expected, deviations of E° (measured) values from this were found to be similar to the junction potentials at those pH values.

$E^{\circ}_{Measured}$	$[H^+]x10^{-3}$	e_j(mV)	E° from graph	$E^{\circ}_{Measured}-e_j$
0·5957	0·747	-0·4	0·5965V	0·5961
0·5947	2·722	-1·6	"	0·5963
0·5938	4·697	-2·9	"	0·5967
0·5922	6·672	-4·1	"	0·5963
0·5911	8·647	-5·3	"	0·5964
0·5904	10·622	-6·4	"	0·5968

The Preparation of Potassium Hydroxide free from Carbon Dioxide.

The method followed here was similar to that recommended by Schwarzenbach and Biedermann. (48).

The apparatus is shown in Figure 4. A glass sinter was sealed into a Pyrex tube of about three inches in length and one inch in diameter, and fitted with B 24 standard taper cones at each end. Two double-necked 1 litre Pyrex flasks could then be fitted, as shown in the diagram. The one, A, was fitted with an escape tube which almost touched the bottom of the flask, and was closed externally by a soda-lime tube. The other, B, was equipped with a fine jet through which nitrogen, free from CO_2, could be passed, and also a tap through which suction was applied as necessary. It was arranged that the whole assembly could be swivelled through 180° in the vertical plane.

42.4675 gm. (0.25 moles) of AnalaR silver nitrate were dissolved in boiled-out redistilled water and precipitated, in flask A, with the escape tube removed, as Ag_2O with a solution of sodium hydroxide which contained as little carbonate as possible. The solid was washed well with boiling water, and then boiled with metal-free water for some time to convert any carbonate to the oxide. After removal of the water, a slight excess of CO_2-free N/2 KCl (a solution containing 37.275 gm. KCl in 500ml.) was added to the silver

oxide. Most of the air was removed from the flask by bubbling in CO_2-free nitrogen. It was then stoppered tightly and shaken for two hours. Nitrogen was passed through flask B and the sinter for 30 minutes. With the apparatus in the inverted position (B uppermost) flask A containing the suspension was fitted and the nitrogen supply cut off. The air tube was placed in the latter vessel, and A gradually brought up to the top. In this ~~was~~ the clear solution of KOH and KCl was obtained, it being absolutely free from CO_2. The small trace of silver it contained had no effect on the titrations.

By dilution with boiled-out metal-free water, the solution was made 0.1 N with respect to KCl. The latter was estimated by titration against standard silver nitrate.

The Preparation of Sodium Hydroxide free from Carbon Dioxide.

A concentrated sodium hydroxide solution was prepared by dissolving pellets of AnalaR NaOH in approximately the same volume of water and allowing the solution to stand for several days. Sodium carbonate, which is insoluble in this syrup, separated and the syrup was sucked into a 100 ml. pipette through a filter stick while a stream of nitrogen was directed into the flask. The solution was then trans-

ferred to a two-necked flask through which nitrogen was passing : one neck was closed with a 'Sofnolite' guard tube, while the other was closed with a serum cap through which a long hypodermic needle was inserted to withdraw NaOH solution as required. It was found that such a strong solution takes up water slowly, but for titration purposes an approximately 3N stock solution was prepared by dilution.

SECTION FOUR.

ORGANIC PREPARATIONS.

ORGANIC PREPARATIONS

Preparation of α-amino-iso-butyric acid.

Reactions :-

$$(Me)_2CO + NaCN + NH_4Cl = (Me)_2C\begin{matrix}OH\\CN\end{matrix} + NaCl + NH_3$$

$$(Me)_2C\begin{matrix}OH\\CN\end{matrix} + NH_3 = (Me)_2C\begin{matrix}NH_2\\CN\end{matrix} + H_2O$$

$$(Me)_2C\begin{matrix}NH_2\\CN\end{matrix} + H_2O_{(cold)} + HCl = (Me)_2C\begin{matrix}NH_2.HCl\\CO.NH_2\end{matrix}$$

$$(Me)_2C\begin{matrix}NH_2.HCl\\CO.NH_2\end{matrix} + H_2O_{(hot)} + HCl = (Me)_2C\begin{matrix}NH_2.HCl\\COOH\end{matrix} + NH_4Cl$$

$$(Me)_2C\begin{matrix}NH_2.HCl\\COOH\end{matrix} + AgOH = (Me)_2C\begin{matrix}NH_2\\COOH\end{matrix} + AgCl + H_2O.$$

(α-amino-iso-butyric acid.)

The method used was a type of Strecker synthesis (49) and for safety all preliminary stages were carried out in a fume-cupboard.

Sodium cyanide (25gm.) were dissolved in water (50ml.) in a litre round-bottomed flask. Ammonium chloride (30gm.) was dissolved in warm water (70ml.) and added to the cyanide solution. Ammonia solution (sp. gr. 0.880, 13ml.)was added to this mixture and the whole cooled with water and stirred mechanically

while acetone (36ml.) in methanol (80ml.) was slowly added. The flask was stoppered and half immersed in a water bath at 60.0° for five hours. The mixture was then saturated, at 0°C., with HCl gas, left to stand overnight and then refluxed for two and a half hours. It was evaporated to dryness under reduced pressure on a water bath and the residue suspended in dry alcohol (250ml.) and boiled on a water bath. The solution was filtered to remove inorganic salts and the residue washed with dry alcohol. Ether (200ml.) was added to the filtrate to precipitate other inorganic material, the solution again filtered and the filtrate evaporated to dryness. The residue was dissolved in water (800ml.) and the solution treated with excess freshly prepared hydrated silver oxide. This reacted with the chloride ions in the amino-acid hydrochloride and decomposed any ammonium salts remaining. The suspension was diluted, filtered, washed with water and the filtrate concentrated to about 200ml. under reduced pressure and again filtered. The filtrate from this operation was saturated with H_2S and the black silver sulphide formed filtered off. The filtrate, containing the the pure amino-acid, was evaporated to dryness under reduced pressure and the amino-acid crystallised twice from 95% aqueous alcohol.

Yield : 14gm. M.Pt : 200° C, 46.6%; H, 8.7%.

Cyclo-hexane-1-amino-1-carboxylic acid.

Zelinsky and Stadnikoff's method (50) was used. Potassium cyanide (6.5gm.) and ammonium chloride (5.4gm.) were dissolved in water (50ml.). Redistilled cyclo-hexanone (9.8gm.) was added followed by sufficient methyl alcohol to give a single phase. The solution was left to react at room temperature for several days and then refluxed for a few minutes to complete formation of the cyanohydrin. After being cooled in ice, an equal volume of hydrochloric acid (concentrated) was added and the solution was saturated with hydrogen chloride. After being left overnight at $0^{\circ}C.$, the mixture was heated under reflux to complete the hydrolysis of the cyanohydrin, (2 Hrs) and then evaporated to dryness under reduced pressure on a water bath. The amino-acid hydrochloride was extracted from the reaction mixture by heating under reflux for a few minutes with dry alcohol (200ml.) containing a little dry ether. The extract was evaporated to dryness, taken up in water (100ml.) and treated with an excess of freshly prepared hydrated silver oxide in a manner identical tothe preparation of α-amino-iso-butyric acid. Excess silver was again removed by saturating with H_2S and, after removal of the precipitated silver sulphide by filtration, the resulting solution was evaporated to dryness. The pure amino-acid was obtained by recrystallising the residue twice from aqueous alcohol.

Yield = 2.8gm (20%)

M.Pt. = 209°C with decomposition.

Found:- C, 58.8; H, 9.2%.

($C_7H_{13}O_2N$ required C, 58.6; H, 9.1%.)

Cyclo-heptane-1-amino-1-carboxylic acid.

The method of preparation was identical to the preparation of cyclo-hexane-1-amino-1-carboxylic acid, cyclo-heptanone replacing cyclohexanone. The materials used were redistilled cyclo-heptanone (11.2gm.), potassium cyanide (6.5gm.) and ammonium chloride (5.4gm.). The pure amino-acid (monohydrate) was obtained by recrystallisation from aqueous alcohol. This is a stoichiometric compound but the molecule of water could be completely removed by drying at 125°C.

Yield = 3.5gm (23%)

M.Pt. = 215°C with decomposition.

Found:- C, 54.9; H, 9.6%.

($C_8H_{15}O_2N,H_2O$ requires C, 54.8; H, 9.8%.)

Phenyliminodiacetic acid.

Two methods of preparation were used, both giving good yields of the required product. In the first method, redistilled aniline (9.3gm., 0.1mol.) was condensed with

sodium chloroacetate (0.3 mol.) in water (100ml.), the sodium chloroacetate being prepared from chloracetic acid (28.2gm.) and sodium hydroxide (12.0gm.). The reaction mixture was well stirred and the temperature maintained at 90-95°C in a water bath. Sodium hydroxide (8.0gm; 0.2 mol.) in water (10ml.) was added slowly from a dropping funnel at such a rate that the pH of the solution was maintained between the change points of phenolphthalein and thymolphthalein. On acidifying the resulting solution and cooling, crystals of phenyliminodiacetic acid separated. These were filtered off at once to minimise contamination and twice recrystallised from aqueous alcohol and dried. It was found that pure starting materials were essential, otherwise an oil was obtained which appeared to decompose further in air, making crystallisation very difficult.

Yield = 60%

M.Pt. = 154°C

Verlander and Mumme's preparation was also used (51). Recrystallised phenylglycine (9.0gm.) and chloroacetic acid (8.4gm.) in water (30ml.) were neutralised with sodium carbonate crystals. The mixture was heated in a boiling water bath and more sodium carbonate crystals added in small portions until the condensation reaction was complete (i.e. no more effervescence). This took about two hours. The resulting solution was then acidified with concentrated HCl,

when an oil first formed. This redissolved in excess acid and crystals of phenyliminodiacetic acid were obtained on cooling. These were recrystallised from aqueous alcohol but purity was essential if oil formation was to be avoided.

Yield = 70%,

M. Pt.= 152°.

The purity of the products was checked by direct titration with alkali and calculation of the acid dissociation constants. The calculated values agreed with those reported by Schwarzenbach (30).

Piperazine-NN'-diacetic acid, PIPDA.

Crude PIPDA was available in the laboratory and was thought to be the monohydrochloride (31). After three recrystallisations from water the chloride content was determined by titration with standard silver nitrate solution using Volhard's method.

(Found : Cl, 14.5. $C_8H_{14}O_4N_2.HCl$ requires Cl, 14.85%).

The purity of the acid was measured by carrying out a potentiometric titration with alkali. The acid was found to be the pure monohydrochloride. A further crystallisation had no effect on either the chloride

content or the titration end-point, so the product was assumed to be the stoichiometric compound, piperazine-NN'-diacetic acid monohydrochloride.

The dihydrochloride was obtained by recrystallisation from concentrated hydrochloric acid, but it was not completely pure so the dissociation constant of the most acidic hydrogen was not calculated.
(Found: Cl, 22.0. $C_8H_{14}O_4N_2.2HCl.2H_2O$ requires Cl, 22.75%).

Titration end-point deviation = 2.5%.

The Preparation of Piperidine-N-monoacetic acid (PIPMA).

Following Kraut's method (52) chloroacetic acid (4.7gm, 0.05 mole) in water (10ml.) was added to redistilled piperidine (14.3gm., 0.1 mole) in water (20ml.) and the reaction mixture left at room temperature for twenty-four hours. After being left for a few minutes a violent reaction commenced, the solution turning slightly brown, but this quickly subsided without excessive decomposition taking place. Unreacted piperidine was then removed from the solution by distillation under reduced pressure and the remaining solution, containing piperidine acetic acid and piperidine hydrochlorides, was diluted with water (80ml.). The solution was brought to the boil and freshly prepared hydrated silver

oxide was added in excess to remove all the chloride ions from solution. Precipitated silver chloride was filtered off and the solution boiled under reduced pressure to remove as much of the free piperidine as possible. It was then diluted with water to 200 ml. and hydrogen sulphide passed to precipitate silver remaining in solution. When precipitation was complete (20 minutes) the solution was boiled, filtered and the filtrate evaporated to dryness. The residue, composed of the required piperidine acetic acid, was twice recrystallized from aqueous ethanol. Crystals of the monohydrate were obtained, the anhydrous acid being formed by drying the monohydrate in an air oven at 85°C.

Yield = 6 gm.

M.Pt. = 214°C.

The Preparation of Diphenylamine-N-propionic Acid.

This compound had been prepared previously by Mann and Millar using an acid catalysed Michael addition reaction to prepare the nitrile :-

$$\phi_2N + CH_2{=}CH\text{-}CN \longrightarrow \phi_2N.CH_2.CH_2.CN$$

which was hydrolysed, in alkaline solution, to the carboxylic acid (53) :-

$$\phi_2N.CH_2.CH_2.CN + 2H_2O \xrightarrow{OH^-} \phi_2N.CH_2.CH_2.COOH + NH_3$$

Although the autoclave and high vacuum distillation apparatus originally used in this synthesis were not available in the laboratory an alternative, but essentially similar, method was devised. It was found that a Carius tube with a wall thickness of 3 mm. could withstand the high pressure developed during the preparation.

The nitrile was prepared as follows :- Diphenylamine (40 gm.), vinyl cyanide (18 cc.), acetic acid (18 cc.), copper acetate (2 gm.) and copper powder (4 gm.) were sealed into a Carius tube of internal diameter 23 mm. and length 35 cm. The tube was heated for 8 hours at 150°C in a steel safety tube inserted into a tube furnace. This consisted of a length of asbestos pipe of suitable diameter around which was wound a length of resistance wire, connected to a 'Variac' transformer. The transformer was then adjusted until the temperature inside the tube was constant at 150°C.

After being allowed to cool slowly the Carius tube was opened, the contents transferred to a 100 ml. flask and volatile constituents removed by distillation under reduced pressure on a boiling water-bath.

At this stage, Mann purified the nitrile by distillation and fractionation at 138°C under a pressure of only 0.05 mm. Such a distillation was attempted but a sufficiently low pressure could not be obtained. With the best vacuum pump available, the boiling point of the reaction mixture was 195°C

and distillation at this temperature left large amounts of involatile material in the distillation flask. On examination the distillate was found to be unreacted diphenylamine, containing only traces of hydrolysable material.

The preparation was then repeated but, after removal of the more volatile constituents of the reaction mixture by distillation, free acetic acid was neutralised with anhydrous sodium carbonate and the mixture heated under reflux with cyclohexane (300 ml.) for a few minutes, to extract the nitrile and unchanged diphenylamine from the copper and polymers formed during the reaction. The solution was filtered while hot and cyclohexane removed from the filtrate by distillation on a water-bath.

The residue, containing the nitrile, was then hydrolysed by heating under reflux for four hours with potassium hydroxide (40 gm.) in water (200 ml.) and ethanol (150 ml.). Ethanol was removed by distillation and the solution allowed to cool. Unreacted diphenylamine separated as an oil from the alkaline solution and eventually solidified; it was then removed by filtration. The filtrate was acidified with concentrated HCl to pH 2-3 when the required acid was precipitated as a bulky, light-brown precipitate, partly in the form of an oil which slowly acidified. This precipitate was collected and crystallized from aqueous ethanol. An oil, containing most of the impurities, was first formed, then

discrete crystals separated. If the solution was again filtered as soon as this stage was reached, the filtrate yielded colourless crystals of diphenylamine-N-propionic acid. These crystals were again recrystallised from aqueous alcohol and dried in an air oven at 80°C.

Yield = 8 gm.

M.Pt. = 210 - 211°C (Literature :- 212°C)

The Copper Complex of Piperazine-NN'-diacetic acid (PIPDA).

A sample of the blue precipitate, which formed at pH 3.6 when a 0.01 M solution of PIPDA was titrated in the presence of copper ions, was collected and dried at 80°C. Part of the sample was analysed for copper by converting it to cupric oxide. A weighed sample (about 20 mg.) of the precipitate was gently heated, in a silica crucible, with a drop of concentrated nitric acid. After being cooled, a further drop of acid was added and the crucible heated to dull red heat to convert the copper nitrate to the oxide. This was weighed and the process repeated to constant weight.

Found :- C, 35.4; H, 5.0; N, 10.5; Cu, 21.0%.

($C_8H_{12}O_4N_2Cu$ requires C, 36.4; H, 4.9; N, 10.6; Cu, 24.1%)

The results indicate that the precipitate approximates to the

1:1 complex, although it was possibly not the simple species Cu.PIPDA.

The Copper^{II} Complex of Phenylalaninediacetic acid (PHENASDA).

The precipitated complex was collected, dried at 80°C and analysed for carbon and hydrogen. The copper content was determined spectrophotometrically with cuproine. A sample of the dried precipitate (10 mg.) was weighed, a drop of concentrated nitric acid added and the solution made up to 250 ml. with water. Hydroxylamine hydrochloride (5 ml. of a 10% solution) was added to a 25 ml. aliquot and the pH adjusted to between five and six with ammonia. A solution of cuproine in amyl alcohol (5 ml. of a 0.1% solution) was added and the mixture shaken with amyl alcohol (10 ml.). The lower aqueous layer was drained off and extracted with a further 10 ml. portion of the alcohol and the combined organic layers were made up to 25 ml. with more amyl alcohol. The absorbancy of this solution was measured in a 1 cm. cell at 536mμ. Standard copper solutions were prepared from weighed lengths of pure copper wire and their absorbancies measured in a similar way. The copper content of the first solution could be found from a graph of absorbancy against

percentage copper.

Found :- C, 34.9; H, 3.2; Cu, 21.4%.

($C_{10}H_9O_4AcCu$ requires C, 36.3; H, 3.0; Cu, 19.2%).

Hence the precipitate appears to be the 1:1 complex, CuPHENACEDA, or possibly a hydroxy-complex of this species.

SECTION FIVE.

METHODS OF CALCULATION.

SECTION FIVE.

METHODS OF CALCULATION.

(i) The Amino-acids.

(a) The Acid Dissociation Constants.

Values for $\bar{n}_A$, the degree of formation of the proton complexes, were determined by Irving and Rossotti's method (8) from the titration curves of a solution of a strong mineral acid (HCl) alone, and a solution of the same concentration of acid in the presence of the amino-acid. The curves were plotted on large sheets of graph paper (100 x 80cm.) to enable accurate measurements to be made.

The degree of formation, $\bar{n}_A$, is defined as:-

$$\bar{n}_A = \frac{\text{total concentration of protons bound to ligand}}{\text{total concentration of ligand.}}$$

$$= \frac{[HL] + 2[H_2L^+]}{[L^-] + [HL] + [H_2L]^+} = \frac{\frac{[H^+]}{K_2} + \frac{2[H^+]^2}{K_1K_2}}{1 + \frac{[H^+]}{K_2} + \frac{[H^+]^2}{K_1K_2}}$$

where $K_1 = \frac{[H^+][HL]}{[H_2L]^+}$ and $K_2 = \frac{[H^+][L^-]}{[HL]}$.

Hence, knowing values for $\bar{n}_A$, values for the dissociation constants can be calculated. Since $K_1 \gg K_2$, and below pH 7, $K_2 \ll [H^+]$ while above pH 7, $K_1 \gg [H^+]$,

$$K_1 = \frac{[H^+](2-\bar{n}_A)}{(\bar{n}_A-1)} \quad \text{and} \quad K_2 = \frac{[H^+](1-\bar{n}_A)}{\bar{n}_A} .$$

These equations hold quite accurately over the ranges $\bar{n}_A$ = 0.2 - 0.8 for K_2 and $\bar{n}_A$ = 1.2 - 1.8 for K_1

(b) <u>The Metal Chelate Stability Constants</u>.

Chelate stability constants were calculated from the 'formation curves' of the chelates (i.e. plots of $\bar{n}$, the degree of formation of the chelate, against pL, the free ligand exponent).

Values for $\bar{n}$ were calculated from different points on the titration curves by Irving and Rossotti's method (8), the curves being drawn on large sheets of graph paper to ensure maximum accuracy.

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

$$= [L^-] + [HL] + [H_2L^+] = [L^-]\left(1 + \frac{[H^+]}{K_2^H} + \frac{[H^+]^2}{K_1^H K_2^H}\right)$$

therefore $[L^-] = \dfrac{T_L - \bar{n}T_M}{1 + \dfrac{[H^+]}{K_2^H} + \dfrac{[H^+]^2}{K_1^H K_2^H}}$. Hence pL may be found.

By definition, $\bar{n}$ = $\dfrac{\text{total ligand bound to metal}}{\text{total metal}}$

$$= \frac{[ML] + 2[ML_2]}{[M] + [ML] + [ML_2]} = \frac{K_1[L] + 2K_1K_2[L]^2}{1 + K_1[L] + K_1K_2[L]^2} \quad \ldots\ldots(1)$$

where $K_1 = \dfrac{[ML]}{[M][L]}$ and $K_2 = \dfrac{[ML_2]}{[ML][L]}$.

Hence, $K_1 = \frac{1}{[L]} \cdot \frac{\bar{n}}{(1-\bar{n}) + (2-\bar{n})K_2[L]}$,

and $K_2 = \frac{1}{[L]} \cdot \frac{(\bar{n}-1) + \bar{n}/K_1[L]}{(2-\bar{n})}$.

i.e. as a crude approximation, $\log K_1 = pL$ when $\bar{n} = 0.5$

and $\log K_2 = pL$ when $\bar{n} = 1.5$.

Therefore, knowing a series of $\bar{n}$ and corresponding [L] values, K_1 and K_2 can be calculated. Whenever possible these constants were calculated by Irving and Rossotti's correction term method (18) but, when precipitation made it impossible to obtain $\bar{n}$ values as high as 1.5, the constants were determined by a graphical solution to equation (i). This equation may be rewritten as $\frac{\bar{n}}{(2-\bar{n})[L]^2} = \frac{(1-\bar{n})K_1}{(2-\bar{n})[L]} + K_1K_2$. Hence, by plotting $\frac{(1-\bar{n})}{(2-\bar{n})[L]}$ against $\frac{\bar{n}}{(2-n)[L]^2}$ a straight line of gradient K_1 and intercept K_1K_2 is obtained. The best values for the constants were determined by a statistical least-squares treatment.

(ii) Other Ligands, including PIPDA.

(a) The Acid Dissociation Constants.

In the general case, a solution of the acid H_pL which is being titrated with potassium hydroxide will contain the following ions :-

H^+, OH^-, K^+, H_pL, $H_{p-1}L^-$, $H_{p-2}L^{2-}$ . . . L^{p-}.

The total acid concentration =

$$C_L = [L^{p-}] + [HL^{(p-1)-}] + [H_2L^{(p-2)-}] \ldots [H_pL] \quad . . \text{(i)}$$

Since electroneutrality must be maintained in solution,

$$[H^+] + aC_L - [OH^-] = p[L^{p-}] + (p-1)[HL^{(p-1)-}] \ldots + [H_{p-1}L^-] \quad . . \text{(ii)}$$

where $aC_L = [X^+]$ =(degree of neutralisation)x(total ligand present)

Considering an acid of formula H_3L (i.e. $p = 3$), the dissociation constants are defined as :-

$$K_1 = \frac{[H_2L][H]}{[H_3L]} \quad . . \text{(iii)} \qquad K_2 = \frac{[HL][H]}{[H_2L]} \quad . . \text{(iv)}$$

$$K_3 = \frac{[L][H]}{[HL]} \quad . . \text{(v)}$$

where, for the sake of clarity, the signs have been omitted. Substituting equations (iii) - (v) in equations (i) and (ii) given the equations :-

$$aC_L + [H] - [OH] = [H_3L](K_1/[H] + 2K_1K_2/[H]^2 + 3K_1K_2K_3/[H]^3) \quad . .\text{(vi)}$$

and

$$C_L = [H_3L](1 + K_1/[H] + K_1K_2/[H]^2 + K_1K_2K_3/[H]^3) \quad . .\text{(vii)}$$

dividing equation (vi) by equation (vii) gives :-

$$\frac{aC_L + [H] - [OH]}{C_L} = \bar{n} = \frac{K_1/[H] + 2K_1K_2/[H]^2 + 3K_1K_2K_3/[H]^3}{1 + K_1/[H] + K_1K_2/[H]^2 + K_1K_2K_3/[H]^3} \quad \ldots \text{(viii)}$$

Hence, from a series of values of [H] and a, dissociation constants can be calculated.

If $K_1 \gg K_2 \gg K_3$,

$$K_1 = \frac{\bar{n}[H]}{(1-\bar{n})} \quad , \quad K_2 = \frac{(\bar{n}-1)[H]}{(2-\bar{n})} \quad , \quad K_3 = \frac{(\bar{n}-2)[H]}{(3-\bar{n})} \quad .$$

If two constants are very similar in magnitude so that the above equation (viii) cannot be simplified so drastically, dissociation constants may be calculated by either successive approximations or a graphical method. For example, in the case of PHENADUA, the constants were calculated from the following equation :-

$$\frac{(\bar{n}-1)}{\bar{n}[H]} = \frac{(2-\bar{n})}{\bar{n}[H]^2} \cdot K_2 - \frac{1}{K_1}$$ which represents a

straight line of gradient K_2 and intercept $\frac{1}{K_1}$.

(b) <u>The Chelate Stability Constants.</u>

Since with these ligands there was no indication of complexes other than the species ML and possibly MHL, the method of calculation could be simplified although essentially it is the same as the $\bar{n}$ - pL method, mentioned earlier.

As an example of the method of calculation, complexes of the ligand H_2L will be considered, assuming the metal (M^{2+}) to be added as MCl_2. Charges will be omitted from the following equations for the sake of clarity.

The total ligand concentration is given by:-

$$C_L = [H_2L] + [HL] + [L] + [ML] + [MHL] \quad \ldots\ldots (i)$$

The total metal ion concentration is given by:-

$$C_m = [M] + [ML] + [MHL] \quad \ldots\ldots\ldots\ldots\ldots (ii)$$

For electroneutrality,

$$aC_L + [H] - [OH] = [HL] + 2[L] + [Cl] - 2[M] - [MHL] \quad \ldots (iii)$$

Since the metal was added as MCl_2, $[Cl] = 2C_m$.

From equation (i),

$$[ML] + [MHL] = C_L - [H_2L] - [HL] - [L] \ ,$$

multiplying by two and substituting in (iii) gives:-

$$(2-a)C_L - [H] + [OH] = 2[H_2L] + [HL] + [MHL]$$

$$= [L](2[H]^2/K_1^H K_2^H + [H]/K_2^H + K_{MHL}^M[M][H]/K_2^H \quad \ldots (iv)$$

Therefore

$$[L] = \frac{(2-a)C_L - [H] + [OH]}{\frac{2[H]^2}{K_1^H K_2^H} + \frac{[H]}{K_2^H} + \frac{[M][H]K_{MHL}^M}{K_2^H}} \quad \ldots\ldots (v)$$

Hence, if K_{MHL}^M can be ignored, [L] can be calculated from the titration curve and a knowledge of the acid dissociation constants.

The elimination of [ML] and [MHL] from equations (i) and (ii) gives:-

$$[M] = (C_m - C_L) + [L]([H]^2/K_1^H K_2^H + [H]/K_2^H + 1) \quad \ldots \text{(vi)}$$

$$= (C_m - C_L) + a[L], \text{where } a = [H]^2/K_1^H K_2^H + [H]/K_2^H + 1$$

Hence, knowing [L], [M] can be calculated.

The value for [ML] may be obtained from (i) , i.e.

$$[ML] = C_L - [H_2L] - [HL] - [L] - [MHL]$$

$$= C_L - a[L] - K_{MHL}^M [M][H]/K_2^H \quad \ldots\ldots\ldots \text{(vii)}$$

Hence, if MHL can be ignored, [ML] can be calculated.

The stability constant of the species ML is defined as:-

$$K_{ML} = \frac{[ML]}{[M][L]} \quad \ldots\ldots\ldots \text{(viii)}$$

Therefore, substituting equations (v), (vi) and (vii) in (viii) and neglecting MHL

$$K_{ML} = \frac{C_L - a[L]}{[L](C_m - C_L + a[L])}$$

Hence K_{ML} may be determined.

If the species MHL is present, values for [M] for each point on the titration curve must be known before accurate values for [L] and [ML] can be found. This difficulty may be partly overcome by using a large excess of metal ions over ligand (e.g. 15:1). It may

then be assumed that the metal ion concentration is approximately constant throughout the titration. If K^{M}_{MHL} is very small compared with K_{ML}, values for [L] calculated by equation (v) will not be influenced greatly by the term including K^{M}_{MHL}. In this case

$$K_{ML}(\text{calculated}) = \frac{([ML]+[MHL])}{[M][L]} = K_{ML} + K^{M}_{MHL}[H]/K^{H}_{2} .$$

A plot of K_{ML}(calculated) against [H] will therefore give a straight line of intercept K_{ML} and gradient K^{M}_{MHL}/K^{H}_{2}. The plot will not be a straight line if [H] is large or if K^{M}_{MHL} is in any way comparable with K_{ML}.

When the 'Mercury' Computor programme was used to calculate the values of both K_{ML} and K^{M}_{MHL}, a value was first obtained for K_{ML}, neglecting K^{M}_{MHL}. Then, by a series of successive approximations, values for [M] in equations (v) and (vii) were refined until self-consistent results were obtained for K_{ML} and K^{M}_{MHL}.

Titrations in the Presence of Silver Ions, in which both $[Ag^{+}]$ and $[H^{+}]$ were measured.

With a ligand such as PHENASDA (H_2L) the total acid concentration is given by :-

$$C_L = [H_2L]+[HL]+[L]+[ML]+[MHL] \quad (+[ML_2] \text{ if this is considered}) \qquad \ldots\ldots\ldots(i)$$

Since $K_{ML} = \frac{[ML]}{[M][L]}$ and $K^{M}_{MHL} = \frac{[MHL]}{[M][HL]}$

$$C_L = [L](1 + [H]/K^{H}_{2} + [H]^2/K^{H}_{1}K^{H}_{2} + [M](K_{ML} + K^{M}_{MHL}[H]/K^{H}_{2})) \quad \ldots(ii)$$

For electroneutrality :-

$$aC_L + [H] - [OH] = 2[L] + [ML] + [MHL] + 2[ML] \ldots(iii)$$

since, if the silver is added as $AgNO_3$, $[NO_3] = C_M = [M] + [ML] + [MHL]$

Therefore :-

$$aC_L + [H] - [OH] = [L](2 + [H]/K^{H}_{2} + [M](2K_{ML} + K^{M}_{MHL}[H]/K^{H}_{2})) \quad \ldots(iv)$$

Dividing (iv) by (ii) gives :-

$$\frac{aC_L + [H] - [OH]}{C_L} = R = \frac{2 + [H]/K^{H}_{2} + [M](2K_{ML} + K^{M}_{MHL}[H]/K^{H}_{2})}{1 + [L]/K^{H}_{2} + [H]^2/K^{H}_{1}K^{H}_{2} + [M](K_{ML} + K^{M}_{MHL}[H]/K^{H}_{2})}$$

i.e.

$$\frac{(2-R) + (1-R)[H]/K^{H}_{2} - [H]^2R/K^{H}_{1}K^{H}_{2}}{[M](R-2)} = \frac{[H](R-1)K^{M}_{MHL}}{K^{H}_{2}(R-2)} = K_{ML} \ldots(v)$$

Equation (v) represents a straight line of the type $y = mx + c$ with a gradient of K^{M}_{MHL} and intercept of K_{ML} when the term on the left of (v) is plotted against $\frac{[H](R-1)K^{M}_{MHL}}{K^{H}_{2}(R-2)}$.

Examples of such plots are shown in Graphs XXV and XXVI when the silver-PHENASDA and silver-chlor-PHENASDPA systems are considered.

The Stability Constants of the Mercury^{II} complexes.

Mercury forms very strong complexes with many ligands hence, in solutions in which the ligand is in large excess, it can be assumed that virtually all the mercury is in the form of the complex. Evidence for this is provided by the measurements of free mercury ion concentrations made during the investigations - they were always very small indeed compared with the total mercury concentration.

In such a case :-

$C_m = [ML] + [MHL] + [ML_2]$ . . . . . (i)

$C_L = \alpha[L] + [ML] + [MHL] + 2[ML_2]$ . . . . . (ii)

where $\alpha = 1 + [H]/K_2^H + [H]^2/K_1^H K_2^H$.

It was first assumed that the only complex species present was ML. In such a case :-

$C_m = [ML]$, $C_L = \alpha[L] + [ML]$, i.e. $[L] = (C_L - C_m)/\alpha$

Therefore $K_{ML} = \dfrac{[ML]}{[M][L]} = \dfrac{C_m \alpha}{[M](C_L - C_m)}$ . . . . .(iii)

Since [M] may be calculated from the potential of the mercury electrode, a value for K_{ML} may be obtained.

If it is now assumed that only the species ML_2 is present, then :- $\beta_2 = \dfrac{[ML_2]}{[M][L]^2} = \dfrac{C_m \alpha^2}{[M](C_L - 2C_m)^2}$ . . (iv)

Similar equations for β_3 and β_4 can be obtained.

Values for K_{ML}, β_2, β_3 and β_4 were calculated over a large pH and ligand:metal ratio range. It was generally found that, except in very acid solutions or at a high metal ion concentration, β_2 was constant indicating that this species was the predominant one in solution and the values calculated for β_2 are reliable. Graph XXVII shows the variations in the constants calculated for the mercury-PHENASDA complex. In this case K_{ML}(calculated) increases as pH increases while β_2 is constant above pH 4.5.

Knowing the value for β_2, K_1 could be calculated for values below pH 4.5 by eliminating [L] from the equations :-

$$C_m = [ML] + [ML_2] \qquad \ldots\ldots\ldots (v)$$

$$C_L = \alpha[L] + [ML] + 2[ML_2] . \qquad \ldots\ldots\ldots (vi)$$

The equation :-

$$\frac{\alpha^2 C_m}{[M]} - \alpha C_m K_{ML} + [M](C_L - C_m)K_{ML}^2 - (C_L - 2C_m)^2\beta_2 = 0$$

is obtained and can be solved for K_{ML}. The values obtained usually showed large drifts in magnitude since the contribution of terms in K_{ML} was small and in all cases $\bar{n}$ was approaching two.

The existance of the species MHL may cause some drift in results. By incorporating this ion in equations (v)

and (vi) attempts were made to calculate the stability constant K^{M}_{MHL}. In all cases the value obtained was meaningless indicating that $K^{M}_{MHL} \ll K_{ML}$.

The zones of existence of the various complexes (which are shown diagrammatically in Section II, Part II) were calculated from the equation :-

$\alpha_n = \frac{[ML_n]}{C_m}$ where α_n = the fraction of the total metal in the form ML_n.

SECTION SIX.

THE EXPERIMENTAL RESULTS.

The Experimental Results.

(a) The Amino-acids.

Titrations of α-alanine (II).

Temp. = 20.0°C. μ = 0.10M (KCl).

Contents of cell :- 20.0ml., [L] = 0.0200M
[HCl] = 0.02025M
[M] = 0.0100M.

Strength of alkali :- 1.726N.

Vol. alkali (ml.)	pH readings. HCl only	HCl + [L]	HCl + [L] + Cu	+ Ni	+ Zn	+ Co
0.0	1.73	2.12	2.13	2.12	2.13	2.14
0.02		2.17	2.18			
0.04		2.24	2.24	2.24		
0.06		2.31	2.31			
0.08		2.40	2.39	2.39		2.40
0.10	2.00	2.49	2.46			
0.12	2.07	2.59	2.56	2.58	2.59	2.60
0.14	2.16	2.69	2.65			
0.16	2.28	2.82	2.75	2.81		2.83
0.18	2.41	3.00	2.85			
0.20	2.61	3.22	2.96	3.21		3.23
0.22	2.99	3.70	3.10	3.72	3.70	3.72
0.23	3.70	4.44		4.46	4.47	4.50
0.24	10.70	8.43	3.25	5.17	5.93	6.12
0.26	11.34	9.06	3.42	5.75	6.52	6.80
0.28	11.60	9.33	3.61	6.08	6.83	7.14

α-alanine titrations (continued)

Vol alkali (ml.)	pH readings. HCl only	HCl + [L]	+ Cu	HCl + Ni	+ Zn	+ Co
0.29	11.69	9.44			6.96	7.27
0.30		9.54	3.85	6.36	7.08	7.40
0.31		9.62	3.96	6.50	7.19	7.51
0.32		9.70	4.09	6.63	7.29	7.63
0.33		9.79	4.24	6.75	7.39	7.74
0.34		9.86	4.38	6.88	7.50	7.86
0.35		9.93	4.53	7.00	7.60	
0.36		10.00	4.69	7.13	7.71	8.08
0.37		10.08	4.85	7.27	7.81*	
0.38		10.15	5.01	7.42		8.31
0.39		10.23	5.19	7.56		
0.40		10.30	5.38	7.73		8.55
0.42		10.49	5.80	8.09		8.78*
0.44		10.73	6.42	8.54		
0.45			6.92	8.88		
0.46			7.91	9.37		
0.47			10.09			
0.48			10.66			

The titration of CC-dimethylglycine with alkali.

Temp. = 20°. μ = 0.10M.

Contents of cell :- [L] = 0.0500M
[HCl] = 0.0506M

Strength of alkali :- 4.169N.

Vol. alkali (ml.)	pH HCl only	pH HCl + [L]	Vol. alkali (ml.)	pH HCl only	pH HCl + [L]
0.00	1.33	1.85	0.25	11.18	8.67
0.02		1.94	0.26	11.57	9.11
0.04		2.03	0.27	11.76	9.35
0.06		2.13	0.28	11.90	9.50
0.08	1.45	2.23	0.30		9.75
0.10		2.33	0.32		9.93
0.12	1.58	2.44	0.34		10.10
0.14		2.57	0.36		10.24
0.16	1.77	2.71	0.38		10.39
0.18	1.91	2.87	0.40		10.54
0.20	2.07	3.07	0.42		10.70
0.22	2.34	3.38	0.44		10.89
0.23	2.58	3.65	0.46		11.12
0.24	3.10	4.24	0.48		11.42

Titrations of CC-dimethyl glycine.

Temp. = 20°. μ = 0.10M.

Contents of cell :- 20.0ml., [L] = 0.0200M
[HCl] = 0.02025M
[M] = 0.0100M

Strength of alkali :- 1.726N.

Vol. alkali (ml.)	HCl only	HCl + [L]	+ Cu	pH readings. + Ni	+ Co	+ Zn
0.00	1.73	2.12	2.13	2.13	2.12	2.12
0.02		2.17				
0.04		2.24	2.24			
0.06		2.32				
0.08		2.40	2.39			
0.10	2.00	2.50	2.47	2.49	2.49	2.50
0.12	2.08	2.60	2.55			
0.14	2.17	2.71	2.64			
0.16	2.28	2.85	2.77	2.82	2.86	2.85
0.18	2.41	3.01	2.88			
0.20	2.61	3.26	3.00	3.22	3.28	3.29
0.22	3.00	3.75	3.18		3.74	3.78
0.23	3.61	4.50		4.45	4.32	4.49
0.24	10.61	8.76	3.36	5.66	6.60	6.40
0.25	11.10	9.16		6.06	7.05	6.76
0.26	11.33	9.38	3.56	6.31	7.32	6.97
0.28	11.62	9.68	3.78	6.66	7.67	7.26

CC-dimethylglycine titrations (continued)

Vol. alkali (ml.)	HCl only	HCl + [L]	pH readings. + Cu	+ Ni	+ Co	+ Zn
0.30		9.88	4.03	6.94	7.92	7.42
0.32		10.04	4.30	7.20	8.14	
0.34		10.20	4.59	7.45	8.33	
0.36		10.34	4.91	7.71	8.50	
0.38		10.49	5.25	7.98	8.65	
0.40		10.64	5.62	8.29		
0.42		10.81	6.07	8.63		
0.44		11.00	6.73	9.06		
0.45			7.28	9.32		
0.46		11.22	8.24	9.60		
0.47			9.93	9.85		
0.48		11.34	10.62	10.08		

Titrations of cyclo-pentane-1-amino-1-carboxylic acid.

(IV).

Temp = 20°. μ = 0.10M.

Contents of cell :- 20.0ml. [L] = 0.0200M
[HCl] = 0.02025M
[M] = 0.0100M

Strength of alkali :- 1.975N.

Vol. alkali (ml.)	pH readings. HCl only	HCl + [L]	HCl + [L] + Cu	+ Ni	+ Zn	+ Co
0.00	1.74	2.18	2.19	2.19	2.19	2.20
0.02		2.25	2.24			
0.04		2.32	2.30			
0.06	1.92	2.40	2.37	2.40	2.42	
0.08	1.99	2.49	2.46			
0.10	2.07	2.60	2.56	2.59	2.62	
0.12	2.17	2.73	2.67			
0.14	2.28	2.90	2.79	2.87	2.91	
0.16	2.44	3.08	2.90	3.05		
0.18	2.70	3.40	3.00	3.37	3.40	
0.20	3.43	4.20	3.16	4.12	4.25	
0.21	10.63	8.63		5.10	5.93	6.23
0.22	11.16	9.19	3.34	5.63	6.45	6.81
0.23	11.40	9.44		5.93	6.71	7.07
0.24	11.56	9.62	3.52	6.16	6.90	7.29
0.26		9.87	3.75	6.51	7.19	7.60
0.28		10.07	4.00	6.83	7.42	7.88

Titrations of IV (continued).

Vol. alkali (ml.)	pH readings. HCl + [L]		HCl + [L]		
	HCl + [L]	+ Cu	+ Ni	+ Zn	+ Co
0.30	10.24	4.31	7.11	7.65	8.13
0.32	10.41	4.66	7.42		8.37
0.34	10.58	5.04	7.76		8.60
0.36	10.76	5.47	8.14		
0.38	10.97	6.07	8.62		
0.40	11.21	7.37	9.36		
0.42	11.45	10.79	10.03		

Titrations of cyclo-hexane-1-amino-1-carboxylic acid (V).

Temp. = 20°. μ = 0.1CM.

Contents of cell :- 20.0ml., [L] = 0.0500M
[HCl] = 0.0506M
[M] = 0.0250M

Strength of alkali :- 4.605N.

Vol. alkali (ml.)	HCl only	HCl + [L]	pH readings. HCl + [L] + Cu	+ Ni	+ Zn	+ Co
0.00		1.94	1.95	1.95	1.95	1.96
0.02		2.01	2.02	2.01	2.01	
0.04		2.10	2.09	2.10		
0.06		2.20	2.15	2.20	2.21	
0.08		2.31	2.23	2.30	2.31	2.30
0.10		2.42	2.32	2.40	2.42	
0.12	1.75	2.55	2.40	2.52	2.56	2.54
0.14	1.82	2.70	2.48	2.66	2.70	2.67
0.16	1.92	2.89	2.57	2.82		
0.18	2.04	3.11	2.67	3.03	3.12	3.06
0.20	2.32	3.48	2.78	3.36	3.50	3.38
0.22	6 -	7 -	2.89	4.42	4.47	4.47
0.24	11.56	9.16	3.01	5.27	5.80	6.28
0.26	11.85	9.48	3.16	5.68	6.19	6.73
0.28	12.01	9.70	3.33	6.00	6.50	7.04
0.30	12.12	9.87	3.54	6.29	6.76	7.31
0.32		10.04	3.78	6.57	6.97	7.55

Titrations of V (Continued).

Vol. alkali (ml.)	HCl only	pH reading. HCl + [L]	+ Cu	+ Ni	+ Zn	+ Co
0.34		10.21	4.07	6.86	7.19	7.82
0.36		10.38	4.40	7.19	7.42	7.80m
0.38		10.58	4.79	7.51	7.65m	
0.40		10.83	5.30			
0.42		11.15	6.15			
0.43		11.35	7.19			
0.44		11.54	10.5			

Repeat titrations with [L] = 0.0196M, [HCl] = 0.02025M
[M] = 0.0100M.

Strength of alkali = 1.901N.

Vol.	HCl	+[L]	+Cu	+Ni	+Zn
0.00	1.73	2.25	2.25	2.26	2.25
0.22	10.73	8.72	3.25	5.32	6.08
0.24	11.42	9.30	3.40	5.92	6.63
0.26		9.58	3.98	6.28	6.92
0.28		9.80	3.79	6.59	7.16
0.30		9.97	4.05	6.88	7.37
0.32		10.14	4.36	7.18	7.59
0.34		10.30	4.70	7.30	
0.36		10.48	5.09	7.35	
0.38		10.69	5.60	8.28	
0.40		10.94	6.43	8.84	

Agreement between results.

[L]	0.0500	0.0196M
Cu		
Log K_1	8.60	8.59
Log K_2	7.26	7.26
Log β_2	15.86	15.85
Ni		
Log K_1	5.53	5.50
Log K_2	4.55	4.55
Log β_2	10.08	10.05
Zn		
Log K_1	4.82	4.78
Log K_2	4.5	4.4
Log β_2	9.34	9.2

The titrations of cyclo-heptane-1-amino-1-carboxylic acid(VI).

Temp. = 20°. μ = 0.10M.

Contents of cell :- 20.0ml. [L] = 0.0500M
[HCl] = 0.0506M
[M] = 0.0250M.

Strength of alkali :- 4.169N.

Vol. alkali (ml.)	HCl only	pH readings. HCl + [L]	+ Cu	+ Ni	+ Zn	+ Co
0.00		1.97	1.98	1.97	1.98	1.98
0.02		2.07				
0.04	1.40	2.18	2.12			
0.06		2.29	2.23			
0.08		2.40	2.32	2.39	2.40	2.41
0.10		2.52	2.41	2.53		
0.12		2.64	2.50	2.64	2.64	2.65
0.14		2.76	2.59			
0.16	1.79	2.90	2.68	2.90	2.90	2.91
0.18		3.07	2.78			
0.20	2.07	3.29	2.87	3.24	3.29	3.31
0.22	2.34	3.61	2.97			
0.24	3.15	4.60	3.09	4.31	4.84	
0.25	11.18	8.82	3.15	5.24	5.95	6.42
0.26	11.57	9.30	3.21	5.67	6.29	6.80
0.28	11.90	9.69	3.35	6.13	6.67	7.21
0.30		9.93	3.51	6.42	6.90	7.48

Titrations of VI (continued)

Vol. alkali (ml.)	HCl only	HCl + [L]	pH readings HCl + [L] + Cu	+ Ni	+ Zn	+ Co
0.32		10.12	3.69		7.10	
0.34		10.28	3.90		7.28	
0.36		10.42	4.15		7.58*	
0.38		10.57	4.43**			
0.40		10.73				
0.42		10.89				
0.44		11.08				
0.46		11.29				
0.48		11.56				

Titrations of PIPDA (VII) with alkaline earth metals.

Temp. = 20°. μ = 0.10M.

Contents of cell :- 100ml. [L] = 0.0010M.
[M] = 0.0010M.

Strength of alkali :- 0.1013N

'a'	PIPDA only	+ Ca	+ Sr	+ Ba
0.00	2.937	2.950	2.954	2.958
0.20	3.059	3.059	3.047	3.064
0.40	3.180			
0.60	3.326	3.317	3.319	3,341
0.80	3.535			
1.00	3.765	3.740	3.760	3.770
1.20	4.036			
1.40	4.345	4.305	4.330	4.326
1.59	4.648			
1.79	5.091	5.033	5.091	5.093
1.89	5.530	5.506	5.519	5.511
1.99	6.981	6.645	6.963	7.007
2.08	7.788	7.570	7.711	7.758
2.18	8.078	7.919	7.994	8.035
2.28	8.291	8.163	8.219	8.262
2.38	8.487	8.371	8.417	8.446
2.48	8.663	8.560	8.580	8.639
2.58	8.836	8.728	8.754	8.814
2.68	9.037	8.912	8.932	9.005
2.78	9.242	9.125	9.220	9.223
2.87	9.529	9.349	9.413	9.505
2.97	9.793	9.639	9.719	9.797
3.07	10.04	9.916	9.979	10.04.

Titrations of PIPDA with transition metals.

Temp.= 20°. μ = 0.10M.

Contents of cell :- 100ml. [L] = 0.002M
[M] = 0.002M

Strength of alkali :- 0.1036N.

Vol. alkali (ml.)	PIPDA only	+ Zn	+ Ni	+ Cu
0.00	2.73	2.74	2.73	2.68
0.20	2.765			
0.40	2.820			
0.80	2.950	2.963		2.835
1.00	3.025	3.040	3.023	2.885
1.20	3.110			2.940
1.40	3.223	3.240		3.000
1.60	3.360	3.371		3.060
1.80	3.518	3.528		3.120
2.00	3.700	3.702	3.650	3.190
2.20	3.882	3.878	3.818	3.270
2.40	4.060	4.052	3.982	3.351
2.60	4.230	4.215	4.153	3.448
2.80	4.404	4.381	4.310	3.553
3.00	4.582	4.961	4.488	3.672
3.20	4.781	4.768	4.686	3.830
3.40	5.040	5.032	4.940	4.000
3.60	5.485	5.480	5.360	4.225
3.80	6.980	6.680	6.282	4.494
4.00	7.784	7.394	6.969	4.761
4.20	8.115	7.665	7.311	5.025
4.40	8.350	7.729*	7.572	5.272*
4.60	8.560		7.800	
4.80	8.755		8.040	
5.00	8.961		8.255	
5.20	9.209		8.470*	

Titrations of PIPMA (VIII) in the presence of metals.

Temp. = 20°. μ = 0.10M.

Contents of cell :- 20ml. (a) [L] = 0.010M
[HCl] = 0.010M

(b) [L] = 0.010M
[M] = 0.005M only

Strength of alkali :- 0.1030N.

(a) Vol alkali (ml.)	pH HCl only	pH HCl + [L]	(b) Vol alkali (ml.)	pH [L]+Cu	pH [L]+Ni
0.00		2.27	0.00	4.52	5.08
0.02		2.31	0.01	5.09	7.20
0.04		2.36	0.02	5.25	7.90
0.06	2.21	2.42	0.03	5.50	8.12
0.08		2.49	0.04	5.66	8.27
0.10	2.35	2.56	0.05	5.81	8.38*
0.12		2.65	0.06	5.94*	
0.14	2.52	2.76			
0.16	2.65	2.90			
0.18	2.83	3.09			
0.20	3.16	3.42			
0.22	8.70	7.95			
0.24	10.95	9.29			
0.26		9.63			
0.28		9.85			
0.30		10.03			
0.32		10.19			
0.34		10.35			
0.36		10.50			
0.38		10.66			
0.40		10.83			

The Titrations of Phenylarsinediacetic Acid (PHENASDA).

Temp. = 20°. μ = 0.10M.

Hydrogen Electrode

100ml. taken (0.001M)

Alkali = 0.101N

'a'	pH
0.00	3.380
0.10	3.450
0.20	3.531
0.30	3.613
0.40	3.704
0.50	3.795
0.60	3.902
0.70	4.006
0.80	4.118
0.90	4.250
0.99	4.376
1.19	4.651
1.29	4.778
1.39	4.914
1.49	5.062
1.59	5.225
1.69	5.425
1.79	5.660
1.88	6.026
1.98	7.977*

(excessive drift due to poisoning of the platinum electrode.)

Titration with silver ions.
Glass Electrode.

Contents of Cell:- 20.0ml. [L] = 0.001
[M] = 0.001

Strength of Alkali = 0.1030N.

Vol. Alkali (ml.)	pH	p[Ag]
0.00	3.25	3.95
0.02	3.29	3.97
0.04	3.34	3.98
0.06	3.39	4.00
0.08	3.45	4.03
0.10	3.51	4.06
0.12	3.57	4.08
0.14	3.64	4.12
0.16	3.72	4.15
0.18	3.80	4.19
0.20	3.89	4.24
0.22	3.97	4.29
0.24	4.07	4.34
0.26	4.19	4.40
0.28	4.32	4.47
0.30	4.47	4.55
0.32	4.67	4.64
0.34	4.93	4.75
0.36	5.39	4.88
0.37	5.95	4.95
0.38	8.75	5.02
0.40	9.83	

The Titrations of p-Chlorophenylenearsine-dipropionic acid (chlor-PHENARSDPA)

Temp. = 20°. μ = 0.10M.

Contents of Cell: 20.0ml. [L] = 0.00094M:
[Ag] = 0.001M.

Strength of Alkali :- 0.1030N.

Vol. alkali (ml.)	pH acid only	in the presence of Silver ions. pH	p[Ag]
0.00	3.70	3.49	3.946
0.02	3.80	3.55	3.955
0.04	3.91	3.62	3.969
0.06	4.02	3.70	3.985
0.08	4.13	3.78	4.004
0.10	4.24	3.86	4.026
0.12	4.34	3.94	4.048
0.14	4.44	4.03	4.074
0.16	4.54	4.11	4.108
0.18	4.64	4.21	4.148
0.20	4.74	4.31	4.187
0.22	4.84	4.41	4.229
0.24	4.96	4.52	4.279
0.26	5.09	4.65	4.335
0.28	5.23	4.80	4.411
0.30	5.39	4.98	4.489
0.32	5.62	5.24	4.590
0.34	5.94	5.64	4.637
0.36	6.43	6.56	4.722
0.38	8.66		

The Titrations of cyclo-hexyliminediacetic Acid .

Temp. = 20°. μ = 0.10M.

Contents of Cell:- 20ml. [L] = 0.001M.
[M] = 0.001M.

Strength of alkali :- 0.1030N.

Vol. alkali (ml.)	Hexda only	+ Cu	+ Zn	+ Ni	+ Cd	+ Ag
0.00	3.11	2.88	3.11	3.12	3.11	3.11
0.02	3.16	2.90				
0.04	3.21	2.93				
0.06	3.27	2.95				
0.08	3.34	2.98	3.34			
0.10	3.43	3.01				
0.12	3.54	3.05	3.53	3.54	3.54	3.55
0.14	3.68	3.09	3.67			
0.16	3.88	3.13	3.87			3.88
0.18	4.26	3.18	4.20			4.88
0.20	7.31	3.23	4.75	4.51	5.09	6.35
0.22	9.65	3.28	5.21	4.86	5.61	8.00
0.24	9.91	3.35	5.53	5.12	5.95	8.47
0.26	10.13	3.43	5.80	5.36	6.46	8.78*
0.28	10.28	3.53	6.05	5.57	6.45	
0.30	10.40	3.65	6.30	5.79	6.69	
0.32	10.50	3.80	6.56	6.03	6.94	
0.34	10.59	4.03	6.87	6.26	7.22	
0.36	10.65	4.44	7.22	6.58	7.56	
0.38	10.70	5.77	7.64*	6.88	8.00*	
0.40	10.74	7.95*		8.8*		

The Titration of Diphenylamine-N-propionic Acid. (in 20% Dioxan)

Temp. = 20°. μ = 0.10M. in 20% dioxan.

Contents of Cell :- 20ml. 0.0010M. acid solution.

Strength of alkali = 0.1030N.

Vol. alkali (ml.)	pH
0.00	4.13
0.01	4.27
0.02	4.40
0.03	4.50
0.04	4.59
0.05	4.68
0.06	4.77
0.07	4.85
0.08	4.93
0.09	5.01
0.10	5.09
0.11	5.17
0.12	5.26
0.13	5.37
0.14	5.49
0.15	5.61
0.16	5.74
0.17	5.90
0.18	6.17
0.19	6.80
0.20	8.90
0.21	9.46
0.22	10.00

Titrations with diphenylphosphine-P-propionic acid.

Temp. = 20°. μ = 0.10M. in 20% Dioxan.

Contents of cell :- 20ml. Acid = 0.0010M.

Vol. alkali (ml.)	pH acid only	[Ag]= 0.001M. acid + Ag (1:1) pH	p[Ag]	[Ag]=0.0005M. acid + Ag (1:0.5) pH	p[Ag]
0.00	4.13	3.91	3.453	3.93	5.563
0.01	4.23				
0.02	4.33	4.06	3.470	4.08	5.580
0.03	4.42				
0.04	4.52	4.20	3.486	4.22	5.611
0.05	4.61				
0.06	4.70	4.34	3.503	4.37	5.652
0.07	4.79				
0.08	4.88	4.49	3.519	4.52	5.695
0.09	4.97				
0.10	5.05	4.65	3.534	4.69	5.730
0.11	5.15				
0.12	5.25	4.82	3.550	4.88	5.793
0.13	5.35				
0.14	5.46	5.03	3.565	5.09	5.848
0.15	5.61				
0.16	5.78	5.31	3.581	5.38	5.905
0.17	6.00				
0.18	6.35	5.85	3.598	5.92	5.982
0.19	6.91				
0.20	8.60	8.00	3.625	8.76	6.059
0.21	9.37				
0.22	9.80				

The titrations of Diphenylarsine-As-propionic acid.

Temp. = 20°. μ = 0.10M. in 20% Dioxan.

Contents of Cell :- 20ml. Acid = 0.000875M:

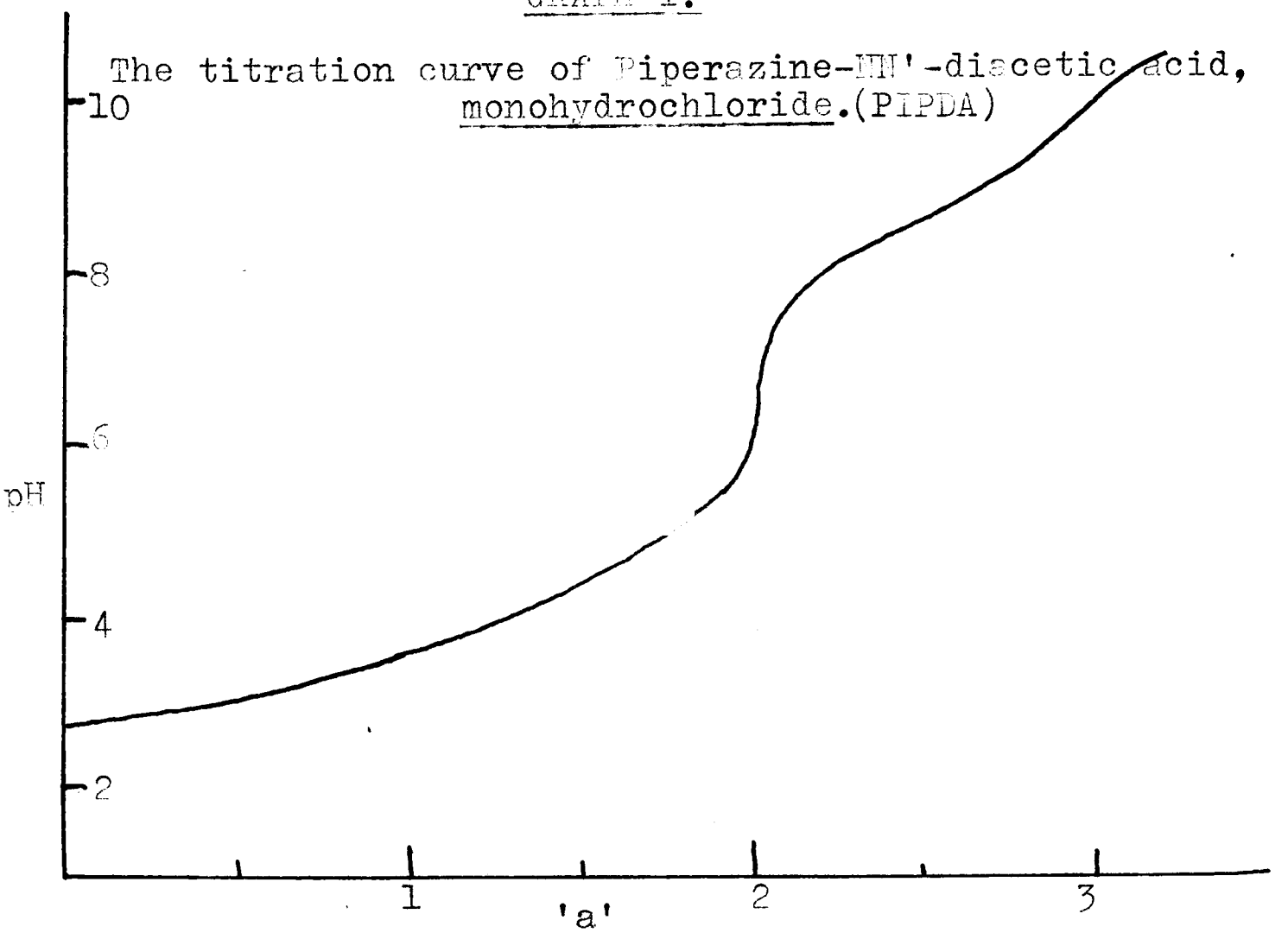
[Ag] = 0.001M.

Strength of Alkali :- 0.1030N.

Vol. alkali (ml.)	pH acid only	Acid + Ag (1:1) pH	p[Ag]
0.00	4.22	3.88	3.696
0.01	4.36		
0.02	4.50	4.03	3.720
0.03	4.63		
0.04	4.75	4.20	3.746
0.05	4.86		
0.06	4.96	4.37	3.768
0.07	5.06		
0.08	5.17	4.55	3.794
0.09	5.27		
0.10	5.38	4.75	3.820
0.11	5.50		
0.12	5.63	5.00	3.854
0.13	5.79		
0.14	5.99	5.36	3.888
0.15	6.35	5.64	3.910
0.16	7.00	6.20	3.940
0.17	9.05		
0.18	9.95	9.66	
0.19	10.27	10.20.	

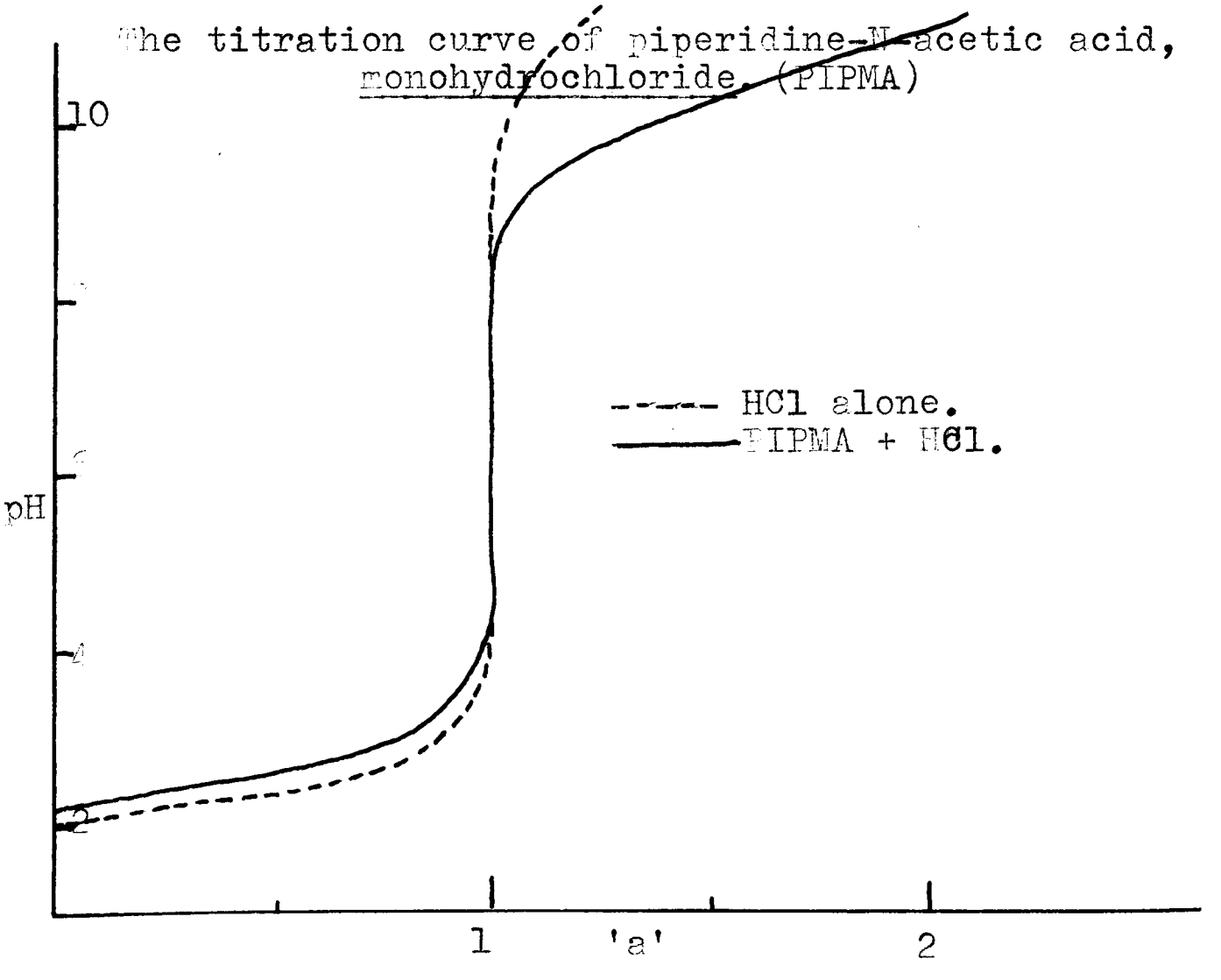
GRAPH I.

The titration curve of Piperazine-NN'-diacetic acid, monohydrochloride.(PIPDA)



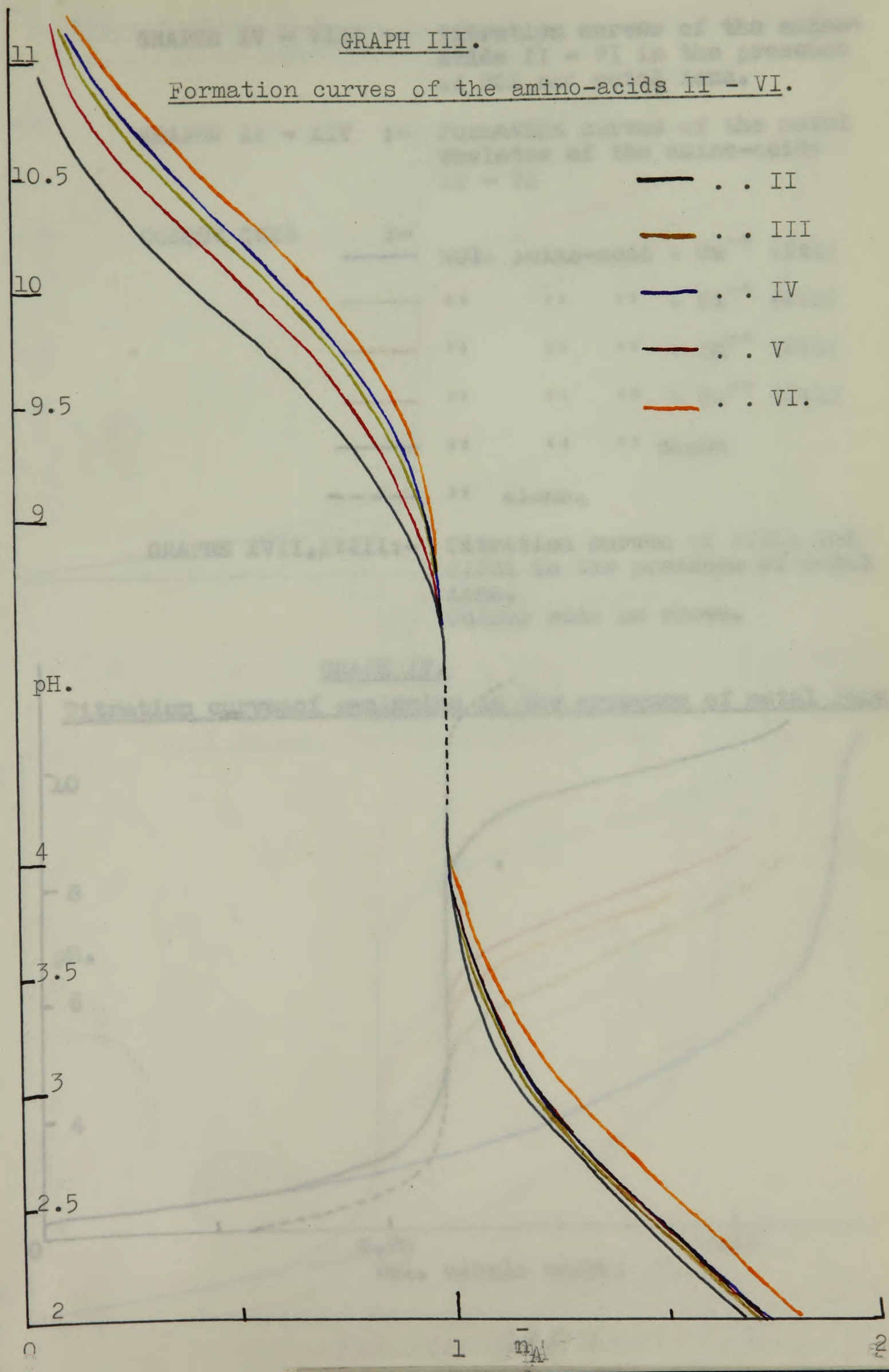
GRAPH II.

The titration curve of piperidine-N-acetic acid, monohydrochloride. (PIPMA)



GRAPH III.

Formation curves of the amino-acids II - VI.



GRAPHS IV - VIII :- Titration curves of the amino-acids II - VI in the presence of HCl and metal ions.

GRAPHS IX - XIV :- Formation curves of the metal chelates of the amino-acids II - VI

COLOUR CODE :-

HCl + Amino-acid + Cu^{++} (2:1)

" " " + Ni^{++} (2:1)

" " " + Zn^{++} (2:1)

" " " + Co^{++} (2:1)

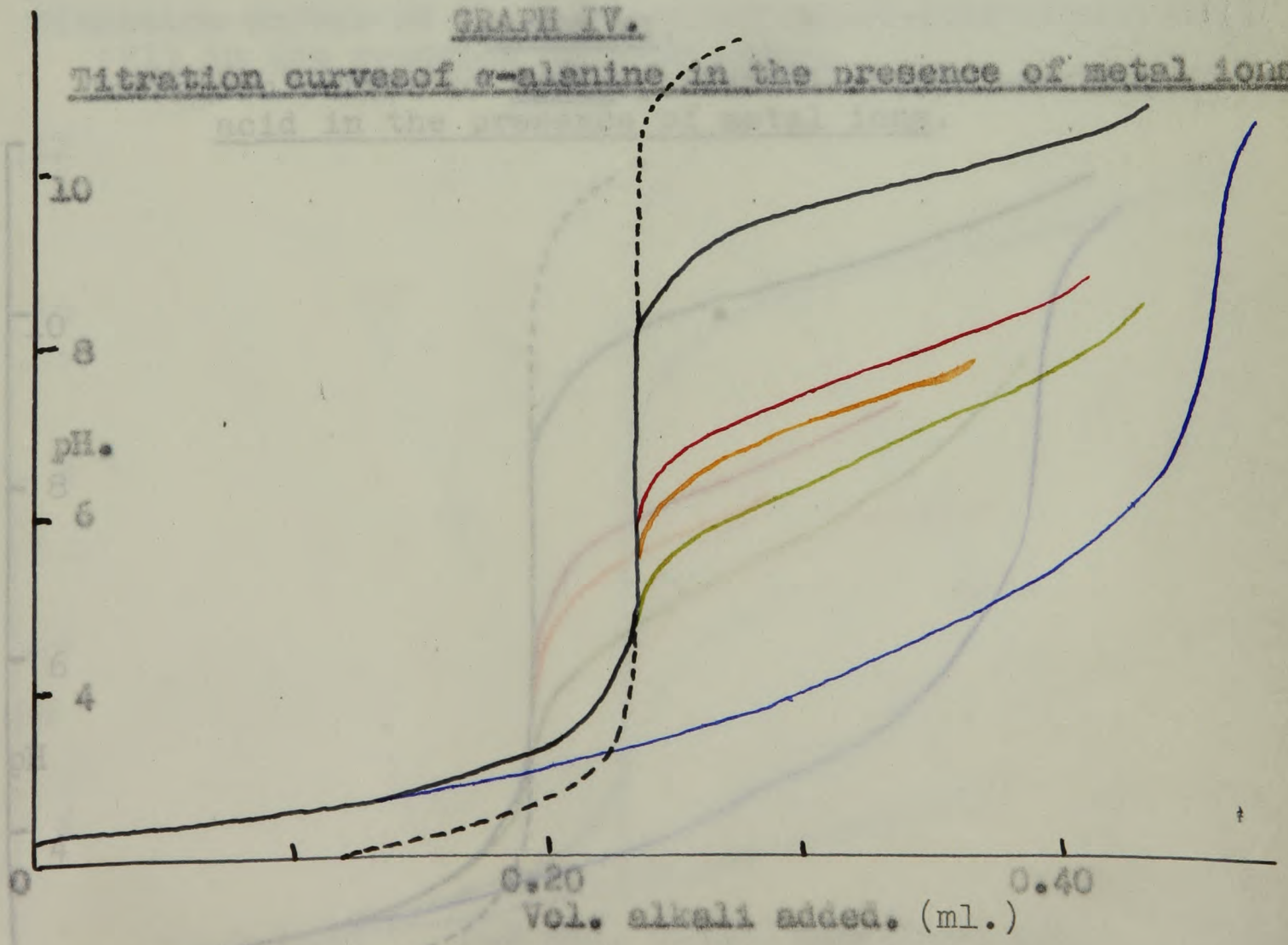
" " " alone

" alone.

GRAPHS XVII, XVIII:- Titration curves of PIPDA and PIPMA in the presence of metal ions.
Colour code as above.

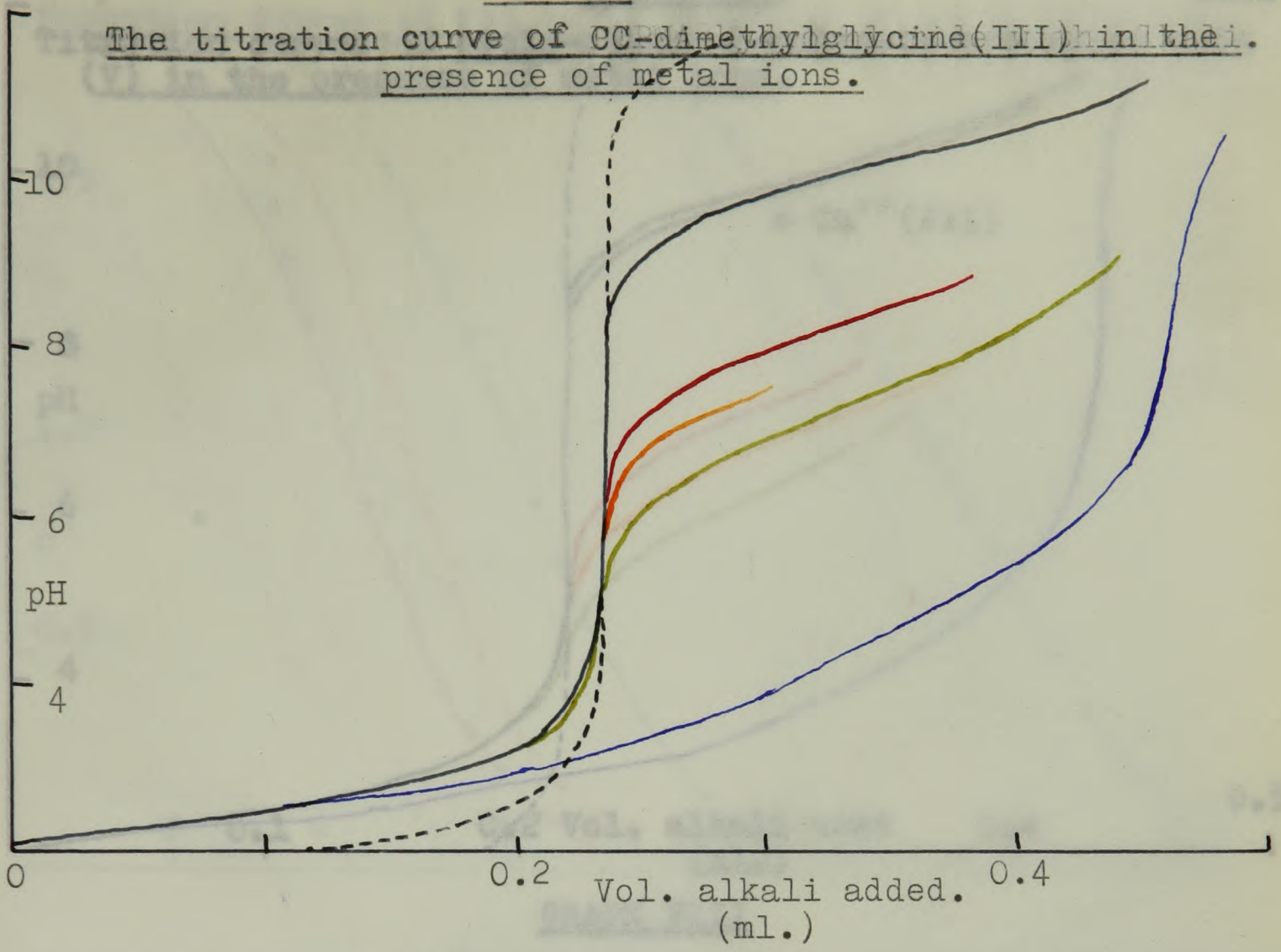
GRAPH IV.

Titration curvesof α-alanine in the presence of metal ions.



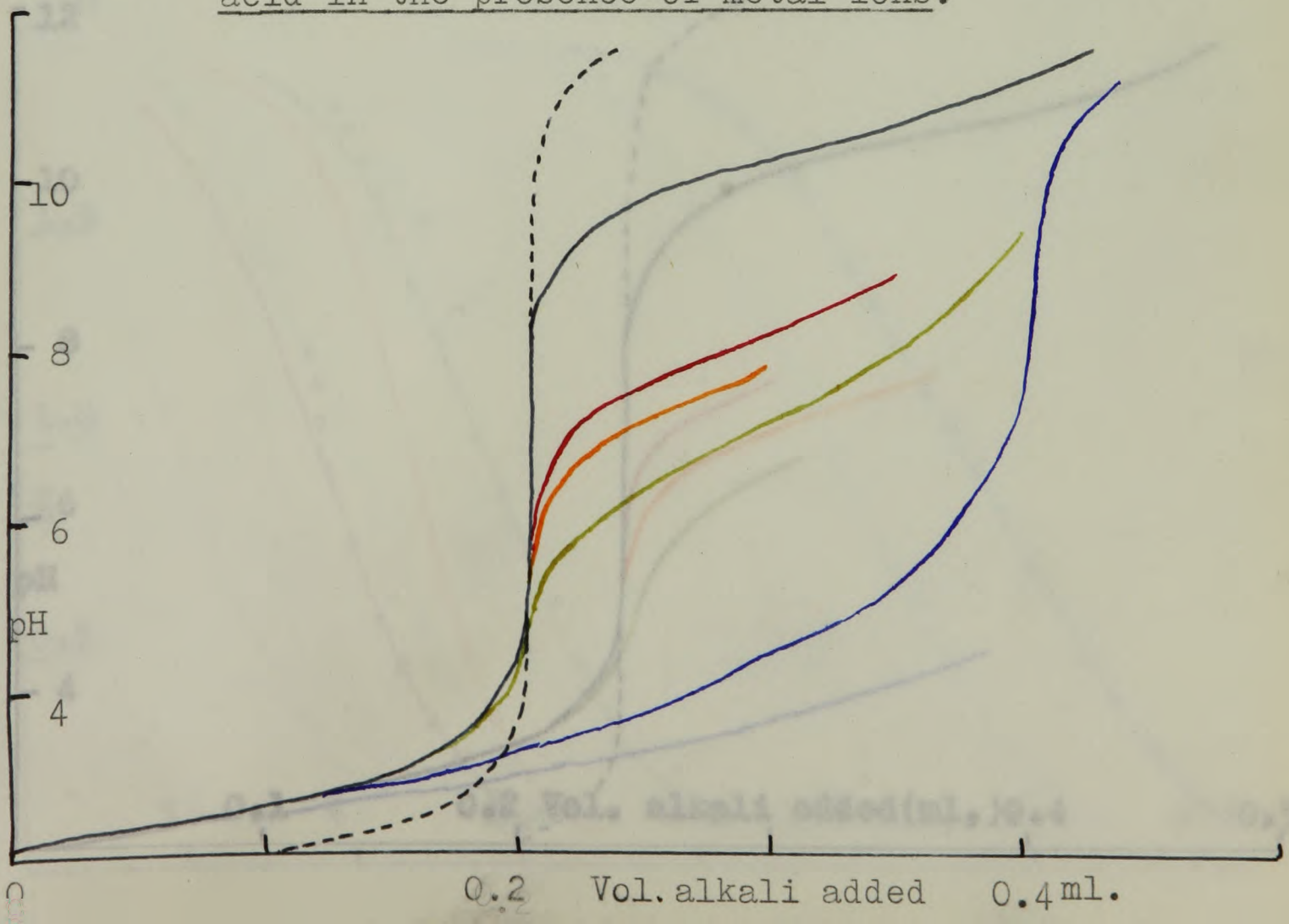
GRAPH V.

The titration curve of CC-dimethylglycine(III) in the presence of metal ions.



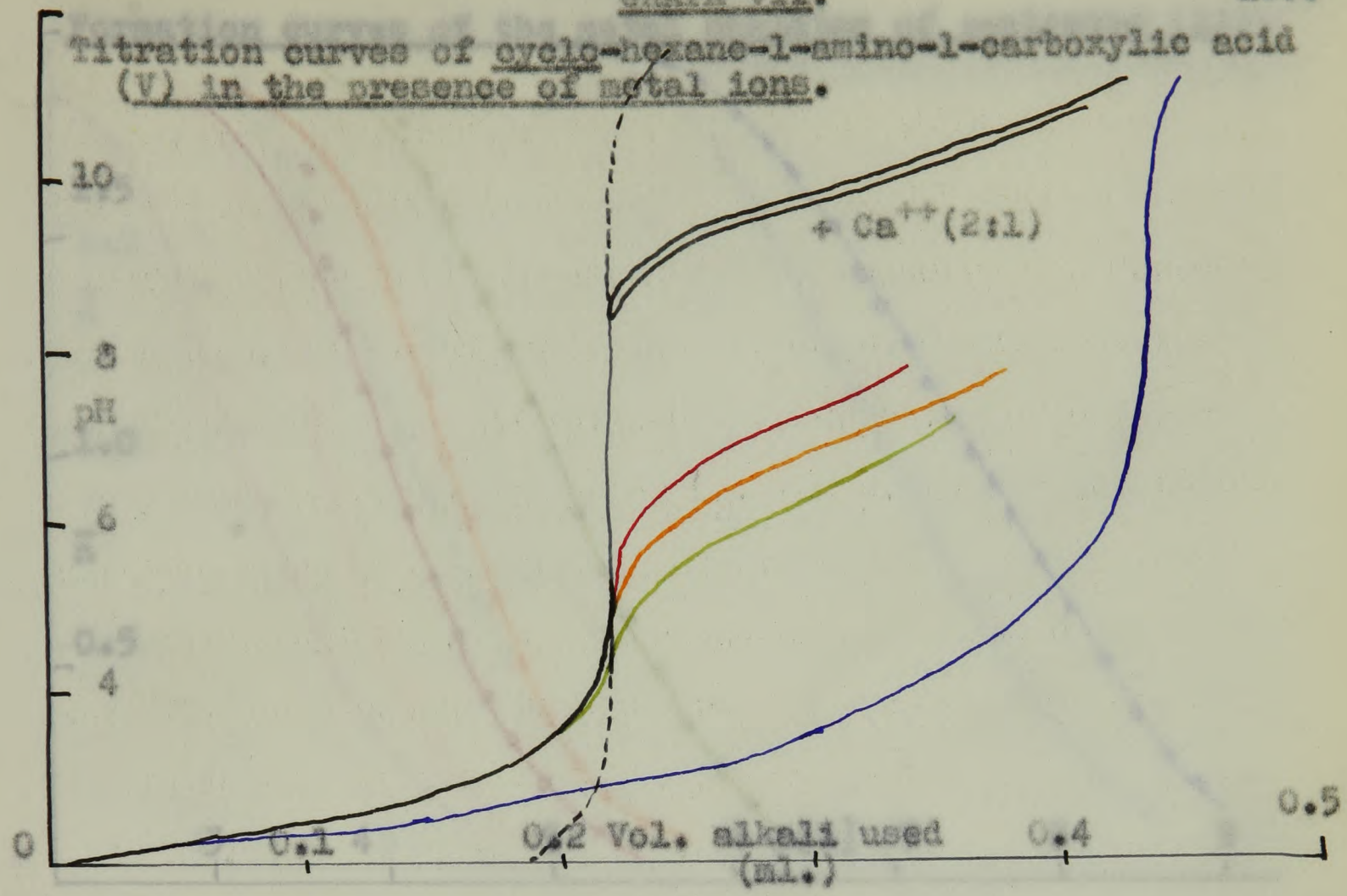
GRAPH VI.

Titration curves of cyclo-pentane-1-amino-1-carboxylic acid in the presence of metal ions.



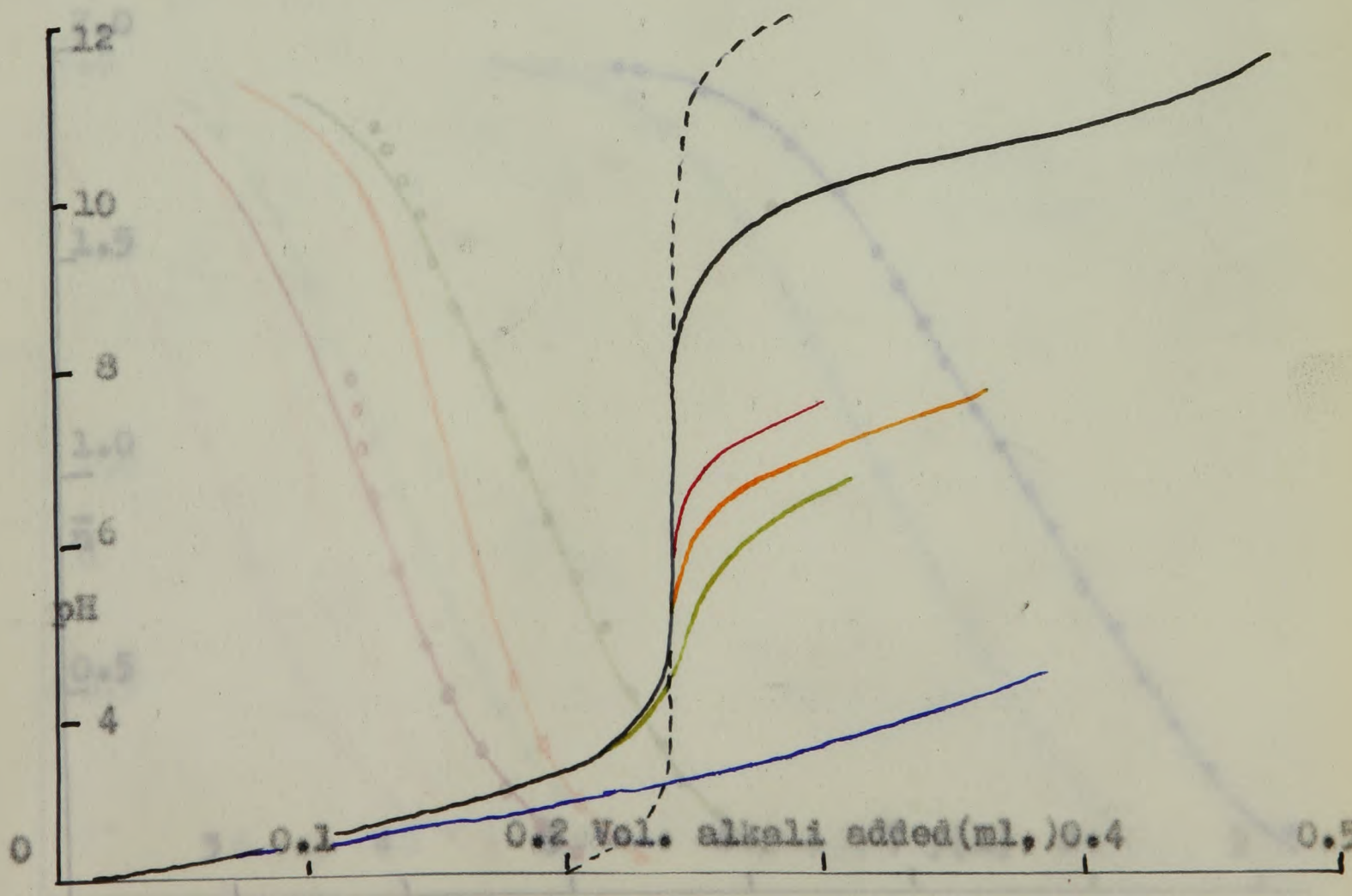
GRAPH VII.

Titration curves of cyclo-hexane-1-amino-1-carboxylic acid (V) in the presence of metal ions.



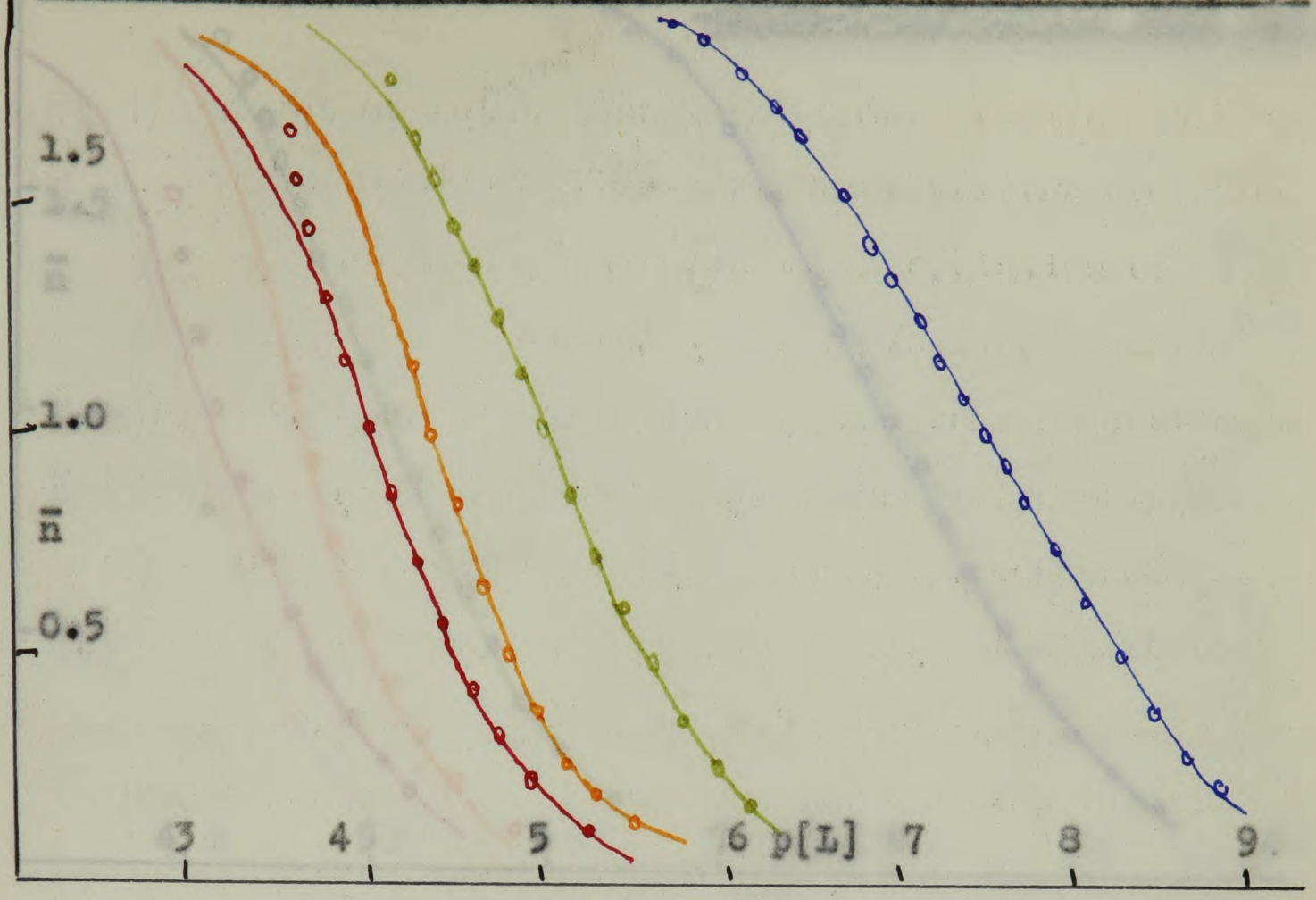
GRAPH VIII

Titration curves of cyclo-heptane-1-amino-1-carboxylic acid (VI) in the presence of metal ions.



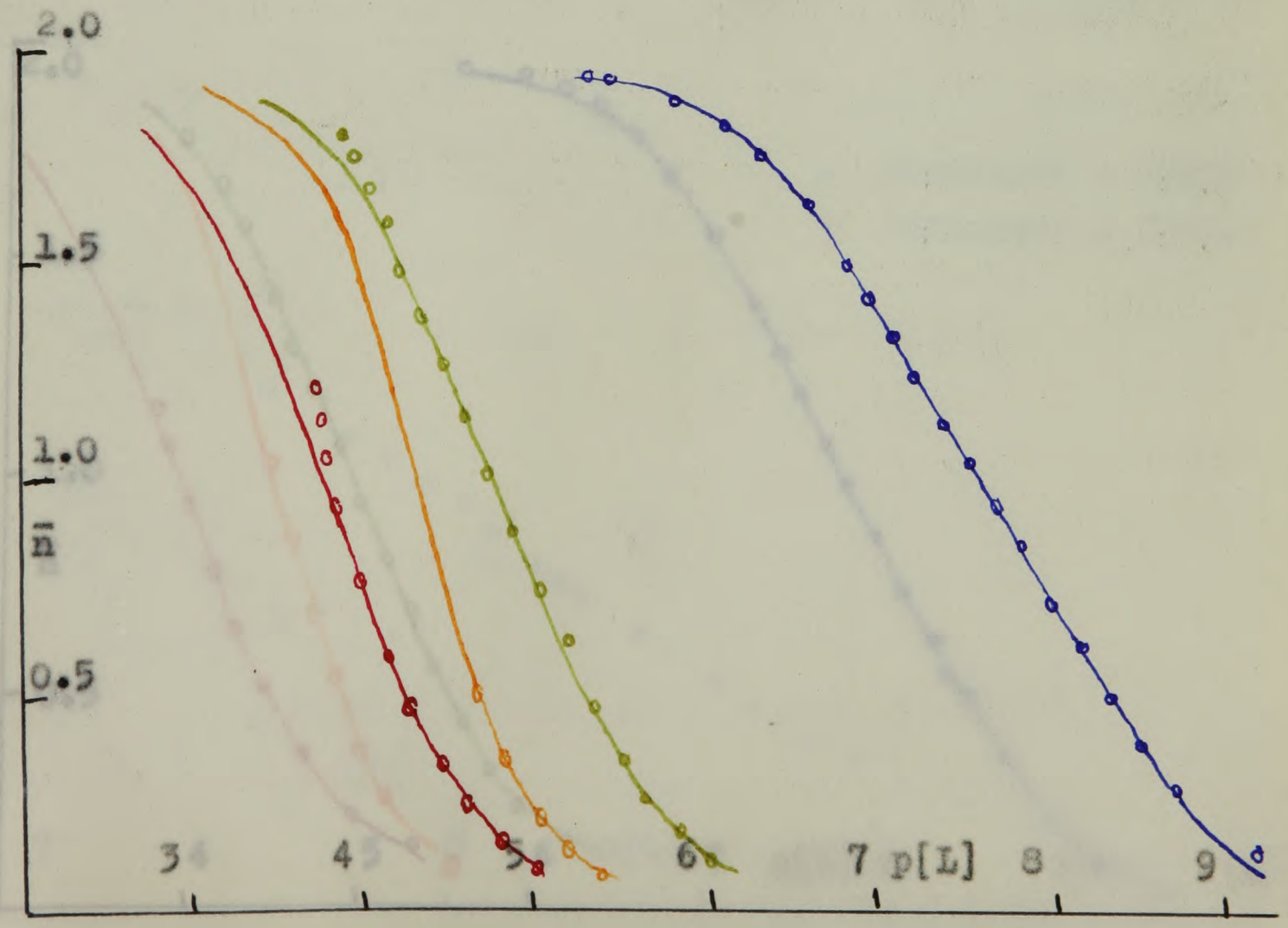
GRAPH IX.

Formation curves of the metal chelates of α-alanine (II).



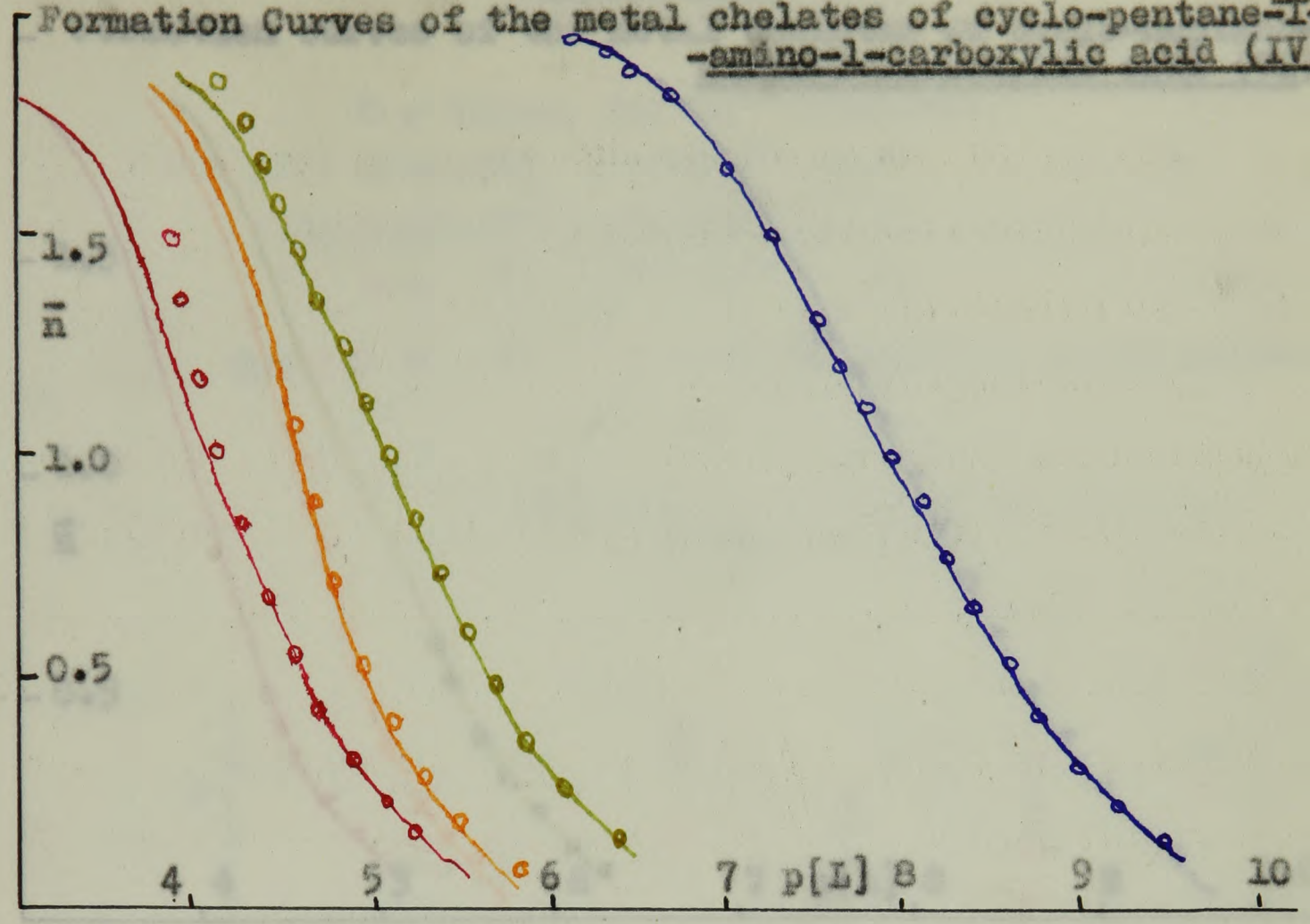
GRAPH X.

Formation curves of the metal chelates of CC-dimethylglycine (III).



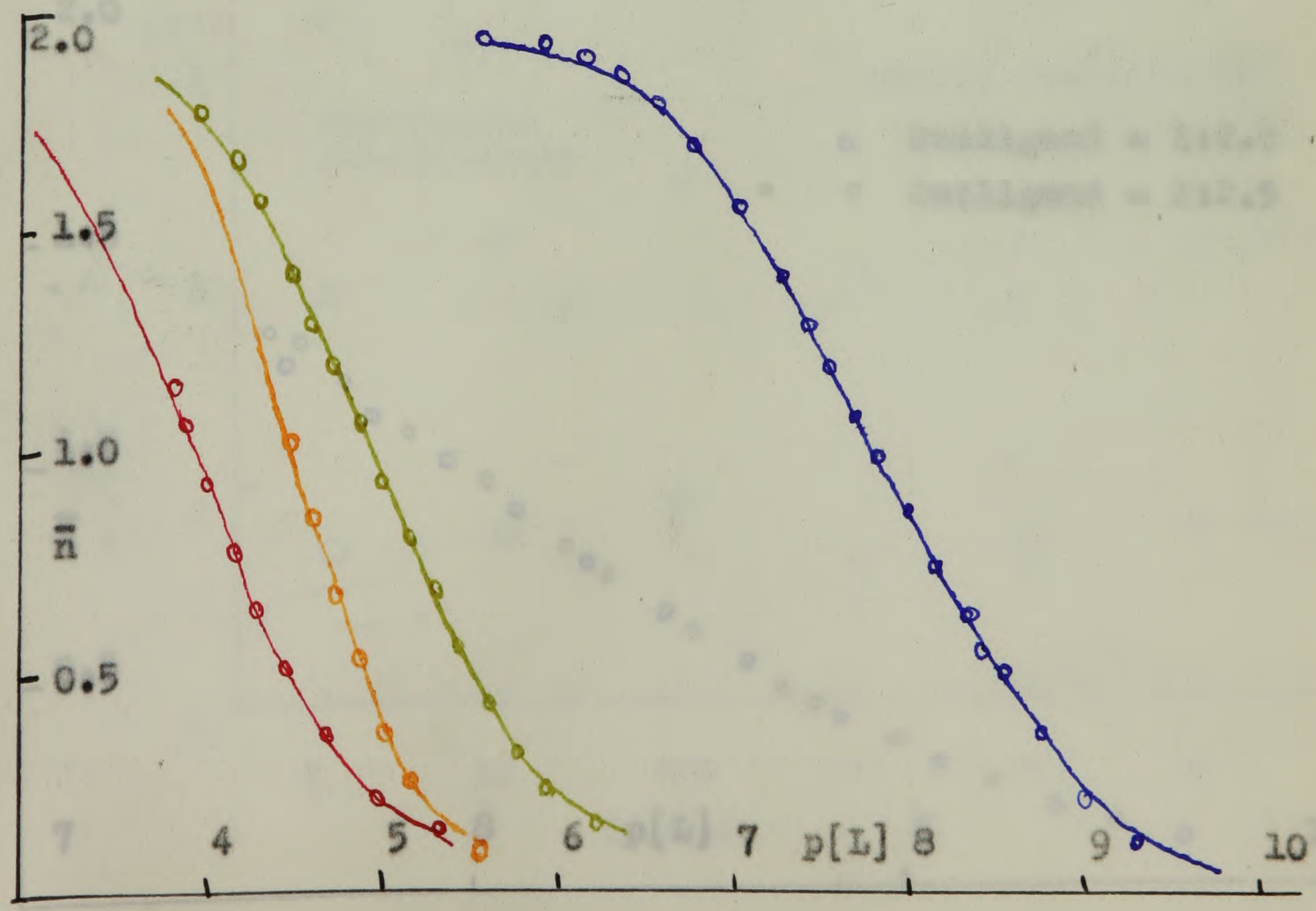
GRAPH XI.

Formation Curves of the metal chelates of cyclo-pentane-1-amino-1-carboxylic acid (IV).



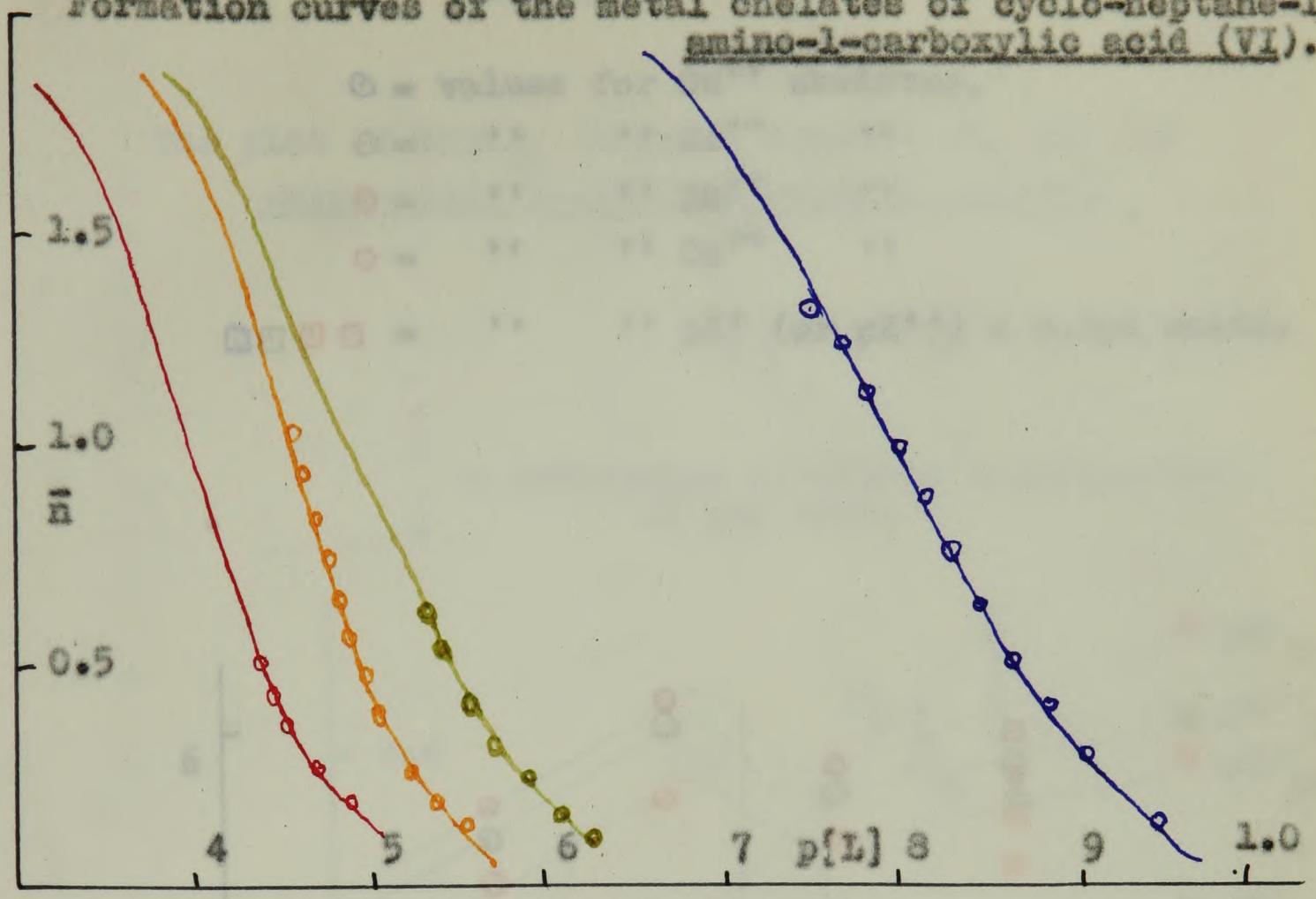
GRAPH XII.

Formation curves of the metal chelates of cyclo-hexane-1-amino-1-carboxylic acid (V).



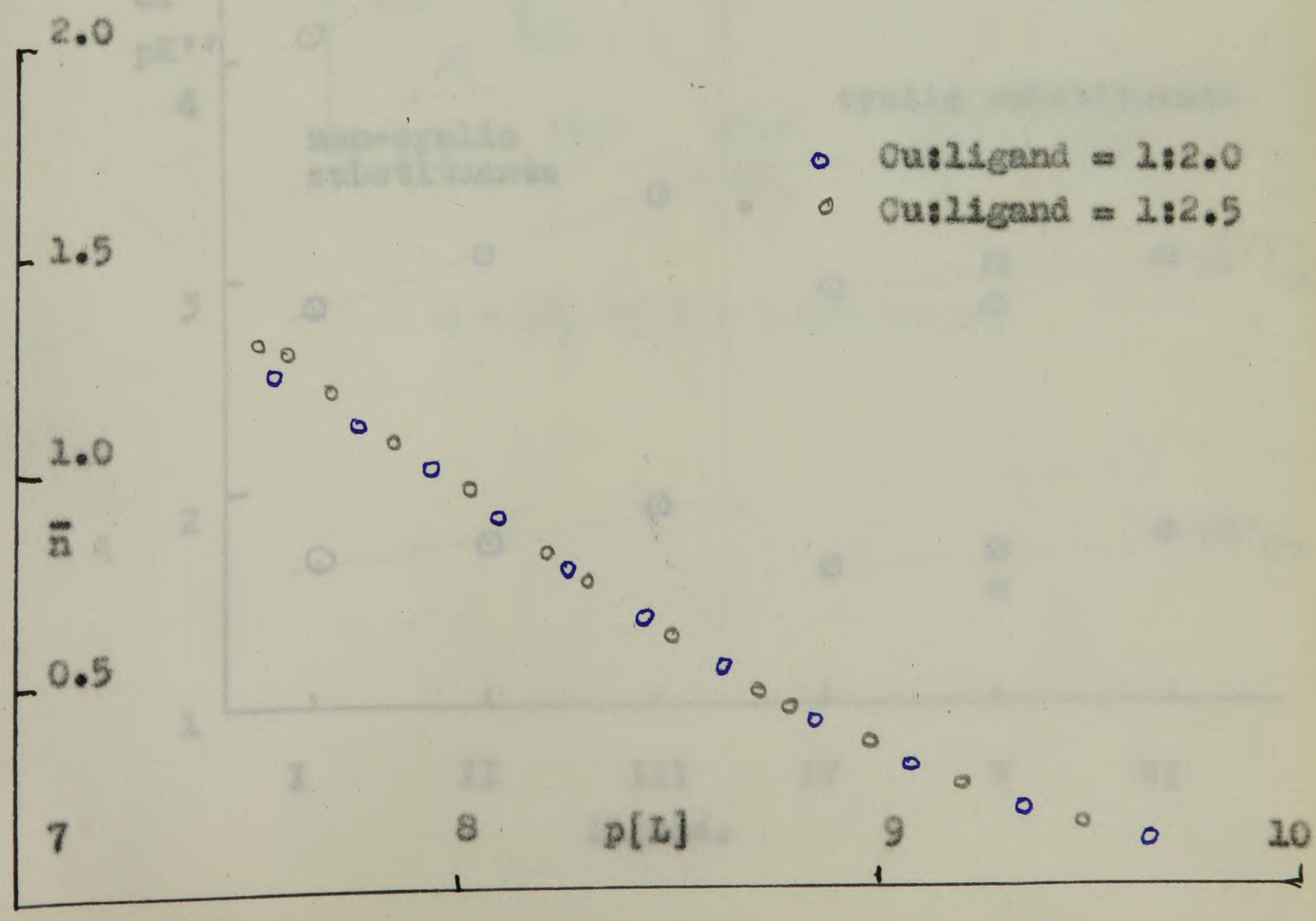
GRAPH XIII.

Formation curves of the metal chelates of cyclo-heptane-1-amino-1-carboxylic acid (VI).



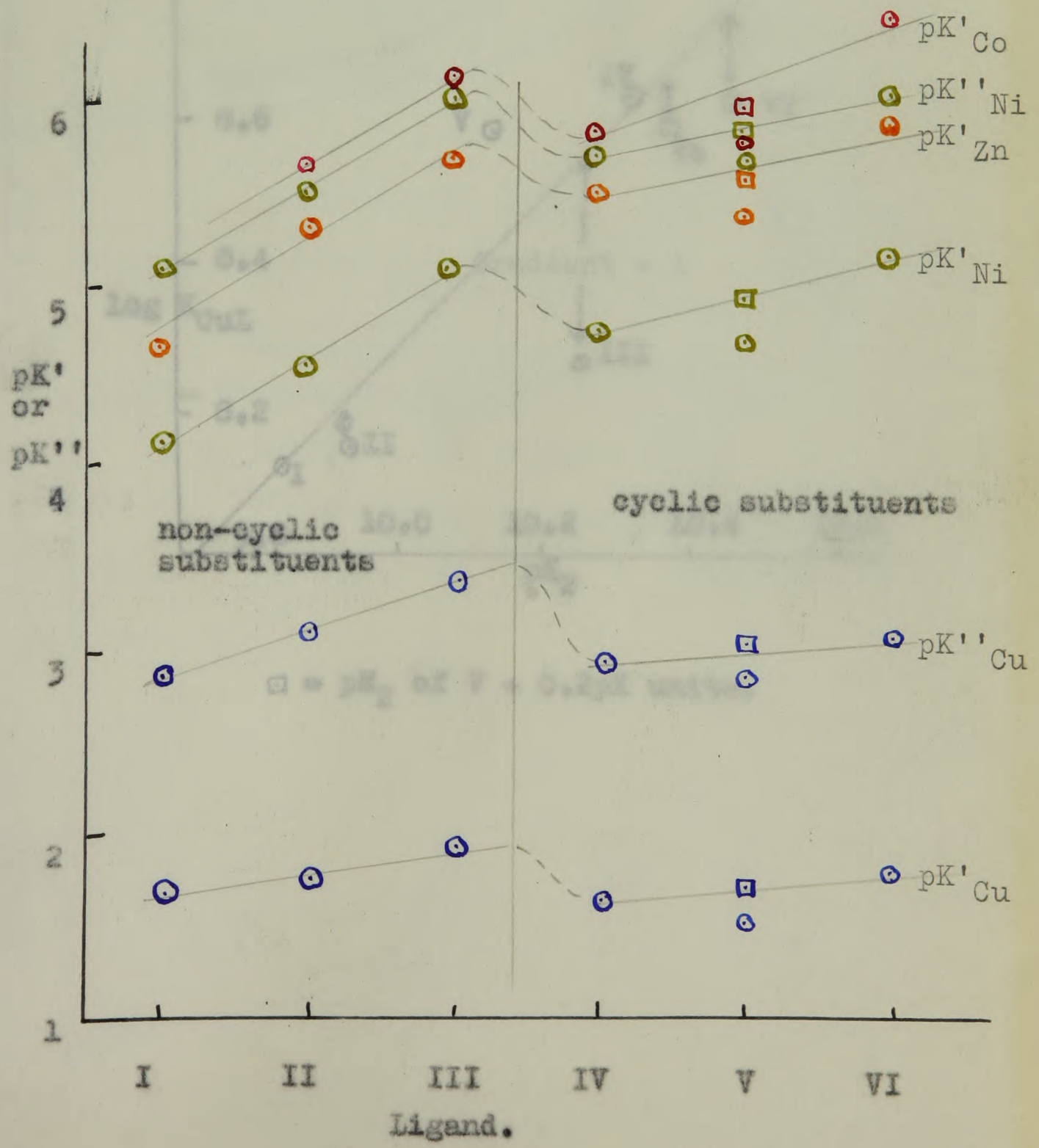
GRAPH XIV.

Formation curve of the copper chelate of VI.



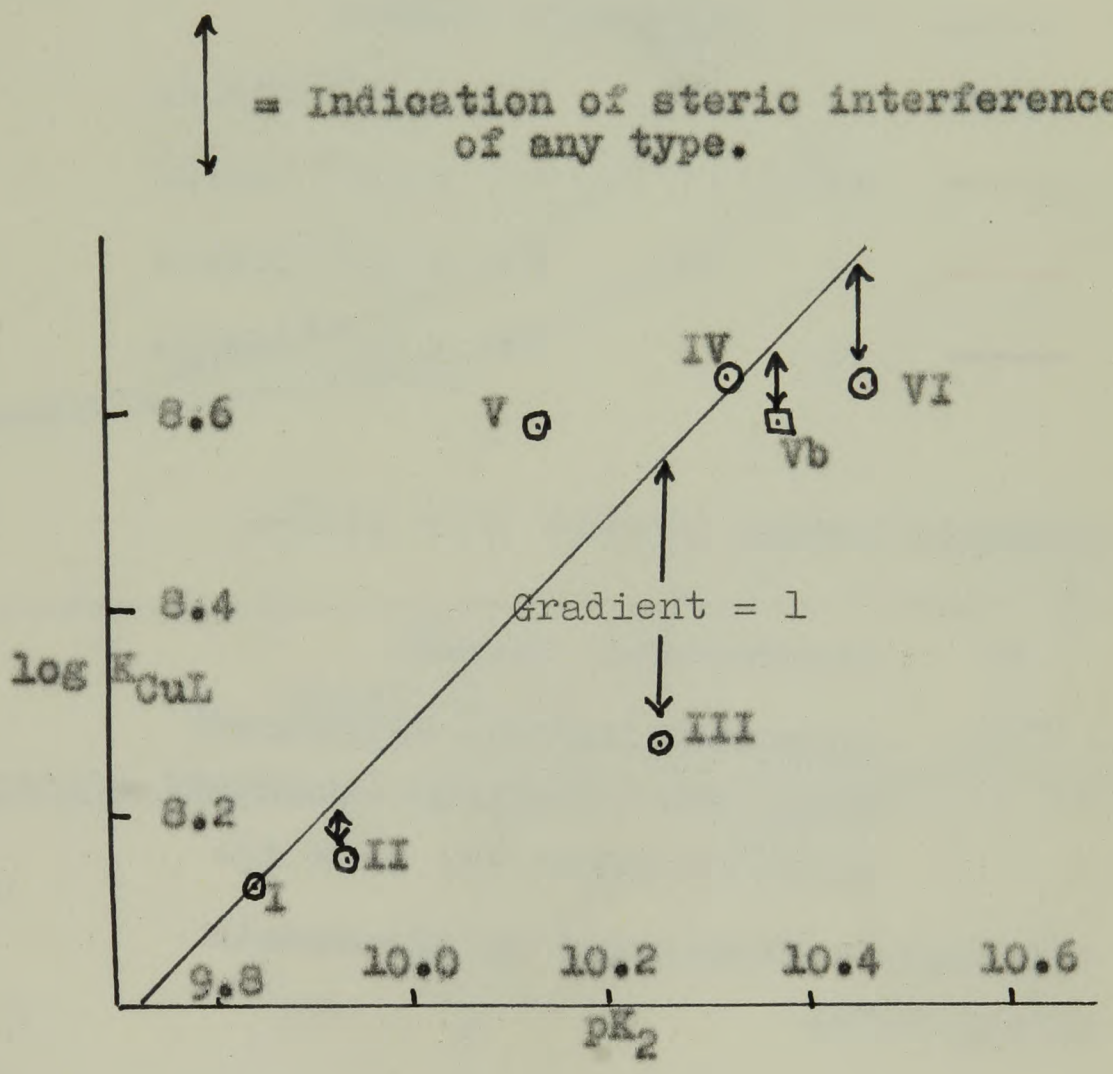
GRAPH XV .(see page 34).

⊙ = values for Cu^{++} chelates,
⊙ = '' '' Ni^{++} ''
⊙ = '' '' Zn^{++} ''
⊙ = '' '' Co^{++} ''
⊡⊡⊡⊡ = '' '' pK' (or pK''!) + 0.2pK units.



GRAPH XVI.

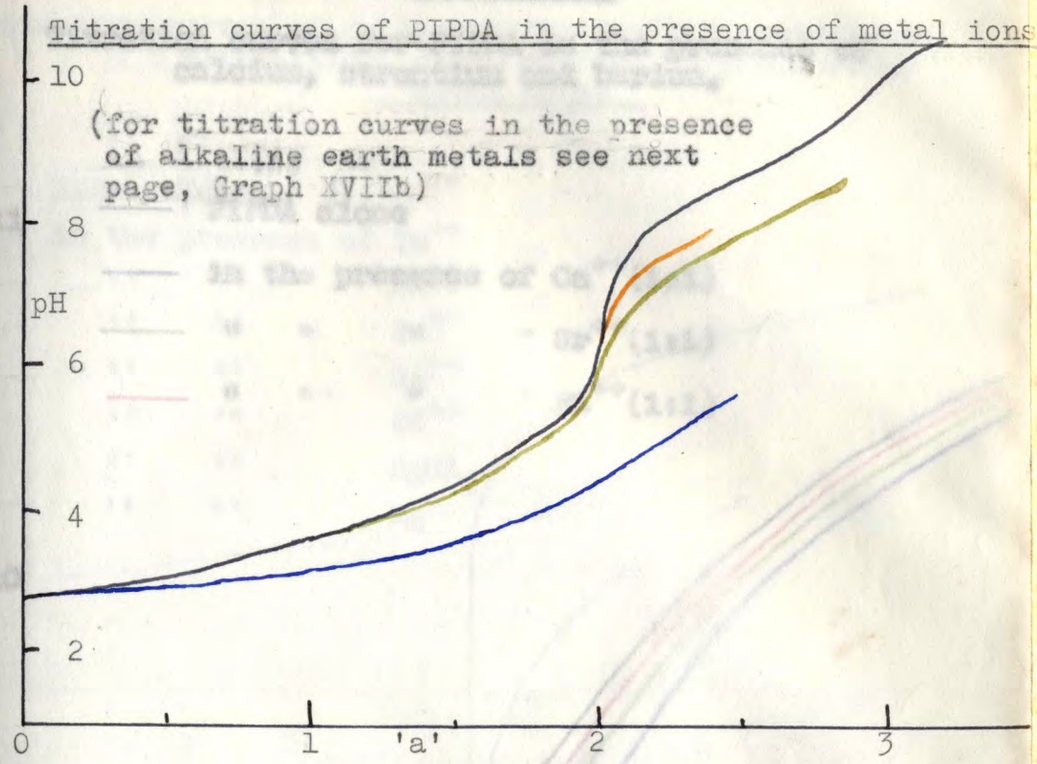
The plot of $\log K_{ML}$ (copper) against pK_2 for the amino-acids I--VI. (see pages 31 and 34).



⊡ = pK_2 of V + 0.2pK units.

GRAPH XVII.

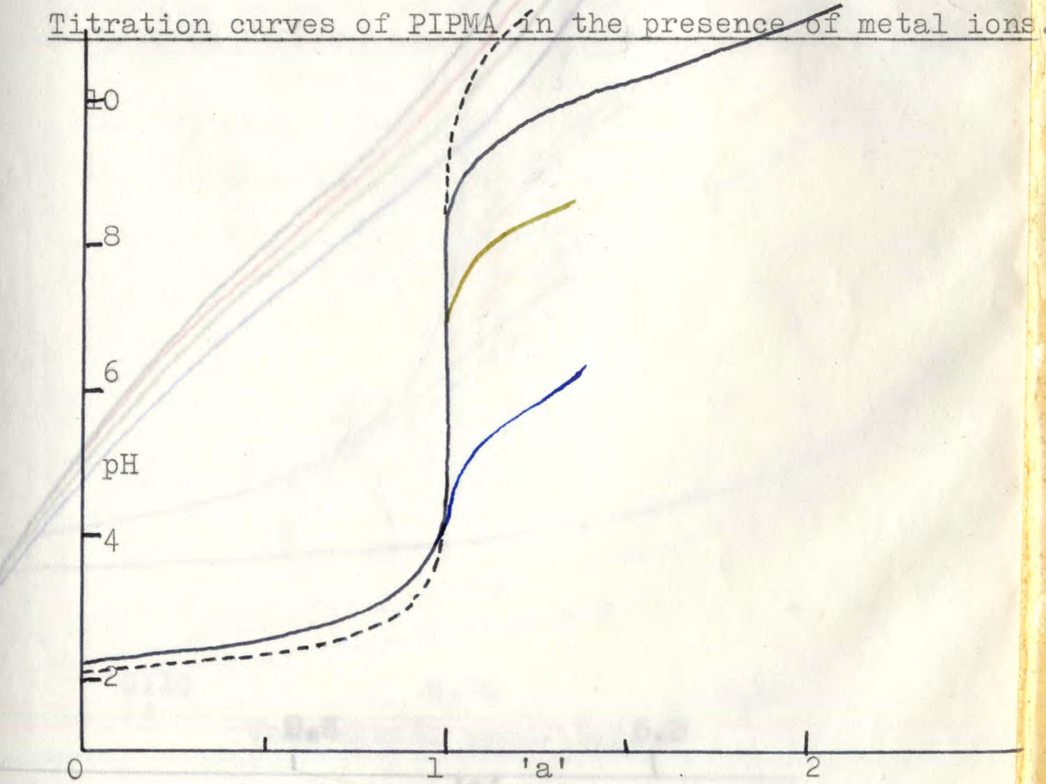
Titration curves of PIPDA in the presence of metal ions.



(for titration curves in the presence of alkaline earth metals see next page, Graph XVIIb)

GRAPH XVIII.

Titration curves of PIPMA in the presence of metal ions.



GRAPHS IV - XVIII.

pH Titration Curves.

- - - - - HCl only.

——— " + Amino-acid alone.

——— " " " + Cu^{++}(2:1).

——— " " " + Ni^{++}(2:1).

——— " " " + Zn^{++}(2:1).

——— " " " + Co^{++}(2:1).

Formation Curves (Graphs IX - XIII).

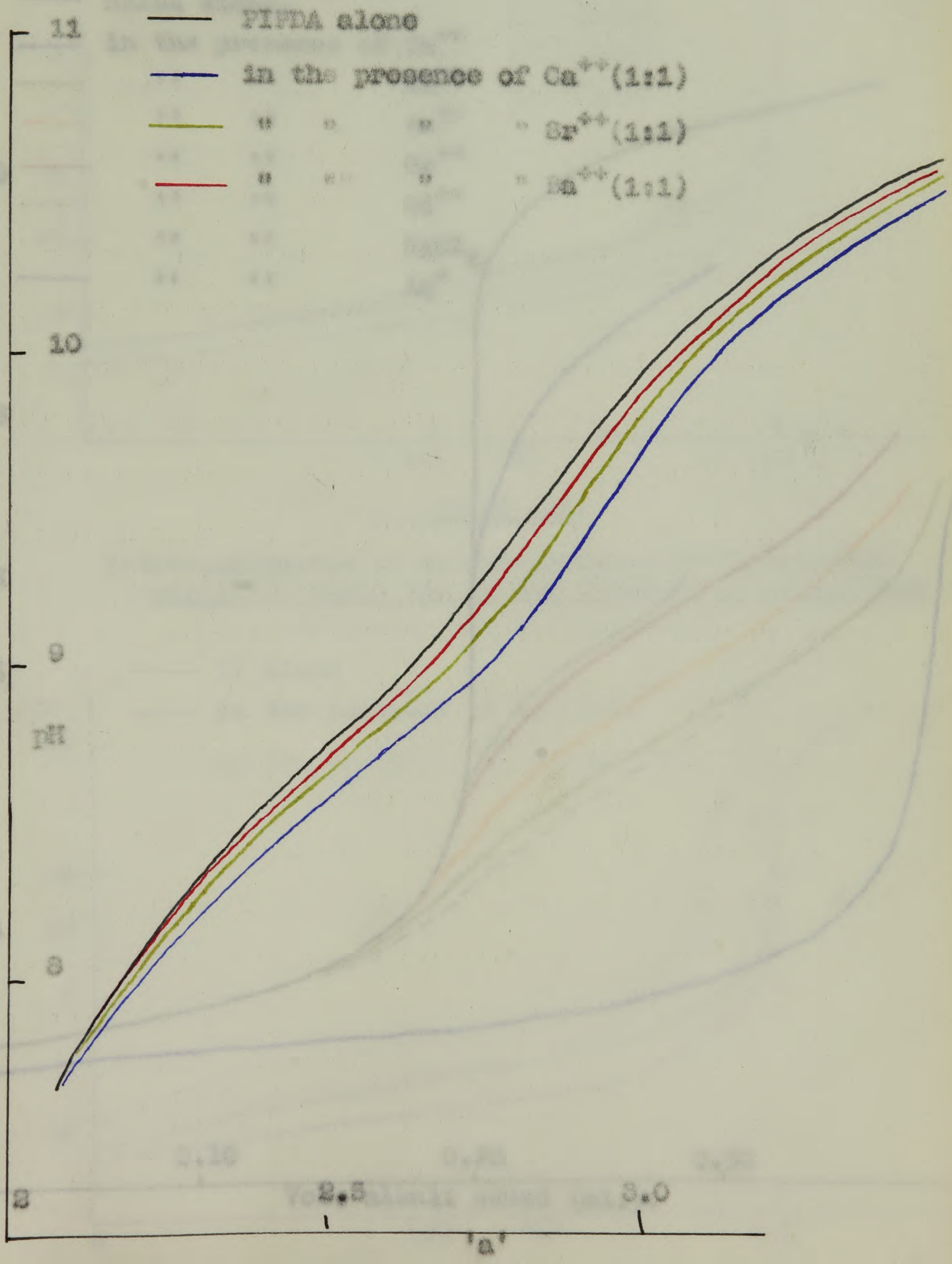
o Experimental Points.

——— Formation Curves, calculated using the Stability Constants given in Table VI, page 40.

The colours correspond to the metals shown above.

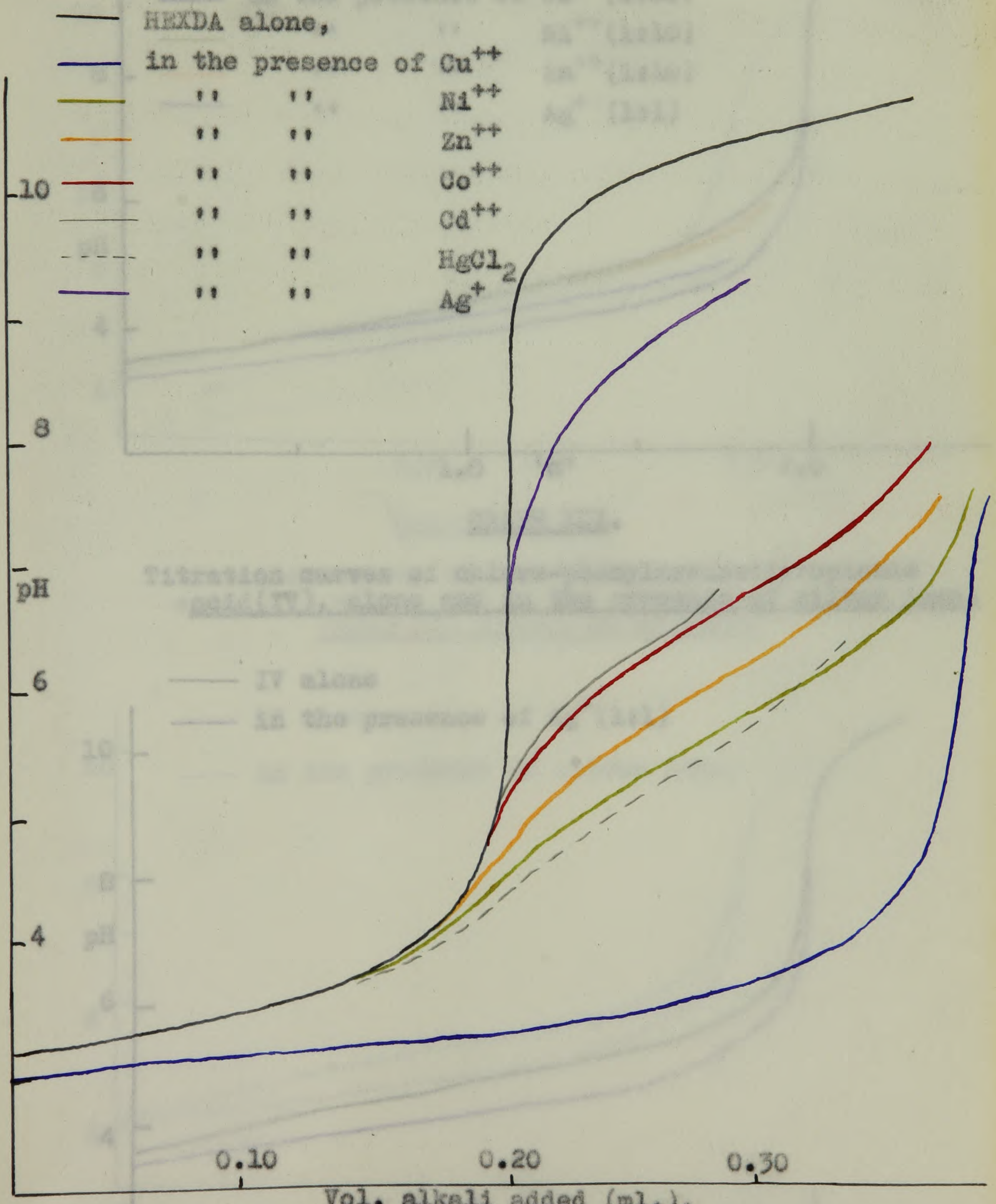
GRAPH XVIIb.

Titration curves for PIPDA in the presence of calcium, strontium and barium.



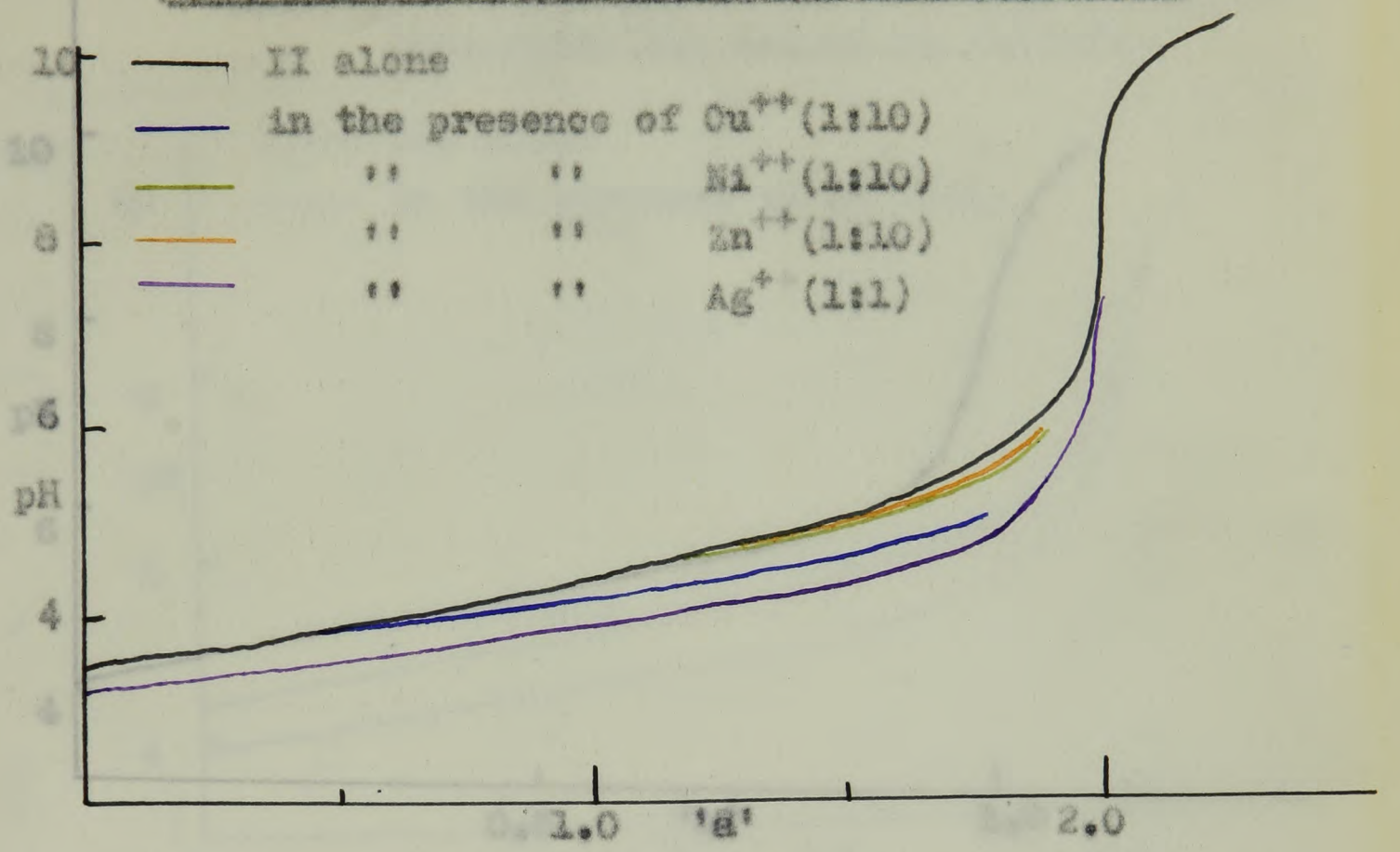
GRAPH XIX.

Titration curves of cyclo-hexylamine-NN-diacetic acid, HEXDA,(III), alone and in the presence of metal ions.



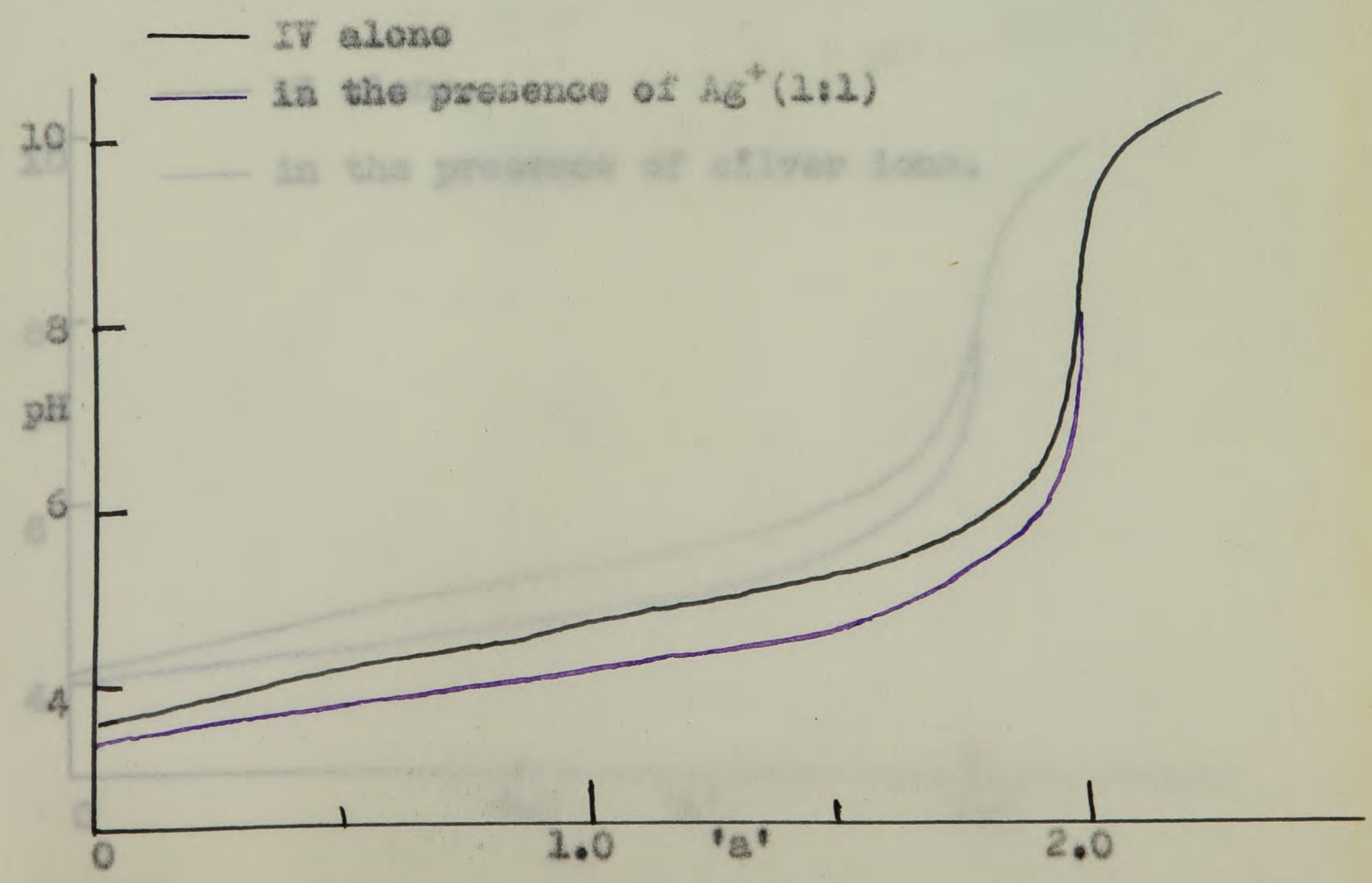
GRAPH XX.

Titration curves of phenylarsinediacetic acid, PHENASDA, (II), alone and in the presence of metal ions.



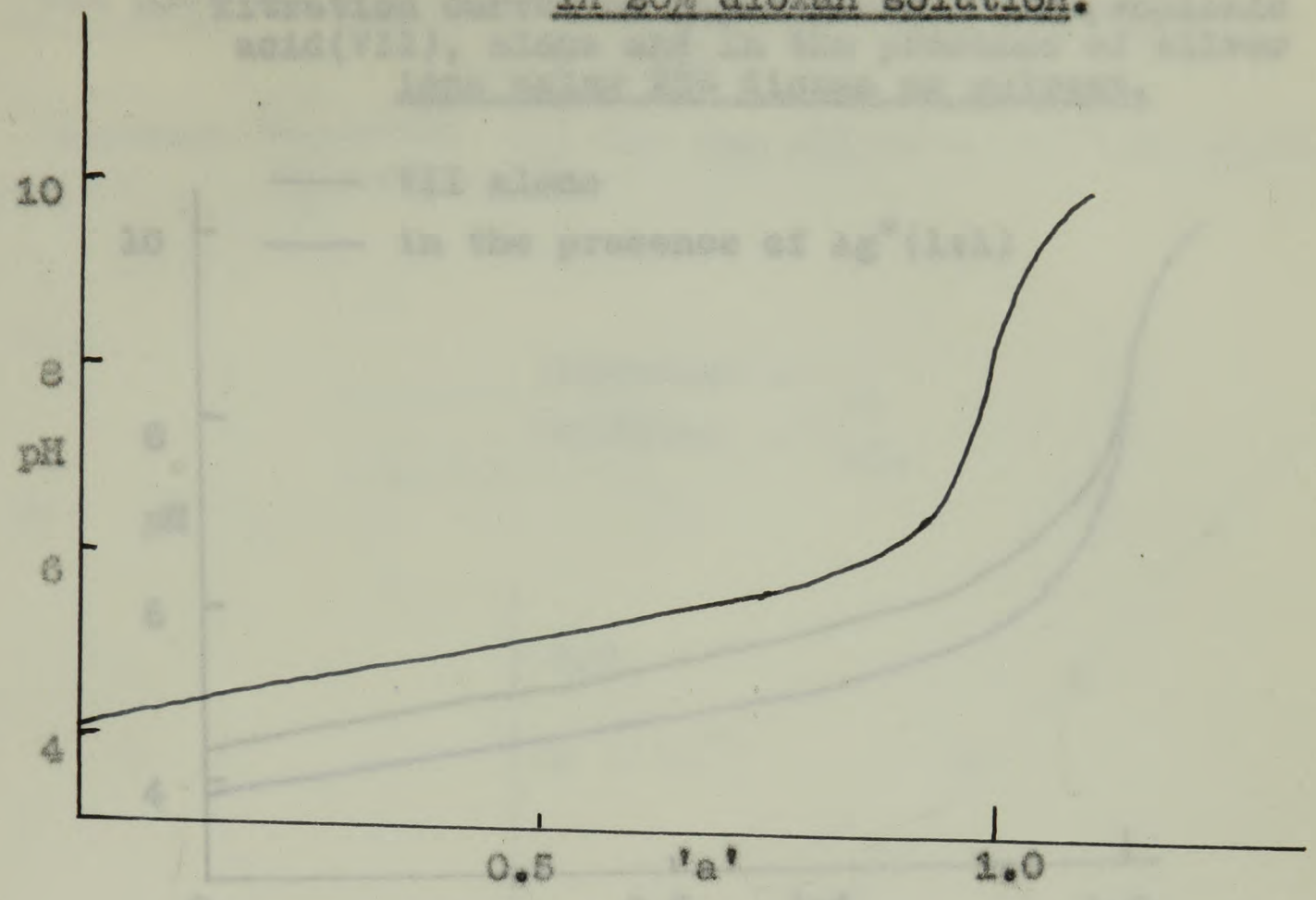
GRAPH XXI.

Titration curves of chloro-phenylarsinedipropionic acid(IV), alone and in the presence of silver ions.



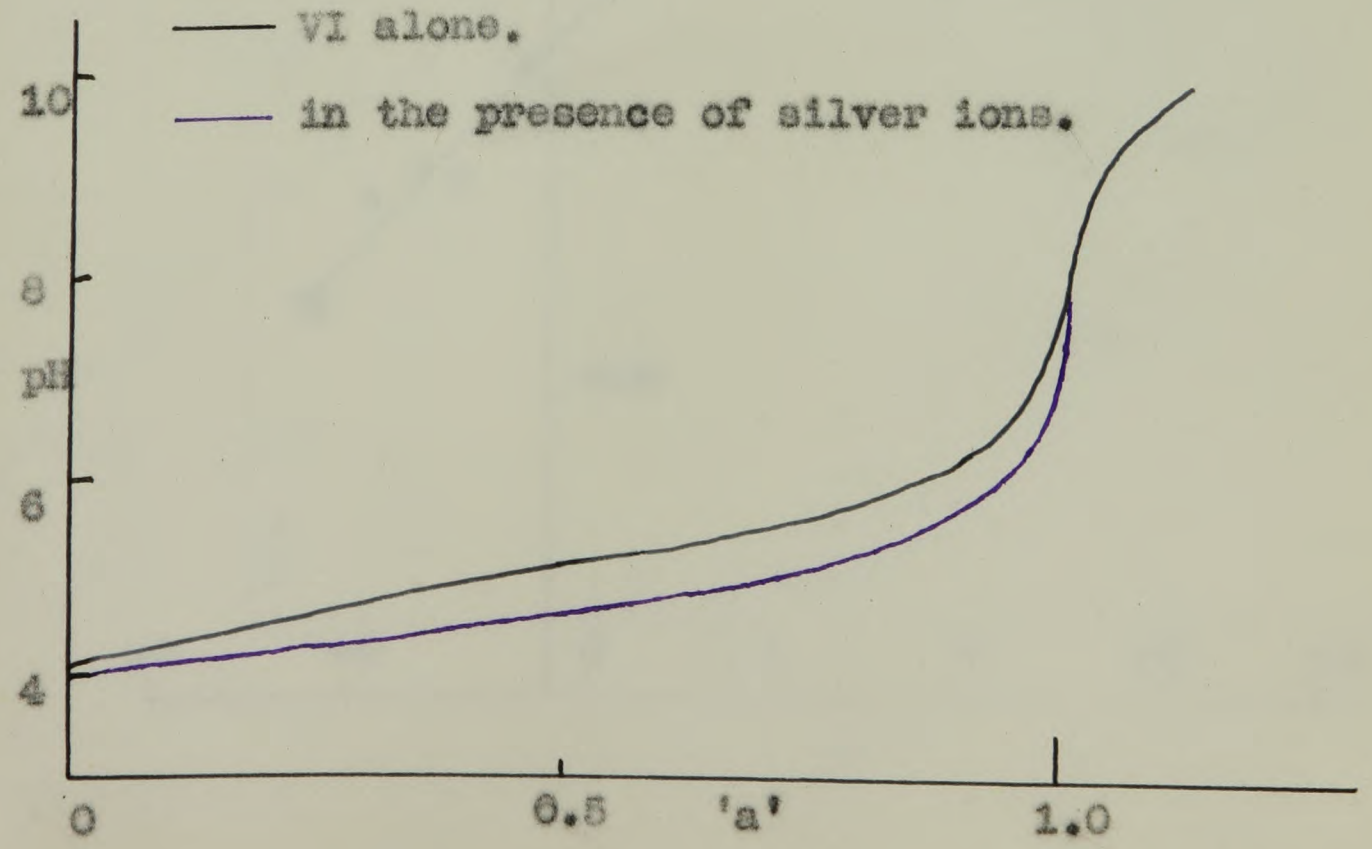
GRAPH XXII.

Titration curve of diphenylamine-N-propionic acid (V) in 20% dioxan solution.



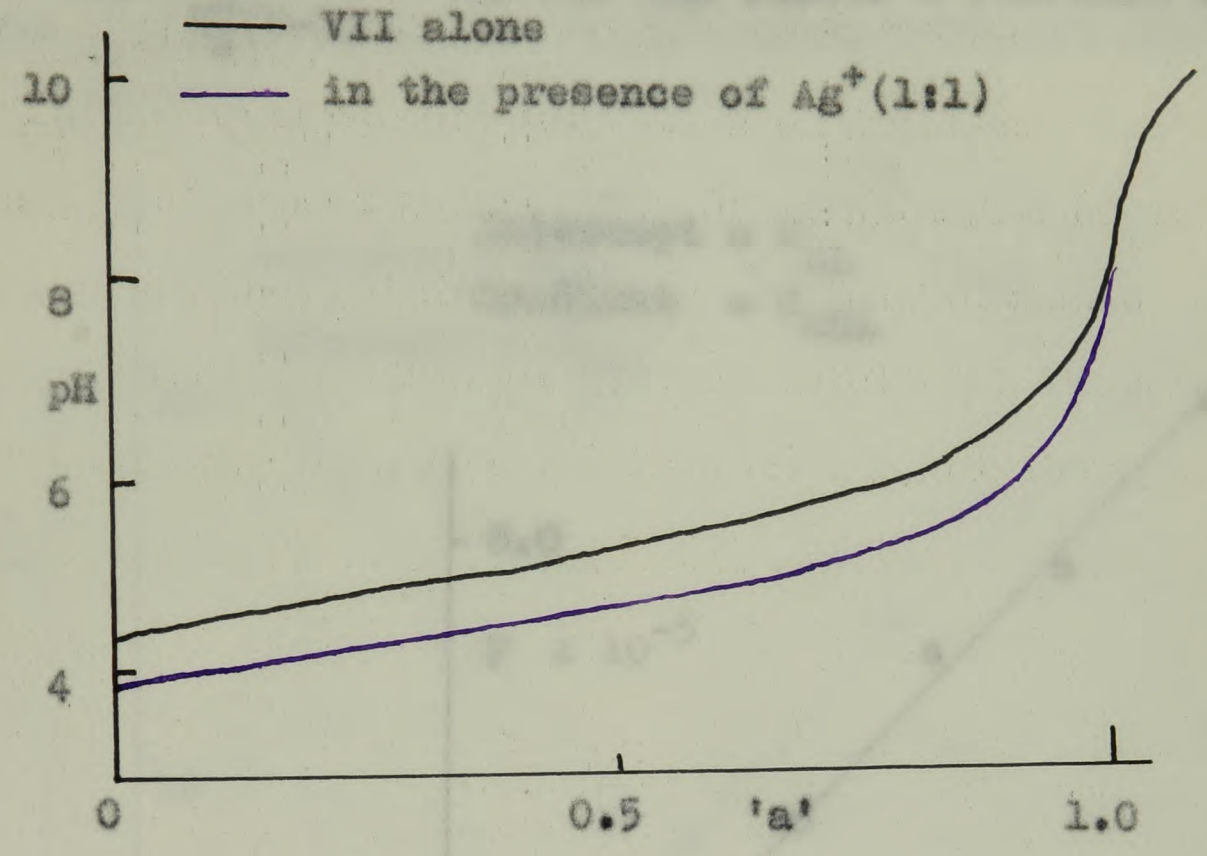
GRAPH XXIII.

Titration curves of diphenylphosphine-P-propionic acid (VI) alone, and in the presence of silver ions using 20% dioxan as solvent.



GRAPH XXIV.

Titration curves of diphenylarsine-As-propionic acid(VII), alone and in the presence of silver ions using 20% dioxan as solvent.



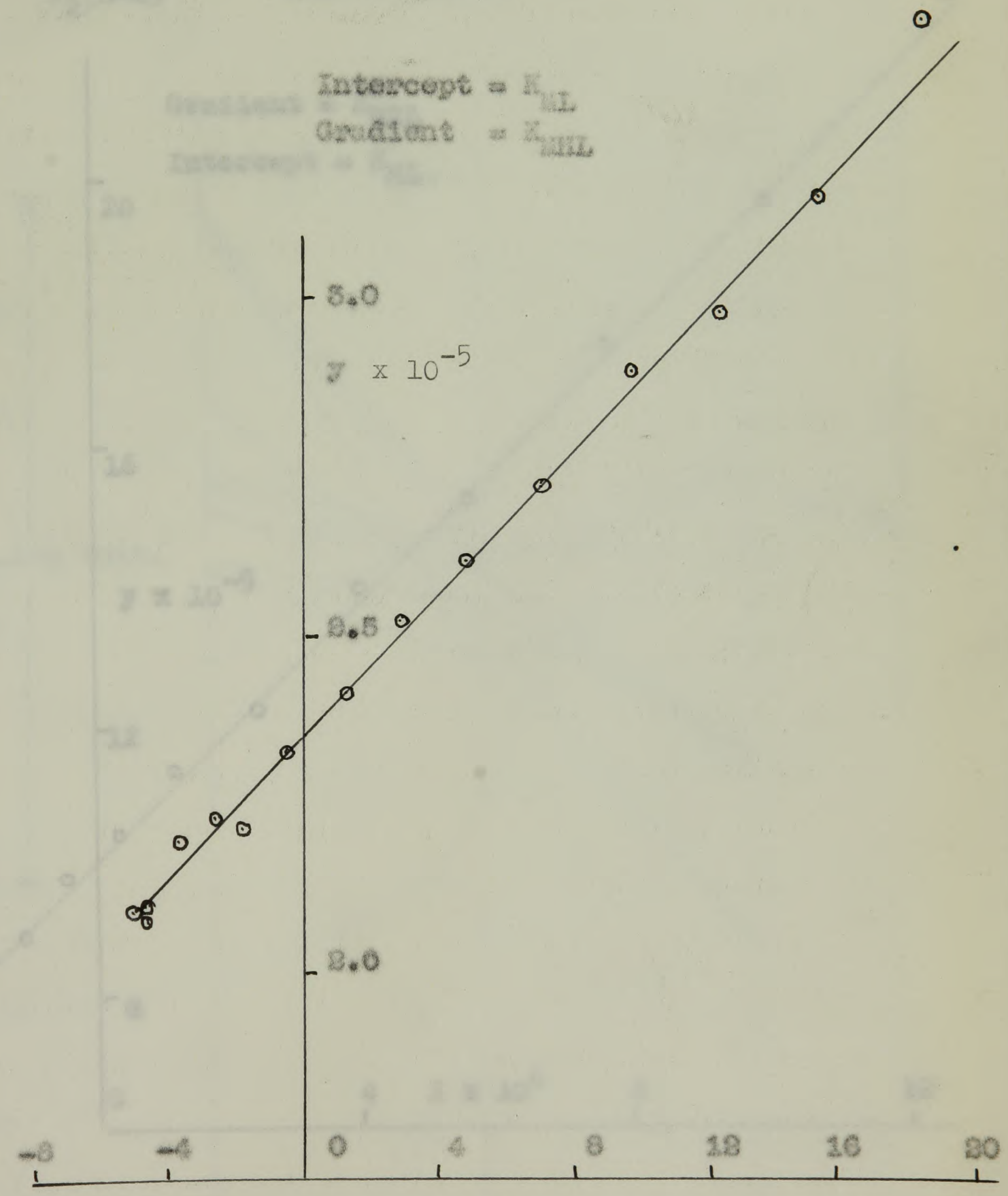
GRAPH XXV.

The plot of $\frac{(2-\bar{n}) + [H^+](1-\bar{n})/K_2^H + [H^+]^2\bar{n}/K_1^H K_2^H}{H^+(\bar{n}-2)}$ (y)

against $\frac{[H^+](2-1)}{K_2^H(\bar{n}-2)}$ (x) for the silver - PHENASDA system.

Intercept = K_{ML}

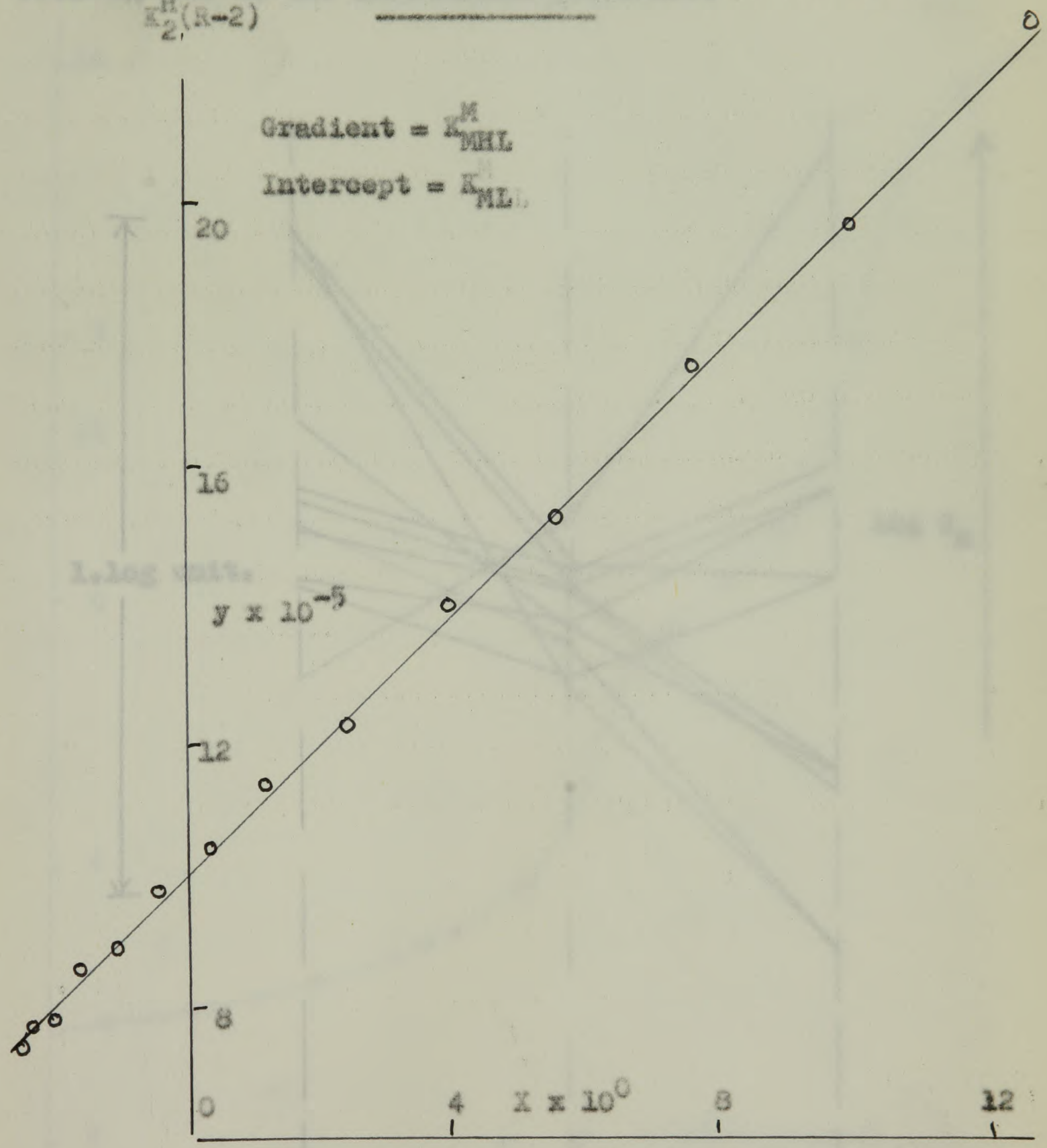
Gradient = K_{MHL}



GRAPH XXVI.

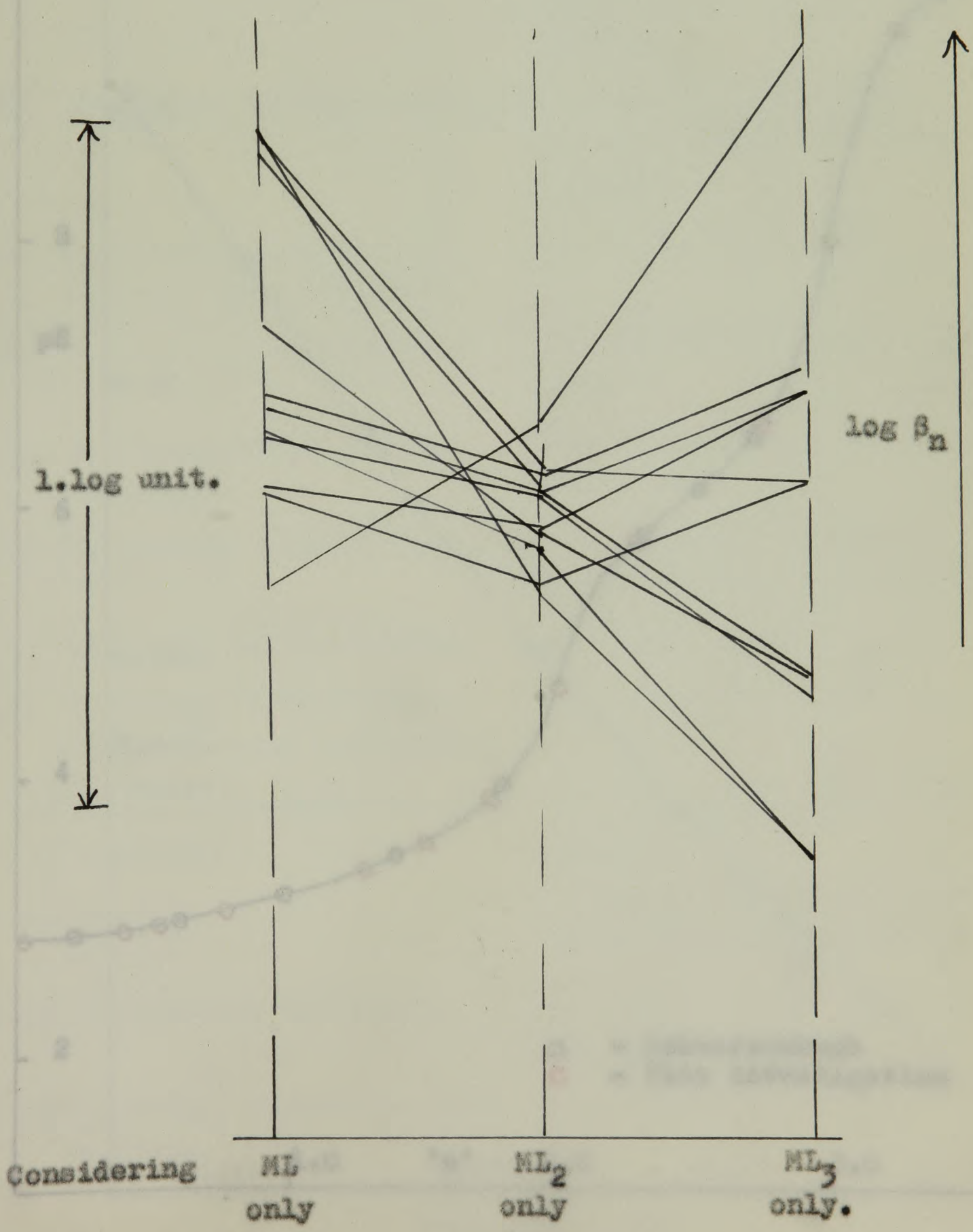
The plot of $\frac{(2-\bar{n}) + [H^+](1-\bar{n})/K_2^H - [H^+]^2\bar{n}/K_1^H K_2^H}{[M](\bar{n}-2)}$ (y)

against $\frac{[H^+](\bar{n}-1)}{K_2^H(\bar{n}-2)}$ for the silver-chlor-PHENASDPA system.



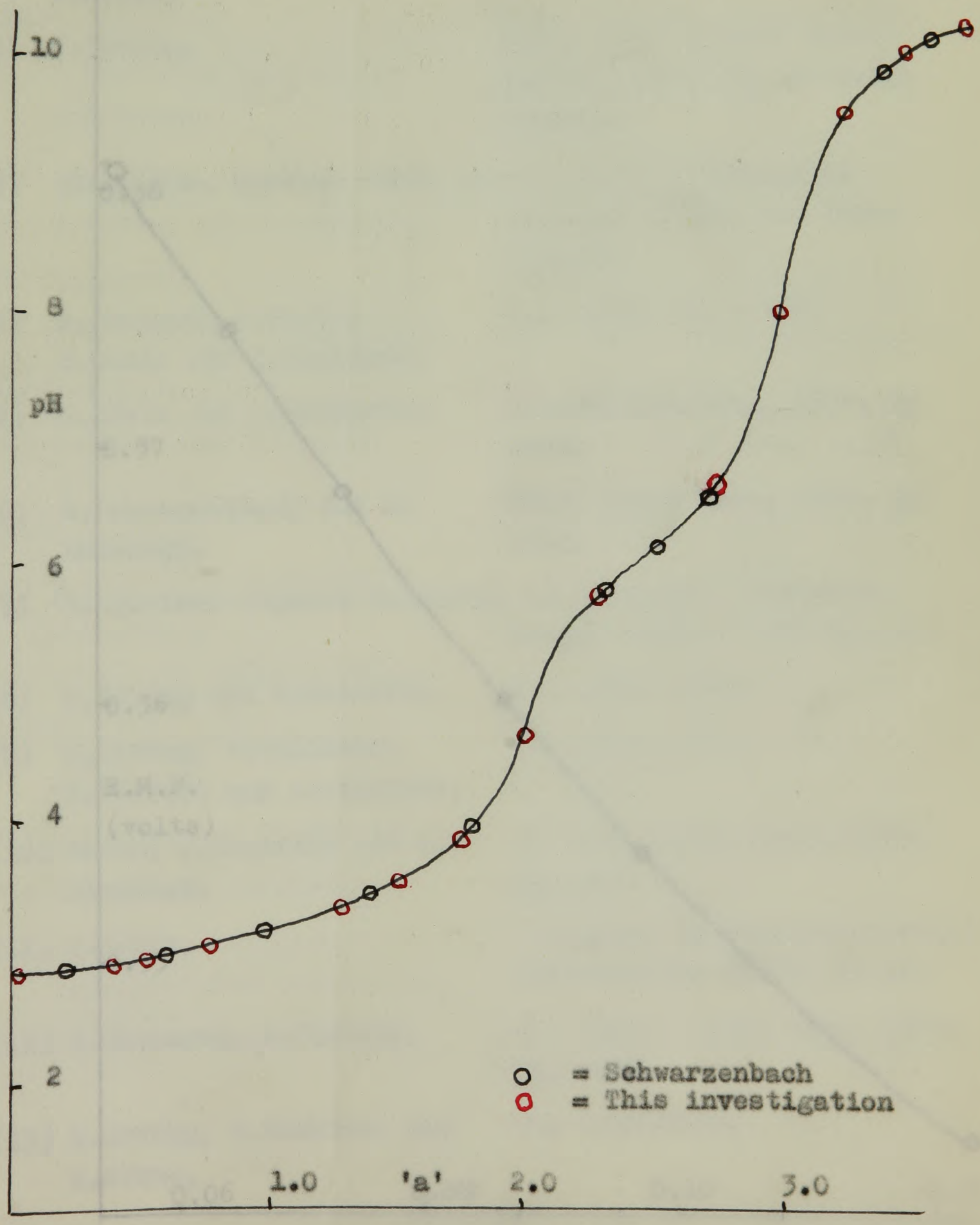
GRAPH XXVII.

A graph to demonstrate the spread in values for β_n for the PHENASDA - mercury^{II} system when the complexes ML, ML_2 and ML_3 are considered separately. Each line represents measurements on the same solution, the differences being entirely due to the calculation procedure.



GRAPH XXVIII.

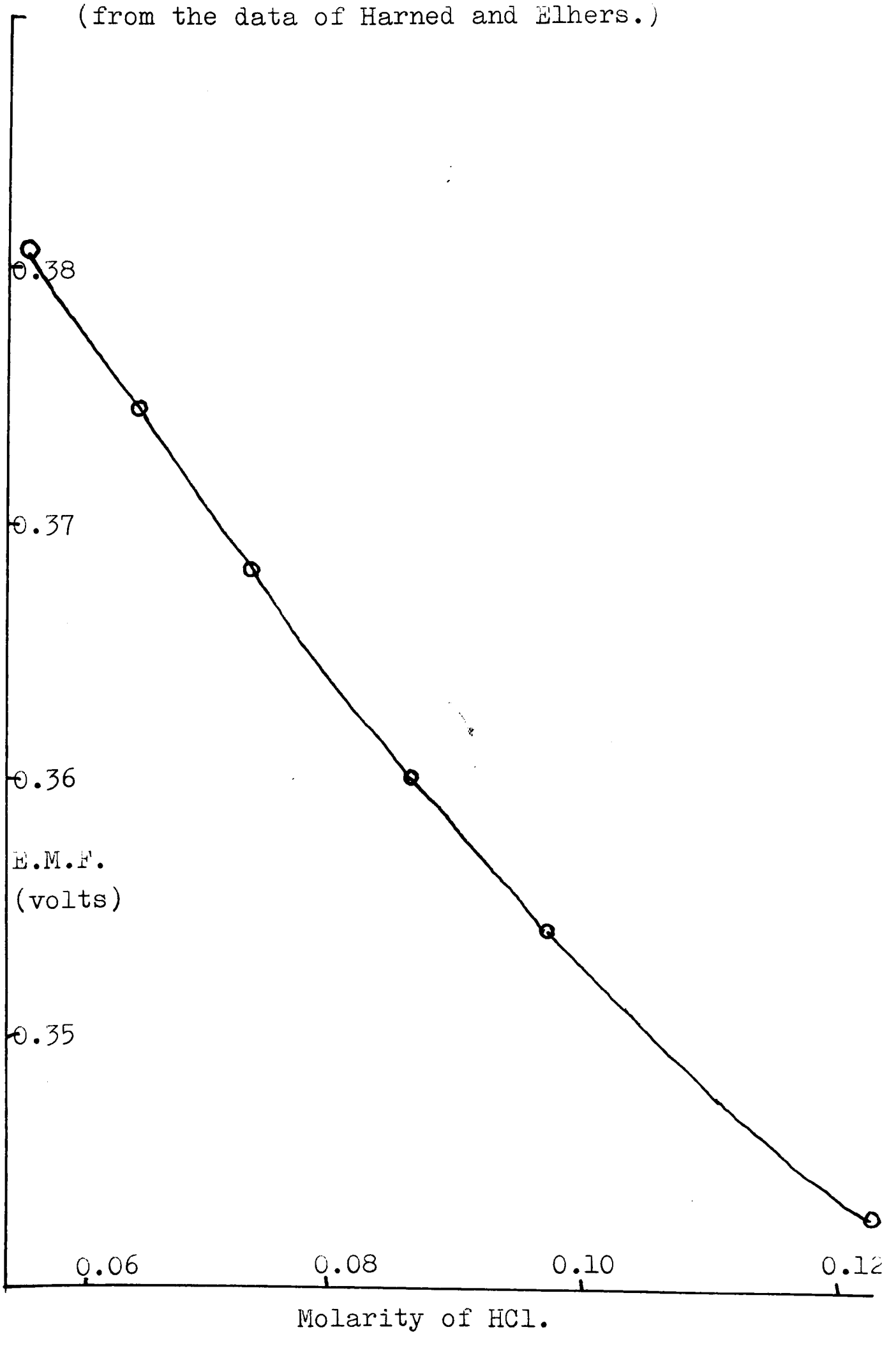
The titration curve of Ethylenediaminetetraacetic acid.



GRAPH XXIX.

The E.M.F. of the cell Ag/AgCl : HCl : H_2/Pt at 20°C.

(from the data of Harned and Elhers.)



REFERENCES.

(1) S.Ahrland, J.Chatt and N.Davis, Quat. Rev. 1958, 12, 265.

(2) H.Irving, Chem. Soc. Special Publ. No. 13, 1959, 13 and refs. therein.

(3) Chem. Soc. Special Publ. No. 6, Part II 'Inorganic Ligands' (1958) and refs. therein.

(4) S.Ahrland, J.Chatt, N.Davis and A.Williams, J., 1958, 264 - 288.

(5) H.Brown and M.Borkowski, J.Amer.Chem.Soc., 1952, 74 1894.

(6) G.Schwarzenbach and G. Anderegg, Helv. Chim. Acta, 1957, 40 1773.

(7) 'Sidgewicks Organic Chemistry of Nitrogen' Clarendon Press, Oxford, 1937 pp.105.

(8) H.Irving and H.Rossotti, J., 1954, 2904.

(9) H.Irving, R.Williams, R.Ferrett and A.Williams, J., 1954, 3494.

(10) Brown, J.Brewster and S. Shechter, J. Amer. Chem. Soc., 1954, 76, 467.

(11) W.Klyne, 'Progress in Stereochemistry' Butterworths (1954) pp.47.

(12) S.Chaberek, A.Martell, J., Amer., Chem. Soc., 1952, 74, 5228.

(13) H.Irving, R.Shelton, and R.Evans, J., 1958,3540.

(14) G.Schwarzenbach and A. Ackermann, Helv. Chim. Acta, 1947, 30, 1798.

(15) F.Basolo and Y.Chen, J. Amer. Chem. Soc., 1954, 76, 953.

(15b) A.Williams, B.Sc. Thesis, Oxford, 1951.

(16) G.Schwarzenbach and A. Ackermann, Helv. Chim. Acta, 1948, 31, 1029.

(17) G.Weber, Perscnal Communication.

(18) H.Irving and H.Rossotti, J., 1953, 3397.

(19) A.Albert, Biochem. J., 1950, 47, 531.

(20) H.Irving and H.Rossotti, Acta Chem. Scand., 1956, 10, 72.

(21) C.Ingold, J., 1921, 305.

(22) E.Corey and J.Bailar, J. Amer. Chem. Soc., 1959, 81, ~~1620~~ 2620

(23) J.Curchod, Ph.D. Thesis, Paris, 1956.

(24) F.Basolo, Y.Chen and R.Murmann, J. Amer. Chem. Soc., 1954, 76, 956.

(25) D.Graddon and L.Munday, Chem. and Ind., 1959, 122.

(26) G.Schwarzenbach and H. Ackermann, Helv. Chim. Acta, 1948, 31, 1034.

(27) O.Hassel and B.Pedersen, Proc. Chem. Soc., 1959, 394.

(28) F.Mann and H.Watson, J., 1958, 2772.

(29) H.Irving, R.Williams, R.Ferrett and A.Williams, J., 1954, 3494.

(30) G.Schwarzenbach et al. Helv. Chim. Acta, 1947, 30, 1303.
Ibid. 1955, 38, 1147.

(31) R.Evans, D.Phil. Thesis, Oxford, 1958.

(32) J.Holloway and C.Reilley, Analyt. Chem., 1960, 32, 249.

(33) H.Rossotti, D.Phil. Thesis, Oxford, 1954.

(34) J.Prue and G.Schwarzenbach, Helv. Chim. Acta, 1950, 33, 963.

(35) B.James, D.Phil. Thesis, Oxford, 1960.

(36) J.Prue and G.Schwarzenbach, Helv. Chim. Acta, 1950, 33, 963.

(37) J.Crenshaw, A.Cope, N. Finkelstein and R.Rogan, J. Amer. Chem. Soc., 1938, 60, 2308.

(38) G.Schwarzenbach, G.Anderegg, W.Schneider and H.Senn, Helv. Chim. Acta, 1955, 38, 1147.

(39) S.Chaberek and A.Martell, J. Amer. Chem. Soc., 1952, 74, 5052.

(40) R.Cannan and A.Kilbrick, J. Amer. Chem. Soc., 1938, 60, 2314.

(41) J.Chatt and A.Williams, J., 1954, 4403.

(42) W.Clarke, 'The Determination of Hydrogen Ions; Bailliere,1928.

(43) Kunz A. J. Phys. Chem., 1928, 32, 1056

(44) H.Harned and R.Ehlers, J. Amer. Chem. Soc., 1932, 54, 1350.

(45) R. Gran, Acta Chem. Scand., 1950, 1, 559.

(46) A.Brown, J. Amer. Chem. Soc., 1934, 56, 646.

(47) Henderson, Z. Phys. Chem., 1907, 59, 118.

G. Lewis and L.Sargent, J. Amer. Chem. Soc., 1909, 31, 363.

(48) G.Schwarzenbach and W.Biedermann, Helv. Chim. Acta, 1948, 31, 331.

(49) Organic Syntheses, 22, 13.

(50) Zelinsky and Stadnikoff, Ber., 1906, 39, 1728.

(51) Vorlander and Mumme, Ber., 1901, 34, 1647.

(52) Kraut, Annalen, 1871, 157, 66.

(53) F.Mann and R.Cookson, J., 1949, 67.

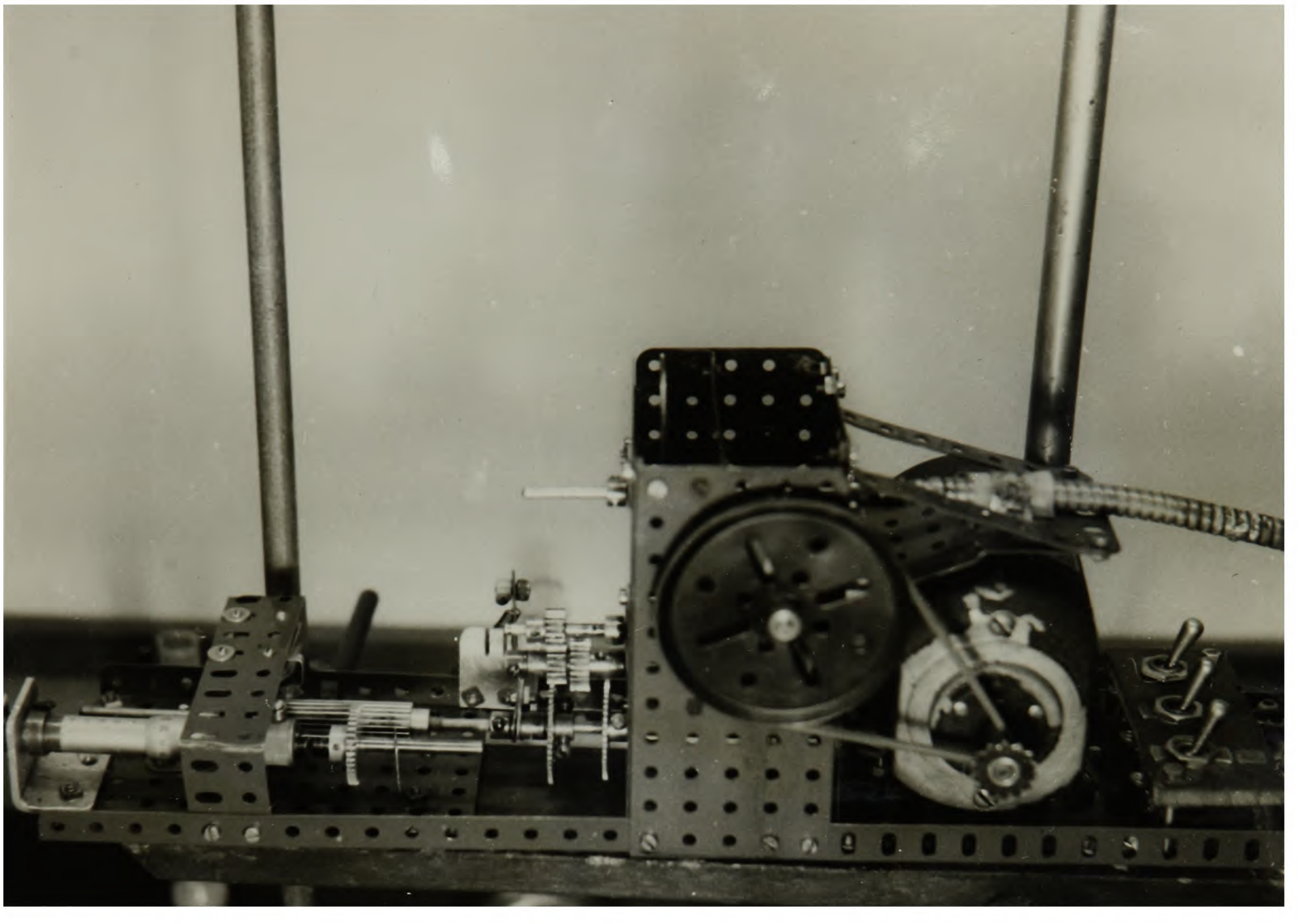
AN AUTOMATIC RECORDING TITRIMETER.

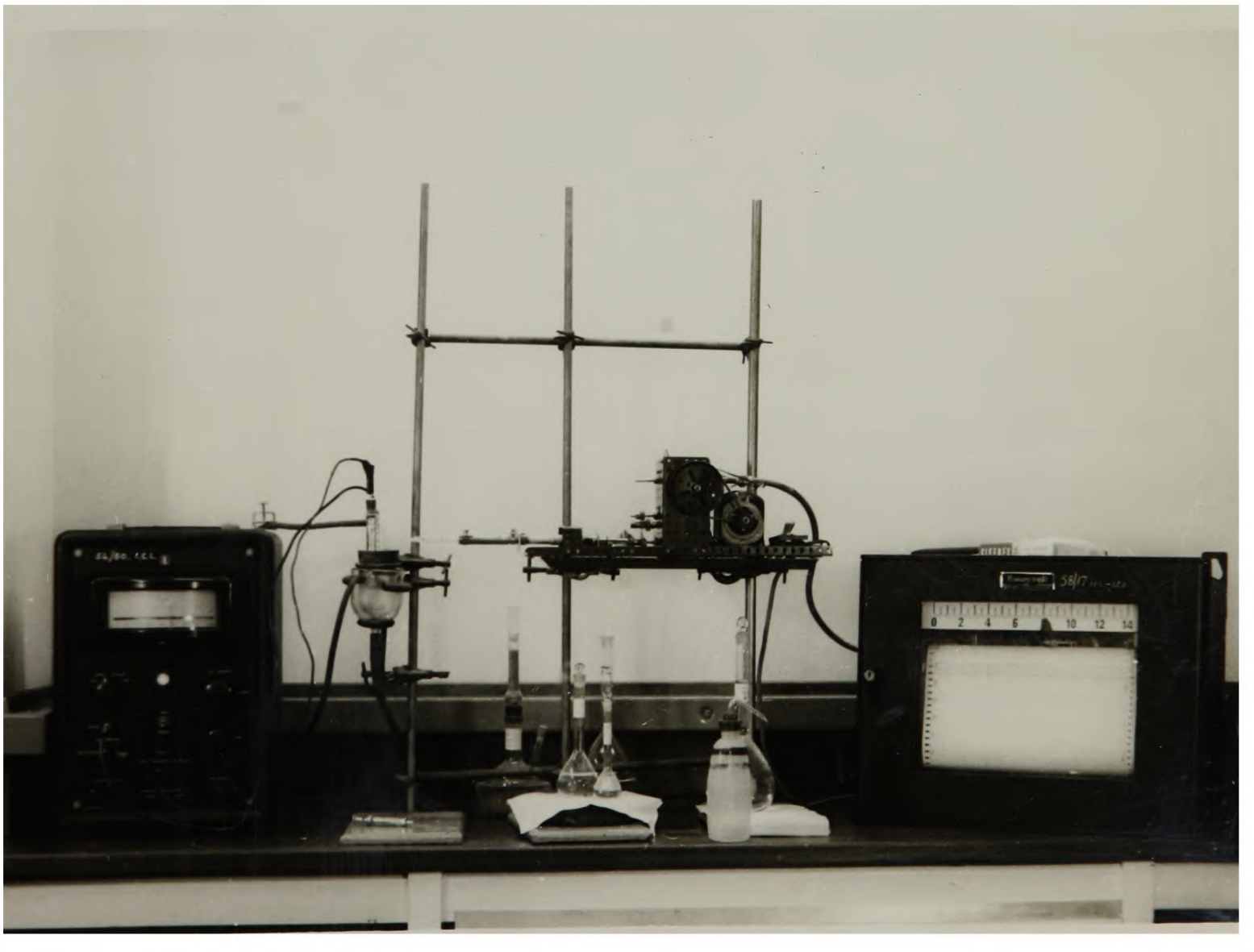
1. INTRODUCTION.

Dissociation constants of weak acids and the stability constants of the complexes which they form with metals may be evaluated from pH measurements made during titrations, with alkali, of the acid (the chelating agent) in the absence and in the presence of metal ions.[1,2,3].

Attempts have been made to facilitate and to increase the accuracy of such potentiometric titrations by employing some mechanical means of delivering the alkali accurately and at a controlled rate.[4,5]. If addition has to be stopped to take a pH reading some mechanism must be employed to raise the tip of the burette from the titration solution to prevent slow effusion and drift of potential. If, on the other hand, the pH is plotted continuously by some recording device both the speed of recorder-chart and the rate of addition of titrant must be constant if a certain length of chart is to correspond exactly to a known volume of added titrant.

On leaving buffer regions the value of d(pH)/dv increases so that more time is required for the solution and electrode system to reach equilibrium. However, if the rate of addition




0 2 4 6 10 12 14

of titrant is reduced, the ordinate scale on the recorder chart will not be uniform and a distorted titration curve will result.

All these disadvantages have been overcome in the titration apparatus described here. The recorder chart and micrometer syringe used to add the titrant are both driven by the same motor through non-slip gears. The speed of this motor may be varied by a 'Variac' transformer so that the rate of addition of titrant does not exceed the rate of attainment of equilibrium. Such changes in speed will, however, affect the chart speed and the rate of addition of titrant equally. Hence on the graph obtained the axis corresponding to the addition of titrant will be linear and the resulting plot will be a 'theoretical' titration curve.

The titrant was added by an 'Agla' micrometer syringe and the pH of the solution was measured with a glass electrode-calomel reference electrode assembly with the aid of a direct reading electronic pH meter ('Electronic Instruments Ltd., model 23). The pH readings were recorded on a chart recorder with a scale reading from 0-14 pH units (Honeywell-Brown model).

With this apparatus up to 0.5ml. of titrant (±0.0002ml.) may be added over periods of time ranging from 100 minutes down to about 25 minutes and pH values read to approximately 0.02 pH units.

Potentiometric Titration Apparatus.

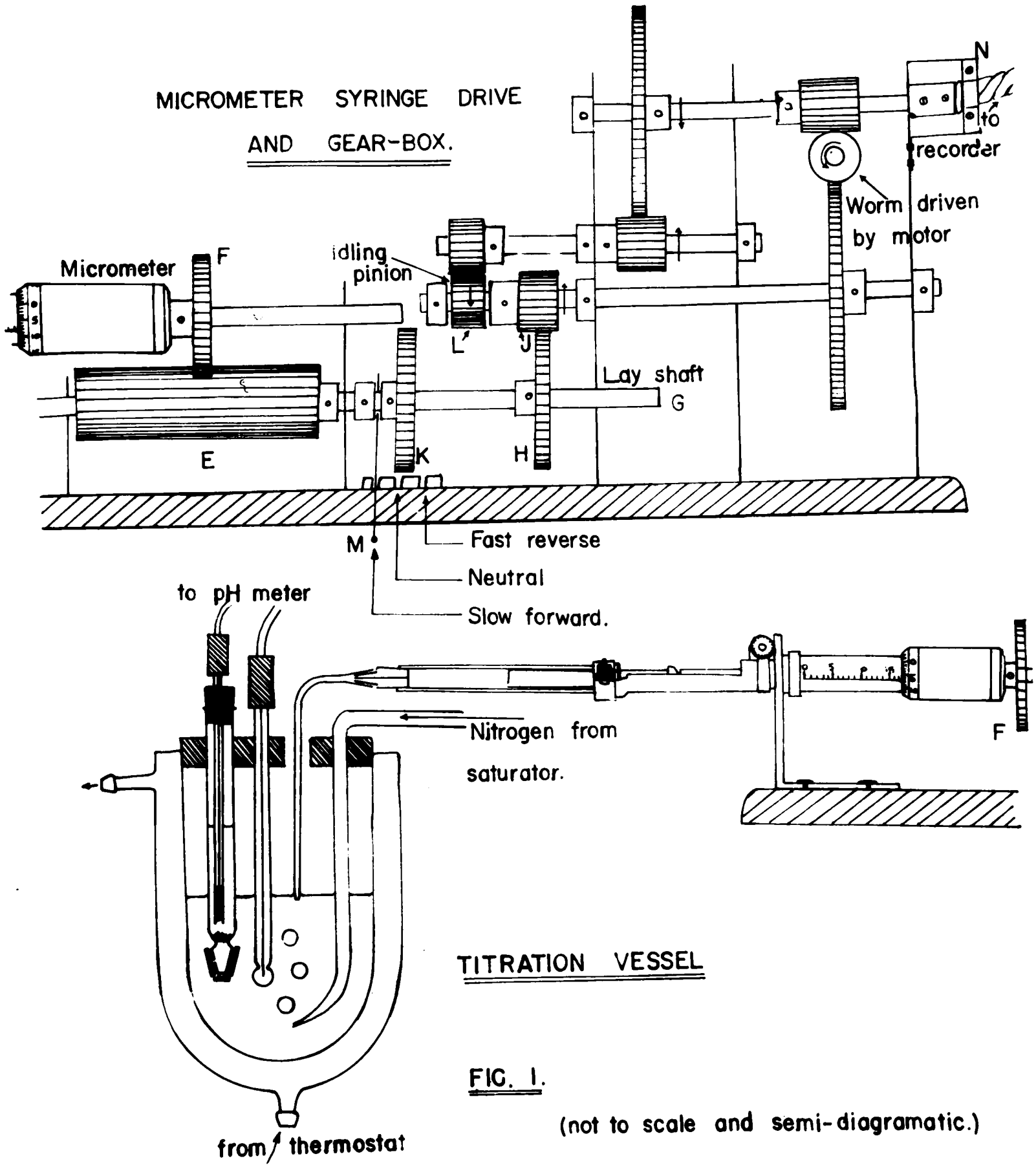


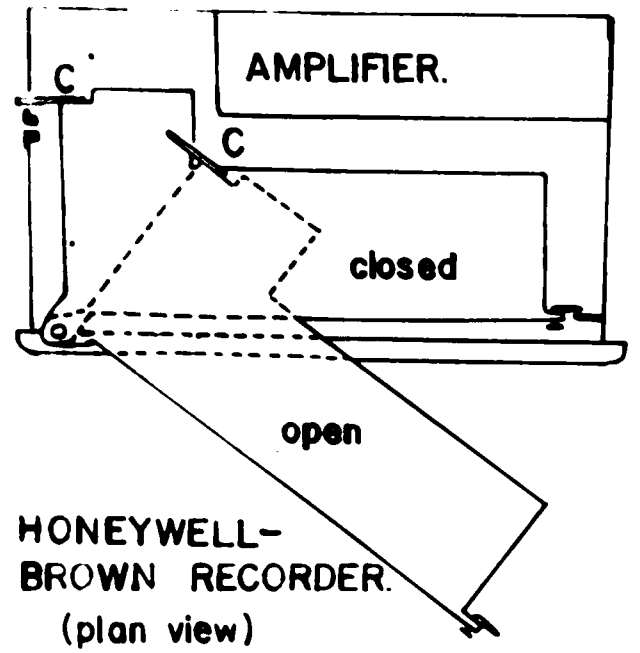
FIG. 1.

(not to scale and semi-diagramatic.)

2. THE TITRATION APPARATUS AND MOTOR-DRIVEN SYRINGE.

The titration vessel consists of a double-walled glass cell through which water from a thermostat is circulated. This is closed by a rubber bung bored with holes for the glass electrode, the reference electrode, for the addition of titrant and for the nitrogen used for stirring. This nitrogen is presaturated with a solution similar to that being investigated. From the syringe titrant is added through a fine capillary jet at right angles to the syringe itself and dipping under the surface of the titration solution. The syringe is driven by a 1/25 H.P. series wound electric motor whose speed is reduced by means of a suitable gearing and is varied by a 'Variac' transformer. This allows fine adjustment in the rate of addition of the titrant.

The drive is transferred from the gears to the micrometer by a pinion, E, of length greater than the maximum traverse of the micrometer (i.e. greater than 25mm.). A suitable gear wheel, F, was attached to the end of the micrometer on a shaft screwed into the thread usually used to secure the ratchet stop. A sensitive micro-switch was situated in such a position that it is actuated by the micrometer gear wheel, F, when the zero mark is reached: this switches off the drive motor and so prevents damage should the apparatus be left unattended. A switch was inserted to by-pass this safety device to enable the micrometer drive to reversed.


C
AMPLIFIER.
C
closed
open
HONEYWELL-
BROWN RECORDER.
(plan view)

0
1·0
2·0 inches
SCALE (approx.)
Ganged 4-pole
2-way switch
S
Chart-drive
Motor
C
A
D
B
N
Flexible drive
Locking-
washer
To chart-drive
mechanism.

FIG 2.

In addition to the slow forward drive a fast reverse and neutral gear were incorporated to facilitate filling the syringe. These gears are engaged by moving the lay shaft, G, to engage either the gear wheel K with the idling pinion L (fast reverse) or the gear wheel H with the pinion J (slow forward). At the half-way position neither H nor K engage so giving a neutral gear. A suitable device was incorporated to lock the shaft G in any of the desired positions, e.g. an arm, M, free to revolve on G, which can engage one of the three slots fixed rigidly to the chassis of the titration apparatus.

3. MODIFICATION OF THE HORWELL-BROWN RECORDER.

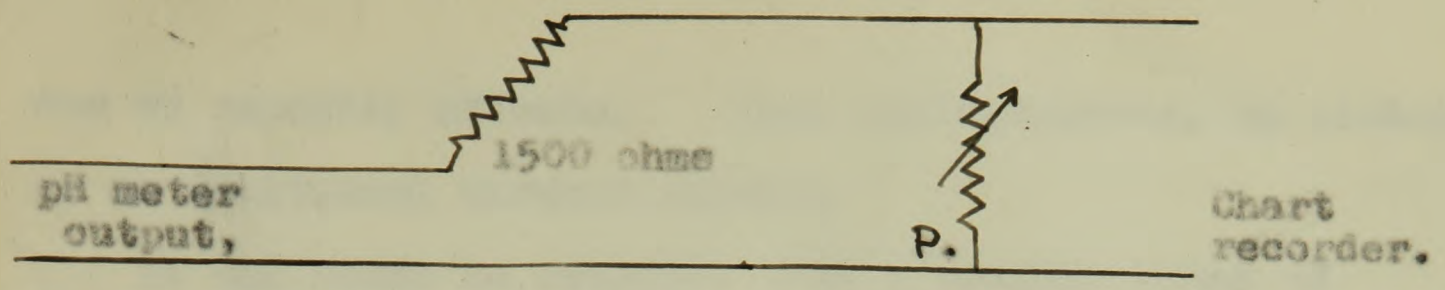
As supplied by the makers the chart of the recorder is driven by a synchronous motor through a gearbox. The four leads to this were cut and a ganged 4-pole, 2-way switch, S in Fig. 2, was inserted. It was then possible to operate the chart by an external motor or to use it, as required, in the manner originally designed.

With the chart motor isolated by S the movement of the chart is controlled by a flexible drive direct from a shaft in the gear-box of the motor driven syringe (Fig. 1). This flexible drive was connected to the pinion A, on the shaft of the chart-drive motor, by means of a shaft, D, with

internal spline ends. One end couples with the teeth of the pinion A while the other has a standard 1/8 inch square key-way to accomodate the standard flexible drive. To prevent the chassis swinging from the recorder case while the drive is connected (see Fig 2, inset) a locking washer, held firmly to the case by the nut B, locks into a groove cut in the rigid brass strip, C. This strip was bolted rigidly to the instrument chassis and protrudes through a hole cut in the recorder case.

The 'Electronic Instruments Ltd.' pH meter, model 23, provides an output of 20mA. per pH unit (i.e. 280mA. full scale deflection) for a recorder of input impedance of less than 1500 ohms. The Honeywell-Brown recorder used was calibrated from 0-14 with a deflection of 20mA. per division and had an impedance of 150 ohms. Hence it could be used directly with this pH meter.

When used in conjunction with the E.I.L. 'Vibron' electrometer, model 33B, and the pH measuring attachment, model 033B, a slight modification was required. Since this unit provides a full scale deflection of 1mA. and requires an impedance of about 1500 ohms when coupled with a recorder, a suitable high stability resistor was connected in series with the recorder and a 100 ohm wire-wound potentiometer, P, was connected in parallel as shown :-



By appropriate adjustment of the range-switches on the 'Vibron' assemblage and the potentiometer P it was possible to arrange for a reading of 10 pH units on the Honeywell-Brown recorder (about 8 inches) to correspond only to one actual pH unit. This enables direct readings to be made from the chart graduations to 0.01 pH units and an estimate made to 0.003. If a particular titration covers a range of several pH units the chart-recorder pen can be re-started at zero when the next higher integral pH value is reached simply by adjusting the 'pH units' switch on the pH measuring attachment and making the corresponding adjustment to the 'Vibron' unit. Hence the pH scale for a titration covering a range of eight pH units will extend for about 64 inches. This makes it possible to exploit the full sensitivity of the 'Vibron'.

When used at this sensitivity it proved essential to shield all leads to the electrodes. In most so-called shielded glass electrodes the shielding stops at the composition collar joining the glass to the screened leads. In our experience this was sufficient to introduce random fluctuations

due to capacity effects. This could, however, be minimised by an additional earthed shield.

It was found in practice that a maximum speed of approximately 0.02 mls. titrant added per minute, corresponding to about 0.75 inches of chart travel, was very convenient. Decreasing the rate of addition of titrant by using the 'Variac' transformer gave a minimum speed of about 0.005 mls. per minute (i.e. about 0.2 inches of chart). That equilibrium had been reached in a particular titration is easily checked by repeating it at a slower speed. In this connection we found that certain glass electrodes did not reach equilibrium fast enough in the more alkaline regions. Of a number examined the T.I.L. GR23 electrodes were found to have an entirely satisfactory and rapid response and, in addition, was accurate over the range 0-13pH units. The shorter range electrode, GR23 (0-10pH), is even faster.

For analytical purposes in which greater interest attaches to the end-point of a reaction or to some intermediate stage at which d(pH)/dv is a maximum, it may be more convenient to plot this derivative on the recorder chart. This can easily be achieved by inserting an electronic differentiating device between the output of the pH meter and the input of the recorder.

An added refinement is to include a cam-operated micro-switch actuated by the micrometer shaft of the syringe by means of which a second 'operations pen' on the recorder can be made to affix a scale of volumes on the right hand side of the chart.

FURTHER APPLICATIONS :-

The Honeywell-Brown recorder used was equipped with two adjustable micro-switches which could be set to open or close external circuits at one or both of two pre-determined pH values. This enabled the titration assembly to be used in a number of useful ways. For example, in the preparation of 'complexones' from amines and sodium chloracetate it is usual to add concentrated alkali to the reaction mixture at such a rate that the pH is maintained between the change points of phenol phthalein and thymol phthalein, i.e. between pH 8.5 and 9.5.[6] This may be done automatically with the apparatus described. Similarly the apparatus may be used to control the addition of alkali (or acid) in order to maintain a constant pH during kinetic studies of hydrolysis and the like.[7]

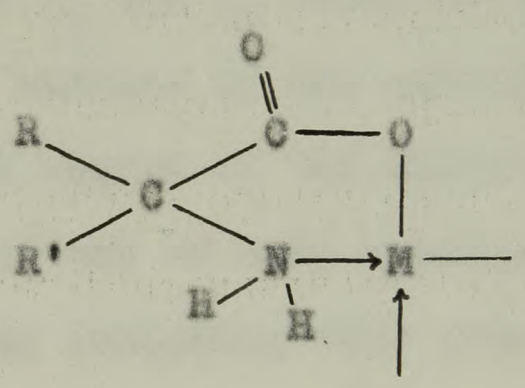
REFERENCES.

(1)	M. Calvin and K. Wilson	J. Amer. Chem. Soc. 1945, 67, 2003.
(2)	H. Irving and H. Rossotti	J., 1954, 2904.
(3)	G. Schwarzenbach and A. Ackermann	Helv. Chim. Acta 1947, 30, 1798.
(4)	H. Irving and H. Rossotti	J., 1954, 2909.
(5)	B. Robinson,	A.E.R.E. report C/M 316, Harwell, 1957.
(6)	G. Schwarzenbach and A. Ackermann	Helv. Chim. Acta, 1948, 31, 1029.
(7)	Nielands and M. Cannon	Analyt. Chem., 1955, 27, 29.

ABSTRACT

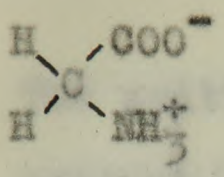
Complex formation between a metal ion (M^{m+}) and a ligand (L^{p-}) produces a series of complexes $ML^{(m-p)+}$, $ML_2^{(m-2p)+}$, etc.. The magnitude of the stability constants of these complexes (defined by $\beta_n = [ML_n^{(m-np)+}]/[M^{m+}][L^{p-}]^n$) will depend upon a variety of factors, e.g. on the nature of the metal acceptor ion, on the nature of the donating atoms, on the structure of the ligand and on various steric and conformational aspects.

The present thesis treats a few of these factors in detail. The first part is concerned with the stability of chelate rings of the type (I) (formed by an α-amino-acid), and discusses the effect of replacing the α-hydrogen atoms of glycine (II) by methyl groups, and of linking these to form aliphatic rings of varying size.

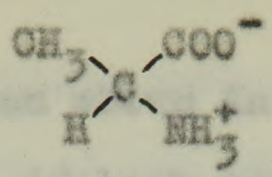


(I)

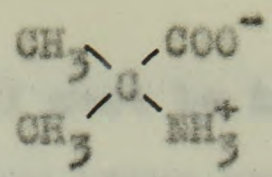
To this end the compounds III - VII were prepared in a state of high purity and their proton dissociation constants were determined at 20.0°C. in a medium of constant ionic strength (μ = 0.10M, KCl) by a precise potentiometric titration procedure. Stability constants of complexes formed by each of these ligands and the



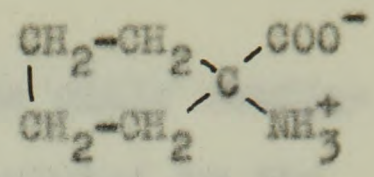
(II)



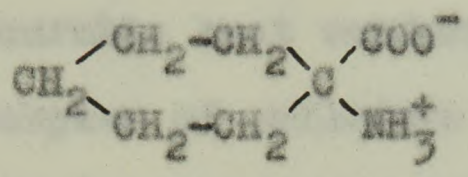
(III)



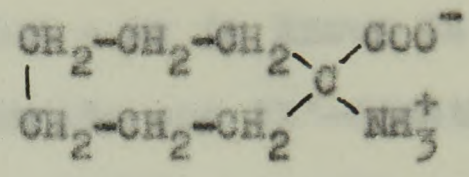
(IV)



(V)



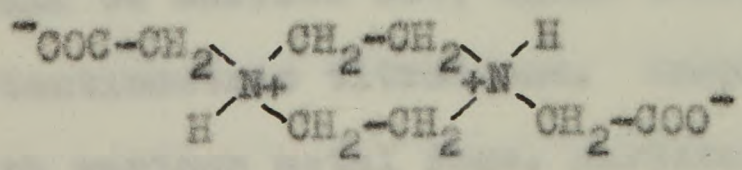
(VI)



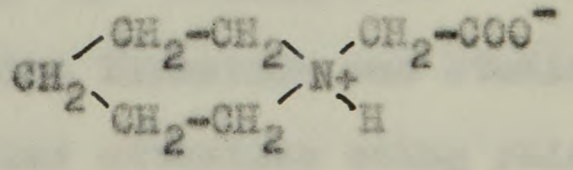
(VII)

divalent ions Co^{++}, Ni^{++}, Cu^{++} and Zn^{++} were determined under the same conditions. In each case the presence of 1:1 and 2:1 complexes was established and there was an indication of a 3:1 complex with nickel. Small changes in the stability constants β_1 and β_2 could be explained in terms of the inductive effects of the substituents, and by changes in the bond angles of the chelate ring produced by substitution of one or both hydrogen atoms on the α-carbon atom, or by including this atom in an aliphatic ring.

Closely connected with this work was the problem of the nature of complexes formed by piperazine-NN'-diacetic acid (VIII).



(VIII)



(IX)

The zwitterion shown in VIII must be in the chair configuration but, if both nitrogen atoms are included in the formation of a chelate ring, the molecule must assume the less favourable boat conformation - as is known to occur in the complex of palladous chloride and NN'-dimethylpiperazine (Hassel and Pedersen, 1959). Complexes of VIII were found to have a comparatively low stability and it appears that the ligand cannot bond effectively to small ions through both nitrogen atoms. This hypothesis was supported by measurements on piperidine-N-acetic acid (IX).

The second part of this work is concerned with the problem of relating the stabilities of metal complexes formed by a series of ligands in which a nitrogen atom is replaced in turn with phosphorus and arsenic. Various factors (e.g. ease of oxidation) prevented the use of purely aliphatic ligands and the only readily accessible ones were not ideally suited to the main purpose. However a comparison of the complexing ability of nitrogen and arsenic in the potentially tridentate ligands X and XI could be carried out, again using the technique of potentiometric titrations. Complex formation was studied with various metal ions, particular attention being paid to copper^{II}, nickel, zinc, silver, and mercury^{II}. The

experimental data were amplified by investigations of the complexes of XII and XIII.

ϕ-N(CH_2-COOH)$_2$ (X)

ϕ-As(CH_2-COOH)$_2$ (XI)

p-Cl-C_6H_4-As(CH_2-CH_2-COOH)$_2$ (XII)

(cyclo-hexyl)-N(CH_2-COOH)$_2$ (XIII)

It was apparent that the behaviour was that expected for metals belonging to the acceptor types classified by Ahrland, Chatt, and Davis (1958) as class (a) and class (b).

Measurements with mercury[11] and the ligands X - XVI were carried out by measuring the E.M.F. and the pH of a cell containing a reversible mercury electrode. In measurements with silver ions and the same ligands a simultaneous measurement of pH and p[Ag] permitted calculation of the stability constants of the metal complex, ML, and of the protonated species MHL ; this latter species was found to have a stability comparable to that of ML when the ligand was XI, XII, XIV, and XV.

The complexes of diphenylphosphine-P-propionic acid (XIV) and its arsenic analogue (XV) have been examined in 20% dioxan solution. The nitrogen analogue (XVI) has

been prepared and its complexes studied to enable a comparison of the donor properties of Group V elements to be made.

ϕ_2P-CH_2-CH_2-COOH (XIV) ϕ_2As-CH_2-CH_2-COOH (XV) ϕ_2N-CH_2-CH_2-COOH. (XVI)

From measurements with the ligands X - XVI it is clear that with class (a) metals bonding is predominantly through the carboxyl groups (and nitrogen) rather than through arsenic or phosphorus. With class (b) metals, however, the strength of bonding increases in the order N < As and N < P, and the contributions to the stabilities of the metal complexes by the formation of chelate rings involving the carboxyl groups are small.