SOME EFFECTS OF
COMPLEX FORMATION
IN ELECTROLYTE
SOLUTIONS

A thesis submitted to the University
of Glasgow for the degree of

DOCTOR OF PHILOSOPHY

by

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September,1962.

This thesis is the original work of the author except in those portions where it is specifically stated to the contrary.

It has not been submitted in whole or part for a degree at any other Univeristy.

PREFACE.

The work described in this thesis was carried out in the Chemistry department of Glasgow University, which is under the direction of Professor J. Monteath Robertson, F.R.S.

The author wishes to express his sincere gratitude for the encouragement and guidance given by Dr. E. Gelles and Dr. G.H.Nancollas, under whose supervision this work was performed. Thanks are also due to Dr. H. S. Dunsmore and Dr. A. McAuley for their help with the Deuce computer, and to the Department of Scientific and Industrial Research for the award of a maintenance grant which made this research possible.

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INTRODUCTION

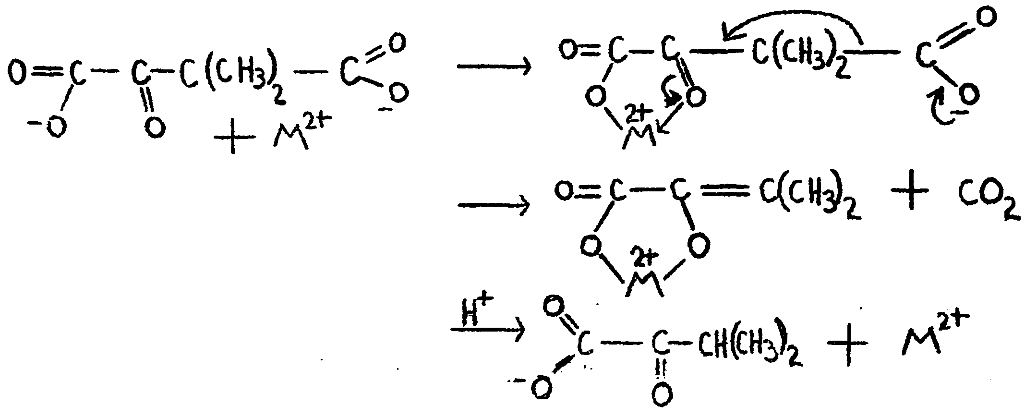
In recent years it has been recognised that metal ions must play an important part in some biological reactions. A large number of enzymes are known to have metal ions associated with them, and the presence of these ions is necessary for the enzymes to exhibit catalytic activity. Among the most common of these metal ion cofactors are manganese, magnesium, calcium, copper, iron, nickel, cobalt and zinc. This interesting observation has aroused much speculation as to the mechanism of metal ion activation of enzymes[1]. In an attempt to find an answer to this problem a study has been made, by several workers, of metal ion catalysis of simple reactions, which are, nevertheless, essentially similar to the enzyme catalysed reactions occurring in nature.

Metal ions may exhibit catalytic activity in two distinct types of reaction in homogeneous systems; (a) reactions in which oxidation and reduction occur, where the metal ion acts as an acceptor or donor of electrons, the mechanism involving a change in the valency of the metal ion; (b) reactions in which catalysis is due to the initially fast formation of a complex between metal ion and substrate followed by some reaction of this complex, which does not involve a change in the valency state of the metal ion.

Specific/

Specific examples of (a) are the catalysis of the decomposition of hydrogen peroxide by metal chelates, studied by Langenbeck[2], and the acceleration of the drying of linseed oil by metal chelates, reported by Myers[3]. Langenbeck showed that the presence of suitable chelating agents such as o-phenanthroline, histidine, argenine and histidine anhydride greatly enhanced the catalytic effect of iron, cobalt and copper in the decomposition of hydrogen peroxide. Myers investigated the catalysis of the drying of linseed oil by a number of metal ions and metal chelates, and proposed a mechanism which explained catalytic ability in terms of electronic structure. Thullier[4] has observed the catalytic effect of iron chelates on the oxidation of vanillin by sodium persulphate in aqueous solution.

Examples of type (b) are numerous. The decarboxylation of some β keto acids has been shown to be catalysed by metal ions and a mechanism, which agrees with the observed kinetics, for the decarboxylation of α,α dimethyl oxaloacetic acid in the presence of a divalent cation M^{2+} has been given by Steinberger and Westheimer[5].



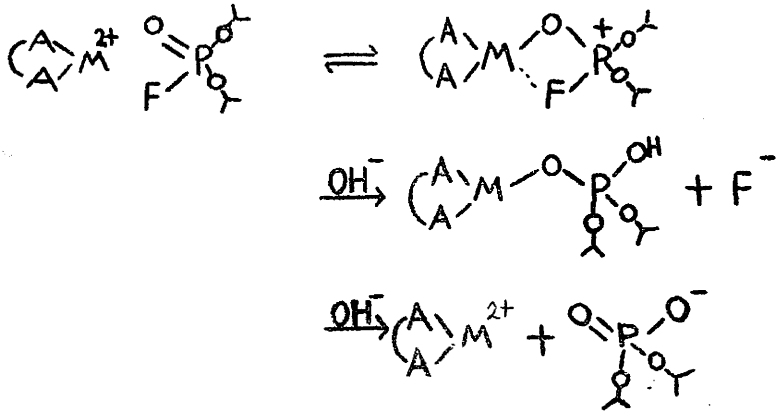
Thus the catalysis of the decarboxylation may be explained in terms of the electron withdrawing power of the metal ion which facilitates the electron shift required tobreak the carbon-carbon bond.

In this type of catalysis the metal ion influences the rate of reaction of a substrate by withdrawing electrons towards the site of attachment, thus increasing the susceptibility to nucleophilic attack of some other part of the substrate molecule. Hence the metal ion behaves as a generalised acid in the Lewis sense, being capable of accepting electrons from donor groups. For a metal ion to exercise any influence on the rate of reaction of a substrate molecule, therefore, it would seem necessary for this molecule to possess at least one atom capable of donating electrons. It is thus not surprising to find that metal ions have been shown to have a catalytic effect in the hydrolysis of some biologically active compounds such as α amino esters, amides and peptides, since these all contain atoms capable of donating electrons.

In 1956 it was shown by Meriwether and Westheimer[6] that the ions of Cu(II), Ni(II) and Co(II) catalysed the hydrolysis of glycine amide and phenylalanyl glycine amide. This catalysis was explained in terms of the initially fast formation of a metal ion - substrate complex which was more subject to attack/

attack by hydroxyl ions or water molecules than the substrate itself.

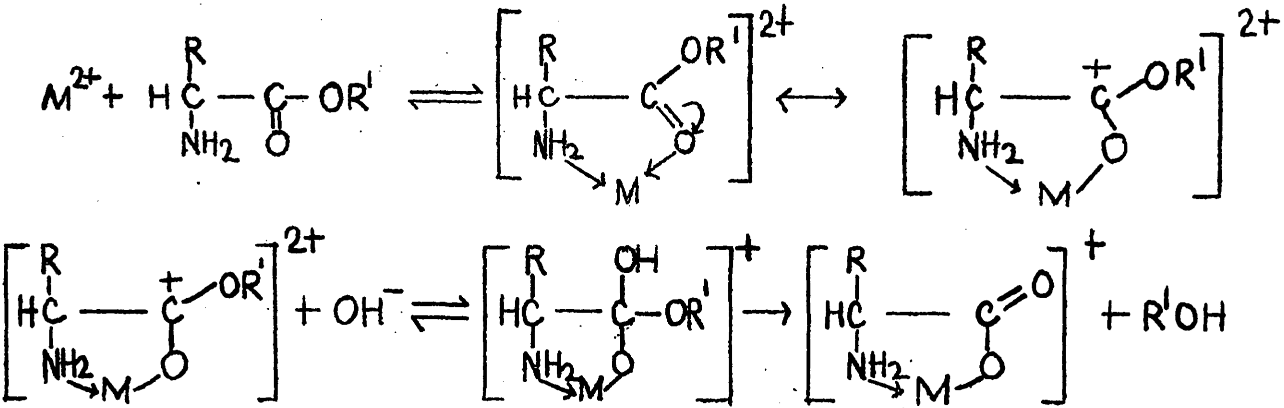
Another metal ion catalysed hydrolysis which has received attention in recent years is the alkaline hydrolysis of diisopropyl fluorophosphonate (D.F.P.). It has been observed that D.F.P. which is rapidly hydrolysed by an enzyme found in blood cells, is also hydrolysed rapidly in the presence of metal chelates. Preliminary work in this field was done by Wagner-Jauregg[7], who found that the 1:1 chelate of copper dipyridyl was the most effective catalyst for the hydrolysis of D.F.P. The catalysis was attributed to the formation of intermediate addition compounds causing an increased polarisation of P=O and P-F bonds, thus facilitating the approach of hydroxyl ions to the P atom, with the expulsion of a fluoride ion,



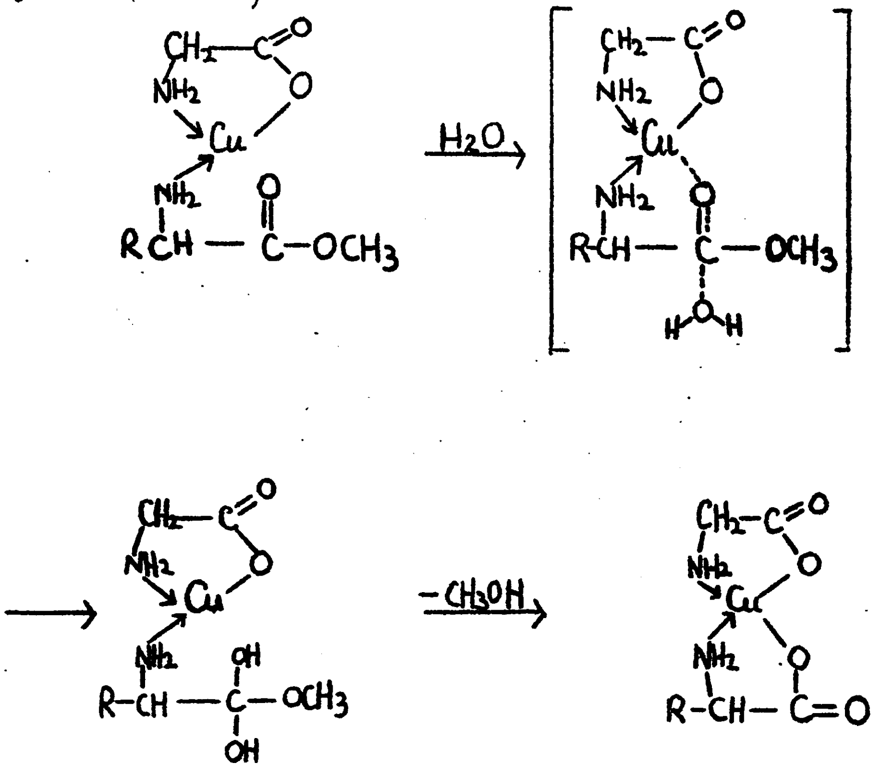
Courtney et al.[8] extended the preliminary work of Wagner-Jauregg /

Jauregg and examined the catalytic activity of a large number of metal chelates in the hydrolysis of D.F.P. and sarin (isopropyl methylphosphonofluoridate). It was found that while the measured rate constants increased with an increase in hydroxyl ion and metal chelate concentrations, in accordance with the mechanism given, they did not increase with the first power of the concentration of these substances and side reactions or equilibria were assumed to be taking place. There was also a correlation between the stability of a chelate and its catalytic activity. In general, the less stable the chelate, the greater was its catalytic activity but a certain minimum stability was of course necessary to avoid precipitation of the metal ion at high pH. In addition it was shown that for chelates to exhibit maximum catalytic activity it was essential that only two of the co-ordination valencies should be filled by the bidentate ligand, the others being filled by water molecules which would allow easy formation of the intermediate complex.

This explanation of catalysis was very similar to that given by Kroll[9] in 1952 to explain the catalysis of the hydrolysis of αamino esters by metal ions. A mechanism was postulated involving a second order reaction between the metal complex of the amino ester and hydroxyl ion as shown below.



In 1957, Bender and Turnquest[10], using a small modification of Kroll's experimental technique made a detailed isotopic and kinetic investigation of the cupric ion catalysed hydrolysis of several α amino esters. The following mechanism was postulated for the hydrolysis of an α amino ester in glycine buffer,

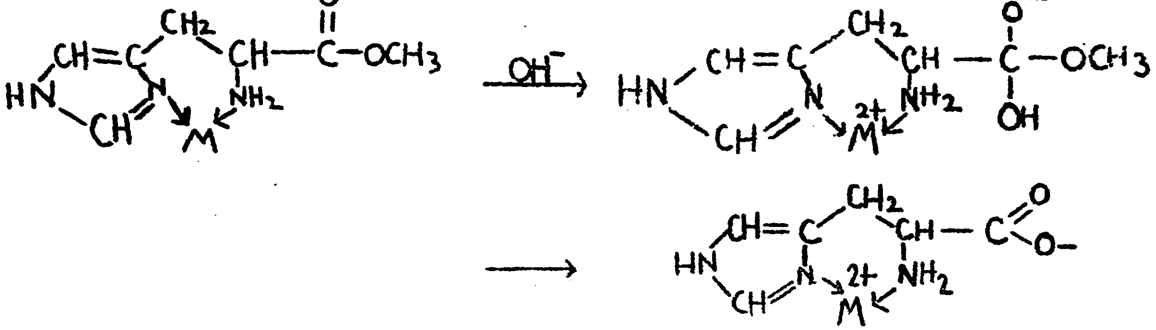


The mechanisms given by both Kroll and Bender and Turnquest for metal ion catalysed hydrolysis of α amino esters differed in one respect only. Kroll envisaged a hydroxyl ion attack on the metal ester complex whereas Bender ruled out this possibility and suggested that a water molecule was in fact the attacking species. These authors agreed however that the metal ion must exert a direct influence on the carbonyl oxygen of the ester group. This hypothesis was not supported by thermodynamic information obtained by White, Manning and Li[11] who, from comparison of the stability constants of metal complexes formed by amino acids and their esters, concluded that in glycine methyl ester complexes the site of binding of the ester to the metal ion was through the amino group only, while for cysteine methyl ester which also contains a sulphur atom capable of donating electrons, the metal ion was attached to both the nitrogen and sulphur atoms. This suggested that in neither of these ester metal complexes was the carbonyl oxygen directly involved. Further evidence for this was provided by the observation that while in copper (II) glycine complexes the maximum number of acid molecules bound is two, more than two glycine ester molecules may co-ordinate to each cupric ion, although the exact number cannot be ascertained because/

because of ester hydrolysis at high pH.

White, Manning and Li also measured the rates of alkaline hydrolysis of cysteine and glycine esters in the absence and presence of various metal ions, in an effort to correlate the stability of the metal ester complexes with the rate at which they hydrolysed. The hydrolysis of the esters, which was followed by a conductivity method, was shown to obey second order kinetics, indicating a bimolecular reaction between hydroxyl ion and ester. The catalytic effect of metal ion was shown to be more pronounced the larger the stability constant of the complex formed and was attributed to the addition of positive charge to the ester with a general withdrawal of electrons away from the carbonyl group, thus facilitating nucleophilic attack by hydroxyl ions.

In 1957, Li, Doody and White[12] extended this work on metal ion catalysed hydrolysis of ∝ amino esters to include histidine methyl ester, whose alkaline hydrolysis was studied in the absence and presence of metalions. Catalysis was again shown to be appreciable and the following mechanism was postulated for part of the reaction:-



From the foregoing resumee of the work done in the field of metal ion catalysed hydrolysis it is clear that a number of questions remain unanswered. It seems to be generally agreed that metal ion catalysis of α amino ester hydrolysis is due to hydrolytic cleavage of metal complexes, but no clear indication has been given as to whether the attacking species is a hydroxyl ion or a water molecule. Kroll[9] and Li[11,12] assume that the reaction is due to the attack of hydroxyl ions on the metal substrate complex while Bender[10] favours water molecule participation. Another question which arises is whether there is any direct interaction of metal ion with the carbonyl oxygen of the ester group. Kroll and Bender suggest that interaction is an essential requisite for metal ion catalysis while Li favours the view that catalysis is due solely to an indirect inductive effect resulting from the proximity of the metal ion to the ester group.

In an attempt to answer these questions it seemed necessary to undertake a detailed study of the metal ion catalysed hydrolysis of an α amino ester, over a range of pH and metal ion concentration, and it was essential that kinetic data should be provided by a suitable experimental technique. It is therefore of interest, at this point, to examine the experimental techniques which have been used in kinetic studies of hydrolytic reactions.

In their work on amino ester hydrolysis both Kroll and Bender performed reactions in buffer solutions of known pH, the course of the reactions being followed by titration of a given volume of reaction mixture to a fixed pH. The interpretation of results obtained by this method is complicated by the fact that the buffers used, trishydroxymethyl amino methane and glycine, both interact appreciably with metal ions being studied. The technique used by Li on the other hand was more direct in that the solutions under study contained only metal ions (when present), substrate, and hydroxyl ions in the ratio 1:3:3, the reaction being followed by the change in resistance of the solution with time. One limitation of this technique is that reactions being studied must not be too rapid compared with the time taken to make conductivity readings. It is also, by the very nature of the technique, impossible to maintain the reaction solution at a constant pH.

The method used by Courtney et al[8], allowed hydrolytic reactions to be studied at constant pH. By use of an automatic titration apparatus, the tendency for the pH to drop as hydrolysis proceeds is counterbalanced by the addition of alkali from a burette. Thus a measure of the acid produced, and hence the extent of hydrolysis at any particular time, is given by the volume of alkali added. One limitation of this/

this method is that the volume of the reaction mixture does not remain constant. For comparative purposes however the technique is quite suitable. An essential for the use of this method is that the substrate-metal ion complex must be sufficiently strong to prevent precipitation of the metal ion in solution of high pH.

The choice of experimental method to be used in this investigation was governed by the advantages and disadvantages of the three methods outlined above. One obvious way of attempting to answer the question of whether hydroxyl ion or water molecule is responsible for hydrolytic attack is to measure the rate of hydrolysis over a range of pH. It was essential therefore that some method of maintaining constant pH should be incorporated and hence the conductivity method could not be used. The other two methods both followed hydrolytic reactions at constant pH, one by buffering and the other by automatic pH control. The latter of these was chosen since it did not have the complication of additional complex formation with buffer ions. An α amino ester suitable for study was histidine methyl ester, since it was known to complex sufficiently well with nickel and copper to prevent precipitation at high pH, and was one whose metal ion catalysed/

catalysed hydrolysis had been studied by another technique.

The work described in this section of the thesis represents an attempt to provide a more detailed understanding of the mechanism of metal ion catalysed hydrolysis of α amino esters. To this end kinetic information has been supplemented by information arising from potentiometric work.

APPARATUS

AND

EXPERIMENTAL TECHNIQUE

Preparation of Reagents:

Standard solutions were made up from A.R. reagents and Grade A volumetric apparatus was used throughout.

Histidine methyl ester-dihydrochloride.

Histidine methyl ester dihydrochloride was prepared by the esterification of histidine in methanol in the presence of dry HCl. The method used was essentially that due to Fisher and Cone[13]. B.D.H. histidine monohydrochloride (10g) was refluxed in dry methyl alcohol (200ml) while dry hydrogen chloride was bubbled through the suspension. The dry hydrogen chloride was generated by mixing concentrated sulphuric and hydrochloric acids, the gas evolved being passed through a column of glass beads containing concentrated sulphuric acid. After refluxing for 2-3 hours a clear solution of histidine methyl ester dihydrochloride remained. On standing and cooling the crude product separated and it was recrystallised twice from dry A.R. methyl alcohol to remove any excess of HCl. (M.pt. 197°C found C, 34.65%; H, 5.35%; N; 17.62%. Calculated for $C_7H_{13}O_2N_3Cl_2$, C, 34.73%; H, 5.41%; N, 17.36%. Found for a dibasic acid by titration with alkali MW. 242.2; Calculated for $C_7H_{13}O_2N_3Cl_2$ M.W. 242.1)

Apparatus.

During this work use was made of an automatic titrimeter (E.I.L.Model 24) to obtain both potentiometric and kinetic information. This consists of a volumetric titration unit in conjunction with a control unit which is in effect an electronic pH meter. Solutions under study were placed in a double walled vessel. Water from a thermostat was circulated to maintain the required temperature, and nitrogen, presaturated with water vapour, was bubbled through solutions to exclude carbon dioxide. The reaction vessel was fitted with a small but efficient stirrer and pH measurements were made by means of a glass electrode incorporated in the cell,

Ag/AgCl/HCl /glass/Solution under study/KCl conc./Calomel electrode.

The electrode system was standardised with three buffers; B.D.H. tabloid phthalate buffer, pH 4.01 at 25°C; B.D.H. tabloid phosphate buffer, pH 6.99 at 25°C; borax buffer pH 9.18 at 25°C. The reaction vessel was sealed with a tightly fitting rubber bung through which the stirrer, nitrogen inlet, burette tip and electrodes passed. The apparatus is shown diagramatically in Figs. 1 and 2.

Figure 1.

a Double Walled Reaction Vessel.
b Rubber Bung.
c Calomel Electrode
d Glass Electrode
e Glass Stirrer
f Nitrogen Inlet
g Burette Tip.

Figure 2.

a Control Unit.
b pH Reading Dials.
c Electrode Terminals and Burette Tap Switch.
d Tap Unit and Stirrer Motor.
e Reaction Vessel.
f Alkali Reservoir

Potentiometric Studies.

Histidine methyl ester dihydrochloride (4×10^{-4} mole) was weighed accurately into the double walled vessel and volumes of distilled water, metal chloride solution (0.1 M when present), and sodium chloride (1M) were added such that the addition of sodium hydroxide (4×10^{-4} mole $\equiv$ 4 ml. 0.1 MNaOH) would bring the total volume of solution to 80 ml. (0.005 M with respect to ester), and give an ionic strength of 0.1 M. When the solution had reached equilibrium, approximately decinormal NaOH was added from the burette and readings of pH of solution with volume of alkali added were taken, time being allowed for equilibrium to be reached after each addition. In this way titration curves were obtained for the ester dihydrochloride in the absence and presence of copper (II) and nickel (II) ions at an ionic strength of 0.1 M. For the titration of the ester dihydrochloride at low ionic strength, the addition of sodium chloride solution was omitted from the above procedure.

Kinetic Studies.

Histidine methyl ester dihydrochloride (4×10^{-4} mole) was weighed out accurately into the double walled reaction vessel and volumes of distilled water, metal chloride solution/

solution (0.1 M when present) and sodium chloride (1M) were added such that the addition of NaOH (8×10^{-4} mole $\equiv$ 8 ml 0.1 MNaOH) would bring the total volume of solution to 80 ml the ionic strength being 0.1M. Approximately 6×10^{-4} moles NaOH were added and the resulting solution, which had a pH considerably less than that at which hydrolysis was appreciable was allowed to reach the required temperature.

A final addition of alkali was made to bring the pH to a sufficiently high value for hydrolysis to occur and a stop clock was started. The total volume of alkali added at zero time was taken to be the initial volume (Vo) and the pH attained by the solution after the addition of Vo was maintained by adding small volumes of alkali from the burette, to counteract the tendency for the pH to be lowered as the ester hydrolysed. If the volume of alkali added at time t was Vt then the amount off ester hydrolysed was proportional to Vt - Vo, and the percentage reaction was given by $\frac{Vt - Vo}{V\infty - Vo} \times 100$, where $V\infty - Vo$ corresponded to the alkali uptake for complete hydrolysis of the ester. Reaction time curves were therefore easily constructed from burette readings at suitable time intervals.

Since this technique involved counteracting, by additions of/

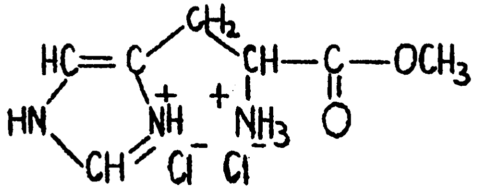
of alkali, the tendency for pH to drop due to hydrolysis, the pH of the solutions under study varied somewhat above and below the required value. When the reaction was monitored automatically by the titrimeter it was found that pH control was no better than ±0.1 units, due to the small time lag between addition of alkali and equilibration of the resulting solution. When the pH of reaction solutions was controlled by manual addition of alkali, volumes of 0.01 ml could be added and the pH could be maintained within ±0.03units. Hence manual addition was used throughout this work.

POTENTIOMETRIC STUDIES

Potentiometric Studies.

In order to evaluate the degree of interaction of a metal ion with the ligand in aqueous solution it is first necessary to understand the behaviour of the ligand towards protons, since complex formation has been looked on as a competition between metal ion and protons for the ligand molecule.

The structure of histidine methyl ester dihydrochloride is shown below



HISTIDINE METHYL ESTER DIHYDROCHLORIDE

In aqueous solution this gives rise to a divalent cation, EH_2^{2+}, which is capable of losing two protons, yielding the uncharged ester molecule, E

$$EH_2^{2+} \rightleftharpoons EH^+ \rightleftharpoons E$$

The ester dihydrochloride clearly behaves as a dibasic acid and the measurement of the two dissociation constants of this acid is the first essential in the investigation of metal ion interaction with the ester.

Conflicting values of the pK's for these equilibria have appeared in the literature and it was therefore thought desirable/

desirable to redetermine them. The method used was that of Speakman[14], applied to EH_2^{2+} as a dibasic acid. The thermodynamic dissociation constants of the divalent ester cation may be defined as follows;

$$EH_2^{2+} \rightleftharpoons EH^+ + H^+ \qquad K_1 = \frac{\{H^+\}\,[EH^+]\,f_1}{[EH_2^{2+}]\,f_2}$$

$$EH^+ \rightleftharpoons E + H^+ \qquad K_2 = \frac{\{H^+\}\,[E]\,f_0}{[EH^+]\,f_1}$$

where fo, f_1 and f_2 are the activity coefficients of the species E, EH^+ and EH_2^{2+} respectively, and the brackets [ ] and { } refer to concentrations and activities respectively.

In a solution of total ester concentration <u>a</u> (molar),

$$\underline{a} = [EH_2^{2+}] + [EH^+] + [E] \quad \ldots\ldots\ldots\ldots\ldots(1)$$

and when a strong monoacid base, which may be taken as completely dissociated, has been added to give a molar concentration <u>b</u> electrical neutrality requires that

$$\underline{b} + 2[EH_2^{2+}] + [EH^+] + [H^+] = 2\underline{a} + [OH^-] \quad \ldots\ldots(2)$$

Substituting (1) in (2),

$$\underline{b} + [H^+] = [EH^+] + 2[E] + [OH^-]$$

If now L, M and N are defined by the equations

$$L = \underline{b} + [H^+] - [OH^-] \quad (= [EH^+] + 2[E]) \ldots\ldots\ldots\ldots\ldots(3)$$

$$M = \underline{a} - \underline{b} - [H^+] + [OH^-] \quad (= [EH_2^{2+}] - [E]) \ldots\ldots\ldots\ldots\ldots(4)$$

$$N = 2\underline{a} - \underline{b} - [H^+] + [OH^-] \quad (= 2[EH_2^{2+}] + [EH^+]) \ldots\ldots\ldots\ldots(5)$$

then it can be shown that

$$\{H^+\}^2 \cdot \frac{\mathrm{fo}}{f_2} \cdot \frac{L}{N} = K_1 \cdot \{H^+\} \cdot \frac{\mathrm{fo}}{f_1} \cdot \frac{M}{N} + K_1K_2$$

which may be rewritten in the form

$$X = K_1Y + K_1K_2,$$

where $X = \{H^+\}^2 \cdot \frac{\mathrm{fo}}{f_2} \cdot \frac{L}{N}$ and $Y = \{H^+\} \cdot \frac{\mathrm{fo}}{f_1} \cdot \frac{M}{N}$

Hence a plot of X vs Y should be a straight line of gradient K_1, with intercept on the X axis, K_1K_2. The values of *b* and $\{H^+\}$ may be obtained from the pH titration of the ester dihydrochloride with standard alkali.

pH Titrations.

Two series of pH titrations were made on the ester dihydrochloride at 25°C; (a) in solution whose ionic strength was adjusted to 0.1 by addition of 1MNaCl; (b) in solution of low ionic strength, without added salt. Part off the titration curves is shown in fig. 3.

The values of b and $\{H^+\}$ obtained from curve A (fig. 3) were substituted in equations (3), (4) and (5) and X and Y calculated. The results are summarised in table I and a plot of X vs Y is shown in fig. 4. The dissociation constants obtained from this linear plot were,

$K_1 = 9.87 \times 10^{-6}$, $K_2 = 5.73 \times 10^{-8}$

i.e. $pK_1 = 5.01$, $pK_2 = 7.24$.

The activity coefficients were calculated by means of the Davies[15] equation

$$\log f_z = -Az^2 \left(\frac{I^{\frac{1}{2}}}{1 + I^{\frac{1}{2}}} - 0.2I \right) \ldots\ldots\ldots\ldots (6)$$

where f_z is the activity coefficient of an ion of valency z in a solution of ionic strength I.

X and Y values shown in table II were obtained from the b and $\{H^+\}$ data of curve B (fig. 3). The calculation of X and Y for any point on curve B involved the determination of the corresponding ionic strength. This in turn required a knowledge/

knowledge of the concentrations of each of the ionic species. Thus the dissociation constants derived from the data of table I were used to estimate the concentrations of the ionic species present at each point in the titration curve. The appropriate activity coefficients were then substituted in the expressions for X and Y and new values of K_1 and K_2 estimated from the resulting plot. These in turn were used to give more accurate values of ionic strength. After two such approximations a set of self consistent values resulted. The final XY plot is shown in fig. 5 and gave

$K_1 = 9.8 \times 15^6$ $\qquad$ $K_2 = 6.12 \times 15^8$

i.e. $pK_{,} = 5.01$ $\qquad$ $pK_2 = 7.21$,

which is in very good agreement with the values obtained by applying activity corrections to the results at constant ionic strength of 0.1 M. $pK_{,}' = 5.38$ and $pK_2 = 7.33$ have been given by Li[12]; and $pK_1 = 5.20$ and $pK_2 = 7.10$, by Bruice[16]. In both cases however it is not clear whether they refer to thermodynamic or concentration values.

Figure 3.

Titration of histidine methyl ester dihydrochloride ($4x\ 10^{-4}$ Moles) with NaOH (0.1N). T=25°C

A. at constant ionic strength (I = 0.1M)

B. at low ionic strength.

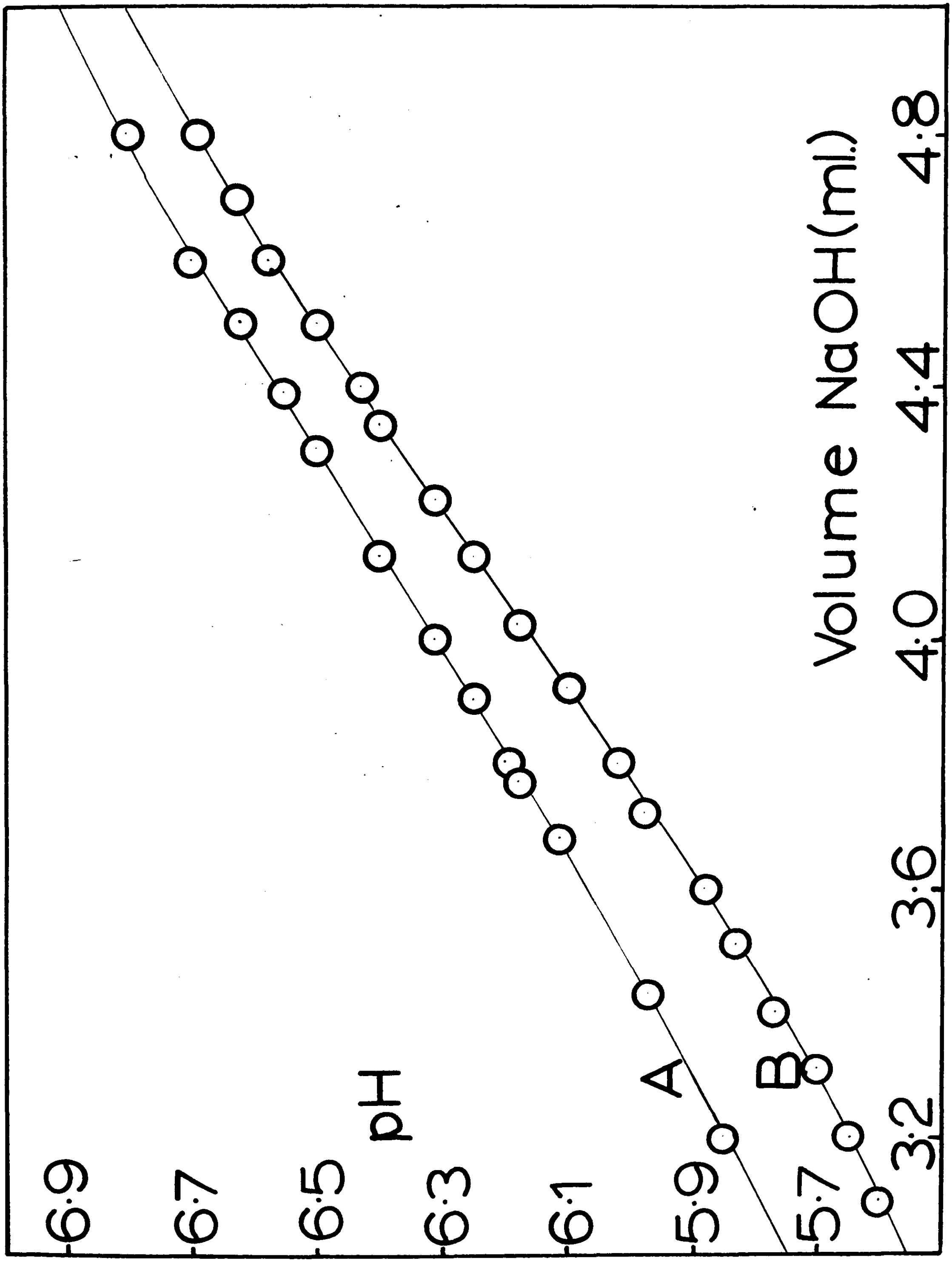


Fig.3

Table I.

Titration of histidine methyl ester dihydrochloride with NaOH, I = 0.1M

pH	$b \times 10^3$ moles/litre	$X.10^{12}$	$Y.10^7$
5.85	4.008	3.627	3.109
5.90	4.128	3.028	2.493
6.00	4.355	2.104	1.528
6.10	4.558	1.446	0.864
6.20	4.736	0.983	0.424
6.60	5.510	0.198	-0.361

Table II.

Titration of histidine methyl ester dihydrochloride with NaOH, at low ionic strength.

pH	$b \times 10^3$ moles/litre	f_1	f_2	$X.10^{12}$	$Y.10^7$
5.650	4.008	0.918	0.703	4.690	4.170
5.705	4.128	0.918	0.704	3.826	3.301
5.820	4.355	0.920	0.706	2.477	1.950
5.925	4.558	0.921	0.708	1.659	1.091
6.025	4.736	0.922	0.710	1.124	0.536
6.485	5.510	0.924	0.721	0.189	-0.436

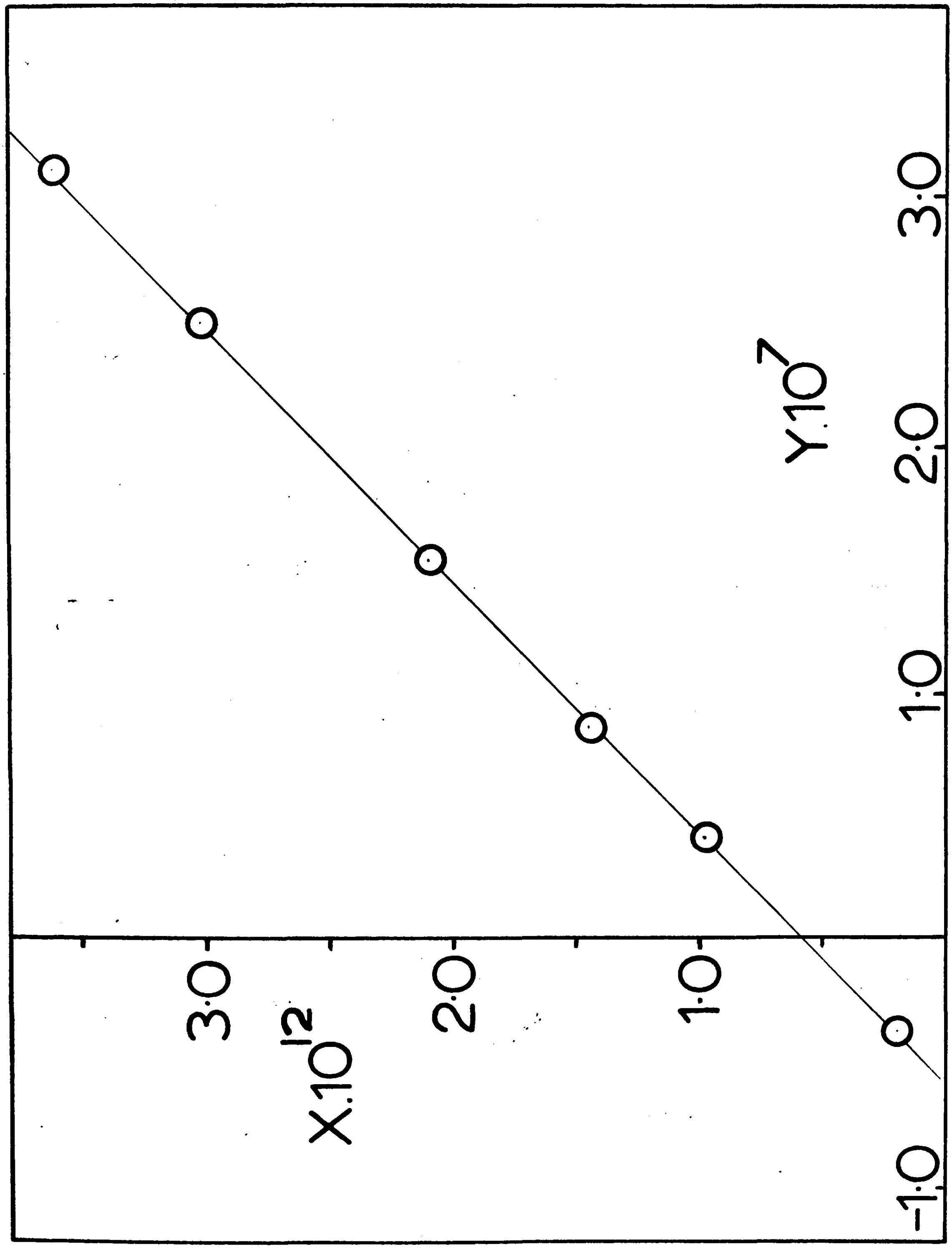


Fig. 4

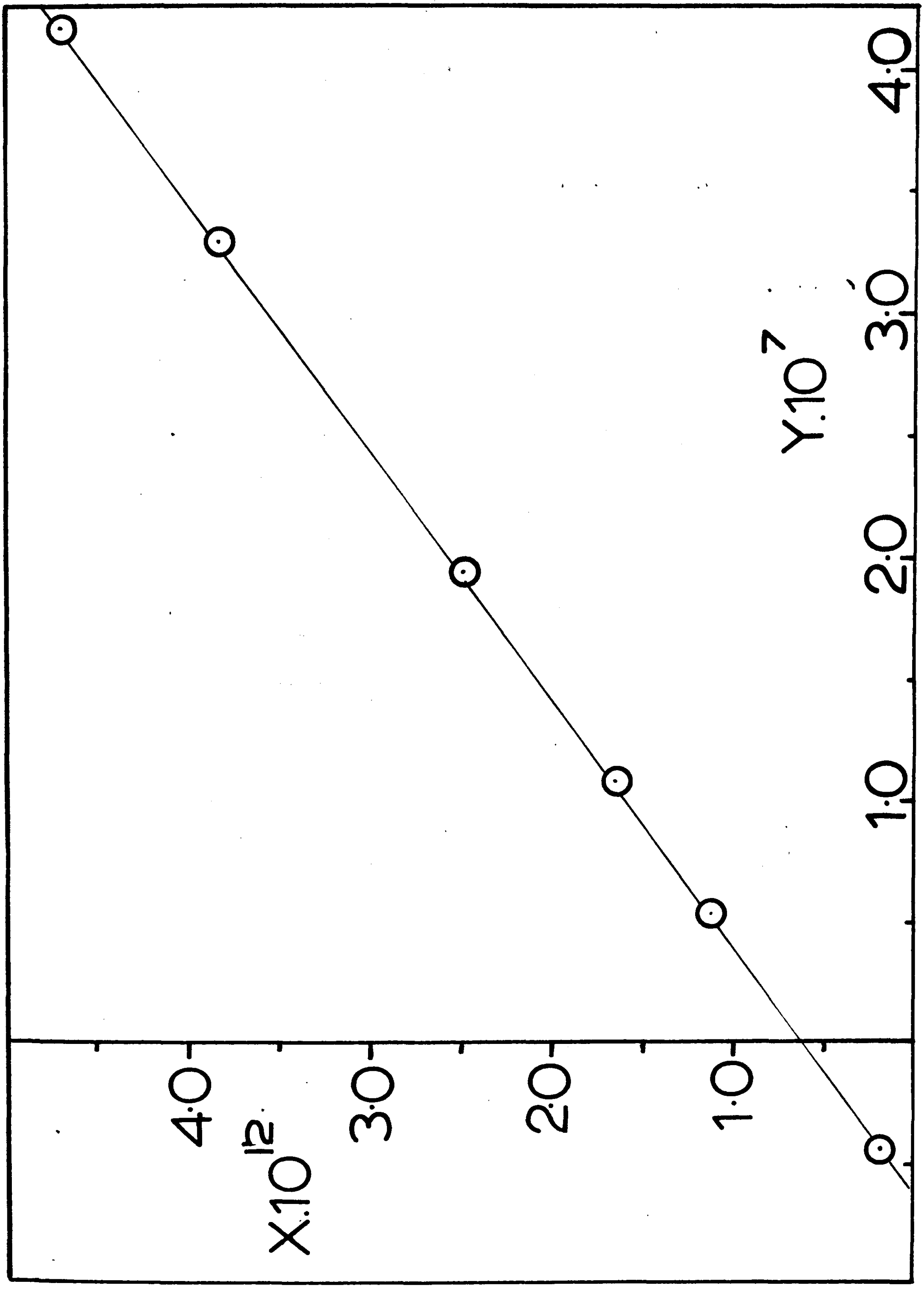


Fig.5

pH Titrations in the presence of metal ions.

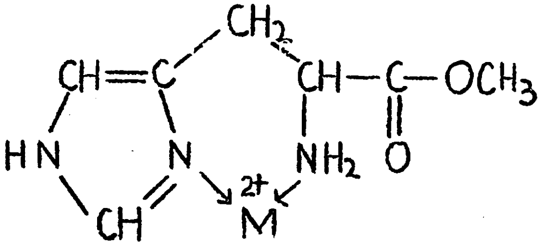
Titrations were next carried out on the ester dihydrochloride in the presence of Cu(II) and Ni(II) ions. When these ions are added to solutions of the dihydrochloride there is a fall in pH and the whole titration curve is lowered until two equivalents of alkali have been added. The titration curves for the ester dihydrochloride alone, in the presence of half an equivalent of Ni(II) ion, and in the presence of half an equivalent of Cu(II) ion are shown in fig.6. This lowering of the titration curve in the presence of metal ions is to be expected since the formation of coordinate bonds between the ligand and metal ion will be accompanied by the liberation of protons from EH_2^{2+}

$$EH_2^{2+} + M^{2+} \rightleftharpoons ME^{2+} + 2H^+$$

Histidine methyl ester possesses four atoms capable of donating electrons to a metal ion; the α amino nitrogen, the "pyrrole" and "pyridine" nitrogens of the imidazole ring and the carbonyl oxygen of the ester group. The formation of chelates involving two of these groups with a metal ion would seem likely, and there is considerable evidence in the literature to suggest which of these four are bound. By comparing the difference in stability of histidine and histidine methyl ester complexes of Cu(II) and Ni(II), with the corresponding/

corresponding difference between glycine and glycine ester complexes Li, Doody and White[12] were able to conclude that the binding sites in histidine ester complexes and histidine complexes were the same. Edsall et al.,[17] have shown, from spectral evidence, that the amino and imidazole groups are the chelating sites in the Cu(II) - histidine complex. Earlier work by Li, White and Doody[18] had shown that the binding site in the imidazole- Cu(II) complex was the "pyridine" rather than the "pyrrole" nitrogen. More recently, Leberman and Rabin[19] have shown that the Cu(II) complexes of histamine and 3 methyl histamine are very similar, indicating that the "pyridine" nitrogen must be involved.

The 1:1 chelate of a divalent metal ion with histidine methyl ester may therefore be represented as follows:-



Although only the 1:1 chelate is shown here it should be pointed out that other chelates are possible, in principle, where the ratio of ester to metal ion is higher. The number of ester molecules which may chelate is governed by the number of valencies in the coordination shell of the metal ion.

Figure 6.

Titration of histidine methyl ester dihydrochloride (4×10^{-4} moles) I = 0.1M. T = 25°C.

A. Ester alone.

B. Ester in the presence of $NiCl_2$ (2×10^{-4} moles)

C. Ester in the presence of $CuCl_2$ (2×10^{-4} moles)

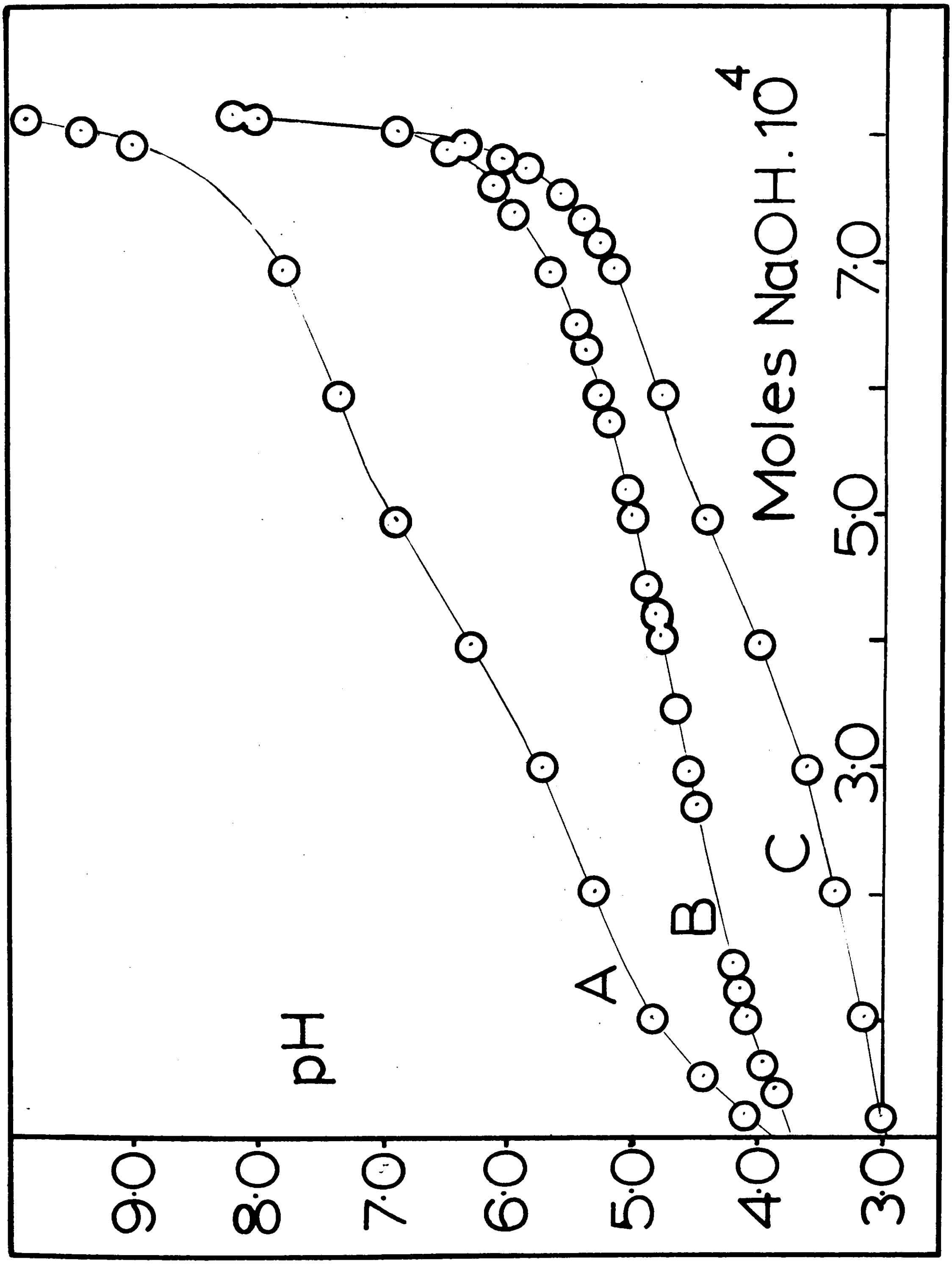


Fig.6

Determination of Stability Constants.

The information required for the evaluation of the stability constants of the 1:1 and 2:1 chelates of histidine methyl ester with copper(11) and nickel(11) may be obtained from pH titration curves for the ester dihydrochloride in the presence of metal ion.

The following equilibria were assumed to be those present in solutions of ester dihydrochloride and metal ions(M^{2+}) to which NaOH was added.

$$EH_2^{2+} \underset{}{\overset{K_1}{\rightleftharpoons}} EH^+ + H^+$$

$$EH^+ \overset{K_2}{\rightleftharpoons} E + H^+$$

$$M^{2+} + E \overset{K_3}{\rightleftharpoons} ME^{2+} \qquad K_3 = \frac{[ME^{2+}]}{[M^{2+}][E]}$$

$$M^{2+} + 2E \overset{K_4}{\rightleftharpoons} ME_2^{2+} \qquad K_4 = \frac{[ME_2^{2+}]}{[M^{2+}][E]^2}$$

Total metal concentration $= C = [M^{2+}] + [ME^{2+}] + [ME_2^{2+}]$. . . . (7)

Total ester concentration $= A = [E]+[EH^+]+[EH_2^{2+}]+[ME^{2+}]+2[ME_2^{2+}]$. .(8)

For electroneutrality,

$$[Na^+] + [H^+] + 2[M^{2+}] + 2[ME^{2+}] + 2[ME_2^{2+}] + [EH^+] + 2[EH_2^{2+}] = [Cl^-] + [OH^-]$$

Now, $[Cl^-] = 2A + 2C$

Therefore,

$$[Na^+] + [H^+] + 2[M^{2+}] + 2[ME^{2+}] + 2[ME_2^{2+}] + [EH^+] + 2[EH_2^{2+}] = 2A + 2C + [OH^-]. \quad (9)$$

From equations (7) & (9),

$$[Na^+] + [H^+] + [EH^+] + 2[EH_2^{2+}] = 2A + [OH^-]$$

i.e. $$[E] = \frac{2A + [OH^-] - [Na^+] - [H^+]}{\frac{\{H^+\}}{K_2 f_1} + \frac{2\{H^+\}^2}{K_1 K_2 f_2}}$$

If $\frac{A}{C} = P$, the ratio of total ester to total metal in solution then A= CP, and combining (7) and(8)

$$P[M^{2+}] + P[ME^{2+}] + P[ME_2^{2+}] = [E] + [EH^+] + [EH_2^{2+}] + [ME^{2+}] + 2[ME_2^{2+}]$$

$$\therefore P[M^{2+}] + (P-1)[ME^{2+}] + (P-2)[ME_2^{2+}] = [E] + [EH^+] + [EH_2^{2+}]$$

$$\therefore [M^{2+}]\left\{P + (P-1)K_3[E] + (P-2)K_4[E]^2\right\} = [E] + [EH^+] + [EH_2^{2+}]$$

Also from equation (7)

$$[M^{2+}]\left\{1 + K_3[E] + K_4[E]^2\right\} = C$$

$$\therefore \frac{[E] + [EH^+] + [EH_2^{2+}]}{P + (P-1)K_3[E] + (P-2)K_4[E]^2} = \frac{C}{1 + K_3[E] + K_4[E]^2}$$

Now let $Q = [E] + [EH^+] + [EH_2^{2+}]$ = concentration of uncomplexed ester.

Then,

$$Q + QK_3[E] + QK_4[E]^2 = PC + (P-1)CK_3[E] + (P-2)CK_4[E]^2$$

i.e. $$K_3\left\{Q[E] - (P-1)[E]C\right\} + K_4\left\{Q[E]^2 - (P-2)C[E]^2\right\} + (Q - PC) = 0$$

Dividing by $K_3(Q-PC)$, we have

$$\frac{Q[E] - (P-1)[E]C}{(Q-PC)} + \frac{K_4}{K_3}\frac{Q[E]^2 - (P-2)C[E]^2}{(Q-PC)} + \frac{1}{K_3} = 0$$

i.e. $$[E]\left\{\frac{Q-(P-1)C}{Q-PC}\right\} = \frac{K_4}{K_3}[E]^2\left\{\frac{Q-(P-2)C}{PC-Q}\right\} - \frac{1}{K_3}$$

This expression is of the form

$$Y = MX + C$$

where

$$Y = [E]\left\{\frac{Q - (P - 1)C}{Q - PC}\right\}$$

and

$$X = [E]^2\left\{\frac{Q - (P - 2)C}{PC - Q}\right\}$$

Hence a plot of Y vs. X should be a straight line of gradient $\frac{K_4}{K_3}$, the intercept on the Y axis being $-\frac{1}{K_3}$.

The titration curves used for the evaluation of K_3 and K_4 were obtained for solutions of ester dihydrochloride in the presence of half an equivalent of metal ion. Thus P = 2 and the expressions for X and Y are somewhat simplified.

Where P = 2

$$Y = [E] \left\{ \frac{Q - C}{Q - 2C} \right\} \quad \text{and} \quad X = [E]^2 \left\{ \frac{Q}{2C - Q} \right\}$$

These curves are shown in fig. 6 and the results are given in tables III and IV. The resulting plots of Y vs X are shown in fig. 7 and 8 respectively. The good linearity of these plots suggested that the scheme of equilibria chosen was in fact a satisfactory one and K_3 and K_4 values are shown in table V. The stability constants given by Li[12] for the corresponding complexes are in all cases slightly higher, and this is accounted for by the differences in K_1 and K_2 already mentioned. The values obtained indicate that the chelates formed by both copper (II) and nickel (II) with histidine methyl ester are fairly stable and the kinetic study of the effect of these metal ions on the hydrolysis of the ester, by the experimental technique outlined, was therefore made. The relative stability of these complexes was as to be expected from the Irving Williams order [20], copper having the greatest affinity of the transition metal ions for ligand molecules.

Table III.

Titration of histidine methyl ester dihydrochloride (4 x 10^{-4} moles) in presence of $CuCl_2$ (2 x 10^{-4} mole.) I= 0.1M

$[Na^+] \times 10^3$ moles/litre	pH	$C \times 10^3$ moles/litre	$[E] \times 10^8$ moles/litre	$Q \times 10^3$ moles/litre	$X . 10^{15}$	$Y . 10^9$
3.807	3.62	2.532	1.125	3.029	0.189	-2.76
4.358	3.77	2.516	2.044	2.779	0.515	-2.38
4.596	3.85	2.510	2.823	2.672	0.907	-1.95
4.997	4.00	2.499	5.184	2.489	2.666	0.207
5.255	4.10	2.492	7.735	2.370	5.424	3.610
5.476	4.20	2.486	11.58	2.271	11.27	9.32
5.743	4.30	2.479	17.03	2.143	22.2	20.3
6.031	4.40	2.471	24.70	2.005	41.6	39.2

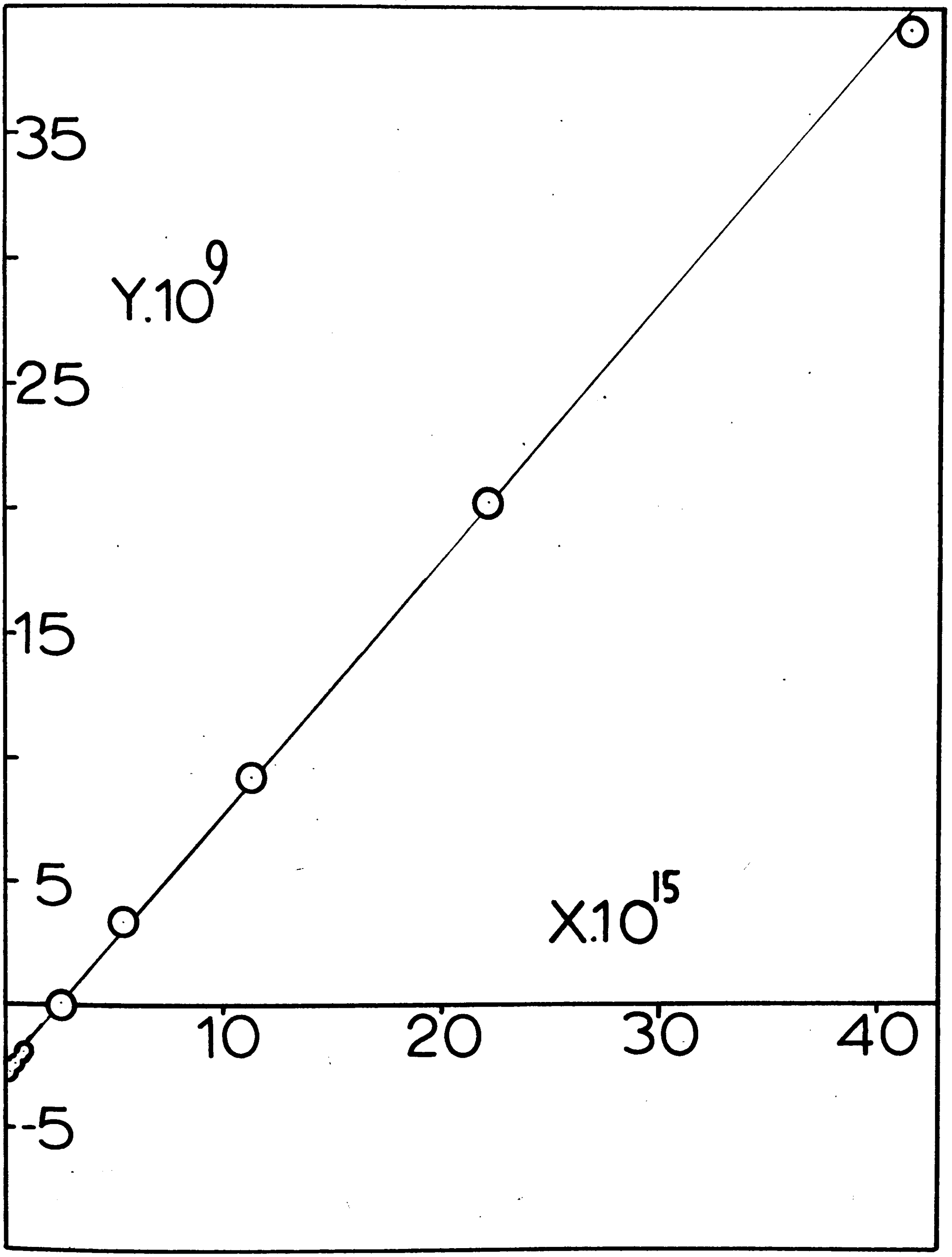


Fig. 7

Table IV.

Titration of histidine methyl ester (4×10^{-4} moles) in presence of Ni^{2+} (2×10^{-4} moles), I. = 0.1M

$[Na^+] \times 10^3$ moles/litre	pH	$C_{\times} 10^3$ moles/litre	$[E] \times 10^6$ moles/litre	$Q \times 10^3$	$X.10^{11}$	$Y.10^7$
3.741	4.570	2.532	0.879	3.425	0.162	-4.794
4.218	4.650	2.519	1.149	3.186	0.227	-4.137
4.455	4.690	2.513	1.308	3.067	0.268	-3.698
4.925	4.781	2.500	1.763	2.836	0.407	-2.737
5.391	4.871	2.488	2.333	2.604	0.597	-1.141
5.851	4.962	2.475	3.051	2.371	0.856	1.23
6.308	5.057	2.463	3.965	2.137	1.205	4.635
6.647	5.145	2.454	5.083	1.968	1.730	8.37

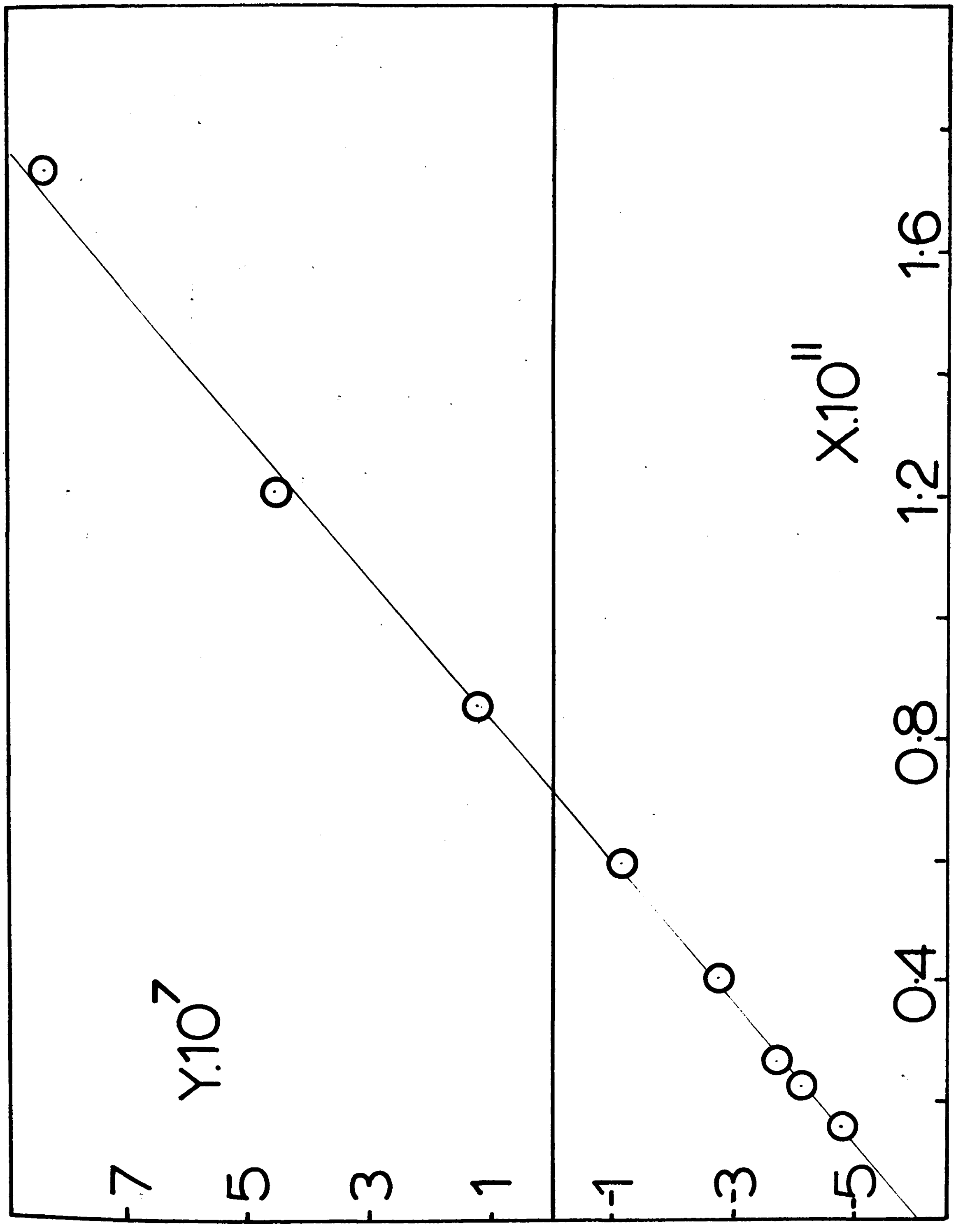


Fig.8

Table V.

Stability constants of Cu(II) and Ni(II) chelates with histidine methyl ester.

Metal Ion	log K_3	log K_4
Cu^{2+}	8.55	14.57
Ni^{2+}	6.21	11.15

TITRATIONS IN THE PRESENCE OF ONE EQUIVALENT OF METAL ION.

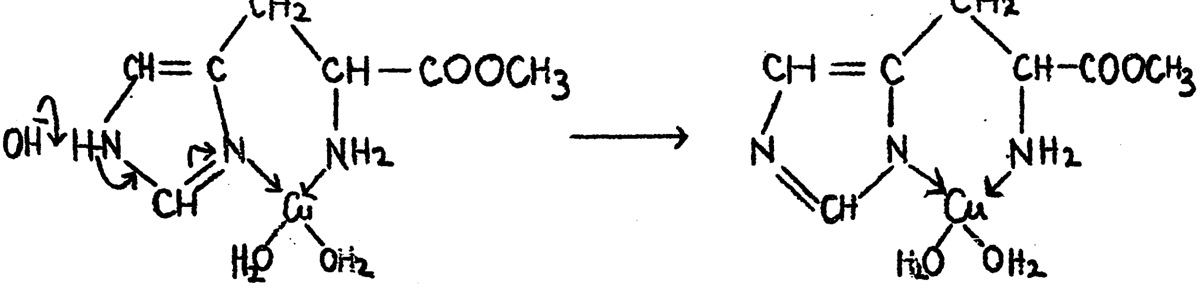
When histidine methyl ester is titrated with alkali in the presence of one equivalent of Cu(II), the pH curve obtained shows a very interesting feature (fig. 9). An equivalence point at about pH 5.5 occurs after the expected alkali uptake of two moles per mole of ester dihydrochloride. This end point however is followed by a further buffer region corresponding to the release of an additional proton per complex molecule, indicating that the following equilibrium must be taking place

$$CuE^{2+} \rightleftharpoons CuE^{+} + H^{+}$$

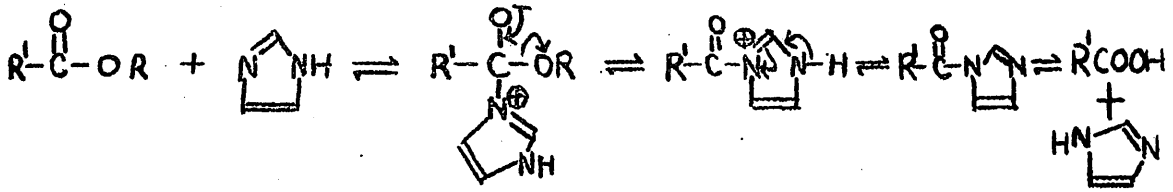
No similar ionisation was found in titrations of the ester in the presence of one equivalent of Ni(II). Several examples of this behaviour of 1:1 copper chelates have been reported in the literature[21-24].

A consideration of the structure of the 1:1 chelate of histidine methyl ester with copper (II) indicates that a proton could be liberated in one of two ways.

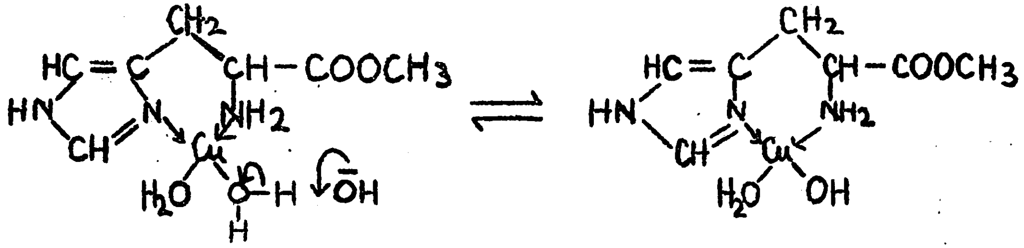
(i) The ionisation of the proton on the pyrrole nitrogen:-



A proton release mechanism of this type has been suggested by Bender[25] as a possible step in the imidazole catalysed hydrolysis of p-nitrophenyl acetate.



(ii) The ionisation of a proton from one of the water molecules bound to the copper ion, giving a monohydroxo complex.



The second of these mechanisms for proton release is more likely since in titrations of ester in the presence of half an equivalent of copper, additional ionisation is not observed although the proton release mechanism (i) would still be expected to operate. Further evidence for this was provided by Leberman and Rabin[19], who showed that the 3-methyl histamine Cu(II) complex released one equivalent of proton, although it does not have a proton on the "pyrrole" nitrogen.

Hence the formation of the hydroxo form of the 1:1 chelate/

chelate affords the best explanation for the release of proton. An accurate value of the dissociation constant for this ionisation was not obtained but the pK_c appeared to be about 7.00 from the titration curve (fig. 9).

Figure 9.

Titration of histidine methyl ester dihydrochloride (4×10^{-4} moles) in the presence of $CuCl_2$ (4×10^{-4} moles)
$I = 0.1M$, $T = 25°C$

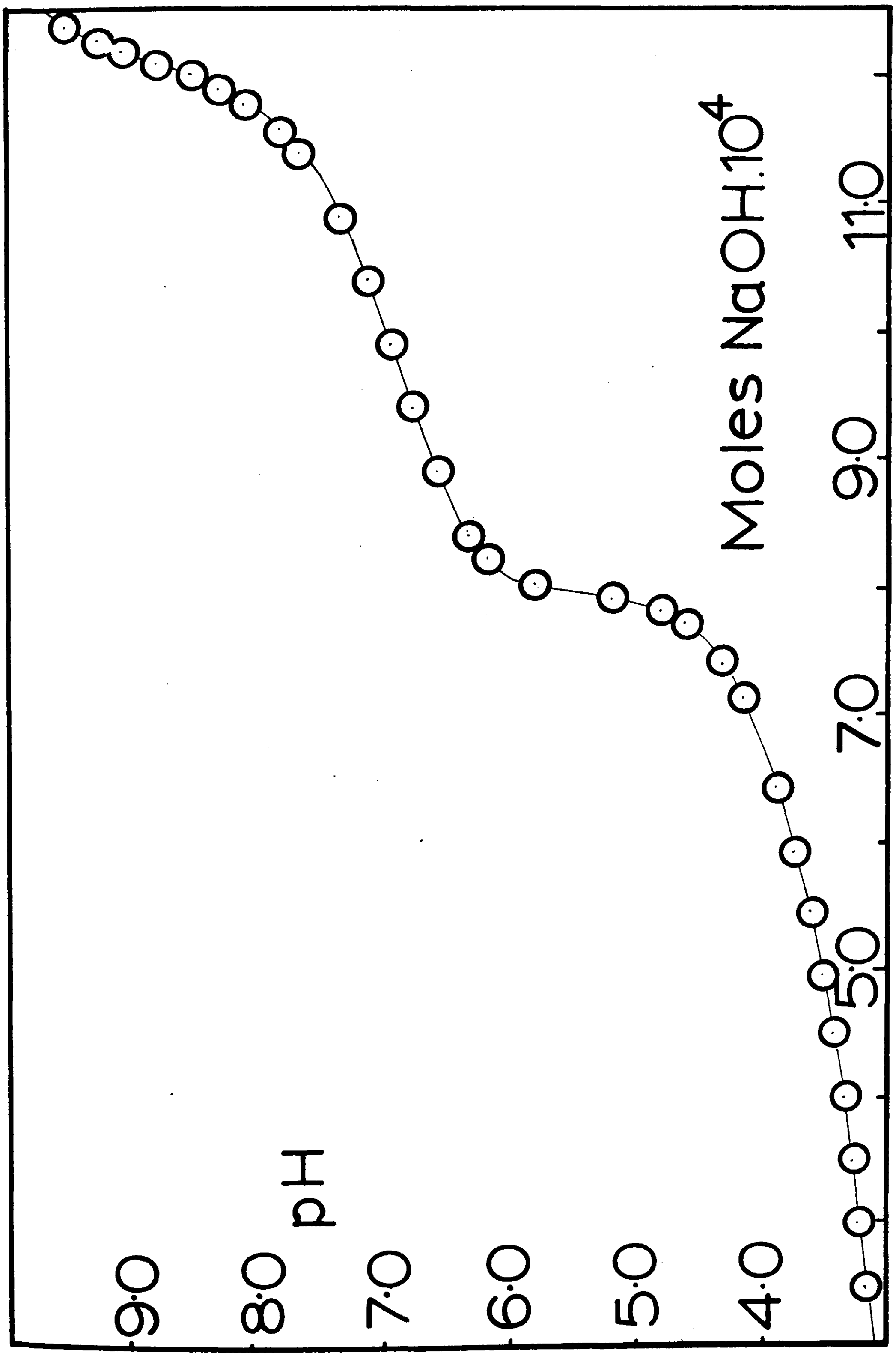


Fig.9

[illegible]

KINETIC STUDIES.

[illegible] value was [illegible] Table VI]. [illegible] uncatalysed [illegible] reaction between [illegible] equation

[illegible] $[OH^-]$ [illegible]

where k_2 [illegible] second order rate constant [illegible]

[illegible]

UNCATALYSED HYDROLYSIS.

If the effect of a metal ion catalyst on the rate of hydrolysis of histidine methyl ester is to be understood it is desirable to know something of the way in which the uncatalysed reaction proceeds over a range of pH. It was found that the ester hydrolysed at a convenient rate in solutions of pH > 9.4 and a series of kinetic runs, using the apparatus and technique previously described, was carried out, in which the hydrolysis of the ester was followed from pH 9.40 to 10.30. From the reaction time curves obtained, first order log plots were drawn (fig. 10) and found to be linear. If the first order rate constants were divided by the appropriate hydroxyl ion concentrations an approximately constant value was obtained (see table VI). This indicates that the uncatalysed hydrolysis proceeds by a simple bimolecular reaction between hydroxyl ion and ester molecule. The rate expression may therefore be written

$$\frac{-d\,[\text{Ester}]}{dt} = k_o\,[OH^-]\,[\text{Ester}]$$

where k_o is the second order rate constant for the reaction. At constant pH, i.e. constant hydroxyl ion concentration, this becomes

$$\frac{-d\,[\text{Ester}]}{dt} = \text{kobs}\,[\text{Ester}]$$

where/

where $\text{kobs} = k_o \left[OH^-\right]$

$$\therefore \frac{\text{kobs}}{[OH^-]} = k_o$$

From table VI, the average value of k_o is 47.1±0.8 litre-mole^{-1}- min.$^{-1}$, which agrees reasonably well with the value 37 litre -mole^{-1}- min.$^{-1}$, obtained by Li[12] from conductivity measurements.

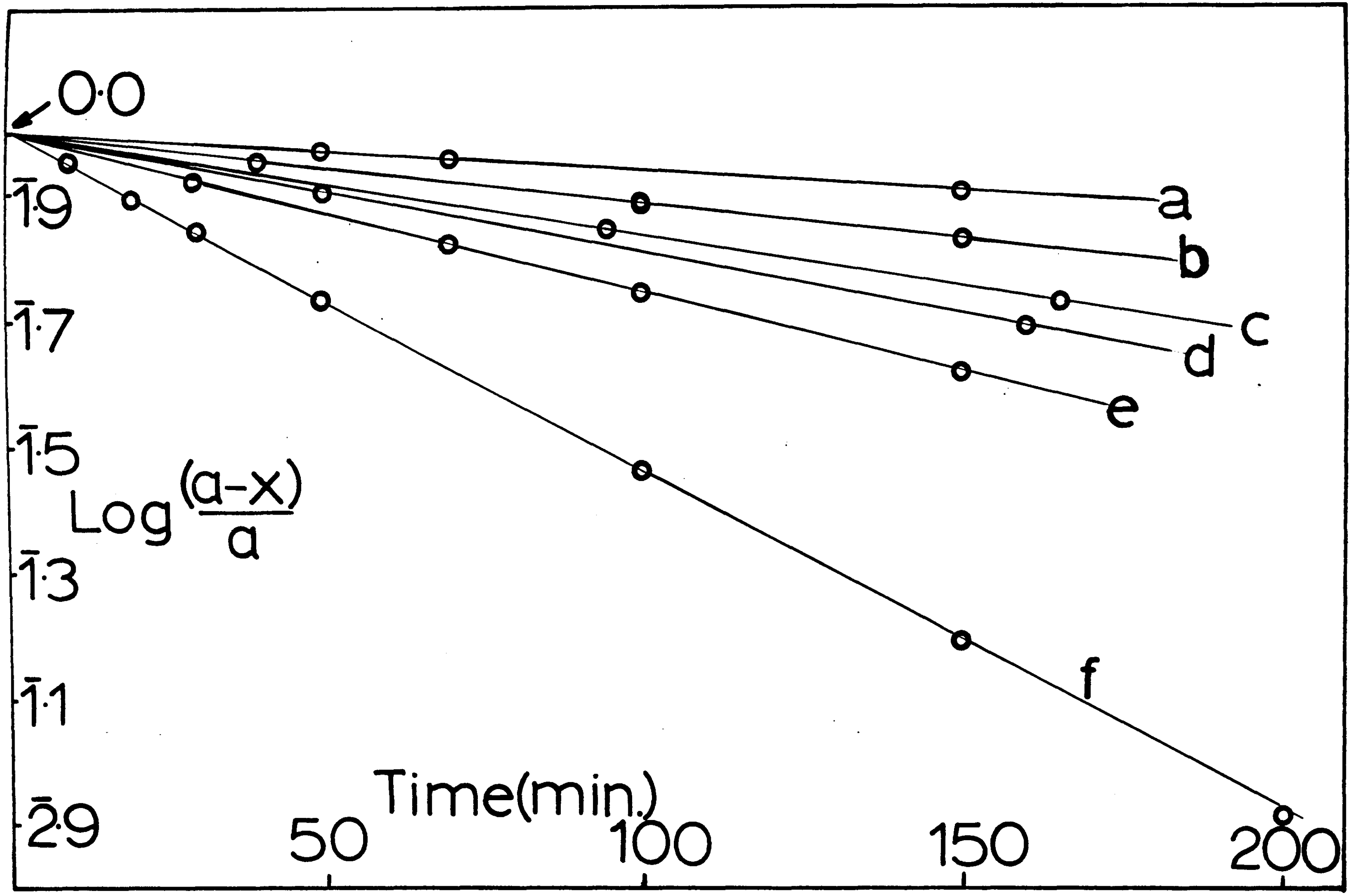
Figure 10.

Hydrolysis of Histidine Methyl Ester at constant pH.

$T = 25^{0}C$, $I. = 0.1$ M.

Plots of $\log \frac{(a - x)}{a}$ vs t.

a - pH 9.40
b - pH 9.65
c - pH 9.80
d - pH 9.90
e - pH 10.00
f - pH 10.30



0·0
$\bar{1}$·9
$\bar{1}$·7
$\bar{1}$·5
$\bar{1}$·3
$\bar{1}$·1
$\bar{2}$·9
$\mathrm{Log}\frac{(a-x)}{a}$
Time(min.)
50
100
150
200
a
b
c
d
e
f

Fig.10

COPPER ION CATALYSIS.

The hydrolysis of histidine methyl ester in the presence of copper ion, over a range of pH, was followed in solutions containing total ester to total copper ratios of 2:1 and 1:1.

Hydrolysis of the 2:1 chelate.

Considering the high stability constant for the chelate CuE_2^{2+} ($\log K_4 = 14.6$) it is reasonable to assume that, in solutions of pH > 7 containing an ester: copper ratio of 2:1, the concentrations of free Cu^{2+}, CuE^{2+}, CuE^{+} and free ester are very small compared with the concentration of CuE_2^{2+}. For the purposes of the kinetic studies on solutions of this type it was assumed that the only species initially present, capable of hydrolysing was the 2:1 chelate, CuE_2^{2+}.

The hydrolysis of the ester in the presence of half an equivalent of Cu(II) was found to proceed at a conveniently measurable rate in solutions of pH >7. The reaction time curves obtained for the hydrolysis at constant pH over a pH range of 7.80 to 9.40 are shown in fig. 11. It is at once obvious that an increase in hydroxyl ion concentration produces an increase in the rate of reaction, which suggests that the hydroxyl ion is the attacking species as suggested by Kroll[9] and Li[12].

The/

Figure 11.

Hydrolysis of Histidine Methyl Ester at constant pH

Ester: Copper = 2:1, T = 25°C, I = 0.1 M.

a pH 7.80
b pH 8.00
c pH 8.10
d pH 8.40
e pH 8.70
f pH 9.00
g pH 9.40

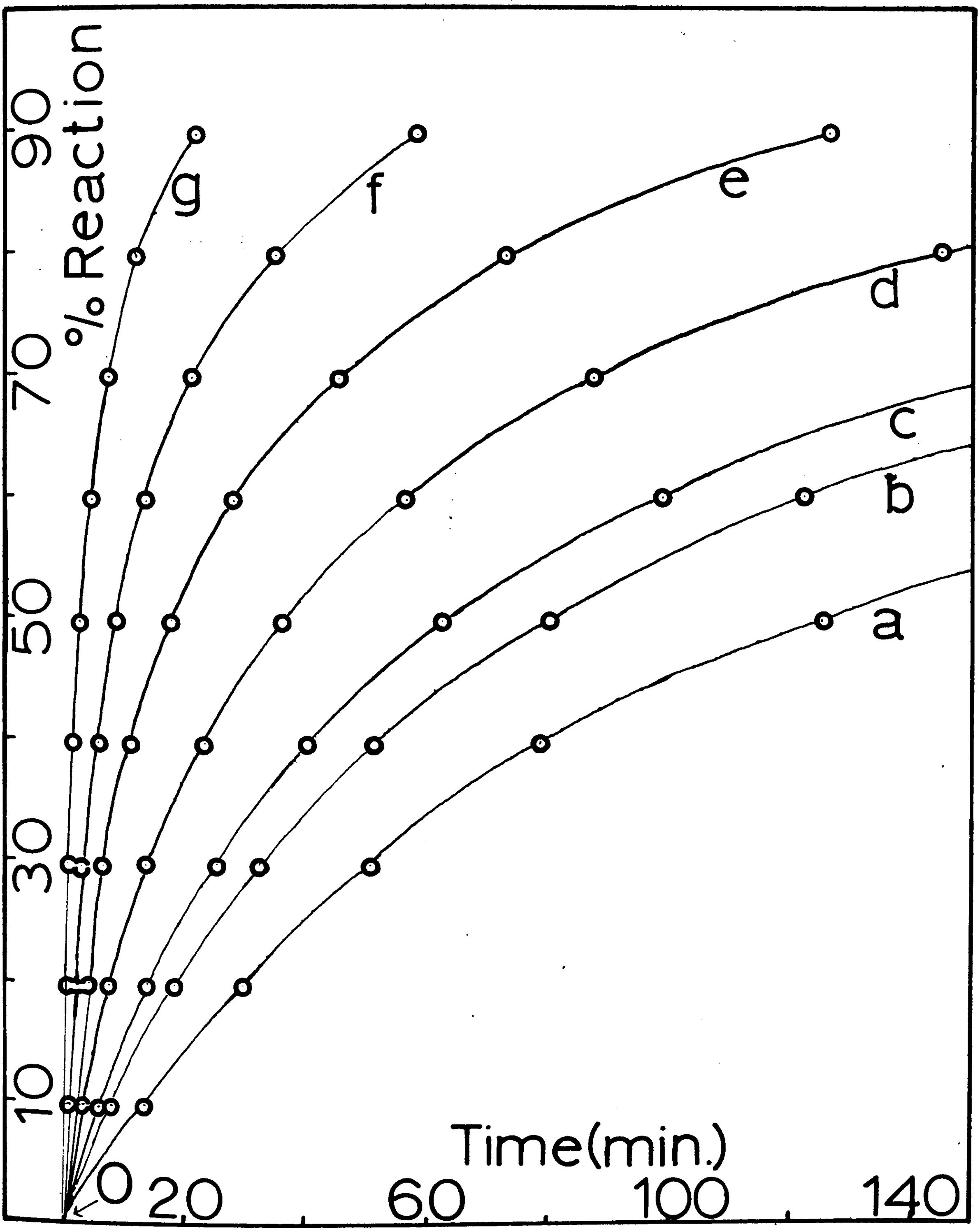


Fig.11

The interpretation of the reaction time curves presented an interesting problem. Assuming a first order expression

$$\log a - \log (a-x) = \frac{kt}{2.303}$$

in which a = initial total concentration of ester (= 4 ml NaOH 0.1N), and x = concentration of acid formed by hydrolysis (= Volume of NaOH, at time t, to maintain constant pH), plots of log $(\frac{a-x}{a})$ vs time were constructed from each of the reaction time curves. These log plots, an example of which is given in fig.12, were all of the same nature, showing initially a marked curvature, which developed into a fairly linear plot after about one half life. This suggested that the hydrolysis of the ester in the presence of half an equivalent of copper was proceeding by two successive reactions, an initially fast reaction of the 2:1 chelate being followed by a slower reaction of the primary product

$$CuE_2^{2+} \xrightarrow{OH^-} CuEA^+$$

$$CuEA^+ \xrightarrow{OH^-} CuA_2$$

where A^- represents the anion of histidine, the hydrolysis product.

This explanation seems all the more probable when one considers the hydroxyl ion to be the attacking species since on electrostatic grounds, the negatively charged reagent would be expected to react at a greater speed with a species having a double positive charge than with one having a single positive charge.

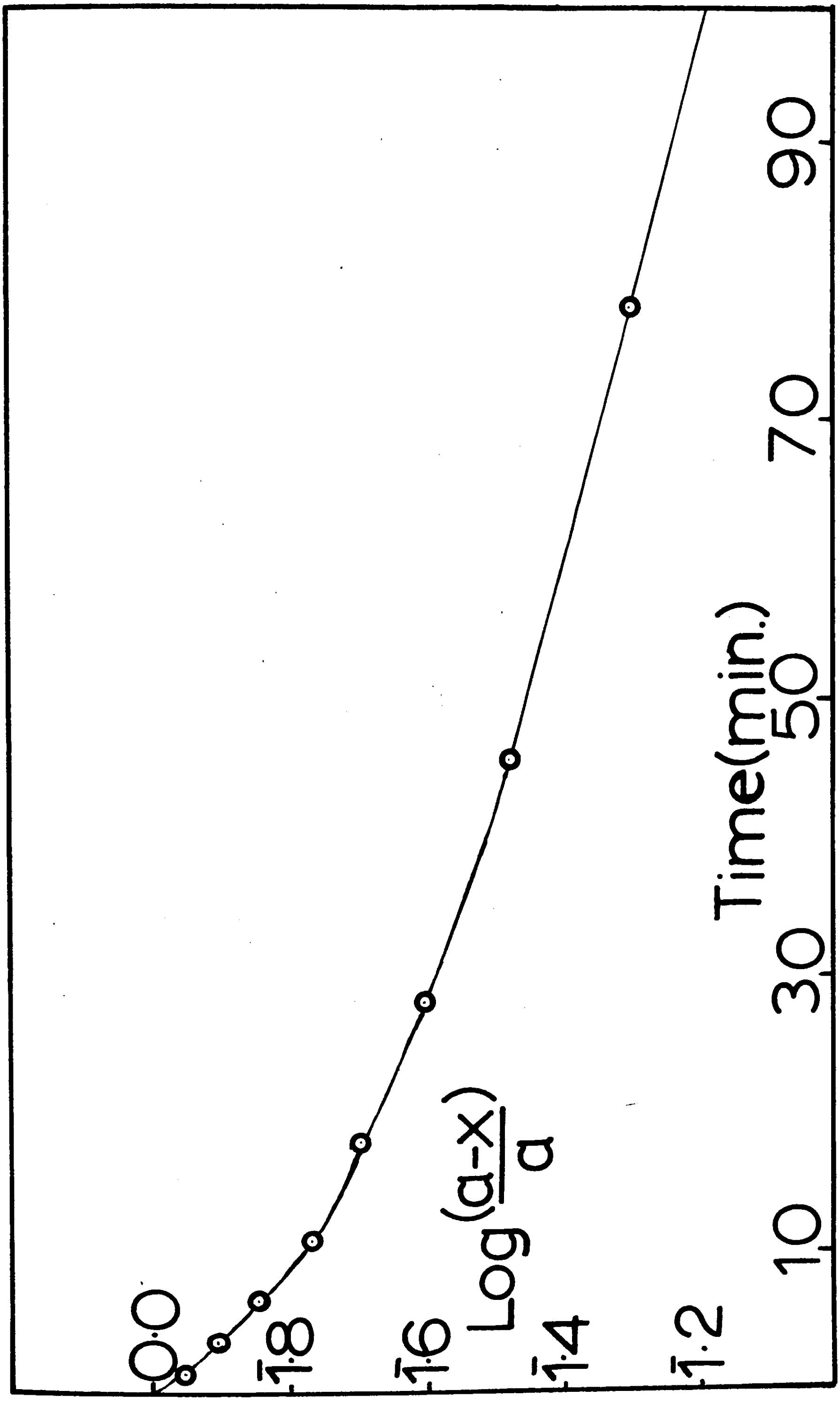


Fig.12

If the difference in the rates of reaction of the two species is sufficiently large in this type of kinetic scheme, then the overall reaction may be considered to proceed in two separate stages, the first step being almost complete before the contribution of the second step becomes appreciable. The rate expression will be given by:-

$$-\frac{d\,[\text{Ester}]}{dt} = k_1\,[OH^-]\,[CuE_2^{2+}] + k_2\,[OH^-]\,[CuEA^+]$$

where k_1 and k_2 are second order constants, which at constant pH simplifies to

$$-\frac{d\,[\text{Ester}]}{dt} = k_1'\,[CuE_2^{2+}] + k_2'\,[CuEA^+] ,$$

where $k_1' = k_1\,[OH^-]$ and $k_2' = k_2\,[OH^-]$.

If $k_1 \gg k_2$ then initially

$$-\frac{d\,[\text{Ester}]}{dt} = k_1'\,[CuE_2^{2+}]$$

Since the initial concentration of CuE_2^{2+} is equal to half the total concentration of ester, then $[CuE_2^{2+}] = \frac{a}{2}$ initially, and a plot of $\log\left(\frac{a-2x}{a}\right)$ vs time taken from the reaction curve should give rise to a straight line of gradient $-k_1'/2.303$. Plots were constructed and shown to be linear initially (fig.13) and the values of k_1', when divided by the appropriate hydroxide ion concentration gave rise to an approximately constant value (table VII). This provided additional evidence that hydroxyl ion is involved in a bimolecular/

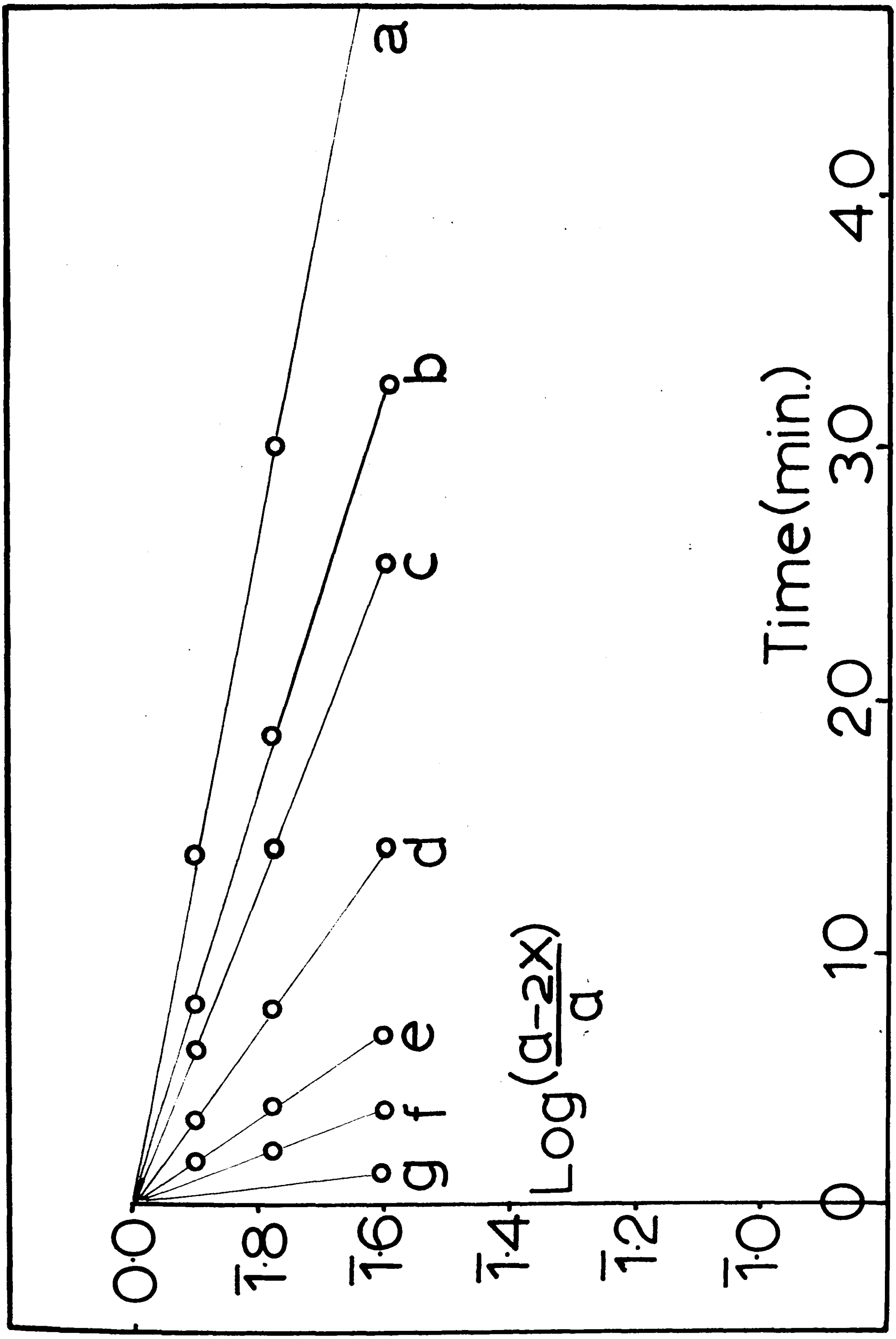
Figure 13.

Hydrolysis of Histidine Methyl Ester at constant pH.

Ester: Copper 2:1, $T = 25^{\circ}C$, $I = 0.1$ M.

Plots of $\log \left(\frac{a - 2x}{a}\right)$ vs t.

a pH 7.80
b pH 8.00
c pH 8.10
d pH 8.40
e pH 8.70
f pH 9.00
g pH 9.40



0·0
1̄·8
1̄·6
1̄·4
1̄·2
1̄·0
0
10
20
30
40
Time(min.)
$\mathrm{Log}\left(\frac{a-2x}{a}\right)$
a
b
c
d
e
f
g

Fig.13

Table VII.

Determination of k_1 from log $\left(\frac{a-2x}{a}\right)$ vs. t plot.

pH	$[OH^-]$ moles/litre	$k_1'.10^2 (min^{-1})$	$k_1'/[OH^-].10^{-4}$ l/mole-min
7.80	8.13×10^{-7}	1.58	1.94
8.00	1.29×10^{-6}	2.70	2.09
8.10	1.62×10^{-6}	3.60	2.22
8.40	3.24×10^{-6}	6.49	2.00
8.70	6.46×10^{-6}	12.2	1.89
9.00	1.29×10^{-5}	23.9	1.85
9.40	3.24×10^{-5}	79.5	2.45

bimolecular reaction with the 2:1 chelate.

The graphical measurement of k_1 given above, clearly had several limitations and it was therefore necessary to apply a more detailed treatment to the reaction time curves in order to obtain values for both k_1' and k_2' at any constant pH. The treatment used was based on the method of Frost[26].

Assuming that there is no disproportionation of the intermediate product $CuEA^+$ (i.e. if $2\ CuEA^+ \nrightarrow CuA_2 + CuE_2^{2+}$) and that chelation is complete such that a 2:1 chelate is the only species capable of hydrolysis at the start of the reaction then the kinetic scheme will involve two consecutive second order reactions.

$$CuE_2^{2+} + OH^- \xrightarrow{k_1} CuEA^+ + CH_3OH$$

$$CuEA^+ + OH^- \xrightarrow{k_2} CuA_2 + CH_3OH$$

At constant pH these will become psuedo first order

$$CuE_2^{2+} \xrightarrow{k_1'} CuEA^+ \xrightarrow{k_2'} CuA_2$$

with rate constants k_1' and k_2'

Now if R_0 is the initial concentration of CuE_2^{2+} and R, S, and U the concentrations of CuE_2^{2+}, $CuEA^+$ and CuA_2 at any time t, the alkali uptake, due to hydrolysis will correspond to $S + 2U$.

The/

The rate expressions for the various species involved may be written as follows:-

$$\frac{dR}{dt} = -k_1' R \ldots\ldots\ldots\ldots\ldots\ldots (10)$$

$$\frac{dS}{dt} = k_1'R - k_2'S \ldots\ldots\ldots\ldots\ldots (11)$$

$$\frac{dU}{dt} = k_2'S \ldots\ldots\ldots\ldots\ldots\ldots\ldots (12)$$

Integration of (10) gives

$$R = R_o e^{-k_1' t} \ldots\ldots\ldots\ldots\ldots (13)$$

Substituting (13) in (11),

$$S = \frac{R_o k_1'}{k_2' - k_1'} \left(e^{-k_1' t} - e^{-k_2' t}\right) \ldots\ldots (14)$$

where $S_o = 0$.

Since, at any time, $R + S + U = R_o$, when S_o and U_o are zero then,

$$\begin{aligned} U &= R_o - R - S \\ &= R_o - R_o e^{-k_1' t} - \frac{R_o k_1'}{k_2' - k_1'} \left(e^{-k_1' t} - e^{-k_2' t}\right) \\ &= R_o \left[1 - \frac{1}{k_1' - k_2'} \left(k_2 e^{-k_1' t} - k_1 e^{-k_2' t}\right)\right] \ldots\ldots (15) \end{aligned}$$

Equations (13), (14) and (15) may be simplified by the introduction of the following dimensionless parameters and variables,

$$\alpha = \frac{R}{R_o}, \quad \beta = \frac{S}{R_o}, \quad \gamma = \frac{U}{R_o} \quad \text{and} \quad \delta = \beta + 2\gamma$$

The values of α, β and γ are the concentrations of R, S and U relative to the initial concentration of R, R_0.

If now we let the parameter $\Upsilon = K_1' t$ and $K = \frac{k_2'}{k_1'}$ then the equations above become

$$\alpha = e^{-\Upsilon} \quad \ldots\ldots (13')$$

$$\beta = \frac{1}{K-1}\left(e^{-\Upsilon} - e^{-K\Upsilon}\right) \quad \ldots\ldots (14')$$

$$\gamma = 1 + \frac{1}{1-K}\left(Ke^{-\Upsilon} - e^{-K\Upsilon}\right) \quad \ldots (15')$$

$$\text{and } \delta = \beta + 2\gamma = 2 - \frac{(1-2K)}{(1-K)} e^{-\Upsilon} - \frac{1}{1-K} e^{-K\Upsilon} \quad \ldots (16)$$

Since the uptake of alkali due to hydrolysis at any time corresponds to S + 2U, the function δ is also related to the amount of alkali used in this time. As the reaction proceeds δ will vary from 0 to 2, and the percentage reaction at any time will be equal to $50 \times \delta$

Equation (16) may be rewritten in the form

$$d = \frac{1-2K}{1-K} e^{-\Upsilon} + \frac{1}{1-K} e^{-K\Upsilon}$$

where $d = 2 - \delta$

In a reaction of this type K, the ratio of the rate constants for the two consecutive reactions is constant, and at any given percentage reaction d must be constant. Hence for a particular value of K, at a particular percentage of/

reaction, Υ will be constant, and the value of Υ will be dependent on the value of K.

Table VIII was constructed showing the way in which the value of Υ at any given percentage reaction varies with K. The evaluation of K for the two stage hydrolysis of the 2:1 chelate at any constant pH was done by a time ratio method. This involved comparing the ratio of the times required for given percentages of reaction with the ratio of Υ values for similar percentages of reaction, over a range of values of K. The value of K for the reaction was that for which the ratio of Υ's equalled the time ratio.

In order to evaluate K therefore, a knowledge of the time for known percentages of reaction was required and this information is given in table IX, which was constructed from reaction time curves.

The data in tables VIII and IX are sufficient to estimate K for the reaction, by the time ratio method. A series of time ratios was chosen at random and is shown in table X. In the construction of this table, time ratios involving very small times or very large times (i.e. times for low percentages of reactions at high pH, and times for high percentages of reaction at low pH), have been excluded; the former because they were subject to large experimental error and the latter because/

Table VIII.

Variation of Υ, at various percentages, with K.

K	Υ_{10}	Υ_{20}	Υ_{30}	Υ_{40}	Υ_{50}	Υ_{60}	Υ_{70}	Υ_{80}	Υ_{90}
.05	0.222	0.502	0.881	1.454	2.556	5.570	11.10	18.33	32.19
.10	0.220	0.494	0.851	1.354	2.149	3.594	6.129	10.217	17.148
.12	0.220	0.491	0.840	1.322	2.049	3.272	5.377	8.701	14.477
.14	0.219	0.488	0.831	1.293	1.967	3.039	4.808	7.630	12.573
.20	0.218	0.479	0.804	1.222	1.787	2.594	3.809	5.730	9.163

Table IX.

Time (minutes) required for completion of given percentage of reaction over range of pH.

δ	0.2	0.4	0.6	0.8	1.0	1.2	1.4	1.6	1.8
pH7.80	14	30	50.5	78.6	125.2	186.5	-	-	-
pH8.00	8	18.7	32.5	51.2	80.4	122.1	-	-	-
pH8.10	6.35	14.4	25.5	40.6	62.7	99.1	157.1	-	-
pH8.40	3.4	7.9	14.3	23.4	36.6	56.5	87.7	145	252
pH8.70	1.90	4.1	6.90	11.4	18.4	28.5	45.9	73.4	127
pH9.00	1	2.3	3.9	6.00	9.4	14.2	21.8	35.5	58.9
pH9.40	<1	<1	1.4	2.1	3.3	5.1	8.2	13.0	23.4

Table X.

Random time ratios for hydrolysis of histidine methyl ester.

pH	t_{90}/t_{60}	t_{80}/t_{20}	t_{70}/t_{20}	t_{60}/t_{10}	t_{60}/t_{30}
7.80	-	-	-	13.32	3.69
8.00	-	-	-	15.26	3.76
8.10	-	-	10.90	15.60	3.89
8.40	4.46	18.35	11.10	16.60	3.95
8.70	4.46	17.90	11.19	15.00	4.13
9.00	4.15	15.43	9.50	14.20	3.64
9.40	4.59	-	-	-	3.64
Average	4.42	17.23	10.68	14.99	3.81

Table XI.

τ ratios comparable with time ratios of Table X.

K	τ_{90}/τ_{60}	τ_{80}/τ_{20}	τ_{70}/τ_{20}	τ_{60}/τ_{10}	τ_{60}/τ_{30}
.05	5.78	36.51	22.11	25.09	6.32
.10	4.77	20.68	12.41	16.34	4.22
.12	4.42	17.72	10.95	14.87	3.90
.14	4.14	15.64	9.85	13.88	3.66
.20	3.53	11.95	7.94	11.91	3.23

because they were not measured.

A comparison of the average time ratios in table X with the corresponding τ ratios for a range of K values (table XI) indicates that $K = 0.12$ gives the best agreement, and this was taken to be K for the reaction. The calculation of individual k_1' and k_2' was now made possible simply by inserting the appropriate value of τ in the expression $k_1' = \frac{\tau}{t}$ Table(XII) shows the values of k_1' obtained in this way for each reaction pH. The average values of k_1' may be compared with the k_1' values derived from the graphical method (table VII). Once again the expression $\frac{k_1'}{[OH^-]}$ remains practically constant, and this is a good indication that the reaction mechanism may be completely described as an attack of hydroxyl ions on the chelates CuE_2^{2+} and $CuEA^+$. The average value of the expression $k_1'/[OH^-]$ was taken as the second order rate constant for the reaction

$$OH^- + CuE_2^{2+} \xrightarrow{k_1} CuEA^+ + CH_3OH$$

$$k_1 = 1.93 \times 10^4 \text{ litres / mole-min.}$$

For the reaction

$$OH^- + CuEA^+ \xrightarrow{k_2} CuA_2 + CH_3OH$$

Since

$$K = \frac{k_2}{k_1}, \quad k_2 = k_1 K = 2.32 \times 10^3 \text{ l-mole}^{-1}\text{- min}^{-1}.$$

Table XII.

Determination of $k_1' = \frac{\Upsilon}{t}$ (min.$^{-1}$ x 10^2)

pH	10%	20%	30%	40%	50%	60%	70%	80%	90%	Average k_1' (min.$^{-1}$)	$k_1'/[OH]$
7.8	1.57	1.64	1.66	1.68	1.64	1.75	-	-	-	1.65	2.04x10^4
8.0	2.75	2.63	2.58	2.58	2.55	2.68	-	-	-	2.63	2.04x10^4
8.1	3.46	3.40	3.29	3.26	3.27	3.30	3.42	-	-	3.34	2.06x10^4
8.4	6.47	6.22	5.87	5.65	5.60	5.79	6.13	6.00	5.74	5.94	1.83x10^4
8.7	11.58	11.98	12.17	11.60	11.14	11.48	11.71	11.85	11.40	11.66	1.80x10^4
9.0	22.00	21.35	21.54	22.00	21.80	23.00	24.70	24.50	24.60	22.83	1.77x10^4
9.4	-	-	60.00	62.95	62.09	64.20	65.60	66.90	61.90	63.38	1.96x10^4

Hydrolysis of the 1:1 chelates.

In the kinetic study of the hydrolysis of histidine methyl ester in the presence of one equivalent of copper it was assumed that in solutions of pH > 6 the amounts of 2:1 chelate, free Cu^{2+}, and free ester were negligible compared with the concentration of 1:1 chelate. The only species in solution capable of hydrolysing were therefore the diaquo chelate, CuE^{2+}, and the monohydroxo chelate CuE^{+}.

Once again hydrolysis was found to proceed at a conveniently measurable rate in solutions of pH > 7 and the reaction time curves obtained over a range of pH from 7.00 to 9.40 are shown in fig.14. The general shape of the reaction time curves was very different from those obtained for the hydrolysis of the 2:1 chelate. First order log plots were again constructed and these are shown in fig. 15. The linearity of the plots indicates that the reaction proceeds, at constant pH, according to a simple first order law with respect to total ester.

The values of the observed first order-rate constants are shown in table XIII, together with $\frac{k_{obs}}{[OH^-]}$. It is clear that the expression $\frac{k_{obs}}{[OH^-]}$ steadily decreases as the pH is raised and tends towards a limiting value at high pH. A plausible explanation of this observation is to be found if it is assumed that the two species present in solution, CuE^{2+} and CuE^{+},/

Figures 14 and 15.

Hydrolysis of Histidine Methyl Ester at constant pH.

Ester: Copper = 1:1. $T = 25^{\circ}C$, $I = 0.1\ M$.

Fig.14 Reaction - time curves.

Fig.15 Plots of $\log \frac{(a-x)}{a}$ vs t.

a	pH	7.00
b	pH	7.50
c	pH	7.80
d	pH	8.00
e	pH	8.20
f	pH	8.90
g	pH	9.10
h	pH	9.20
i	pH	9.40

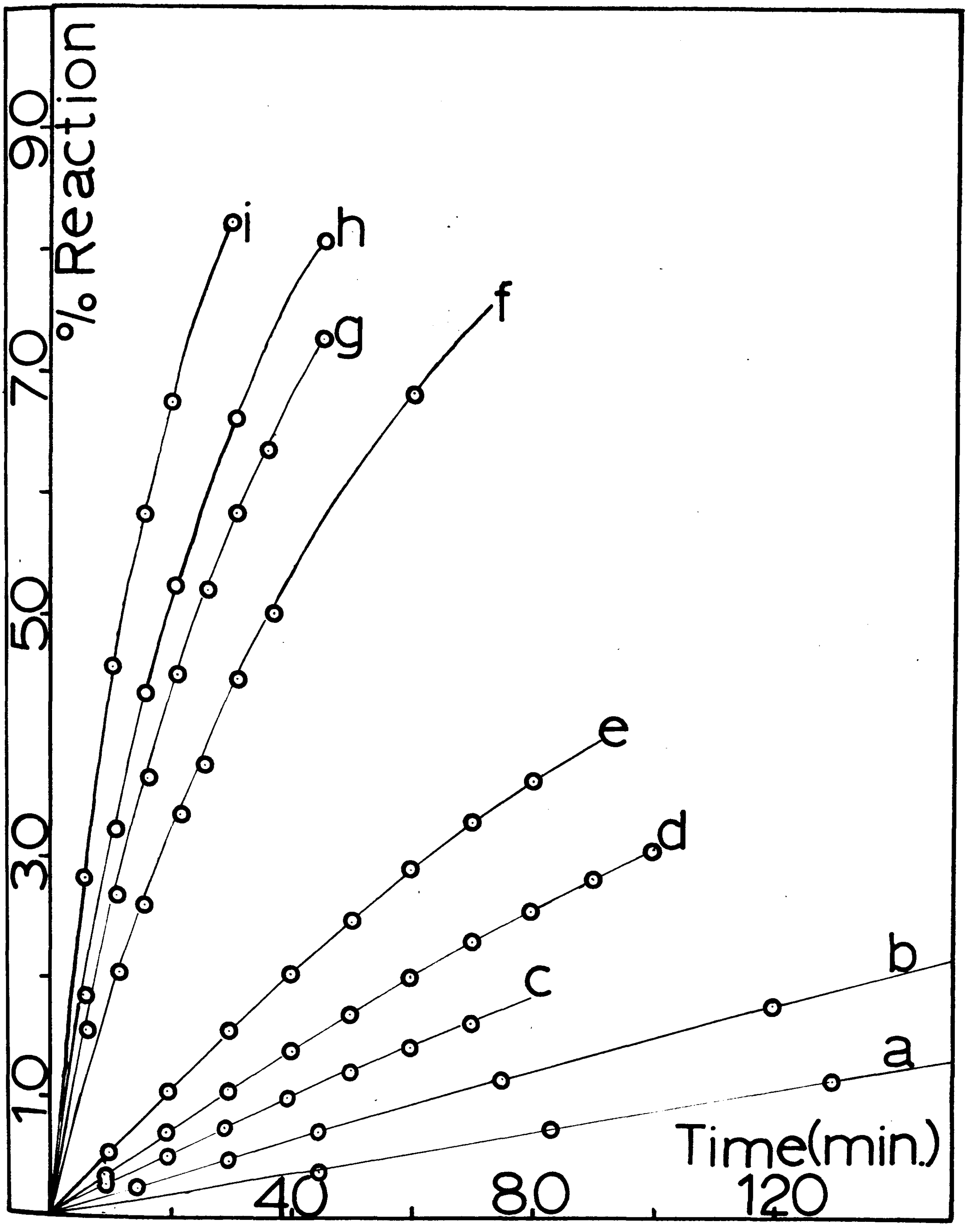


Fig.14

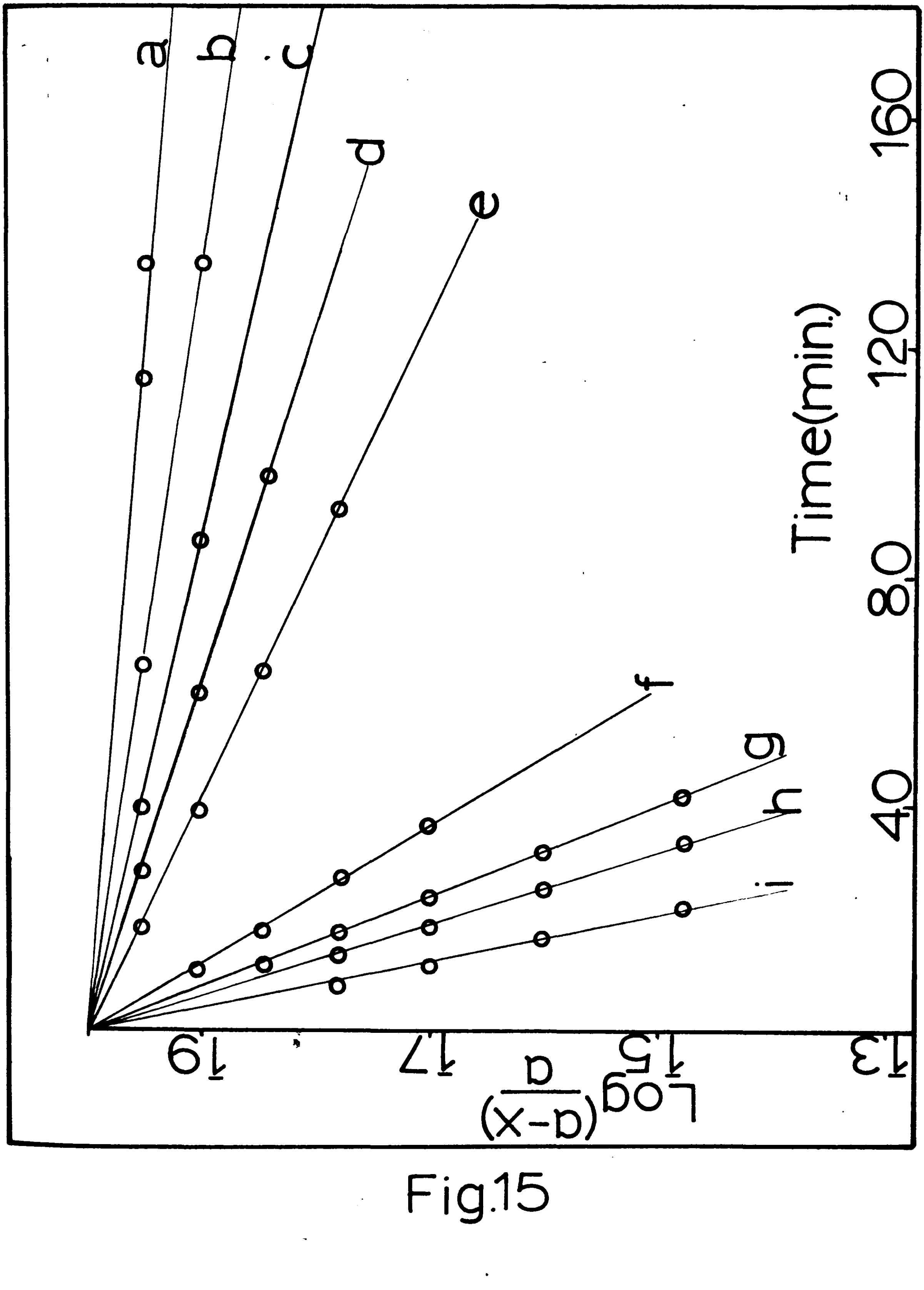

a
b
c
d
e
f
g
h
i
Time(min.)
40
80
120
160
$\bar{1}.9$
$\bar{1}.7$
$\bar{1}.5$
$\bar{1}.3$
$\mathrm{Log}\left(\frac{a}{a-x}\right)$

Fig.15

Table XIII.

Hydrolysis of histidine methyl ester in presence of one equivalent of Cu(II), I = 0.1M T=25°C

pH	$[OH^-]$ mole/litre	$k_{obs.}$ (min^{-1})	$\frac{k_{obs.}}{[OH^-]}$ litre-mole^{-1}-min^{-1}
7.00	1.29×10^{-7}	9.72×10^{-4}	$7.53 \times 10^{+3}$
7.50	4.07×10^{-7}	1.68×10^{-3}	4.13×10^{3}
7.80	8.13×10^{-7}	2.67×10^{-3}	3.28×10^{3}
8.00	1.29×10^{-6}	3.72×10^{-3}	2.88×10^{3}
8.20	2.04×10^{-6}	5.53×10^{-3}	2.71×10^{3}
8.90	1.02×10^{-5}	1.91×10^{-2}	1.87×10^{3}
9.10	1.62×10^{-5}	2.88×10^{-2}	1.78×10^{3}
9.20	2.04×10^{-5}	3.57×10^{-2}	1.75×10^{3}
9.40	3.24×10^{-5}	5.60×10^{-2}	1.73×10^{3}

CuE^+, react at different rates. The rate expression for the hydrolysis of the ester is then given by

$$\frac{-d[\text{Ester}]}{dt} = k_3 [OH^-][CuE^{2+}] + k_4 [CuE^+][OH^-]$$
$$= \text{kobs} \begin{bmatrix}\text{Total}\\\text{Ester}\end{bmatrix}$$

where k_3 and k_4 are the second order rate constants for the alkaline hydrolysis of CuE^{2+} and CuE^+ respectively. The rate of hydrolysis will thus depend on the relative values of k_3 and k_4, and the relative concentrations of CuE^{2+} and CuE^+, which in turn will be dependent on pH. At high pH the concentration of CuE^{2+} is very small compared to that of CuE^+ and the overall rate will be due almost entirely to the hydrolysis of CuE^+ i.e.

$$\text{kobs} [\text{Total Ester}] = k_4 [OH^-] [CuE^+].$$

Hence in the limit, $\frac{\text{kobs}}{[OH^-]} = k_4$. This, therefore, would explain the fact that a limiting value for $\frac{\text{kobs}}{[OH^-]}$ is found.

On the basis of the above scheme a quantitative treatment was applied as follows. Assuming the concentrations of free copper, free ester and 2:1 chelate to be negligible compared with the concentration of the 1:1 chelate, then

$$\text{Total Ester} = A = [CuE^{2+}] + [CuE^+] \ldots\ldots\ldots\ldots (17)$$

If the above reaction scheme is correct, then

kobs/

$$\text{kobs}.A = k_3[OH^-][CuE^{2+}] + k_4[OH^-][CuE^+]$$

and $\frac{\text{kobs}}{[OH^-]}.A = k_3[CuE^{2+}] + k_4[CuE^+]$ ....(18)

Let Ki be the dissociation constant for the equilibtium

$$CuE^{2+} \xrightleftharpoons{Ki} CuE^+ + H^+$$

i.e. $Ki = \frac{[CuE^+]}{[CuE^{2+}]} . \{H^+\} . \frac{f_1}{f_2}$

$\therefore [CuE^+] = \frac{Ki\frac{f_2}{f_1}}{\{H^+\}} [CuE^{2+}]$ ....(19)

Substituting (19) in (18), we have

$\frac{\text{kobs}}{[OH^-]}.A = k_3[CuE^{2+}] + k_4 \frac{Ki\frac{f2}{f1}}{\{H^+\}} [CuE^{2+}]$ ....(20)

From (19)

$$\frac{[CuE^+] + [CuE^{2+}]}{[CuE^{2+}]} = 1 + \frac{Ki\frac{f2}{f1}}{\{H^+\}}$$

$\therefore \frac{A}{[CuE^{2+}]} = 1 + \frac{Ki\frac{f2}{f1}}{\{H^+\}}$ ....(21)

Substituting (21) in (20),

$$\frac{\text{kobs}}{[OH^-]}.A = k_3\frac{A}{1 + \frac{Ki\frac{f2}{f1}}{\{H^+\}}} + k_4\frac{Ki\frac{f2}{f1}}{\{H^+\}} . \frac{A}{1 + \frac{Ki\frac{f2}{f1}}{\{H^+\}}}$$

$\therefore \frac{\text{kobs}}{[OH^-]}\left(\frac{\{H^+\}}{Ki\frac{f2}{f1}} + 1\right) = \frac{\{H^+\}}{Ki\frac{f2}{f1}} . k_3 + k_4$ ...(22)

This is of the form $Y = MX + C$, where

$$Y = \frac{kobs}{[OH^-]}\left(\frac{\{H^+\}}{Ki\frac{f2}{f1}} + 1\right) \quad \text{and} \quad X = \frac{\{H^+\}}{Ki\frac{f2}{f1}}$$

A plot of Y vs X should therefore be linear, the slope being k_3 and Y intercept k_4. From the potentiometric data $Ki\frac{f2}{f1} \approx 10^{-7}$ (fig. 9) and this value was used in the construction of an X,Y plot (fig. 16) which proved to be a straight line, within experimental error. The values of k_3 and k_4 obtained from this plot were 1.29×10^4 l-mole.$^{-1}$-min.$^{-1}$ and 1.70×10^3 l-mole.$^{-1}$-min.$^{-1}$, respectively.

Figure 16.

Plot of Y vs X from the data of Table XIII, where,
$$Y = \frac{k\ \text{obs.}}{[OH^-]} \left[\frac{\{H^+\}}{Ki \frac{f_2}{f_1}} + 1 \right]$$

and
$$X = \frac{\{H^+\}}{Ki \frac{f_2}{f_1}}$$

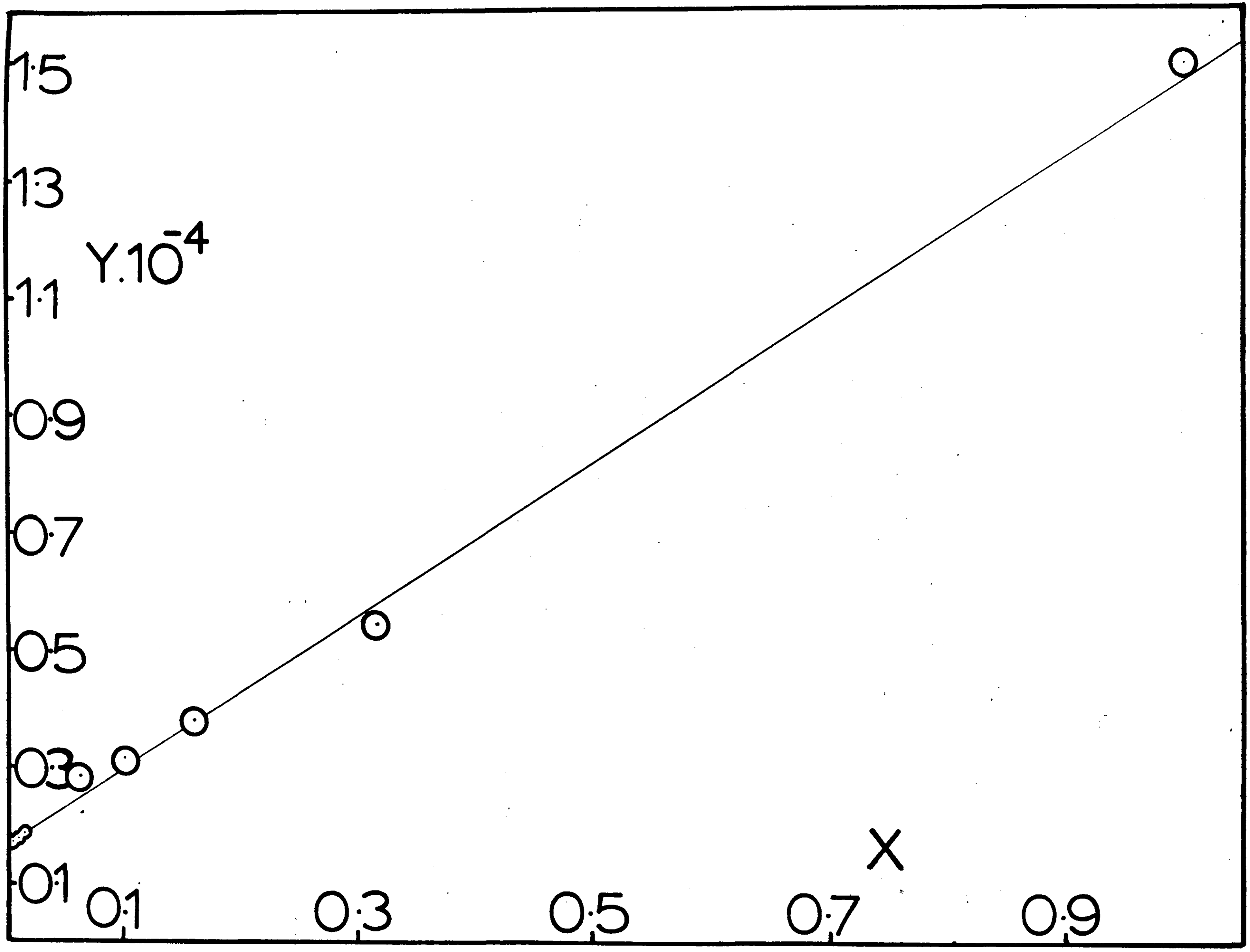


Fig.16

Nickel Ion Catalysis.

Having established the nature of the copper (II) catalysis of the hydrolysis of histidine methyl ester, a study of the nickel (II) catalysis was made in order to compare the catalytic effect of these two ions with the stability of the chelates formed. Preliminary experiments showed that a similar hydrolysis pattern was to be expected in the Ni(II)-ester system.

Hydrolysis of the 2:1 chelate.

The relative values of K_3 and K_4 for the Ni(II) ester system, (table V) are such that in solutions of pH > 7.00 where the ester: Ni ratio is 2:1, there is a not insignificant dissociation of the 2:1 complex

$$NiE_2^{2+} \rightleftharpoons NiE^{2+} + E$$

To ensure that effectively all the Ni(II) was present as the 2:1 complex, it was therefore necessary to observe hydrolysis in solutions containing an excess of free ester. For this reason, hydrolysis of NiE_2^{2+} was observed in solutions where the ester-Ni ratio was 10:3, and corrections were made to the reaction time curves to allow for the slow hydrolysis of the free ester which was almost, but not quite negligible in the pH range studied. The times for completion of given percentages of hydrolysis of the 2:1 chelate, NiE_2^{2+}, over the pH/

pH range 8.40 to8.90 are given in Table XIV. Calculation of appropriate time ratios (table XV) and comparison with the γ ratios of table XI, lead to a K value of 0.14. Values of k_1', calculated assuming K = 0.14 are shown in table XVI, along with average k_1' values and $k_1'/[OH^-]$. The expression $\frac{k_1'}{[OH^-]}$ was again found to be approximately constant and the average, $k_1 = 7.09 \times 10^3$ l-mole^{-1}-min^{-1}, was therefore taken to be the second order rate constant for the alkaline hydrolysis of the 2:1 nickel chelate. It follows that the second order constant k_2 for the hydrolysis of $NiEA^+$ is 9.92×10^2 litre-mole.$^{-1}$-min.$^{-1}$

Hydrolysis of the 1:1 chelate.

Solutions containing ester and nickel in the ratio 1:1 showed a tendency to precipitate nickel hydroxide, due to slight local alkalinity at the burette tip. This caused any kinetic measurements made on such solutions to be subject to much larger experimental error than in solutions where no precipitation occurred. It is for this reason that only a very approximate value, 4.7×10^3 litre-mole.$^{-1}$-min.$^{-1}$, can be assigned to the second order rate constant for the hydrolysis of the 1:1 chelate NiE^{2+}.

Table XIV

Time (min) for completion of given percentage of reactions in hydrolysis of NiE_2^{2+}. $T = 25°C$, $I = 0.1 M$

pH	t_{10}	t_{20}	t_{30}	t_{40}	t_{50}	t_{60}	t_{70}	t_{80}
8.40	9.60	21.5	37	59	86	132	-	-
8.60	6.0	13.5	23.0	36.5	55	83	135	-
8.90	2.9	6.5	11.2	18.0	27.0	40.0	62.0	103

TABLE XV.

Time ratios for hydrolysis of NiE_2^{2+}

pH	t_{70}/t_{20}	t_{60}/t_{10}	t_{60}/t_{30}	t_{80}/t_{20}
8.40	-	13.75	3.57	-
8.60	10.00	13.83	3.61	-
8.90	9.54	13.79	3.57	15.85

Table XVI.

k_1' for the hydrolysis of NiE_2^{2+} ($min.^{-1} \times 10^2$)

pH	10%	20%	30%	40%	50%	60%	70%	80%	K_1 mean	$K_1/[OH^-]$
8.40	2.28	2.27	2.25	2.19	2.24	2.30	-	-	2.26	6.98×10^3
8.60	3.65	3.62	3.61	3.54	3.58	3.66	3.56	-	3.60	7.02×10^3
8.90	7.55	7.51	7.42	7.18	7.29	7.60	7.7	7.27	7.44	7.29×10^3

GENERAL DISCUSSION

The hydrolysis of histidine methyl ester has been shown to proceed via a bimolecular reaction between a hydroxyl ion and an ester molecule, either free in solution or bound to a metal ion. The reactions studied and the second order rate constants obtained are shown below -

1. $E + OH^- \longrightarrow A^-$ $k_o = 4{\cdot}7 \times 10^1$ litre-mole^{-1}-min^{-1}.
2. $CuE_2^{2+} + OH^- \longrightarrow CuEA^+$ $k_{1CuE_2^{2+}} = 1{\cdot}94 \times 10^4$ " " "
3. $CuEA^+ + OH^- \longrightarrow CuA_2$ $k_{2CuEA^+} = 2{\cdot}33 \times 10^3$ " " "
4. $CuE^{2+} + OH^- \longrightarrow CuA^+$ $k_{3CuE^{2+}} = 1{\cdot}29 \times 10^4$ " " "
5. $CuE^+ + OH^- \longrightarrow CuA$ $k_{4CuE^+} = 1{\cdot}70 \times 10^3$ " " "
6. $NiE_2^{2+} + OH^- \longrightarrow NiEA^+$ $k_{1NiE_2^{2+}} = 7{\cdot}08 \times 10^3$ " " "
7. $NiEA^+ + OH^- \longrightarrow NiA_2$ $k_{2NiEA^+} = 9{\cdot}9 \times 10^2$ " " "
8. $NiE^{2+} + OH^- \longrightarrow NiA^+$ $k_{3NiE^{2+}} = 4{\cdot}7 \times 10^3$ " " "

From the above information an order of reactivity for the various species, capable of hydrolysing, may be constructed, as follows:-

$CuE_2^{2+} > CuE^{2+} > NiE_2^{2+} > NiE^{2+} > CuEA^+ > CuE^+ > NiEA^+ > E$.

Several conclusions may be drawn from this, concerning the factors influencing the catalysis of the hydrolysis of the ester.

It/

It may be seen that the reactivity of a species depends to a large extent on the overall positive charge, since species possessing two positive charges are more reactive than those possessing one positive charge, and the reactivities of both of these are much greater than that of the uncharged ester molecule. Another factor is the number of ester molecules present in the species, since species of similar charge, but having different numbers of ester molecules present have different reactivities.

These two factors do not, however, account entirely for the order of reactivity given above. If the reactivities of copper and nickel chelates of similar charge and possessing equal numbers of ester molecules, are compared it is found that in all cases the copper chelate is more reactive than the nickel. An explanation of this observation may be found from a consideration of the relative stabilities of the copper and nickel chelates with histidine methyl ester, (table V). The formation constants of copper chelates are considerably greater than those of similar nickel chelates and the reactivity of a chelate towards hydroxyl ion would thus seem to depend on the degree of interaction of the metal ion with the ester molecule.

Metal ion catalysis of the hydrolysis of histidine methyl ester, therefore, may be regarded as being due to three effects.

(i)/

(i) Introduction of positive charge into the ester molecule.

(ii) Statistical effect.

(iii) Electron withdrawal effect.

These obviously must be intimately connected with one another, and it would be very difficult to assign quantitatively the contribution made by each to the overall catalytic effect. It is however, useful to compare the reactivities of suitable hydrolysing species, bearing the three catalytic effects in mind.

(1) The overall effect of the introduction of positive charge to the ester molecule may be seen by comparing the reactivities of the uncharged ester, with the reactivities of the metal chelates bearing one and two positive charges respectively.

$$\frac{k_{3\,CuE^{2+}}}{k_o} \approx 2.6 \times 10^2 \qquad \frac{k_{4CuE^+}}{k_o} \approx 4 \times 10^1$$

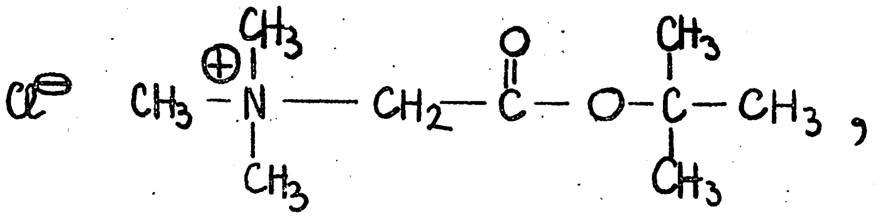
$$\frac{k_{3NiE^{2+}}}{k_o} \approx 1 \times 10^2 \qquad \frac{k_{2NiEA^+}}{k_o} \approx 2 \times 10^1$$

The reactivity ratios must also include the electron withdrawal effect of the metal ion and hence the ratios for copper chelates are somewhat larger than those for similarly charged nickel chelates. It would seem reasonable to assume, however, that the/

the introduction of a net single charge in the vicinity of the ester group increases the rate of hydrolysis by at least a factor of ten, where as the introduction of a double positive charge increases the rate by at least a factor of 50.

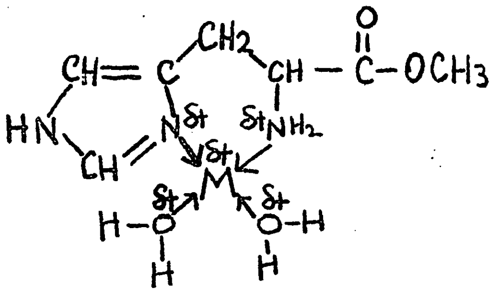
The increase in hydrolytic rate is easily understood if we bear in mind that the attacking species is a negatively charged hydroxyl ion. The introduction of positive charge to the vicinity of the ester group would have the effect of increasing the concentration of hydroxyl ions in the neighbourhood of the ester molecule, thus increasing the chance of effective collisions.

The effect of introduction of positive charge on alkaline hydrolysis has been studied. Westheimer and Shookhoff[27] measured the rates of alkaline hydrolysis of t-butyl dimethyl glycinate and t-butyl betainium chloride and found that the rate of hydrolysis was increased by a factor of 10^3, on introduction of positive charge on the α nitrogen. At first sight the results of the present work might seem to be in disagreement with those of Westheimer, in that introduction of a single positive charge has been shown to have a very much smaller effect. In t-butyl betainium chloride, however, the α nitrogen bears a single positive charge,



$$Cl^{\ominus}\quad CH_3-\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{\overset{\oplus}{N}}}-CH_2-\overset{\overset{O}{\|}}{C}-O-\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}-CH_3\,,$$

and must therefore exert a very powerful inductive effect, withdrawing electrons away from the ester carbonyl group, and greatly enhancing its reactivity. In a charged metal chelate on the otherhand, the positive charge is distributed over several atoms and the inductive effect of the α nitrogen will be greatly reduced compared with that in the betainium ion.



Thus fractional positive charge on the α nitrogen provides a plausible explanation for the apparent difference.

(11) The statistical effect observed may be explained as a corollary of effect (1), since the introduction of additional ester groups into a region of positive charge will further increase the chance of reaction. When the rates of reaction of similarly charged chelates containing one and two ester/

ester molecules are compared it is found that these are not 2 as would be expected on statistical grounds, but about 1.5

$$\frac{k_{1CuE_2^{2+}}}{k_{3CuE^{2+}}} \simeq 1.5 \qquad \frac{k_{1NiE_2^{2+}}}{k_{3NiE^{2+}}} \simeq 1.5$$

A possible explanation of this may lie in the difference in distribution of the positive charge in the diaquo 1:1 chelate, and in the 2:1 chelate, causing the α nitrogen to exhibit a different inductive effect.

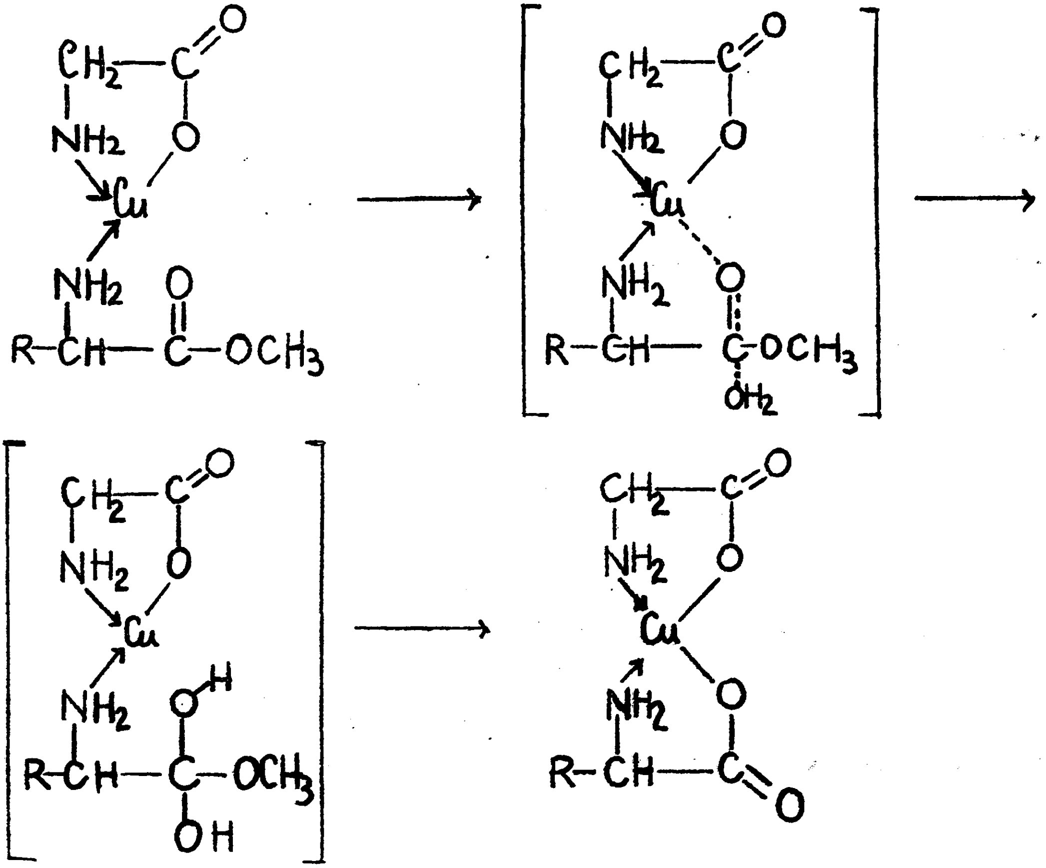
(111) A measure of the relative electron withdrawal effect of the copper and nickel ions in the hydrolysis of histidine methyl ester may be estimated by comparing the reactivities of similar copper and nickel chelates.

$$\frac{k_{1CuE_2^{2+}}}{k_{1NiE_2^{2+}}} \simeq 2.7 \qquad \frac{k_{3Cu^{2+}}}{k_{3NiE^{2+}}} \simeq 2.7 \qquad \frac{k_{2CuEA^{+}}}{k_{2NiEA^{+}}} \simeq 2.4$$

We can conclude that the reactivities of copper chelates are about two and a half times as great as the reactivities of similar nickel chelates. Since it has been shown that copper has a greater interaction with histidine methyl ester than does nickel it is not unreasonable to suppose that the effect of the presence of a copper ion on the electron distribution within the ester molecule would be more pronounced than the effect of/

of a nickel ion. The withdrawal of electrons towards the metal increases the susceptibility to nucleophilic attack of the ester carbonyl group.

Very few comparisons of metal ion catalysed and uncatalysed hydrolysis of α amino esters have appeared in the literature, but it is of interest to examine them. In 1957 Bender and Turnquest[10] measured the rates of hydrolysis of several α amino esters, in copper glycine buffer solutions, and concluded that the mechanism for the catalysed hydrolysis was as follows:-



This mechanism clearly involved direct interaction between the carbonyl oxygen of the ester group and the metal ion. The evidence for this was based on a comparison of the calculated rates of acid and alkaline hydrolysis with the rate of the metal ion catalysed reaction. The alkaline and cupric ion catalysed hydrolyses were compared for the hydrolysis of phenylalanine ethyl ester and the ratio of the rate constants was found to be of the order of 10^6. It had been shown previously[27] that the introduction of a positive charge two atoms away from the carbonyl group of an ester increased the rate constant for alkaline hydrolysis by a factor of 10^3. Hence Bender and Turnquest favoured the view that the catalysis could not be due to the attack of hydroxyl ions on the positively charged ester molecule, but that the metal ion was acting as a super catalyst, interacting directly with the carbonyl group. The ratio of rate constants derived by Bender is subject to some doubt, since the catalysed rate constant involves buffer interaction, and the alkaline rate constant was calculated from a second order constant for alkaline hydrolysis measured in 85% ethanol[28].

A more direct comparison of catalysed and uncatalysed rates of hydrolysis was made by Li, Doody and White[12]. By a conductivity method they measured the rates of alkaline hydrolysis/

lysis of histidine methyl ester in the absence and presence of copper and nickel ions. The solutions under study contained metal ions (when present), ester and hydroxyl ions in the ratio 1:3:3, and the second order constants which they obtained are shown in table XVII. They found that the presence of nickel and copper increased the measured rate constant by a factor of 2.5 and 4.5 respectively, which is vastly different from the factor of 10^6 observed by Bender and Turnquest for copper catalysis and considerably different from the values of rate constant ratios measured in the present work which ranged from 20 to 400.

An explanation of the difference in the results obtained by Li, Doody and White and those obtained in the present work is to be found in the reaction conditions employed by these authors. Since the solutions contained ester, hydroxyl ions and metal ion in the ratio 3:3:1, the species present initially would be ME_2^{2+} and E in equal proportions, and the initial rate expression would be given by

$$\frac{-d\,[\text{Ester}]}{dt} = k_1\,[OH^-]\left[ME_2^{2+}\right] + k_0\,[OH^-][E]$$

Since it is known from the present work that $k_1 \gg k_0$ for both nickel and copper, the chelate ME_2^{2+} will be almost completely hydrolysed to MA_2, before an appreciable amount of free/

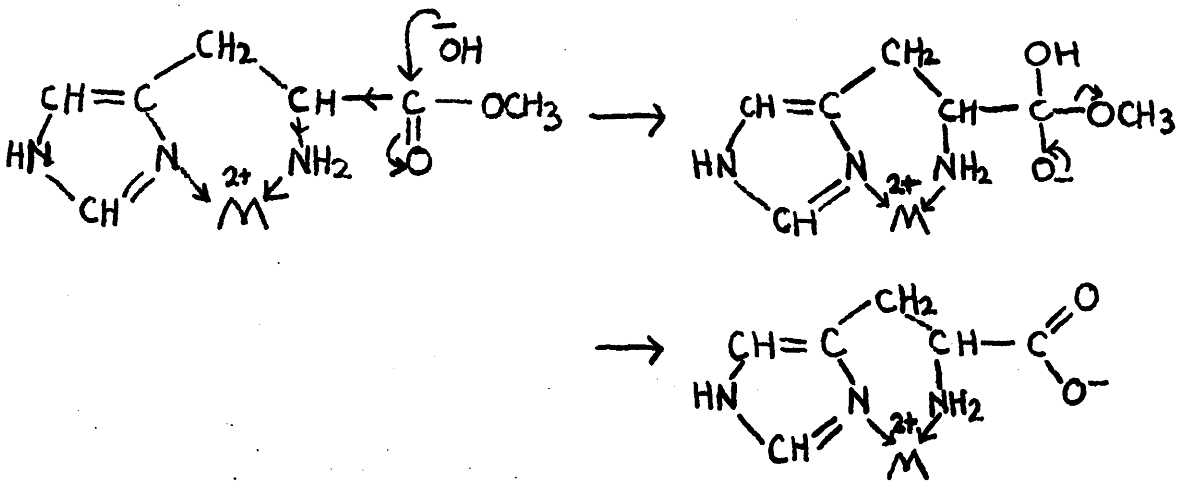
Table XVII.[12]

Initial Ester Concentration	Metal Ion	k obs. (litre/mole-min)
.00478 M	-	3.72×10^1
.00382 M	Ni^{2+}	9.44×10^1
.00382 M	Cu^{2+}	17.04×10^1

free ester has reacted. This means that after complete hydrolysis of the chelates the alkali concentration will still be one third of its initial value. In the kinetic runs reported the initial total ester and alkali concentration was 3.8×10^{-3}M and hence after complete hydrolysis of the chelate ME_2^{2+} the alkali concentration must have been about 1×10^{-3} M, i.e. the pH must have been at least 11 during the hydrolysis of the chelate. From the kinetic information derived during the present work, the times taken for 90% hydrolysis of NiE_2^{2+} and CuE_2^{2+} at pH11 are 1.8 min. and 0.7 min. respectively. It is therefore doubtful whether very much of the hydrolysis of the metal chelates could have been followed by a conductivity method in solutions of such high hydroxyl ion concentration.

In conclusion, the work presented here has shown that the metal ions Ni(II) and Cu(II) catalyse the hydrolysis of histidine methyl ester by chelate formation which increases the reactivity of the ester towards hydroxyl ions. The overall catalytic effect may arise in three ways; (i) the introduction of positive charge (ii) a statistical effect (iii) an electron withdrawal effect. A comparison of the ratios of catalysed and uncatalysed reactions shows that the mechanism of catalysis may be described in terms of these three effects and

and need not involve direct interaction of metal ion with the carbonyl oxygen.



Part II.

THE CONDUCTIVITY OF SOME SYMMETRICAL RARE EARTH SALTS IN WATER AND DIOXAN—WATER MIXTURES

INTRODUCTION

The behaviour of electrolytes in solution is a subject which has fascinated physical chemists for over a century. The first attempt at a quantitative description of the properties of ions in solution was given by Arrhenius, who observed that the euqivalent conductance of electrolytes decreased with increasing concentration. He explained this by assuming that dynamic equilibrium existed between neutral, non conducting molecules of electrolyte and the free ions into which the electrolyte dissociated.

$$MX \rightleftharpoons M^{Z+} + X^{Z-}$$

Application of the mass action law to the equilibrium gave the equation,

$$K = \frac{[M^{Z+}][X^{Z-}]}{[MX]} = \frac{m\gamma^2}{1-\gamma} \quad \ldots\ldots\ldots\ldots (23)$$

where γ was the fraction of free ions produced and m the molar concentration. He next assumed that

$$\gamma = \frac{\Lambda}{\Lambda_0} \quad \ldots\ldots\ldots\ldots (24)$$

where Λ was the equivalent conductivity and Λ_0 the conductivity at infinite dilution. A combination of (23) and (24) led to the Ostwald dilution law,

$$\frac{1}{\Lambda} = \frac{1}{\Lambda_0} + \frac{m\Lambda}{K\Lambda_0^2} \quad \ldots\ldots\ldots (25),$$

and when this was tested experimentally by plotting Λ^{-1} against/

against $m\Lambda$ it was found that equation (25) described fairly well the behaviour of electrolytes for which γ was small, but was inadequate for those electrolytes which were highly dissociated. These two classes were defined as being weak and strong electrolytes respectively. Typical of the first class were the carboxylic acids while examples of the second were simple uni-univalent inorganic salts.

In his treatment of electrolyte solutions Arrhenius had assumed that the mobilities of ions were independent of concentration and that any deviation of Λ from Λ_0 was due entirely to incomplete dissociation. Kohlrausch, a contemporary of Arrhenius, had observed that for those salts, whose behaviour was not described by the Ostwald dilution law, the equivalent conductivity decreased linearly with the square root of the concentration.

With the advent of structure determination by X-ray crystallography in the early part of this century, it became evident that inorganic salts consisted of separate ions held together in a crystal lattice, there being no individual molecule within the crystal. The fact that ions in the lattice were held together by electrostatic forces, suggested that these forces might continue to exert considerable influence after dissolution of the crystal in a solvent. The consequences to be expected/

expected from this were that the movement of ions under the influence of an electric field would be somewhat restricted by ions of opposite charge, and a decrease in equivalent conductivity with increasing concentration was thus explained.

It was also realised about this time that the activity coefficient of an ion would be influenced by these Coulombic forces and several workers attempted to give a quantitative treatment of electrolyte solutions, which would take into account ionic interactions. The first major success was achieved in 1923 by Debye and Huckel[29], who pictured an electrolyte solution as consisting of completely dissociated, rigid spherically symmetrical ions. Having chosen a reference ion, all the other ions were replaced by a continuous space charge whose density was assumed to be a function of the distance from the origin. The electrostatic potential around the reference ion was related to the charge density and dielectric constant of the surrounding medium by means of the Poisson equation. Application of the Boltzmann distribution to describe local concentrations, allowed the density in the Poisson equation to be replaced by the stoichiometric concentrations, charges and potentials of the ions. This led to the well known Debye Huckel equation for the mean activity coefficient of an ion,

$$\log f_{\pm} = \frac{A z_1 z_2 \sqrt{I}}{1 + \beta \mathring{a} \sqrt{I}} \quad - - - - - (26)$$

where A and B are defined by the temperature and nature of the solvent and a^{o} is the distance of closest approach of the ions.

Using the same concept of an ionic atmosphere of ions of one type around a central ion of opposite charge, Onsager[30] gave the first successful quantitative treatment of conductance of completely dissociated electrolytes. Two effects of interionic attraction were considered; the relaxation and electrophoretic effects. The former described the retarding force exerted by the ionic atmosphere on an ion, under the influence of an electric field, when it moved from the centre of its atmosphere; the latter described the slowing of an ion by solvent molecules moving in the other direction and a tendency for the ion to drag such molecules along with it. Consideration of these effects gave rise to the familiar Onsager equation;

$$\Delta = \Delta_o - (\alpha \Delta_o + \beta)\sqrt{C} \qquad \ldots\ldots\ldots (27)$$

where the two constants α and β are described by temperature, viscosity, and dielectric constant of the medium, the valency type of the solute and physical constants. This had the same form as Kohlrausch's equation.

Both the Debye-Hückel and Onsager equations held only at very low concentrations. This was a natural consequence of/

of the choice of a model in which ions were considered to be point charges. Since then, both equations have been improved and extended to allow for finite ionic size. Higher terms in the mathematical expansions which were neglected in the preliminary derivations, and forces other than ion-ion forces which may occur in solution have also been taken into account.

While the Onsager equation was very successful in predicting the conductivities, in water, of many salts which hadnot obeyed the Ostwald dilution law, negative deviations from the predicted Onsager slope were known to occur for some salts in water, and still more puzzling was the fact that electrolytes, which appeared strong in water gave conductivity curves typical of weak electrolytes in liquid ammonia. Deviations of this type were successfully explained by a return to the Arrhenius theory of incomplete dissociation. In the case of weak electrolytes such as carboxylic acids the equilibrium was assumed to involve neutral molecules,

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

where as with the inorganic salts there was no unionised neutral molecule to dissociate and the process was considered to be an association of ions to form an ion pair.

$$M^{m+} + X^{x-} \rightleftharpoons MX^{(m-x)+}$$

A/

A quantitative theory of ion pair formation was given by Bjerrum[31] in 1926, which arose from a consideration of the effects of electrostatic forces on rigid, unpolarisable, charged spheres of diameter "a", in a medium of dielectric constant, D. Non polar quantum bonds between ions were neglected as were ion solvent interactions. He showed that the probability of finding an ion of type "i" in any unit volume at a distance r from an ion of type "j", of opposite charge, was at a minimum at a distance q given by

$$q = \frac{e^2|z_i z_j|}{2DkT}$$

It follows that q is the distance of separation of ions for which the mutual potential energy is 2kT. For values of r less than q the probability increases rapidly as r decreases; for $r > q$ the probability increases slowly. Bjerrum assumed that two ions at a distance $r < q$ were associated, so that all ions at a distance r where "a" $< r < q$ were considered to be paired and to exhibit properties characteristic of the new entity. A relationship between the dissociation constant K, the dielectric constant D, and the distance of closest approach "a" was derived in the form

$$\log K = \text{const} - 3 \log D + \log Q(b)$$

$$-\log b = \text{const} + \log D + \log \text{"}a\text{"},$$

where/

where $Q(b) = \int_2^b e^Y . Y^{-4} dY$

and $b = \frac{Z_1 Z_2 e^2}{a D k T}$

With the introduction of a quantitative theory of ion pair formation, the measurement of dissociation constants took on a new significance and the theory has been verified for many systems over a range of dielectric constants and temperature. Fuoss and Kraus[32], for example, have shown that the Bjerrum theory adequately described the observed conductance of tetraisoamylammonium nitrate in water-dioxane mixtures of low dielectric constant.

The actual methods of deriving constants will be described in the next section and it is sufficient at present to say that they are based on the Arrhenius and Ostwald theories with suitable modifications to allow for ionic interaction. The use of conductivity measurements is particularly applicable to the study of symmetrical salts since the ion pair formed is uncharged and does not conduct electricity. The work of Fuoss and Kraus on 1:1 electrolytes at low dielectric constants has been mentioned. In solutions of high dielectric constant such as aqueous solutions, appreciable ion association is to be expected only with high valency type electrolytes. The dissociation of lanthanum ferricyanide in water and other solvents of high dielectric/

dielectric constant has been studied,[33, 34, 35] and it has been shown that the use of the limiting forms of the Debye Hückel and Onsager equations gives satisfactory dissociation constants, whose values vary with dielectric constant in a way very close to that predicted by the Bjerrum theory.

In an attempt to extend the work on 3:3 electrolytes, Atkinson[36] measured the conductivities of several rare earth cobalticyanides in water and dioxane-water mixtures. The constants derived from these data indicated a completely anomalous behvaiour, for while the Δ_0 values in each solvent were in complete accord with what was to be expected from independent ion mobilities, the dissociation constants differed considerably through the series. Although Walden's rule was closely obeyed, indicating that ionic radii remained the same in each solvent, the "a" values were apparently not constant. Monk[37] pointed out that consistent K values could not be obtained, using many of the Δ_0 values reported and that large differences in dissociation constants were not to be expected in a series of rare earth salts. In view of the excellent agreement of lanthanum ferricyanide with its behaviour predicted by the Bjerrum theory of ion association, Monk suggested that the apparent anomalies in the cobalticyanide series were of experimental nature. The object of the present work was to provide accurate conductivity data for a series of rare earth salts and to examine these in the light of the Bjerrum theory of ion association.

DETERMINATION of CONSTANTS from CONDUCTANCE DATA.

Where negative deviations from the limiting Onsager slope occur even at very low concentrations these can be attributed to the formation of ion pairs in solution,

$$M^{z+} + X^{z-} \rightleftharpoons M^{z+}X^{z-}$$

Methods of evaluating the equilibrium constant,

$$K = \frac{\{M^{z+}\}\{X^{z-}\}}{\{MX\}} = \frac{Cf^2\gamma^2}{Z(1-\gamma)} \quad \ldots\ldots(28)$$

where C is the equivalent concentration, have been given by Davies[38], Fuoss[39], Shedlovsky[40], Wirth[41] and Ives[42]. These are all based on the Ostwald-Arrhenius theory of incomplete dissociation, suitably modified to allow for interionic effects on both mobility and activity of ions.

The basic assumption is that the degree of dissociation is given by

$$\gamma = \frac{\Lambda}{\Lambda_x} \quad \ldots\ldots\ldots(29),$$

where Λ is the measured equivalent conductivity and Λ_x is the conductivity of a solution of ionic concentration, $C\gamma$ calculated according to a theoretical conductance equation.

In 1933, Davies[38] applied these ideas to the study of ion association in metal sulphate solutions. Where Λ_0 is known γ may be calculated by successive approximations from the equation

$$\Lambda_x = \Lambda_0 - (\alpha\Lambda_0 + \beta)\left(C\frac{\Lambda}{\Lambda_x}\right)^{\frac{1}{2}} \quad \ldots\ldots(30)$$

by taking $\Lambda_x = \Lambda_0$ as a first approximation on the right hand side and repeating the calculation until Λ_x is constant. The value of γ which results may be used in the limiting Debye-Hückel equation written in the form

$$-\log f_{\pm} = Az^2\sqrt{I} = Az^{\frac{5}{2}}\sqrt{\gamma C}.$$

By substituting the values of f, c and γ in (28), K may be calculated. This procedure is repeated for each measured concentration and a constant value of K is an indication of a correct choice of equilibrium.

Conductance data may also be used to provide both K and Λ_0 in cases where the latter may not be readily available. Using the same basic assumptions as above, Fuoss[39] chose a preliminary value of Λ_0 from a rough extrapolation of a $\Lambda - \sqrt{C}$ plot, and calculated γ and f. These were then substituted in the equation

$$f\sqrt{C} = \sqrt{zK}\sqrt{X} \quad \ldots\ldots\ldots\ldots (31)$$

which is derived by rearranging equation (28) putting $X = \frac{1-\gamma}{\gamma^2}$. A correct value of Λ_0 results in a straight line of zero intercept on the $f\sqrt{C}$ axis, and gradient $\sqrt{zK}$. Λ_0 is varied and the procedure repeated until a plot satisfying these conditions is found when the dissociation constant may be evaluated./

evaluated.

This procedure is obviously tedious, and time consuming, when done manually and a more rapid method has been given by Fuoss[43].

The degree of dissociation was written

$$\gamma = \frac{\Lambda}{\Lambda_0\left\{1-(\alpha\Lambda_0+\beta)(\gamma C)^{\frac{1}{2}}/\Lambda_0\right\}} \quad \ldots\ldots (32)$$

The terms in $\{\ \}$ brackets were replaced by a function F(z) where

$$F(z) = 1 - Z\left(1 - Z\left(1-Z\left\{\ldots\right\}^{-\frac{1}{2}}\right\}^{-\frac{1}{2}}\right\}^{-\frac{1}{2}} = \frac{4}{3}\cos^2\frac{1}{3}\cos^{-1}\left[\frac{-3\sqrt{3}z}{2}\right]$$

and

$$Z = (\alpha\Lambda_0+\beta)\left(\frac{\Lambda C^{\frac{1}{2}}}{\Lambda_0^{3/2}}\right)$$

i.e.

$$\gamma = \frac{\Lambda}{\Lambda_0}F(z)$$

Tables have been constructed[43] of F(z) and Z, so that having chosen a Λ_0 value, γ and f may be found quickly. Substitution of (32) in (28) leads to the the expression

$$\frac{F(z)}{\Lambda} = \frac{1}{\Lambda_0} + \frac{C\Lambda f^2}{F(z)Kz\Lambda_0^2}$$

A plot of $\frac{F(z)}{\Lambda}$ vs $\frac{C\Lambda f^2}{F(z)}$ gives a new value of Λ_0 from the intercept and this process is repeated until a consistent Λ_0 is obtained when K may be evaluated from the slope.

In Shedlovsky's treatment[40] a slightly different form of the limiting conductance equation was used,

$$\Lambda = \Lambda_0 - (\alpha\Lambda_0+\beta)\frac{\Lambda}{\Lambda_0}\sqrt{C},$$

and a solution for γ was found in terms of a function

$$S(z) = \left(\frac{z}{2} + \sqrt{1+\left(\frac{z}{2}\right)^2}\right)^2 ,$$

leading to an equation of the form

$$\frac{1}{\Lambda} = \frac{1}{\Lambda_0} + \frac{C\Lambda S(z) f^2}{z K_s \Lambda_0^2} \quad \ldots\ldots\ldots\ldots\ (33)$$

Values of Λ_0 and K were obtained by similar plotting procedures. The relationship between the Fuoss and Shedlovsky constants, K_f and K_s respectively, has been shown[44] to be

$$\frac{1}{K_S} = \frac{1}{K_F} + \frac{(\alpha\Lambda_0 + \beta)^2}{\Lambda_0^2}$$

Where $K > 10^{-3}$ the Shedlovsky value is to be preferred since the limiting conductance equation used by him agrees with observed conductivities over a larger concentration range. Where $K < 10^{-3}$ the two methods are equivalent and give K values which agree within experimental error.

Recently, Wirth[41] has suggested a modification of the Fuoss method in which γ in the denominator of equation (32) is replaced by $\frac{\Lambda}{\Lambda_0}$. The equation may be then written

$$\gamma = \frac{\Lambda}{\Lambda_0 W(z)}$$

where $W(z) = 1 - Z$, which leads to an equation

$$\frac{W(z)}{\Lambda} = \frac{1}{\Lambda_0} + \frac{C\Lambda f_{\pm}^2}{W(z) K z \Lambda_0^2} ,$$

in which f is calculated by means of extended form of the Debye-Hückel equation for activity coefficients.

From/

From equations (28) and (29) Ives[42] derived the expression

$$\Lambda - \Lambda_x = \frac{-\Lambda^2 f^2 c}{\Lambda_x z K},$$

and when Λ_0 is added to each side this becomes

$$\Lambda + (\alpha\Lambda_0 + \beta)\sqrt{\gamma c} = \Lambda_0 - \frac{\Lambda^2 f^2 c}{\Lambda_x z K},$$

which is of the form

$$Y = \Lambda_0 - \frac{X}{K}$$

Λ_0 is obtained by least squares and the calculation repeated until constant values of Λ_0 and K are obtained.

The methods given above are all restricted to cases where deviations from the Onsager equation are large, and ion association effects are very much greater than the approximations involved in the original conductance equation The most recent advance has been the application of the Fuoss Onsager conductance equation[45], to the problem of ion association in cases where the extent of association is small.

Fuoss and Onsager wrote the conductance equation for unassociated electrolytes in the form

$$\Lambda = \Lambda_0 - Sc^{\frac{1}{2}} + Ec\log c + J_1 c(1 - \alpha c^{\frac{1}{2}})\left(1 - \frac{J_2 c^{\frac{1}{2}}}{J_1}\right),$$

Where S was the Onsager slope E dependent on properties of solvent but independent of ion size and J_1 and J_2 functions of ion size. Fuoss[46] used the above equation to describe the conductance due to the free ions in solutions of and associated electrolyte by rewriting in the form

$$\Lambda_x = \Lambda_0 - S(\gamma c)^{\frac{1}{2}} + E\gamma c\log\gamma c + J_1\gamma c(1 - \alpha(\gamma c)^{\frac{1}{2}})\left(1 - \frac{J_2(\gamma c)^{\frac{1}{2}}}{J_1}\right),$$

and when this was used in conjunction with the extended Debye-Hückel equation for activity coefficients a graphical method for deriving K, 'a' and Λ_o for 1:1 electrolytes in water-dioxan mixtures was described.

Fuoss and Kraus[48] showed that where K was less than 10^{-2}, earlier methods, which made use of limiting laws could be adopted without great loss in accuracy; this was also found by Nash and Monk[49]. Since 3:3 electrolytes had been shown [34] to have dissociation constants of the order of 10^{-4}, the use of one of the earlier methods in the present work was justified. Although the original Fuoss method[39] is extremely tedious, when done manually, the reiterative mathematical operations involved are ideally suited for a high speed computer. A programme has been constructed for the Deuce high speed electronic computer, which enables Λ_o and K values to be calculated rapidly from Λ and $\sqrt{C}$ data.

Determination of Λ_o

The determination of Λ_o by the methods outlined above places a great deal of reliance on the applicability of the limiting Onsager and Debye Hückel laws to ionic solutions of finite concentration. It is therefore fortunate that other methods are available for measuring Λ_o

The/

The original method for deriving Λ_0 from conductivity data was simply to construct a Λ-$\sqrt{c}$ plot and extrapolate to zero concentration. For highly dissociated electrolytes at low concentrations this leads to values of Λ_0 which are reasonably accurate. Owen[50] has proposed a more sensitive determination of Λ_0, based on a conductance equation

$$\Lambda = \Lambda_0 - Sc^{\frac{1}{2}} + Ac\log c + Bc ,$$

which may be rewritten in the form

$$\frac{\Lambda + Sc^{\frac{1}{2}} - \Lambda_0}{c} = A\log c + B \quad . \; . \; . \; . \; . \; (34)$$

A plot of the left-hand side of (34) against log C will be linear for a correctly chosen Λ_0. At low concentrations it is highly sensitive to small changes in Λ_0, and the method has been shown to be applicable to partly associated electrolytes[51].

Where association is appreciable this method is rather insensitive to changes in Λ_0 and it is better to obtain it from mobility data for the corresponding strong electrolytes. It becomes increasingly difficult to find such completely dissociated salts in solutions of low dielectric constant, and Walden's rule[52] ($\Lambda_0 \eta_0 = \text{const.}$) may be used in such cases. Such calculations are however necessarily approximate since the rule is based on the application of Stokes' law to the motion of an ion through solvent molecules which are in most/

most cases of comparable size. Where K and Λ_0 are calculated simultaneously much more reliance may be placed on the former, if the latter is in agreement with a limiting conductance derived by an independent method.

While the treatment of symmetrical electrolytes has so far been discussed exclusively, it should be mentioned that conductivity measurements have been applied successfully to the treatment of unsymmetrical electrolytes, although there is the obvious difficulty of assigning a conductivity to the charged product of ion association. The normal practise is to assume that the limiting conductance is some fraction of the conductance of one of the ions involved. Thus Jenkins and Monk[53] assumed $\frac{\lambda^0 La^{3+}}{3} = \lambda^0 LaSO_4^+ = 23{\cdot}2$, whereas Spedding and Jaffe[54] assumed $\frac{\lambda^0 SO_4^=}{2} = \lambda LaSO_4^+ = 40$. Since both treatments gave very similar dissociation constants the mobility of the ion pair does not greatly influence the calculated dissociation constant.

APPARATUS

AND

EXPERIMENTAL TECHNIQUE

Measurement of Resistance.

Resistances were measured on an a-c screened Wheatstone bridge of the type described by Jones and Joseph[55] and by Shedlovsky[56], which incorporated the modifications for minimising capacitance and inductance effects arising from various parts of the bridge network. The circuit is shown in fig. 17. R_1 was the conductivity cell and R_2 a Sullivan non reactive resistance, the total resistance being subdivided into 10^5 parts by two concentric dials. The output from the bridge was amplified before passing to the Earphones by a twostage high gain mains operated Sullivan amplifier. A mains operated oscillator (Advance model H-1), which gave frequencies from 15 to 15,000 cycles per second, was placed about eight feet from the bridge to prevent interaction, and measurements were normally taken at a frequency of 1000 cycles per second, this being the optimum frequency. The oscillator was connected to the bridge by screened and grounded leads via a Sullivan balanced and screened transformer, which was designed to screen the supply source from the bridge without upsetting the balance of the latter to earth. A considerable improvement in the sharpness of the sound minimum in the detector was effected by earthing the bridge. A modified Wagner earth, described by Jones and Joseph[55], ensured the telephone/

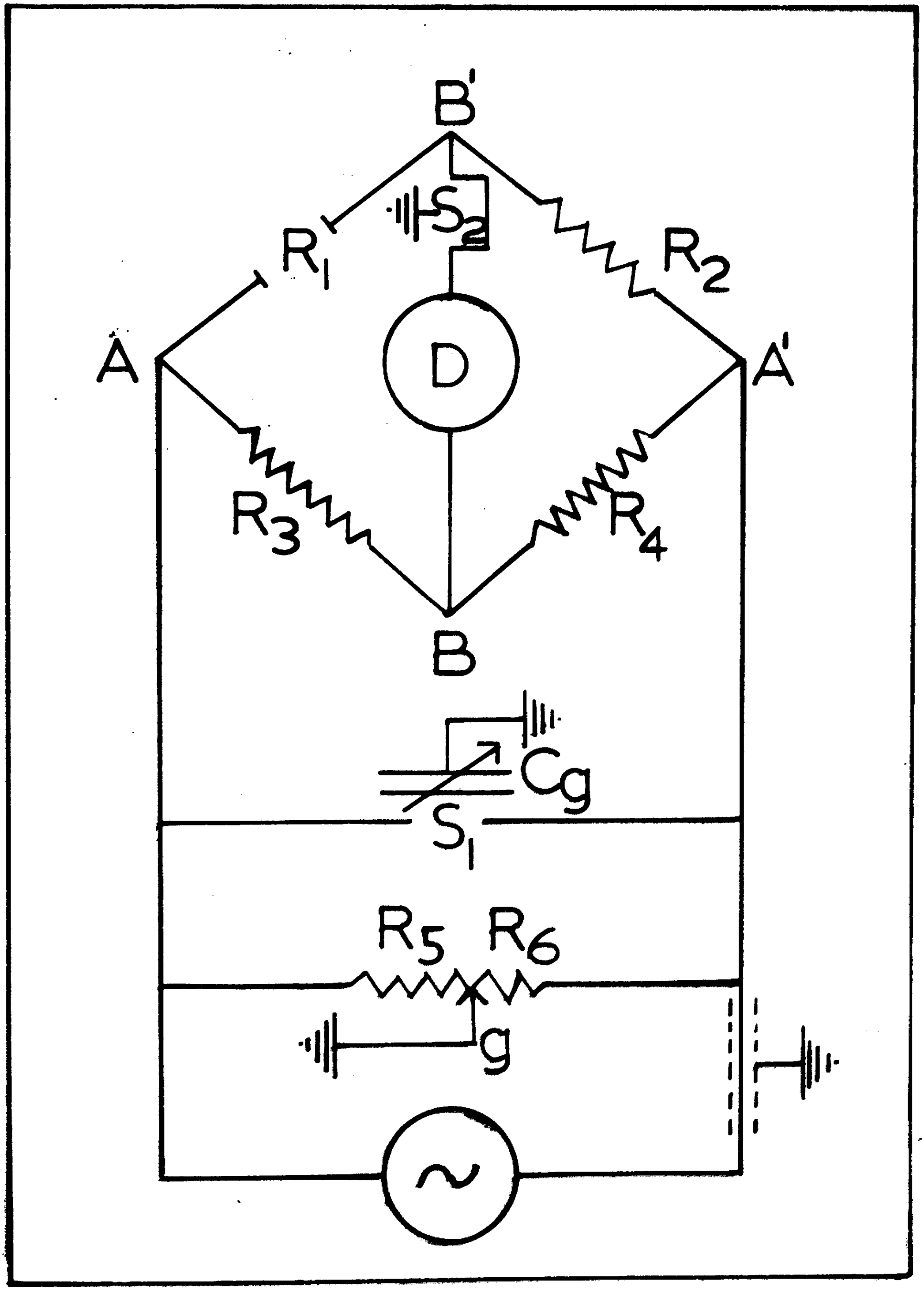


Fig.17

telephone earpiece being maintained at ground potential, thus eliminating any leakage of current due to capacity between the operator and the telephone coils. The Wagner earth is represented in the figure by the resistances R_5, R_6, the contact g and the variable condenser C . The bridge was balanced in the usual way and the detector was connected to ground by switch S_2. B was then brought to ground potential by adjustment of the contact g . The bridge was again balanced and the process repeated if there was any change. During the latter part of this work the amplifier and ear-phones were replaced by a tuned amplifier and null detector (General Radio Company type 1232-A).

Since the cell acts as a condenser it was necessary to balance out the capacity effects associated with it. This was done by means of a Sullivan decade stable mica condenser reading from 0 to 0.01 μF connected across either R_1 or R_2. The cell was connected to the bridge by taking leads from the electrodes to two mercury cups supported in the thermostat. This prevented heat interchange between the cell and the room. The copper leads were of equal length and thickness to minimise resistance effects. The connections to the cell and the resistance box were interchangeable by means of a mercury commutator of the rocking type. When pure solvent and/

and solutions of high resistance were being measured, a 10,000 ohm, non-reactive, standard resistance was connected in parallel with the cell.

Thermostat and Temperature Control.

The thermostat was a large, earthed and heat insulated metal tank filled with transformer oil to reduce capacity errors[56]. Stirring was effected by an electrically operated multiple paddle stirrer. The temperature of the bath was controlled by a mercury-toluene spiral regulator, connected in series with a 60 watt bulb through a vacuum relay. The temperature was measured by means of a Beckmann thermometer which had been standardised against a calibrated platinum resistance thermometer[57] and control was accurate to ± 0.005°C. The complete conductivity apparatus was kept in a constant temperature room thermostated to 25°C, which prevented excessive condensation in the conductivity cell cap.

The Conductivity Cell.

This was of the Hartley-Barret[58] type, and was constructed from pyrex glass. The body had a capacity of about 400 ml, and the cap carried the electrodes, an aperture to allow additions of solutions, and a side arm fitted with a three way stop cock, which enabled CO_2-free, solvent saturated air to be passed over the surface of solutions. The cap and body were joined in the same position relative to one another for each experiment by aligning marks on the male and female joints.

The electrodes which were lightly coated with platinum black[47] were held at a fixed distance from one another by four small pyrex glass rivets, and were connected to the electrode supports by platinum wires. Since it is not possible to seal platinum into glass, a little Araldite epoxy resin was set in the bottom of each support. This provided a permanent seal which prevented leakage of mercury into the cell solution.

The Carbon Dioxide Free Air Supply.

For accurate conductivity measurements it is important that solvents should be as free as possible from conducting impurities. In studies in aqueous solvents the most persistent impurity is carbon dioxide which forms the weakly dissociated carbonic acid on dissolution in water. This may be prevented by passing a current of CO_2-free air over the cell solutions for the duration of the experiment.

Carbon dioxide free air was produced by filtering the available compressed air supply through a jar of cotton wool, bubbling through 2N Sulphuric acid to remove ammoniacal vapours, and passing through a series of towers packed with glass beads containing 50% potassium hydroxide. The air was then passed through a water scrubber and a column of pure solvent. Before entering the cell, the air was bubbled through pure solvent in a presaturator supported in the thermostat.

Purification of solvents.

Distilled water was deionised by passing it through a mixed bed resin[59]. The resins used were Amberlite 1R 120 (H) acid resin and Amberlite 1RA 140 basic resin intimately mixed in a proportion 1:2 by volume. Water of specific conductivity less than 0.15 gemmhos was obtained by this method.

Dioxan was purified by the method of Kraus and Vingee[60]. Commercially obtainable "pure" 1:4 dioxan (L.Light and Co.Ltd.) was refluxed over metallic sodium for several days in an all glass apparatus carrying a silica gel guard tube. It was then distilled and refluxed with fresh sodium. This procedure was repeated until the sodium metal remained bright. Prior to use the pure dioxan, thus obtained, was refluxed over sodium for several hours and distilled directly into the flask in which the mixed solvent was to be prepared.

Filling the Cell.

After rinsing the cell several times with conductivity water a stream of pure air was passed through for about 15 minutes and it was then filled directly from the resin column. The cell and contents were weighed, placed in the thermostat and connected to the supply of presaturated pure air. It was gently shaken at frequent intervals and the water resistance noted. After becoming constant, no further change in resistance occurred for periods of up to 8 hours.

The above procedure was modified in mixed solvent runs. Purified dioxan, which had been refluxed over sodium for several hours was distilled directly into the weighed stock flask, and after reweighing, a known amount of conductivity water was added to give the required mixed solvent composition. Carbon dioxide was then removed by bubbling presaturated pure air through the mixed solvent for about 1 hour. (Fig.18) The cell was then rinsed several times by blowing over small quantities of solvent, and finally filled quickly, weighed, and placed in the thermostat. Once again equilibrium was attained within a short time.

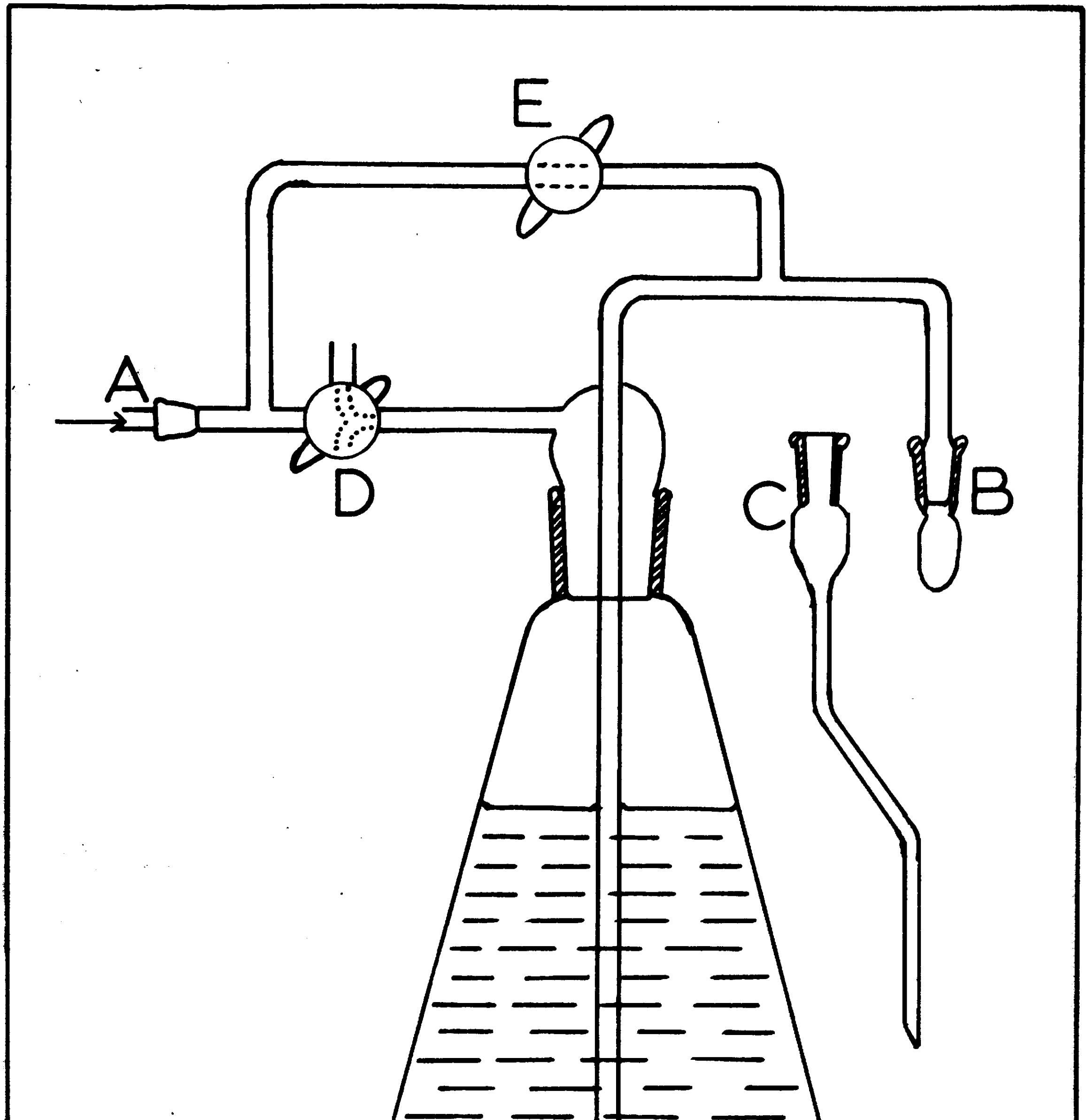


Fig.18

Preparation of Stock Solutions.

A sample of the solid substance in a small glass tube was weighed by difference into a clean, steamed out and weighed Pyrex flask. A suitable amount of conductivity water was added and the flask and contents re-weighed. In the preparation of mixed solvent solutions the salt was dissolved in water and the appropriate amount of dioxan was added. This procedure was adopted because of the extremely slow rate of dissolution of $La\,Co(CN)_6$ in water-dioxan mixtures, compared with the rate of dissolution of the salt in water alone.

Measurement of Conductivity.

When the solvent in the cell had reached equilibrium, a weight of stock solution, never less than 1g., was added by means of a weight burette through the aperture in the cell cap. The cell was then shaken at intervals and solution resistance normally became constant within an hour. For two settings of the resistance box, R_2, the specific conductivities, calculated from ratio arm measurements, normally agreed to within 0.01%.

Four or five additions from the weight burette were normally made during a run, at the end of which the cell was removed and weighed. This provided a means of detecting any evaporation/

evaporation which had occurred, and this never amounted to more than about 0.03%.

In view of the limited solubility of the neodymium and gadolinium salts the normal dilution method provided concentrations of less than 3×10^{-4}N in the cell. For measurements at higher concentrations it was therefore necessary to prepare a stock solution in the cell, after noting the solvent resistance, by weighing the salt directly into the cell. Additional points could be obtained by adding pure solvent from a weight burette.

Cell Constant Determination.

B.D.H. Analar potassium chloride was recrystallised three times from conductivity water, drained as free as possible from the mother liquor, and dried at 100°C. Prior to use in cell constant determinations the crystals were heated to dull redness in a platinum dish, which was allowed to cool in a dessicator.

The cell was standardised by the method of Fraser and Hartley[61]. Several series of resistance measurements were made on potassium chloride solutions, in the concentration range subsequently to be used. Conductivities were corrected, where necessary for interionic attraction effects. The cell constant was then found by comparing each measured value with the conductivities derived from the equation[62]

$$\Lambda = 149{\cdot}92 - 93{\cdot}85\sqrt{C} + 50C$$

Seven cell constant runs gave a mean value of 0.07360 with a mean deviation of 0.02%.

Preparation of Rare Earth Salts.

Potassium cobalticyanide was prepared by the oxidation, with pure air, of a solution containing an equivalent mixture of B.D.H. "Analar" cobaltous chloride and "Analar" potassium cyanide. The resulting solution was filtered and carefully neutralised with dilute acetic acid. Dioxan was then added dropwise with constant stirring, until the bulk of the cobalticyanide had been precipitated. After washing with water-dioxan mixture and pure acetone, the precipitate was air dried. The crude product was purified by dissolving in a small amount of conductivity water, partially precipitating with dioxan and washing and drying as before. This process was repeated three times and the final product was dried over phosphorus pentoxide.

Potassium ferricyanide was prepared by recrystalisation of the Analar material three times from conductivity water.

The rare earth salts were prepared by the method of James and Willard[63]. A strong solution of lanthanide chloride was made by dissolving the appropriate oxide in the stoichiometric amount of constant boiling hydrochloric acid, and to this solution, at 60°C, was, added a solution containing the calculated amount of potassium ferricyanide or cobalticyanide. The salts were precipitated almost immediately/

ly and since they were of limited solubility, they were not recrystallised but were washed extensively with conductivity water. On drying over phosphorus pentoxide, constant weight was attained in about two weeks. Analysis for the rare earth was made[63] and in each case corresponded to a salt composition of $L^{3+}X^{3-}\cdot 4H_2O$ (Table XVIII). This is in agreement with the findings of James[64] who prepared lanthanum ferricyanide and cobalticyanide in the form of the pentahydrate by drying over the partially dehydrated salt. James observed that on drying over concentrated sulphuric acid, there was a loss in weight which corresponded to the loss of one water molecule from the pentahydrate. It is of interest to note that the salts prepared by Atkinson[36] were dried over concentrated sulphuric acid, but were reported as having a general formula $R\,Co\,(CN)_6 5H_2O$.

Table XVIII

Analysis of Rare Earth Salts.

Salt	% Rare Earth.	
	Calc.($RX.4H_2O$)	Found
$LaCo(CN)_6$	32·61	32·45
$LaFe(CN)_6$	31·36	31·30
$NdFe(CN)_6$	33·69	33·76
$GdFe(CN)_6$	35·58	35·45

RESULTS.

Lanthanum cobalticyanide.

The conductivity of dilute lanthanum cobalticyanide solutions in water and in 10% and 20% (W/W) dioxan-water mixtures has been measured at 25 ± 0.005°C. The phoreograms shown in figs. 19 and 20 were constructed from the data of Tables XIX, XX and XXI. For purposes of comparison fig. 19 includes a few of the data of James and Monk[65] for lanthanum cobalticyanide in water. The data of Atkinson[36] for the salt in 10% and 20% dioxan-water mixtures are shown in fig. 20. Calculation of K and Λ_0, shown in these tables, was done by the method of Fuoss[39], for which a suitable computer programme was constructed. From Λ and $\sqrt{C}$ data, and an approximate starting value for Λ_0, the value of Λ_0 was computed for which a plot of equation (31) showed linearity and had a zero intercept on the $f\sqrt{C}$ axis. Using this value of Λ_0, a K value was calculated for each conductivity measurement.

The limiting forms of the Onsager, and Debye-Hückel equations are written

$$\Lambda = \Lambda_0 - (\alpha\Lambda_0 + \beta)C^{\frac{1}{2}}$$

and

$$\log f \pm = - AC^{\frac{1}{2}},$$ respectively, and when recent values of physical constants[66], and viscosity and dielectric constant data for water-dioxan mixtures[67] are incorporated, the/

the numerical values of α, β and A at 25°C, shown in table XXII, are obtained.

Rare earth ferricyanides.

The conductivity of dilute aqueous solutions of lanthanum, neodymium and gadolinium ferricyanide has been measured at 25± 0.005°C. The phoreograms shown in fig. 21 were constructed from the data of tables XXIII, XXIV and XXV. Use of the computer programme gave the K and Λ_0 values shown.

Table XXII

%Dioxan	α	β	A
0	3·5729	314·817	7·9453
10	4·2116	275·839	9·3656
20	5·1056	245·213	11·3536

Table XIX

The conductivity of lanthanum cobalticyanide in water at 25°C

$C \times 10^4$	$\sqrt{C} \times 10^2$	Λ	$K \times 10^4$	$\Delta K \times 10^4$
1.9455	1.3948	130.530	1.796	0.030
2.8164	1.6782	123.718	1.829	0.003
3.7218	1.9292	118.189	1.844	0.018
0.8561	0.9253	144.308	1.850	0.024
1.4320	1.1967	136.545	1.860	0.034
0.8724	0.9340	143.847	1.819	0.007
1.8902	1.3749	130.906	1.778	0.048
3.5391	1.8813	118.826	1.809	0.017
5.3768	2.3188	110.254	1.831	0.005
2.4520	1.5659	126.618	1.845	0.019
1.7202	1.3116	133.321	1.855	0.029
1.6123	1.2698	133.823	1.784	0.042
0.5882	0.76691	148.861	1.817	0.009
0.9788	0.9894	142.186	1.817	0.009
1.7226	1.3125	133.118	1.835	0.009
2.4861	1.5768	126.439	1.854	0.028

$\Lambda_0 = 166.98$, Mean K $= 1.826 \pm 0.021 \times 10^{-4}$

Table XX

The conductivity of lanthanum cobalticyanide in 10% dioxan-water at 25°C.

$C \times 10^4$	$\sqrt{C} \times 10^2$	Λ	$K \times 10^5$	$\Delta K \times 10^5$
0.7045	0.8393	107.861	7.822	0.400
1.0112	1.0056	102.734	8.058	0.164
0.3273	0.5721	117.967	8.114	0.108
1.6231	1.2740	95.459	8.389	0.167
2.3145	1.5214	89.251	8.436	0.214
0.2818	0.5308	120.636	9.345	1.123
0.6448	0.8030	109.789	8.202	0.020
0.9791	0.9895	103.304	8.084	0.138
1.4731	1.2137	96.687	8.180	0.042
2.5262	1.5893	87.120	8.207	0.015
1.5175	1.2318	95.927	8.070	0.152
2.9211	1.7091	84.327	8.150	0.072
4.0906	2.0225	78.380	8.223	0.001
5.2119	2.2829	74.005	8.209	0.013
0.49010	0.7001	112.963	7.886	0.336
1.0251	1.0124	102.592	8.096	0.126
1.5780	1.2561	95.572	8.216	0.006
2.1271	1.4584	96.462	8.302	0.080

Λ_0 = 133.98, Mean K = 8.222 ± 0.12 x 10^{-5}

Table XXI.

The conductivity of lanthanum cobalticyanide in 20% dioxan-water.

$C.10^4$	$\sqrt{C}.10^2$	Λ	$K.10^5$	$10^5.\Delta K$
2.1811	1.4769	54.188	2.470	0.054
2.6680	1.6334	51.231	2.484	0.040
3.5814	1.8925	47.141	2.510	0.014
0.4237	0.6509	80.259	2.426	0.098
0.8630	0.9290	68.978	2.446	0.078
1.3567	1.1647	61.707	2.467	0.057
0.1491	0.3861	94.281	2.443	0.081
0.7088	0.8419	72.410	2.474	0.050
1.3657	1.1686	61.862	2.502	0.022
2.0098	1.4177	55.863	2.526	0.002
2.5613	1.6004	52.321	2.551	0.027
4.8484	2.2020	43.445	2.573	0.049
0.6485	0.8053	74.732	2.603	0.079
1.0314	1.0156	67.058	2.587	0.063
1.4513	1.2047	61.430	2.579	0.055
2.8630	1.6921	50.234	2.491	0.033
3.5209	1.8764	47.345	2.505	0.019
0.6791	0.8241	73.866	2.585	0.061
1.4522	1.2051	61.361	2.571	0.047
2.0437	1.4296	55.957	2.575	0.051
0.8001	0.8945	71.253	2.593	0.069
1.5947	1.2628	60.230	2.624	0.100
2.3002	1.5167	53.362	2.469	0.055
2.9090	1.7056	50.251	2.526	0.002

Λ_0 = 111.06, Mean K = 2.524 ± 0.05 x 10^{-5}

Figure 19.

The conductivity of Lanthanum Cobalticyanide in Water at 25 ± 0.005°C

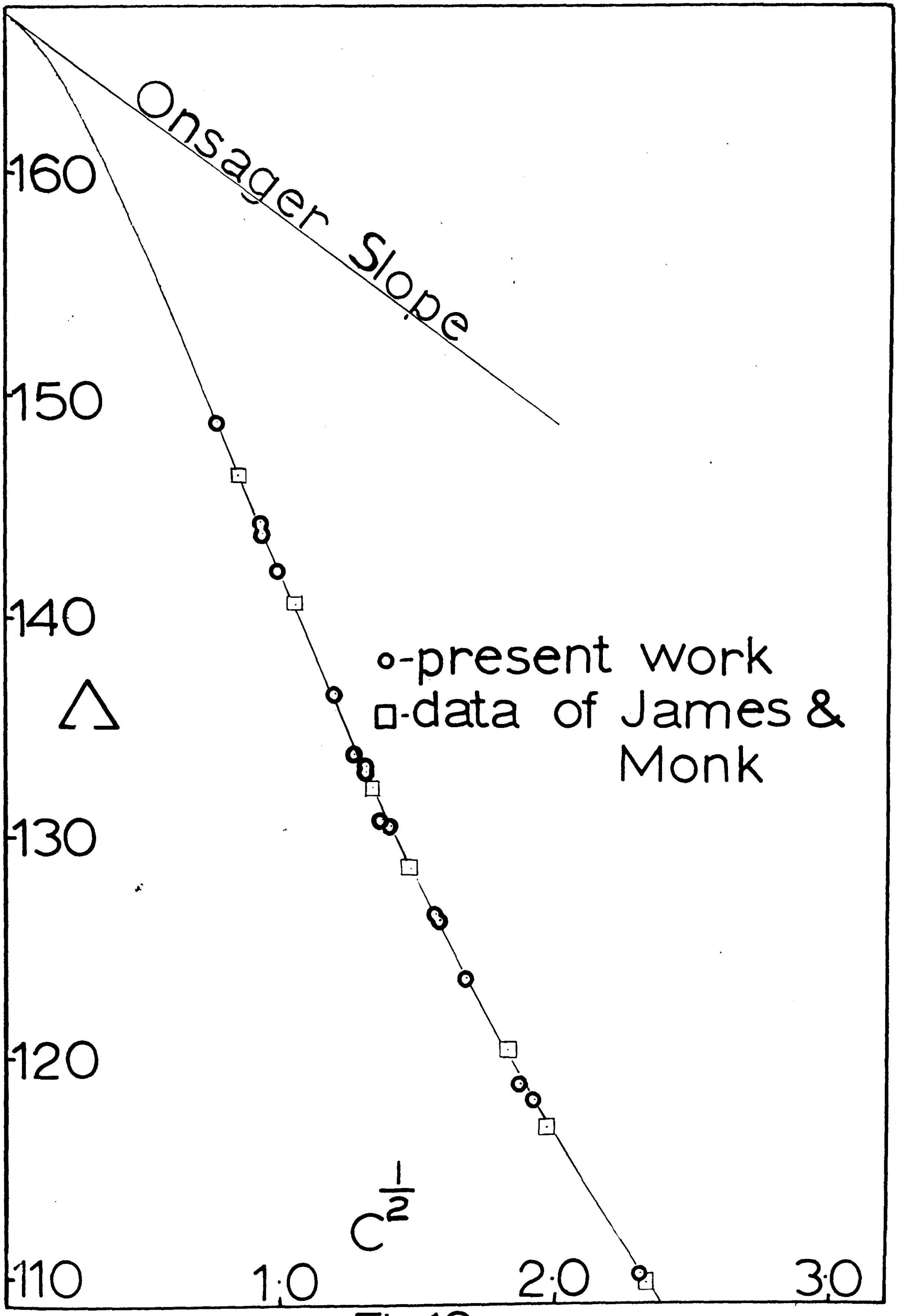

Onsager Slope
160
150
140
130
120
110
Δ
o-present work
□-data of James & Monk
$C^{\frac{1}{2}}$
1.0
2.0
3.0

Fig.19

Figure 20.

The conductivity of Lanthanum Cobalticyanide in mixed solvents at 25 ± 0.005°C

A - 10% dioxan-water (W/W).

B - 20% dioxan-water (W/W).

✤ - Atkinson's data[36].

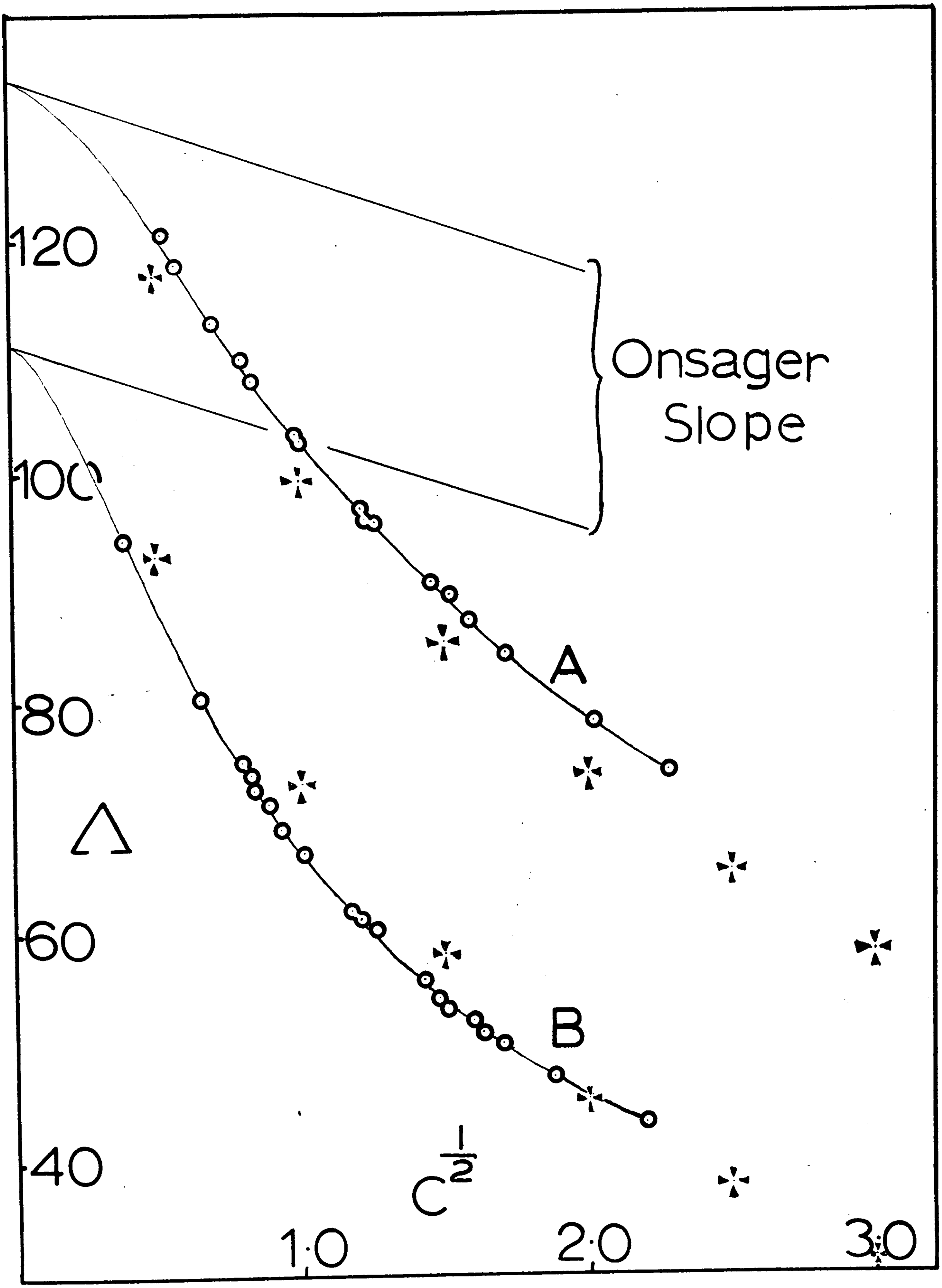


Fig. 20

Table XXIII

The conductivity of lanthanum ferricyanide in water at 25°C

$C.10^4$	$\sqrt{C}.10^2$	Δ	$K.10^4$	$\Delta K.10^4$
0.9794	0.9896	144.328	1.8049	0.0106
2.2629	1.5043	130.074	1.8320	0.0165
3.3378	1.8269	122.200	1.8294	0.0139
4.4313	2.1051	116.327	1.8401	0.0356
6.2455	2.4991	108.451	1.8051	0.0104
5.4459	2.3337	111.265	1.7925	0.0230
5.2560	2.2925	112.268	1.8098	0.0057
1.2034	1.0970	141.175	1.8114	0.0041
1.7241	1.3131	135.216	1.8354	0.0199
2.3509	1.5333	129.577	1.8558	0.0403
0.8094	0.8997	146.991	1.7825	0.0330
2.0501	1.4318	131.810	1.8160	0.0005
2.9914	1.7295	124.338	1.8181	0.0026
2.1544	1.4678	130.414	1.7736	0.0419
4.1950	2.0482	117.329	1.8261	0.0106

Δ_o = 169.57 , Mean K = 1.8155 ± 0.017 x 10^{-4}

Table XXIV

The conductivity of neodymium ferricyanide in water at 25°C

$C \times 10^4$	$\sqrt{C} \cdot 10^2$	Λ	$K \times 10^4$	$\Delta K \times 10^4$
0.8975	0.9474	145.406	1.7943	0.0471
1.4379	1.1991	138.210	1.8261	0.0153
1.8650	1.3656	133.814	1.8516	0.0102
2.6755	1.6357	127.141	1.8781	0.0367
1.2067	1.0985	141.318	1.8503	0.0189
1.7366	1.3178	135.046	1.8441	0.0027
1.5465	1.2436	136.320	1.7585	0.0829
2.1607	1.4699	130.464	1.7947	0.0467
3.1219	1.7669	123.331	1.8169	0.0245
4.2825	2.0694	116.976	1.8421	0.0007
0.6774	0.8230	149.369	1.8198	0.0216
1.2900	1.1358	139.977	1.8190	0.0224
2.4728	1.5725	128.287	1.8385	0.0029
3.4893	1.8680	121.515	1.8600	0.0186
0.6459	0.2542	165.560	2.0960	0.2546
0.3247	0.5698	158.690	1.7720	0.0694

$\Lambda_0 = 169.42$, Mean K = $1.8414 \pm 0.042 \times 10^{-4}$

Table XXV

The Conductivity of Gadolinium Ferricyanide in water at 25°C

$C.10^4$	$\sqrt{C}.10^2$	Λ	$K \times 10^4$	$\Delta K \times 10^4$
4.1588	2.0393	115.082	1.817	0.006
4.3314	2.0812	114.276	1.821	0.010
0.2924	0.5408	154.994	1.831	0.020
0.5507	0.74207	148.801	1.775	0.036
0.3458	0.58801	153.656	1.836	0.025
0.5880	0.7668	148.319	1.825	0.014
1.3814	1.1754	136.080	1.800	0.011
2.6234	1.6197	124.370	1.805	0.006
2.3972	1.5483	125.990	1.792	0.019

$\Lambda_0 = 166.33$, Mean K = $1.811 \pm 0.016 \times 10^{-4}$

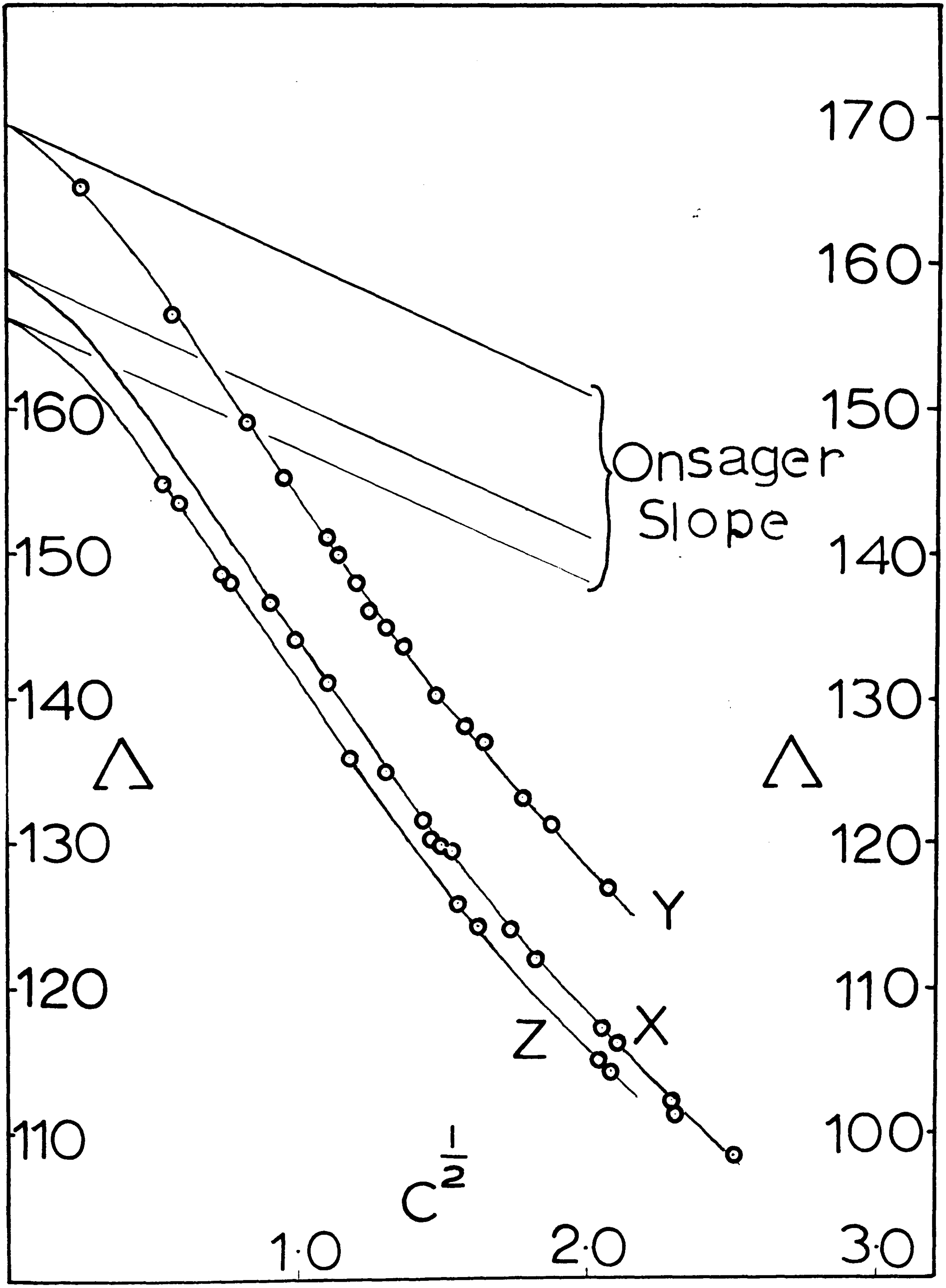
Figure 21.

The conductivity of rare earth ferricyanides in water at 25 ± 0.005°C

X – Lanthanum Ferricyanide.

Y – Neodymium Ferricyanide (righthand Λ axis)

Z – Gadolinium Ferricyanide.



Onsager
Slope
Y
X
Z
Λ
Λ
$C^{\frac{1}{2}}$
160
150
140
130
120
110
170
160
150
140
130
120
110
100
1·0
2·0
3·0

Fig.21

DISCUSSION.

The relationship between the dissociation constant of an electrolyte and the dielectric constant of a solvent is expressed by the equations[31]

$$K^{-1} = \frac{4\pi N}{1000}\left\{\frac{|Z_1 Z_2| e^2}{kDT}\right\}^3 Q(b) \quad \ldots\ldots\ldots(35)$$

and

$$b = \frac{|Z_1 Z_2| e^2}{\text{"a"} DkT} \quad \ldots\ldots\ldots(36)$$

where K is the dissociation constant, D the dielectric constant, "a" the mean distance of closest approach of the ions of charge Z_1 and Z_2, and

$$Q(b) = \int_2^b e^Y . Y^{-4}\, dY$$

For 3-3 electrolytes, writing equations (35) and (36) in logarithmic form,

$$-\log K = 8.9906 - 3\log D + \log Q(b) \quad \ldots\ldots\ldots(37)$$

$$-\log b = 4.2973 + \log D + \log \text{"a"} \quad \ldots\ldots\ldots(38)$$

Hence when the measured dissociation constant and the appropriate values of D are substituted in (37), log Q(b) may be calculated and b interpolated from tabulated b vs log Q(b) data[68]. "a" may then be obtained by substitution in (38)

Table XXVI

% Dioxan	Λ_o	$K.10^4$	% Mean Deviation	"a" (Å)
0	166.98 (1)	1.826	± 1.1	7.31
	167.20 (2)	1.799	± 0.9	7.28
	166.51 (3)	1.797	± 4.1	7.28
10	133.98 (1)	0.8222	± 1.5	7.27
	134.50 (3)	0.6143	± 5.6	6.85
20	111.06 (1)	0.2524	± 2.0	7.15

(1) Present Work.

(2) James and Monk.[65]

(3) Atkinson.[36]

Lanthanum Cobalticyanide.

Table XXVI shows the "a" values obtained in the present work and also those computed from the data of James[65] and of Atkinson[36]. As was to be expected from the phoreograms, the constants derived for the salt in water were in good agreement, although the mean deviation in K was somewhat larger for Atkinson's data.

When the constants calculated for different solvents are examined it may be seen that while in the present work there is a change of only 0.15Å in the "a" value, there is a difference of 0.42Å in "a" between Atkinsons water and 10% dioxan results, and the mean deviation in his dissociation constant for the latter solvent is once again very large.

Atkinson's results at 20% dioxan were recalculated by Monk[37] who showed that for the reported Λ_0 (=116.6), K decreased steadily as the concentration increased, and it was suggested that the use of a higher Λ_0 value might give a better fit. Accordingly these data were recalculated in the present work using an impossibly large range of starting Λ_0 values, 111 to 141. It was impossible to obtain consistent results and this provides evidence that the apparent deviations from the Bjerrum theory reported by Atkinson/

Atkinson must have been due to a fault on an experimental nature.

The results of the present work would therefore suggest that lanthanum cobalticyanide exhibits no substantial deviation from the Bjerrum model of ion association in the range of solvent dielectric constants studied, which is in accord with James' results for lanthanum ferricyanide[34].

The Rare Earth Ferricyanides.

Atkinson[36] measured the donductances of several rare earth cobalticyanides and found that while the Λ_0 values agreed with those evaluated from independent ion mobilities, the dissociation constants differed considerably within the series for a given solvent. For example the dissociation constant for lanthanum cobalticyanide in water was approximately twice that for neodymium cobalticyanide, while the difference in Λ_0 for these salts was only 0.13 units. The close similarity in the limiting mobilities of lanthanum and neodymium ions suggests that the radii of the solvated ions must be very nearly the same and one would expect that the distance of closest approach and hence the dissociation constants for their salts in water would be very similar if association is due solely to electrostatic forces. Although Monk[37] pointed out that the actual values/

values of dissociation constants given by Atkinson are in error by a factor of three, due to the omission of z in the Shedlovsky equation (33), the relative values of dissociation constants remain unaltered. This would suggest that since association was more marked in neodymium cobalticyanide solutions, forces other than simple electrostatic were involved.

This was not to be expected from previous work[54] in which the dissociation constants of a number of lanthanide sulphates were measured in water and were found to be very similar. It seemed likely therefore, that Atkinson's experimental measurements were once again suspect. Accordingly conductance measurements for a series of lanthanide salts have been made.

Neodymium cobalticyanide was prepared, but it was found that its solubility (approximately 10^{-5}M) was much too low for accurate conductivity measurements to be made. Surprisingly, Atkinson reports conductivities for cell solution concentrations of 3 x 10^{-4}M. Since the rare earth ferricyanides are more soluble than the cobalticyanides, those of lanthanum, neodymium and gadolinium were used.

The Λ_0 values, 169.56, 169.42, and 166.33 for lanthanum, neodymium and gadolinium ferricyanides respectively are probably satisfactory. There is a considerable variation in values reported for the limiting conductance of the individual ions. Thus Hartley and Donaldson[69] for $Fe(CN)_6^{3-}$ give $\lambda_o = 100.9$ and James and Monk[65], 99.1. For La^{3+} the λ_o values vary from 69.5 to 69.7, for Nd^{3+}, 69.3 to 69.4; and for Gd^{3+}, $\lambda_o = 67.3$.[70-73]. For example lanthanum ferricyanide could be considered to have $\Lambda_o = 168.55$ or 170.60.

The important result of the present work is that the dissociation constants for lanthanum, neodymium and gadolinium ferricyanides in water at 25°C, 1.81×10^{-4}, 1.84×10^{-4} and 1.81×10^{-4} respectively, are the same within experimental error, which confirms the prediction that one would not expect to find large differences in the dissociation constants for a series of rare earth salts in the same solvent.

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SUMMARY.

Part I

The increased rate of hydrolysis of histidine methyl ester in the presence of copper (II) and nickel (II) ions has been investigated. Potentiometric studies have indicated that in the pH range in which ester hydrolysis proceeds, several ester-metal ion chelates may exist, depending on the relative concentrations of ester and metal ion. Formation constants for the chelates CuE_2^{2+}, CuE^{2+}, CuE^{+}, NiE_2^{2+} and NiE^{2+}, have been measured, where E represents the ester.

Kinetic studies have shown that in all cases hydrolysis proceeds via a simple bimolecular reaction between hydroxyl ion and ester, the latter being either free in solution or bound to metal ion. In the case of the 2:1 chelates the reaction involves two consecutive competitive reactions

$$ME_2^{2+} + OH^- \longrightarrow MEA^+$$
$$MEA^+ + OH^- \longrightarrow MA_2 ,$$

where A^- represents the anion of histidine, the hydrolysis product.

A comparison of the second order rate constants for the alkaline hydrolysis of the ester in the absence and presence of metal ions, has shown that metal ion catalysis is due to chelate formation which increases the reactivity of the ester towards hydroxyl ions. The overall catalytic effect may arise

in three ways:

1. Introduction of positive charge into the ester molecule
2. A statistical effect.
3. An electron withdrawal effect.

The introduction of positive charge into the vicinity of the ester molecule increases the chance of effective collisons. A statistical effect is introduced by the fact that more than one ester molecule may complex with the positively charged matal ion. In view of the consistent relative difference in the rates of hydrolysis of similarly charged copper and nickel chelates, an electron withdrawal, or inductive, effect which depends on the degree of interaction between metal ion and ester is also considered to contribute towards catalysis.

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Part II

The conductivity of lanthanum cobalticyanide in water and in 10% and 20% (W/W) dioxan water mixtures has been measured. Negative deviations fron the conductivities predicted by the Onsager equation have been attributed to ion pair formation and dissociation constants have been evaluated. Calculation of "a" the distance of closest approach of ions has shown that the Bjerrum theory of ion association adequately describes the behaviour of this salt in the range of dielectric constants studied, which is in accord with previous results for lanthanum ferricyanide.

The ferricyanides of lanthanum, neodymium and gadolinium, have been prepared and conductivity measurements have been used to evaluate dissociation constants for these salts in water. The close similarity in the dissociation constants confirm the prediction that one would not expect to find large differences for a series of rare earth salts in the same solvent.