CHAPTER - IV

Mixed-Ligand Complexes Containing Tertiaryamines and Ambivalent Secondary Ligands

In recent years considerable attention has been paid to the investigation of Copper(II) binary and ternary complexes containing the imidazole group as a ligand, since this is one of the important binding sites for copper in many biological systems. It was shown that histidyl residues in protein are typically nonchelating and therefore the ternary system of Cu(II) with unsubstituted imidazole as a ligand have been studied exhaustively.[12,139-145] It has also been explained that ligands co-ordinating through tertiary nitrogen as imidazole, histamine or histidine have N ----> M σ bond and also M ----> N π bond formation and this brings in interesting properties of these complexes.

Cu(II) complexes of imidazole also show a discriminating tendency in the formation of ternary complex i.e. it reacts preferably with oxygen donor ligands rather than nitrogen donor ligands.[143-147,52,91]

Imidazole is unidentate and histamine is bidentate, co-ordinating through one nitrogen and one amino nitrogen. Binary complexes of imidazole or histamine have been studied in detail by many workers.[26,148,149] Ternary complexes of the type [M 2,2'-dipyridyl L] are more stable than the complexes [M histamine L] complexes. This observation has been explained[91] in terms of the extent of M ----> A π interaction. Histamine has only imidazole ring, whereas bipyridyl has two pyridine rings over which π delocalization is possible. Hence

M ---> histamine π interaction is less than M ----> dipyridyl π interaction.

The importance of histidyl residues as metal binding sites in biological systems is well recognized. Many of these systems are enzymes and are mostly involved in oxygen transport[150-153] electron transfer[154,155] or oxygen activation.[155-159] The interaction of derivatives of histidine with metal ions has been extensively studied, particularly for Cu(II).[148,160,161]

Histidine is ambidentate in nature and shows more distinctive tridentate character than any other amino acid component of proteins. The three co-ordinating sites are imidazole nitrogen, amino nitrogen and carboxyl oxygen. Only metal ions with an octahedral co-ordination sphere can combine with two tridentate histidinate anion. With metal ion having a square-planar co-ordination sphere, histidine forms stable bis complex but has little tendency to form tris complex because of steric factor.[161,162] Binary complexes with histidine have been studied in detail by many workers.[144,161] In $\left[M(Histidine)_2\right]$ there are two possiblities:[159-168]

(i) Both the histidinate anions bind to the metal ion histamine like, i.e. from imidazole nitrogen and amino nitrogen.

(ii) Both the histidinate anions bound to the metal ion glycine like, i.e. the co-ordination is from amino nitrogen and carboxyl oxygen.

Hence, in Cu(II)-histidine binary system, there is possibility of two types of [Cu-histidine] (1 : 1) complexes, $[Cu(H\text{-}Hist)]^{2+}$ and $[Cu(Hist)]^{+}$, in which only two binding sites (amino acid site or histamine site respectively) are attached to the metal ion.[161-162] A third type of co-ordination was suggested earlier[166,167] considering that in the species [Cu(H.Hist)], co-ordination is from imidazole nitrogen and carboxyl oxygen, the amino nitrogen remaining unco-ordinated and protonated. However, this will give rise to a less stable seven membered ring. A crystal structure study[169] of the $[Cu(LH)_2]$ complex has shown that the co-ordination is from amino nitrogen and carboxyl oxygen as in amino acids, and the imidazole nitrogen remains protonated. It has been further confirmed by Pettit and coworkers[163] by the determination of formation constants in solution. In the species $[CuL]^{+}$, co-ordination is from amino nitrogen and imidazole nitrogen.[144,161] There may be a weak co-ordination of carboxyl oxygen also. The formation constants of various possible binary species such as [CuLH], [CuL], $[CuL_2H]$ and $[CuL_2]$ have been reported by several workers.[144,162,164]

It has been indicated by Pettit and coworkers that in the pH range 3.5 to 4.7 species [Cu(Hist)] is formed

with co-ordination from amino nitrogen and imidazole nitrogen. There may be a weak co-ordination of carboxyl oxygen also. At very low pH i.e. 1.8 to 3.2, there is formation of $[Cu(H.Hist)]$ species involving glycine like co-ordination and imidazole nitrogen remains protonated. Thus, initially there is formation of the species $[Cu(H.Hist)]$ or $[Cu(Hist)]$. At still higher pH range 4.1 to 6.0, there is co-ordination of the second histidinate moiety Hist or H.Hist respectively, resulting in the formation of $[Cu(Hist)(H.Hist)]$. In $[Cu(Hist)(H.Hist)]$ one histidine molecule binds to Copper(II) from imidazole nitrogen and amino nitrogen and other histidine molecule binds to the metal ion glycine like i.e. from amino nitrogen and carboxyl oxygen, imidazole nitrogen remaining protonated.

Ni(II) complex of histidine, $[Ni(hist)_2]$ is, however, known to be octahedral[170] with histidine acting as a tridentate ligand.

In the present investigation, we have studied mixed ligand complexes $[MAL]$, where M = Cu(II) or Ni(II), A = 5-nitro-1,10-phenanthroline (A^1), 2,2'-dipyridyl-ketone (A^2) or 2,2'-dipyridylamine (A^3) and L = histidine (L^{21}) or histamine (L^{22}) in 50% dioxan-water (1 : 1, v/v) medium at initially constant ionic strength 0.2M and temperature 30°C.

Experimental

Standardization of all the required solutions of metal perchlorate, sodium hydroxide, perchloric acid were done in the same way as detailed in chapter II A. The primary ligands (A^1 to A^3) were also of the same quality as detailed in chapter II A and secondary ligands were also of A.R. grade (BDH pure). The caliberation of microburettes, pipettes, pH-meter was done as stated earlier.

The titration data for 50% dioxan-water (1 : 1, v/v) medium are given in figures IVA 1 to IVA 12. The concentration of various reagents taken have been shown in the figures.

The formation constants of ternary complexes were determined using Irving-Rossotti titration technique. The values were refined by using computer program SCOGS. In the case of histidine the values were refined by using the computer method in two ways :

(i) By considering complete formation of [CuA] and the species present in the solution to be LH_3, LH_2, LH, L, [CuA], [CuAL] and [CuALH].

(ii) By taking into account all possible species present in solution i.e. AH_2, AH, A, LH_3, LH_2, LH, L, Cu(II), [CuA], [CuA_2], [CuLH], [CuL], [CuL(LH)], [CuL_2], [CuAL], [CuALH].

In case of [CuA histamine] complexes, the species considered were LH_2, LH, L, [CuA], [CuAL] in the first computer method and AH_2, AH, A, LH_2, LH, L, Cu(II), [CuA], [CuA_2], [CuL], [CuL_2] and [CuAL] in the second computer method.

In case of nickel(II) complexes, it was observed that on considering the presence of protonated species $[Ni(H.Hist)]^{+}$, no convergency was obtained in the computer run. In mixed ligand complexes also same observation is true. It is thus indicated that Ni(II) combines with histidine from the histamine sites only. Hence, the species considered in the first computer method were LH_3, LH_2, LH, L, [NiA] and [NiAL] and in the second computer method were AH_2, AH, A, LH_3, LH_2, LH, L, Ni, [NiA], [NiA_2], [NiL], [NiL_2], and [NiAL].

The formation constants of mixed ligand complexes in 50% dioxan-water (1 : 1, v/v) medium have been tabulated in Table IVA 1 and IVA 2.

The plots of concentrations of different species against pH in [CuA^1 histidine] and [NiA^1 histidine] system are shown in Figures IVA 13 and IVA 14.

Table IVA 1

Ternary complex stability constants of Copper(II) in dioxan-water (1 : 1, v/v) medium and 0.2M $NaClO_4$ at 30°C, with standard deviation $\sigma\beta$ in parentheses

Ligands	A^1		A^2		A^3	
	$\log K^{CuA}_{CuALH}$	$\log K^{CuA}_{CuAL}$	$\log K^{CuA}_{CuALH}$	$\log K^{CuA}_{CuAL}$	$\log K^{CuA}_{CuALH}$	$\log K^{CuA}_{CuAL}$
	$\Delta \log K$	$\Delta \log K$	$\Delta \log K$	$\Delta \log K$	$\Delta \log K$	$\Delta \log K$
L^{21}	10.17 (±0.08)	+ 0.23	10.13 (±0.06)	- 1.30	10.01 (±0.05)	+ 0.07	9.96 (±0.08)	- 1.47	9.48 (±0.06)	- 0.56	9.6 (±0.11)	- 1.83
L^{22}	-	-	8.7 (±0.03)	- 1.27	-	-	8.55 (±0.09)	- 1.42	-	-	7.92 (±0.06)	- 2.05

Table IVA 2

Ternary complex stability constants of Nickel(II) in dioxan-water (1 : 1, v/v) medium at 0.2M $NaClO_4$ at 30°C, with standard deviation $\sigma\beta$ in parentheses

Ligands	$\log K^{NiA}_{NiAL}$					
	A^1	$\Delta \log K$	A^2	$\Delta \log K$	A^3	$\Delta \log K$
L^4	9.92 (± 0.12)	- 0.27	9.82 (± 0.09)	- 0.37	9.65 (± 0.13)	- 0.37
L^5	6.68 (± 0.07)	- 0.31	6.51 (± 0.14)	- 0.48	5.63 (± 0.12)	- 1.36

Table IVA 3

Visible spectra of Mixed ligand Complexes in dioxan-water (1 : 1, v/v) medium at different pH

Complex	pH	λ_{max} nm
$[CuA^1H.Hist]$	3.5	610
$[CuA^1Hist]$	6.5	666.7
$[CuA^1Histamine]$	4.0	667.0
$[CuA^1Histamine]$	6.5	666.7

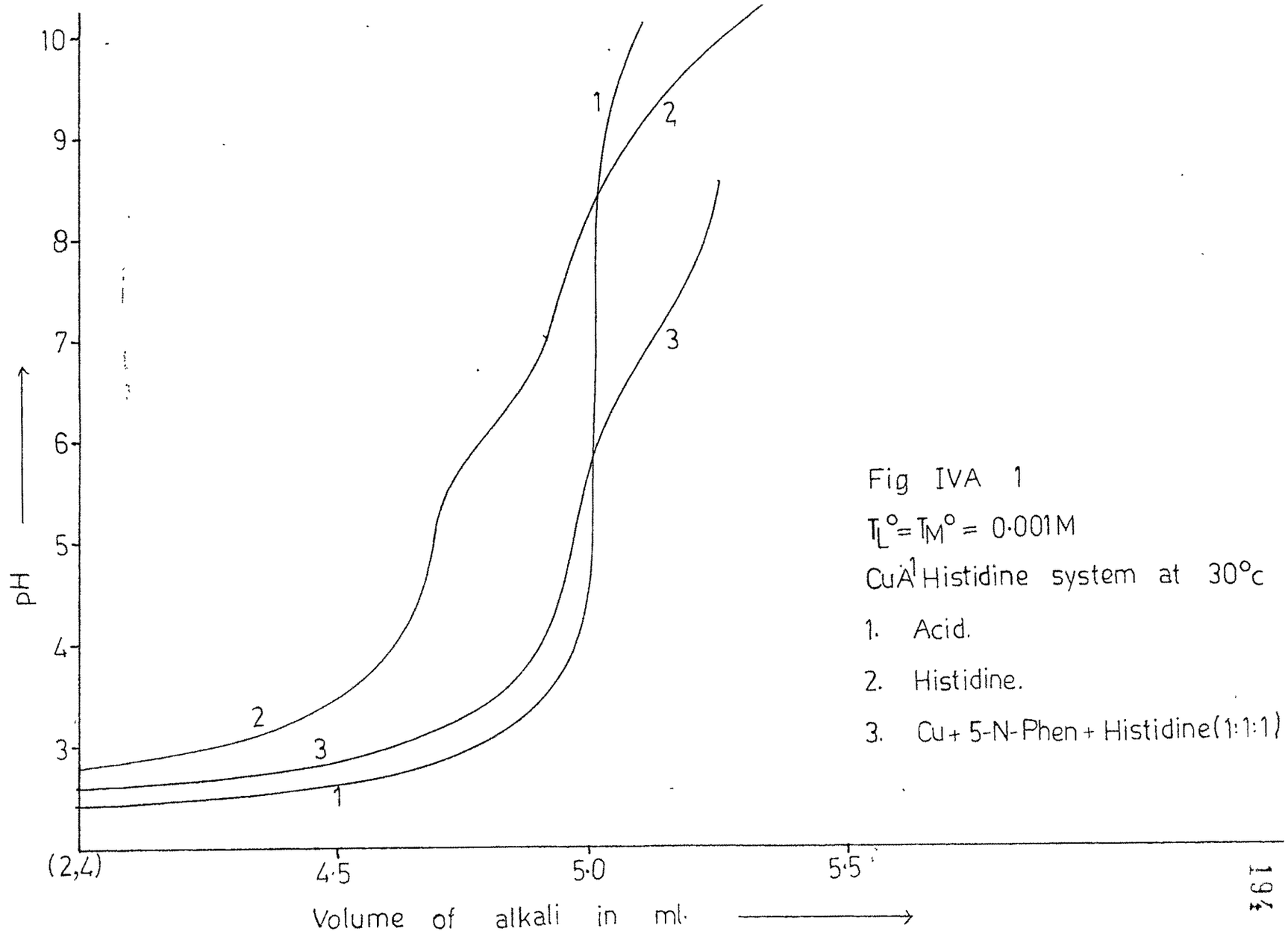


Fig IVA 1

$T_L^\circ = T_M^\circ = 0.001M$

CuA^1 Histidine system at 30°c

1. Acid.
2. Histidine.
3. Cu + 5-N-Phen + Histidine (1:1:1)

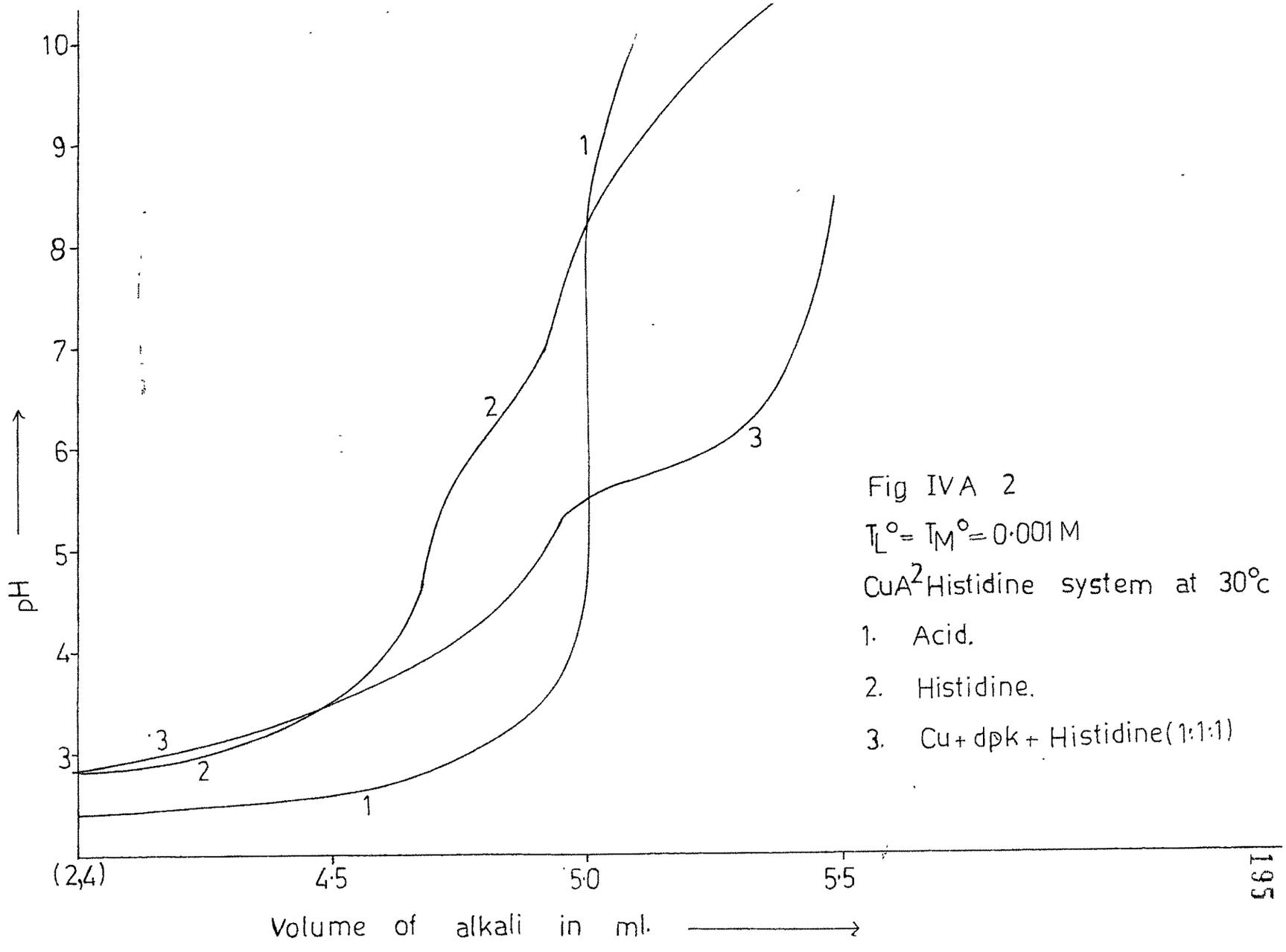


Fig IV A 2

$T_L^\circ = T_M^\circ = 0{\cdot}001\,M$

CuA^2 Histidine system at 30°c

1. Acid.
2. Histidine.
3. Cu + dpk + Histidine (1:1:1)

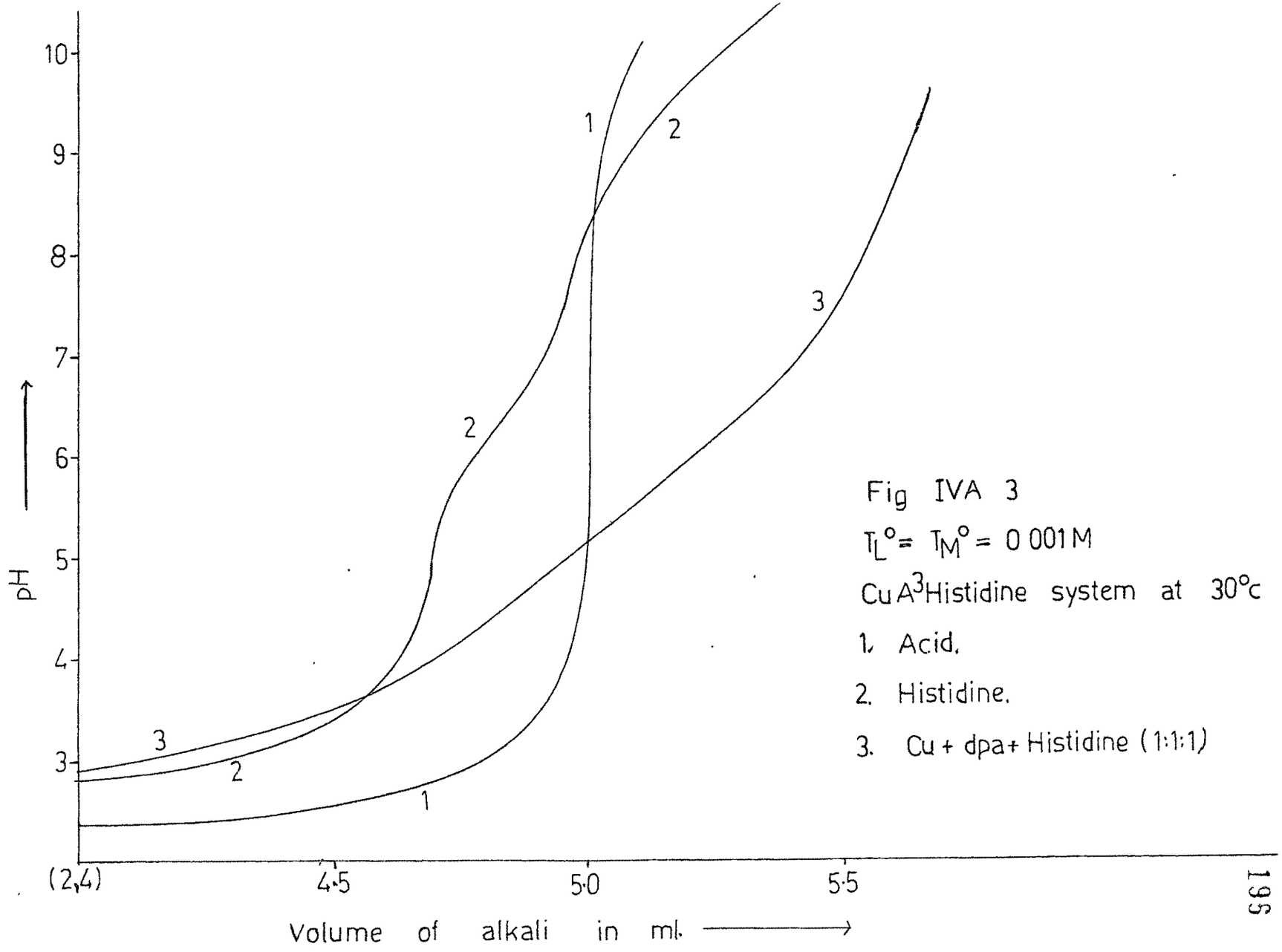


Fig IVA 3

$T_L^\circ = T_M^\circ = 0.001\,M$

Cu A^3 Histidine system at 30°c

1. Acid.
2. Histidine.
3. Cu + dpa + Histidine (1:1:1)

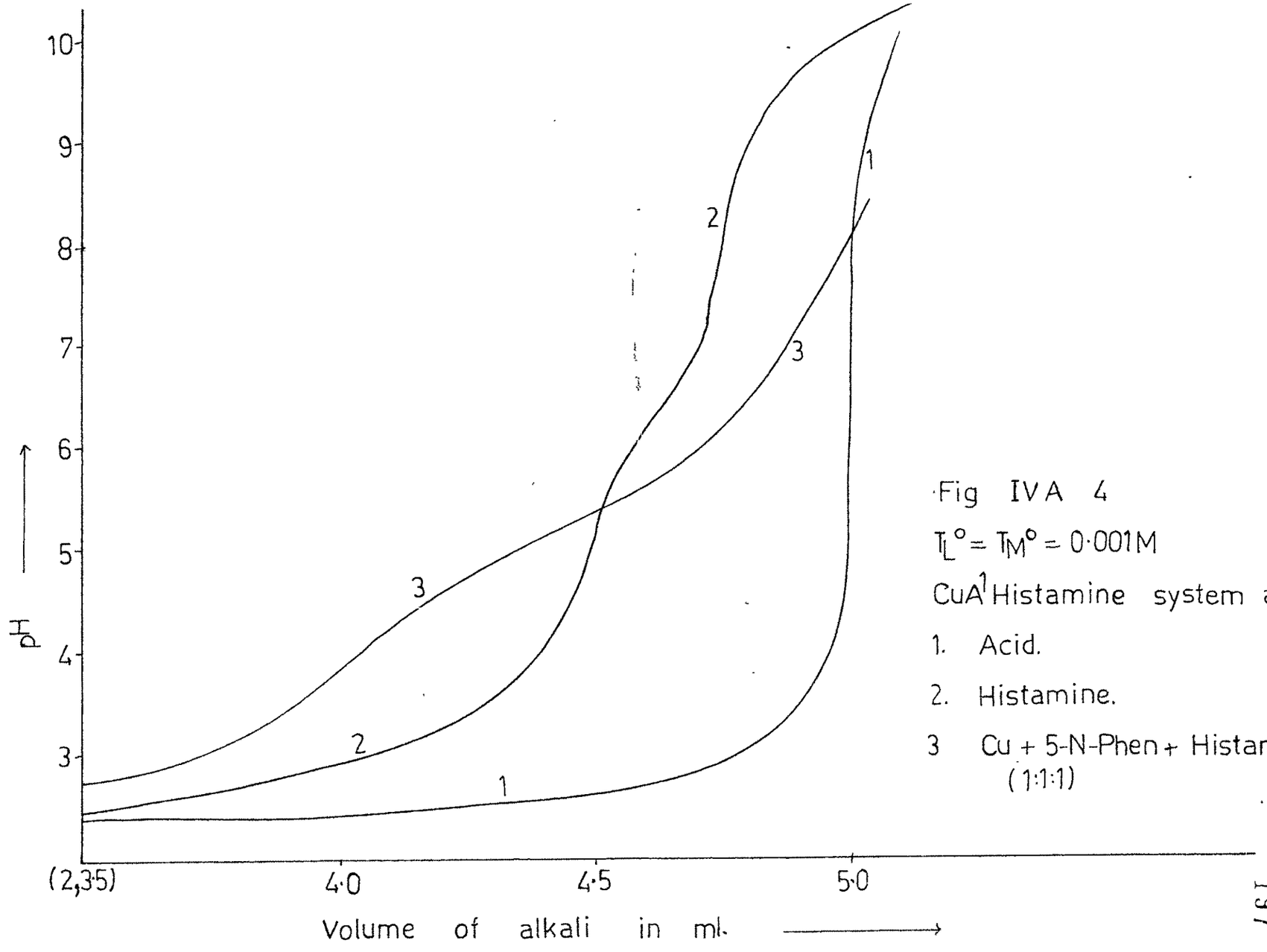


Fig IV A 4

$T_L^\circ = T_M^\circ = 0{\cdot}001M$

CuA^1 Histamine system at 30°c

1. Acid.
2. Histamine.
3. Cu + 5-N-Phen + Histamine (1:1:1)

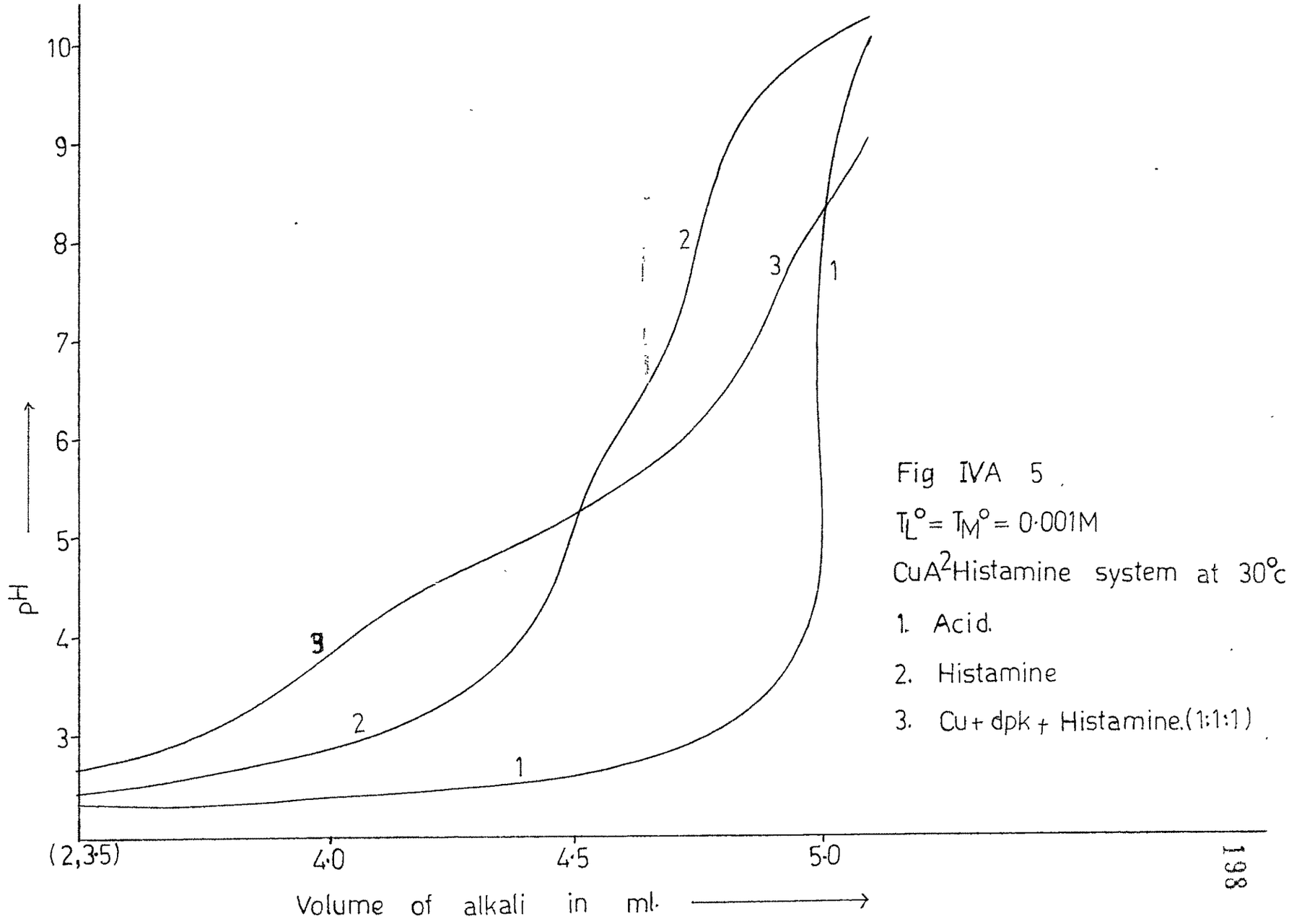


Fig IVA 5

$T_L^\circ = T_M^\circ = 0.001M$

CuA^2Histamine system at 30°c

1. Acid.
2. Histamine
3. Cu + dpk + Histamine.(1:1:1)

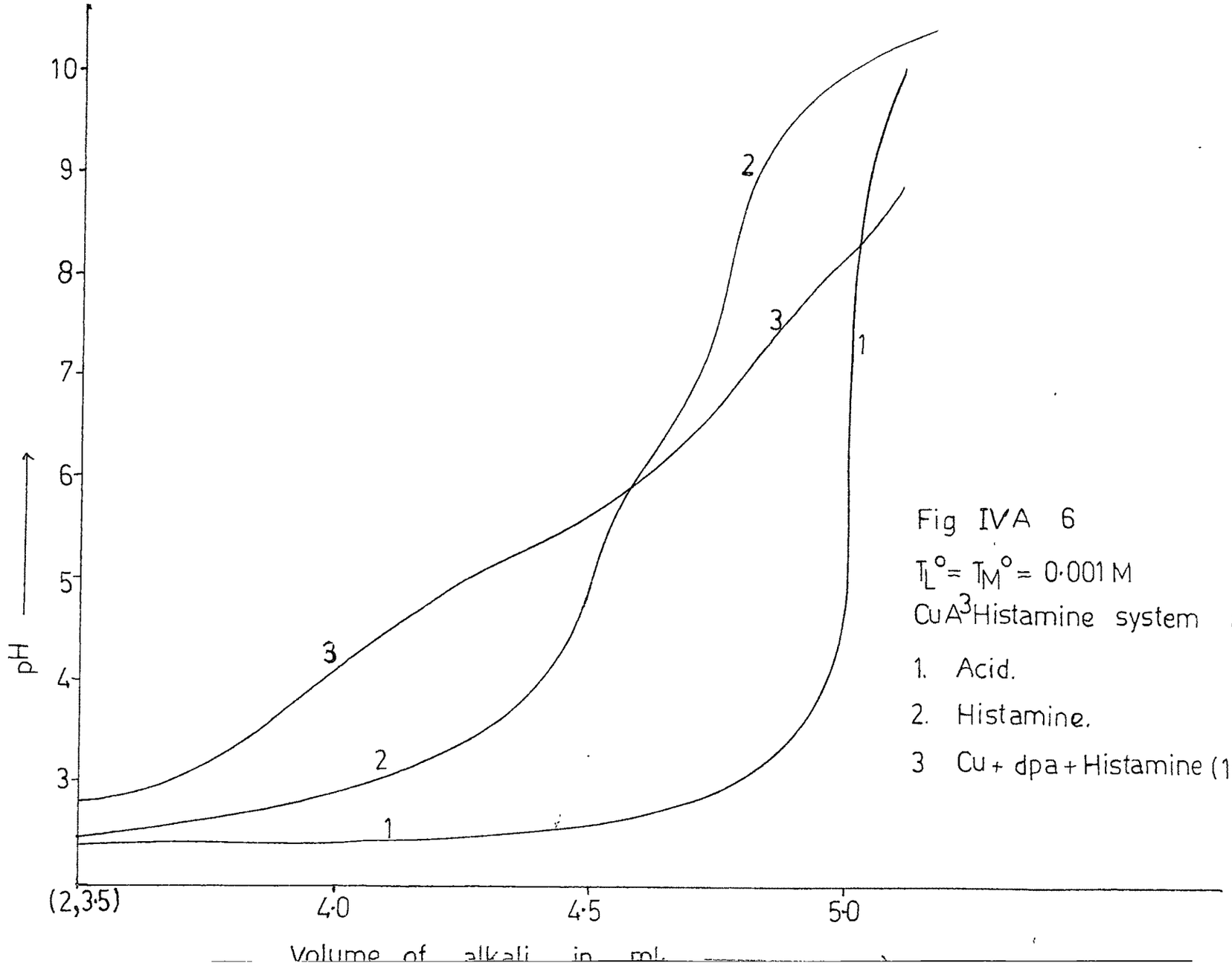


Fig IVA 6

$T_L^\circ = T_M^\circ = 0{\cdot}001$ M

CuA^3Histamine system at 30°c

1. Acid.
2. Histamine.
3. Cu + dpa + Histamine (1:1:1)

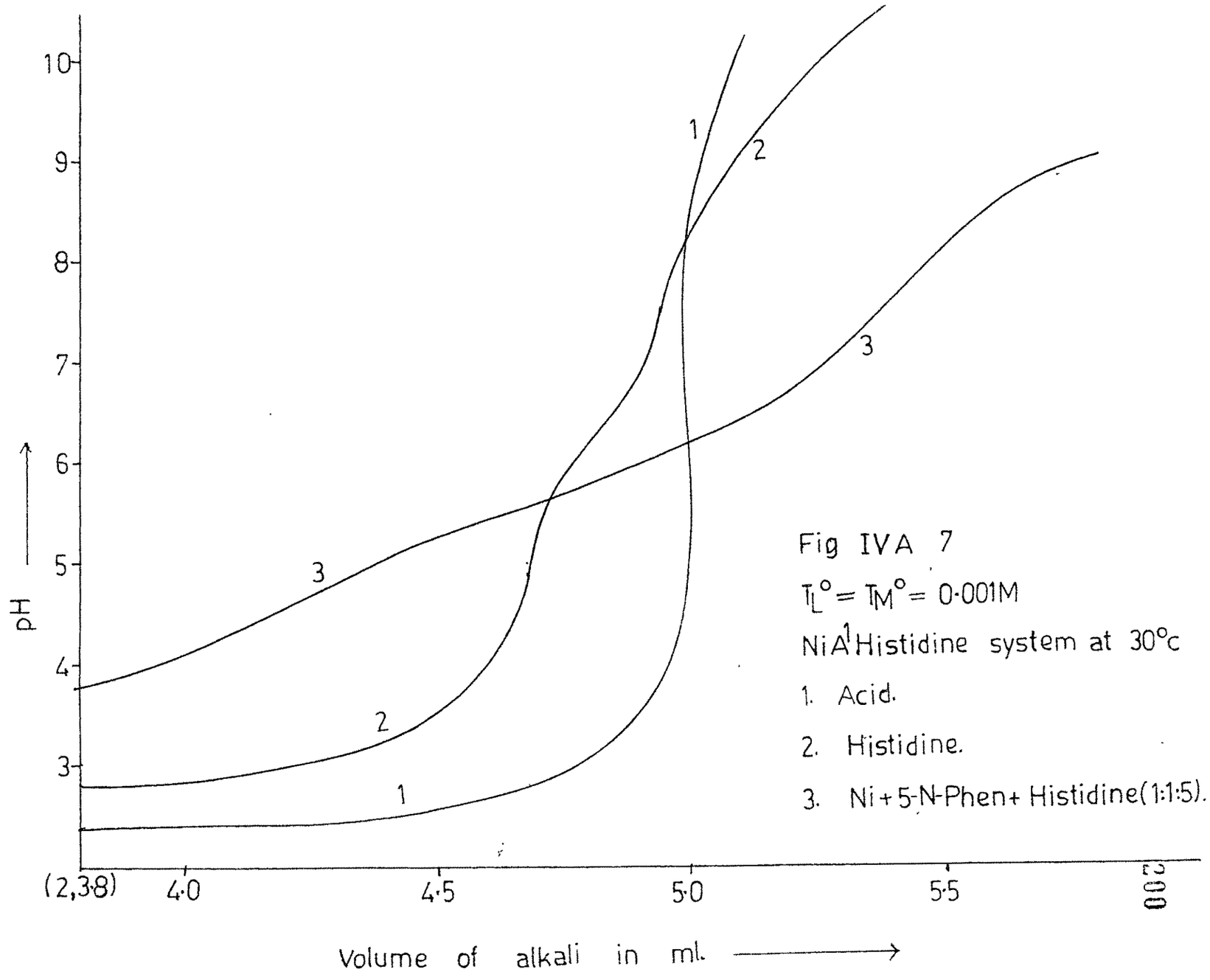


Fig IVA 7

$T_L^\circ = T_M^\circ = 0.001M$

NiA^1 Histidine system at 30°c

1. Acid.
2. Histidine.
3. Ni + 5-N-Phen + Histidine (1:1:5).

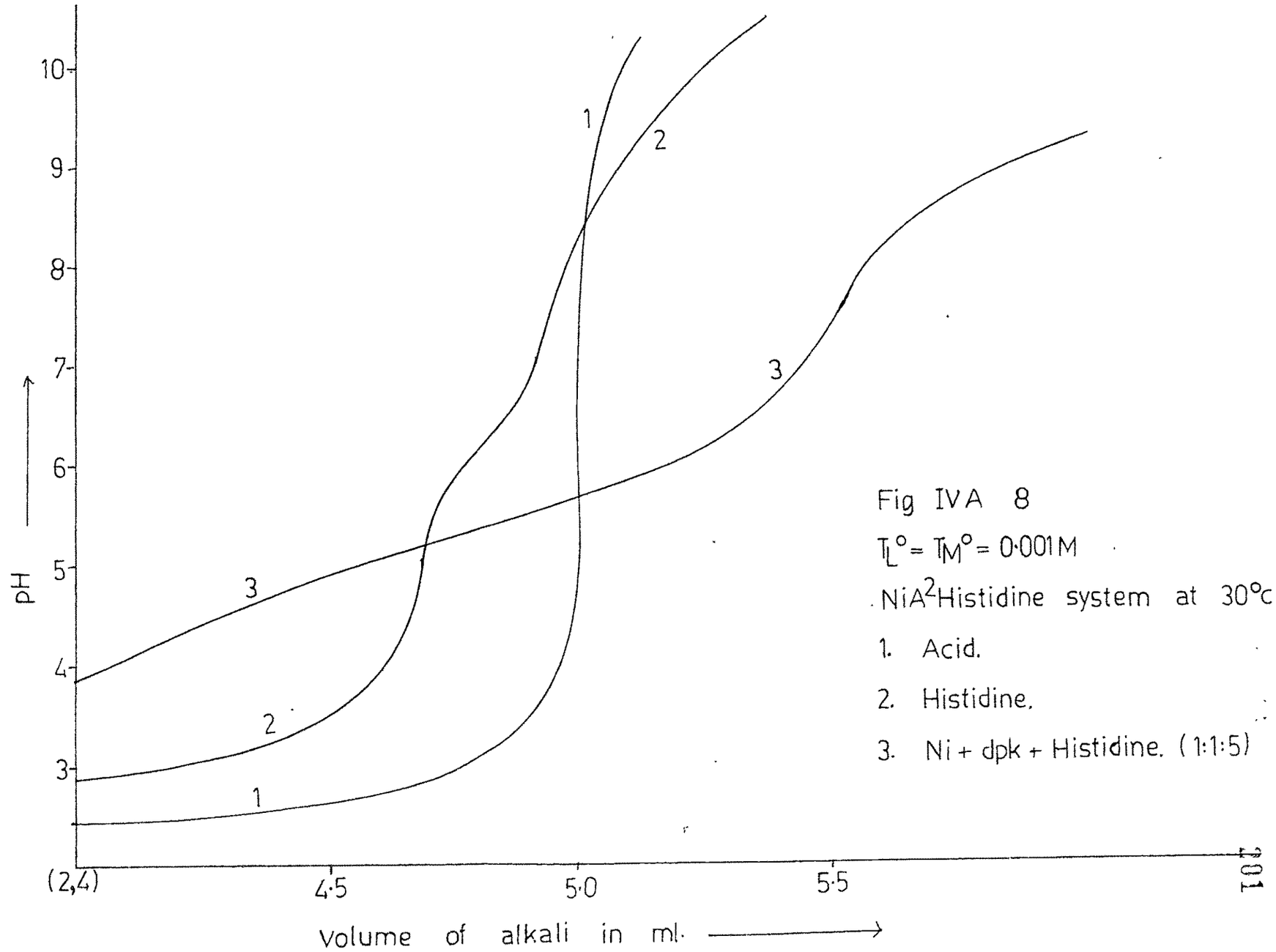


Fig IV A 8

$T_L^\circ = T_M^\circ = 0{\cdot}001\,M$

NiA^2Histidine system at 30°c

1. Acid.
2. Histidine.
3. Ni + dpk + Histidine. (1:1:5)

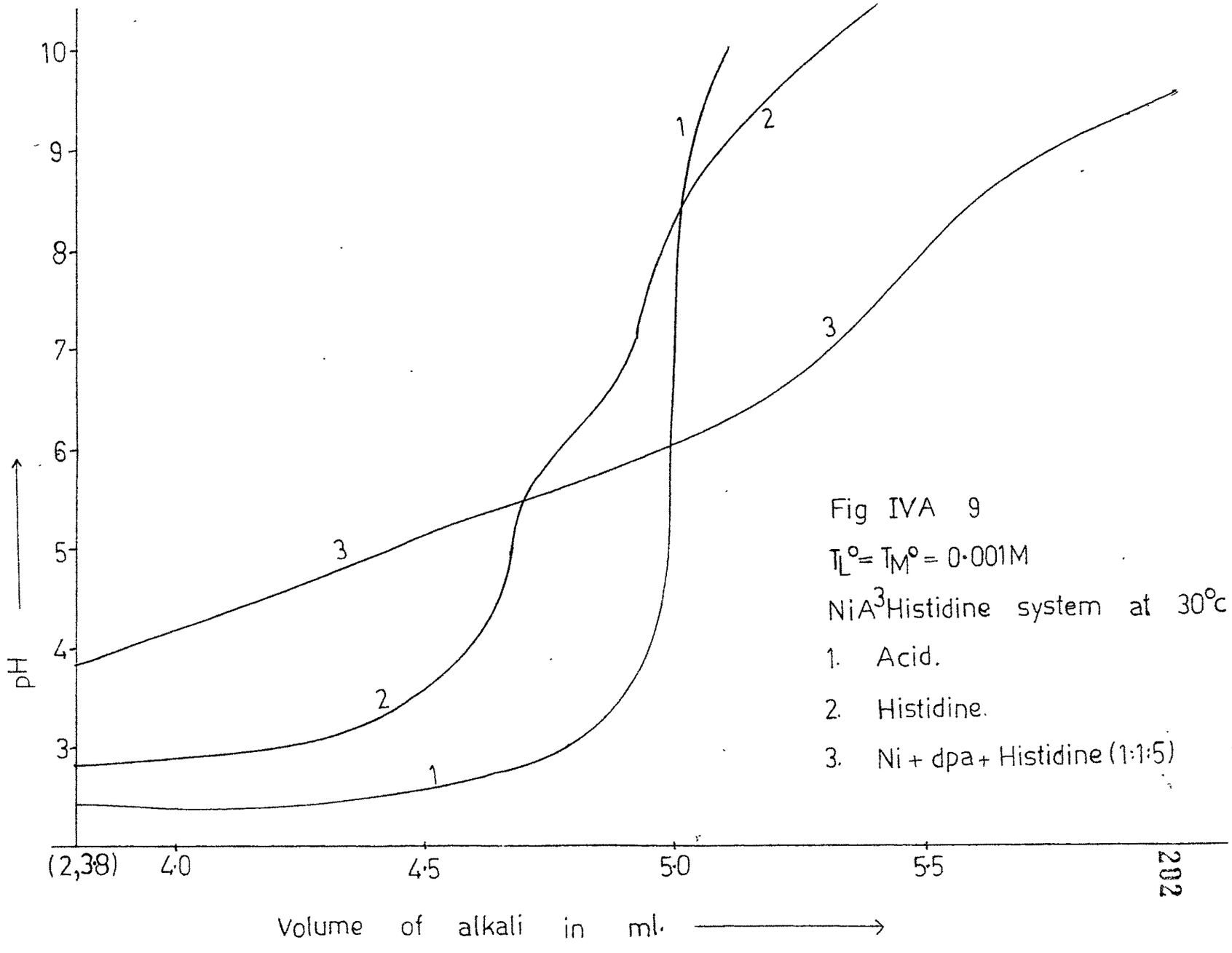


Fig IVA 9

$T_L^\circ = T_M^\circ = 0{\cdot}001M$

NiA^3Histidine system at 30°c

1. Acid.
2. Histidine.
3. Ni + dpa + Histidine (1:1:5)

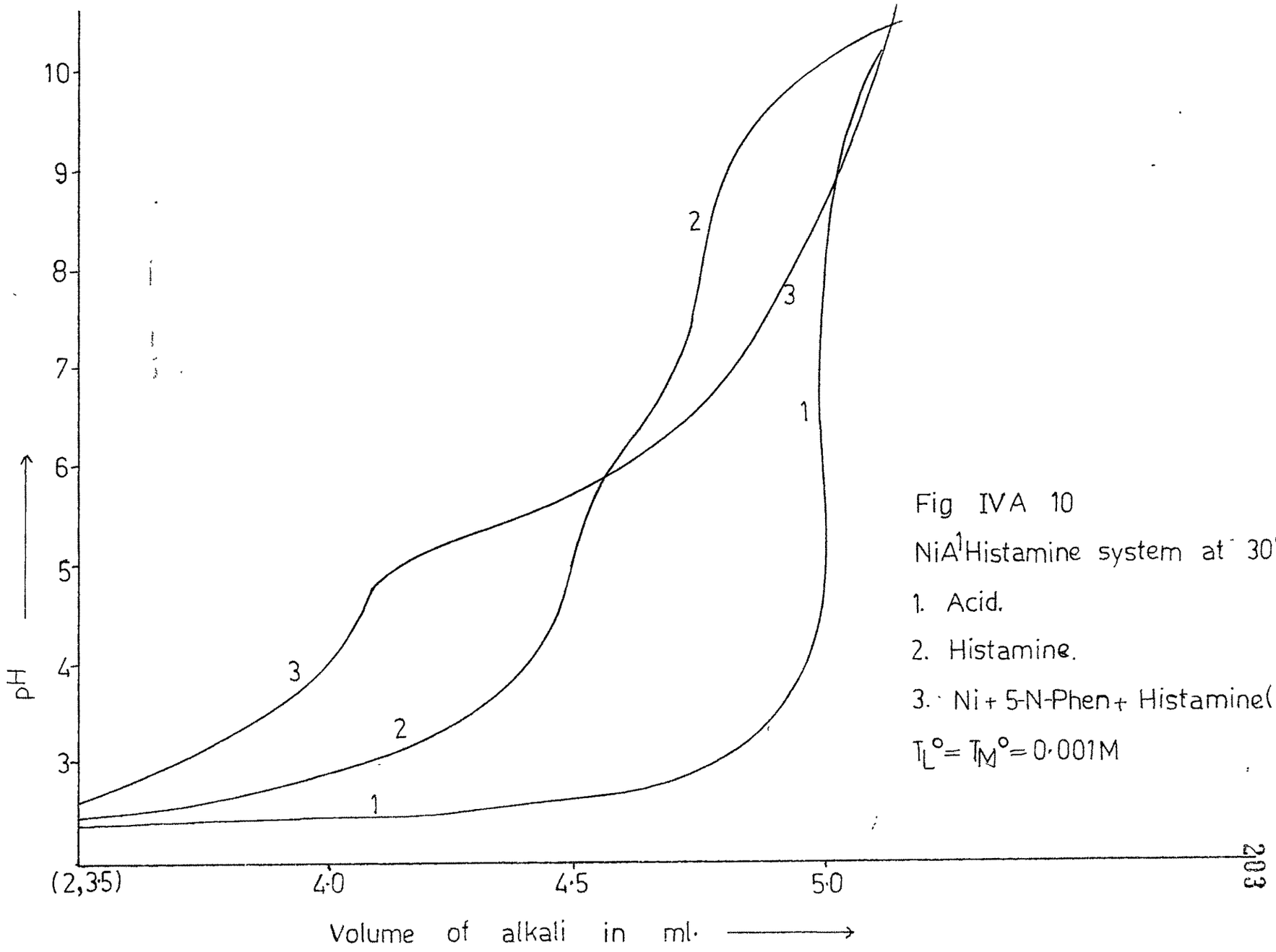


Fig IVA 10

NiA[1]Histamine system at 30°c.

1. Acid.
2. Histamine.
3. Ni + 5-N-Phen + Histamine (1:1:5)

$T_L^\circ = T_M^\circ = 0.001M$

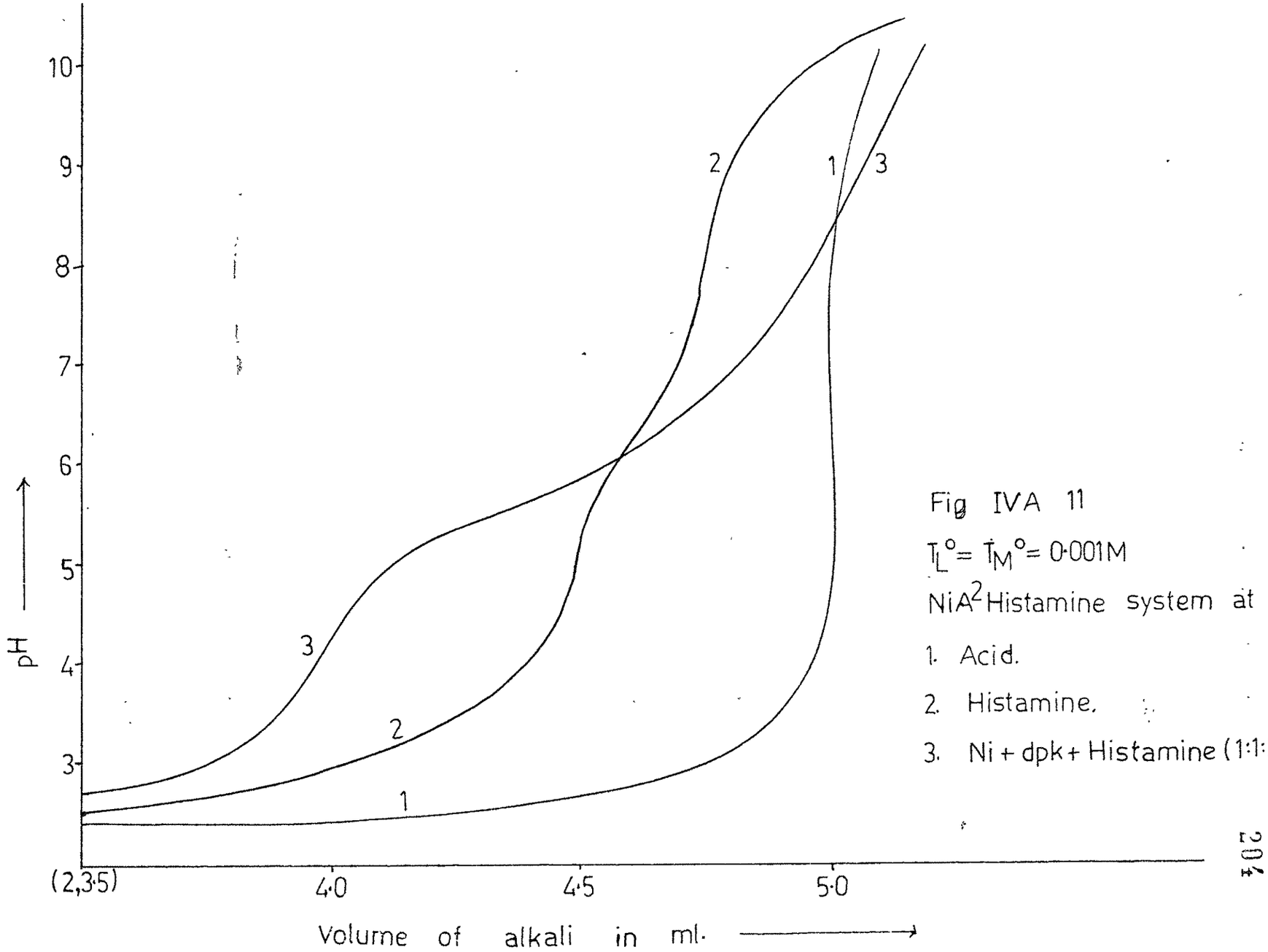


Fig IVA 11

$T_L^\circ = T_M^\circ = 0.001M$

NiA^2 Histamine system at 30°c

1. Acid.
2. Histamine.
3. Ni + dpk + Histamine (1:1:5)

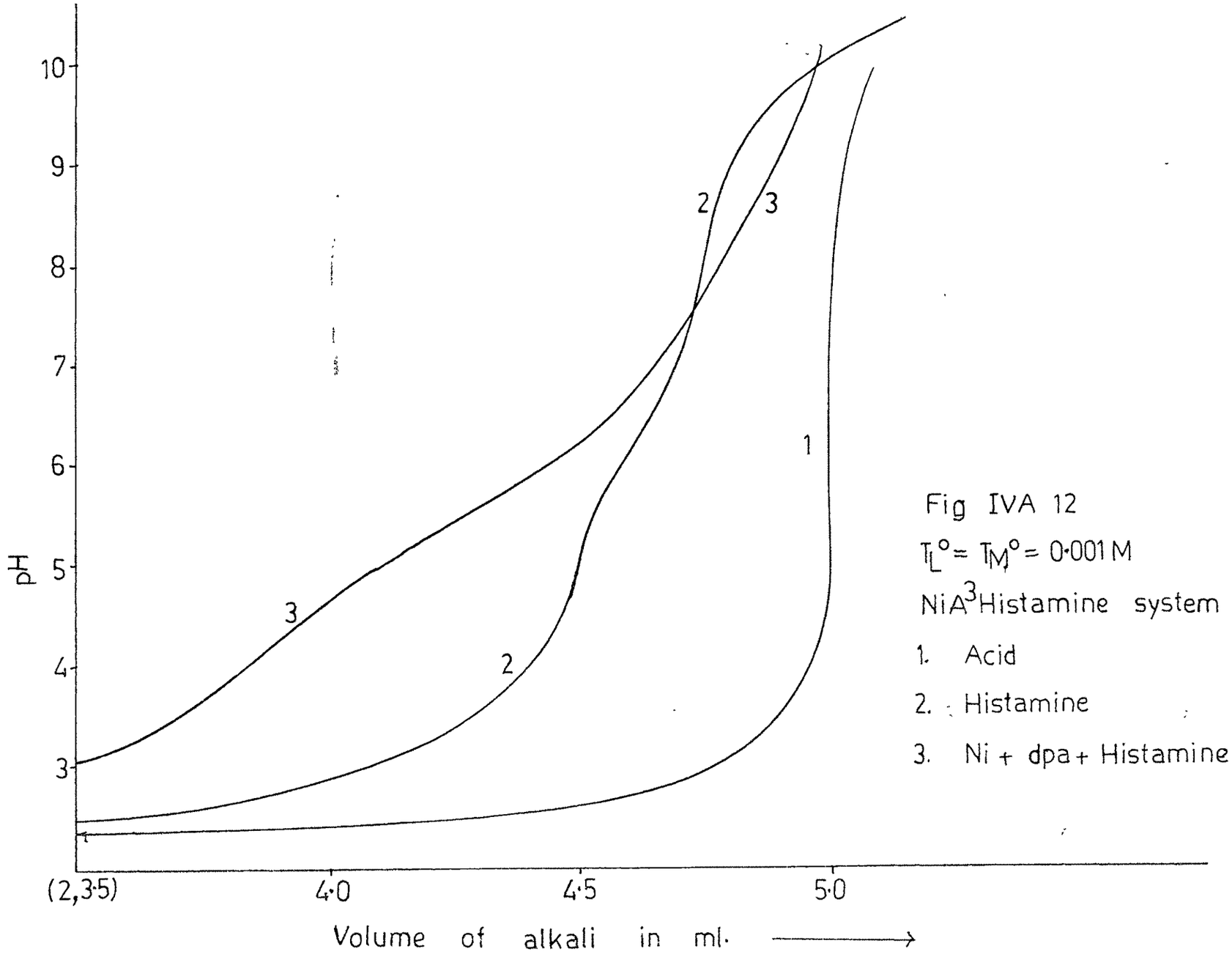


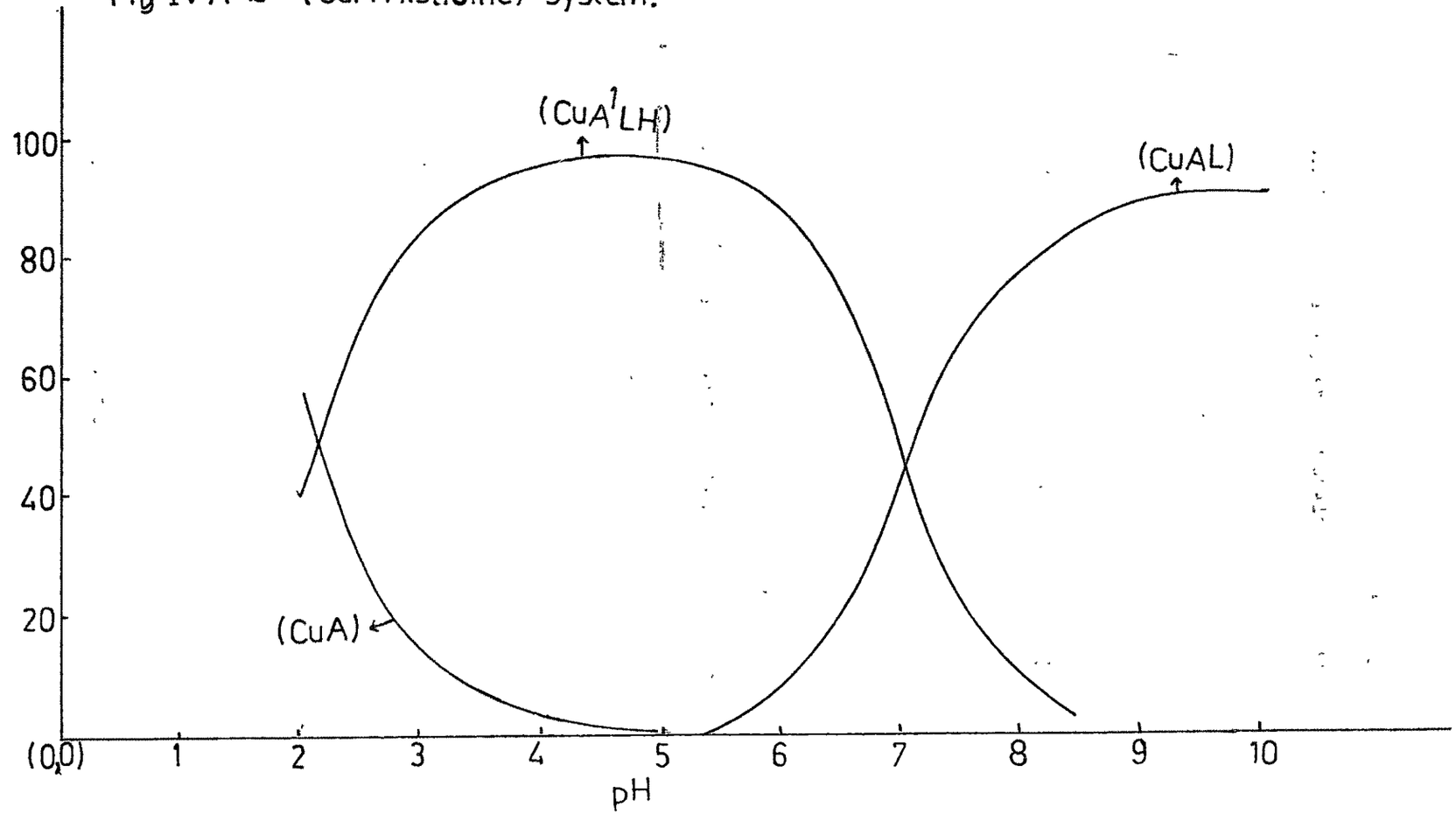
Fig IVA 12

$T_L^\circ = T_M^\circ = 0.001\,M$

NiA^3 Histamine system at 30°c

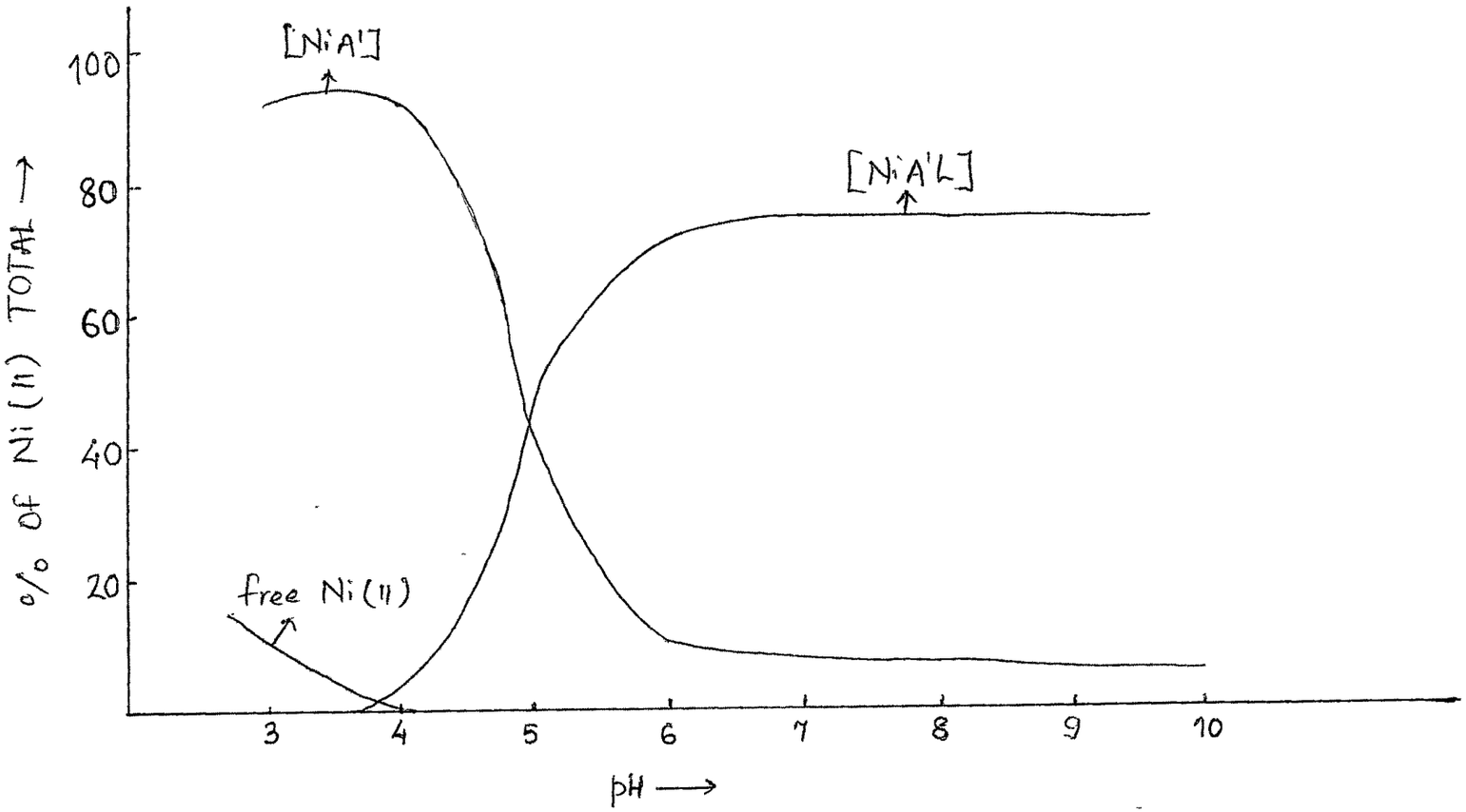
1. Acid
2. Histamine
3. Ni + dpa + Histamine (1:1:5)

Fig IV A 13 (CuA^1 Histidine) system.



Variation of concentrations of different species with pH

FIG IV A 14 (NiA'Histidine) system.



Variation of concentrations of different species with pH —

Results & Discussion

The plot of concentrations of the species against pH (figure IVA 13) shows that [CuA] is the major species in the lower pH range and then the co-ordination of histidine takes place in steps :

$$[CuA] + H.Hist \rightleftharpoons [CuAH.Hist]$$

$$[CuA] + Hist \rightleftharpoons [CuA\ Hist]$$

It is observed in the plot of the concentrations of the species that [CuA.H.Hist] is maximum 52% at pH 5.0 and [CuAHist] is maximum 89% at pH 6.5. In the lower pH range (pH 3.0 to 5.0) there is formation of [CuAH.Hist] due to the co-ordination from amino nitrogen and carboxyl oxygen, imidazole nitrogen remaining protonated as in binary complex [CuH.Hist]. The [CuAHist] formation starts at higher pH $\sim$ 4.8 due to co-ordination from imidazole nitrogen and amino nitrogen. As pH is increased, the concentration of [CuAL] also increases.

The value of Δ log K for the [CuA^1LH] species (Δ log K = + 0.20) is comparable with that of [CuA^1glycine] (Δ log K = + 0.23) indicating that in the species [CuALH] coordination is glycine like i.e. from amino nitrogen and carboxyl oxygen. The value of Δ log K for the species [CuA^1L] (Δ log K = - 1.30) is comparable to that of [CuA^1histamine] (Δ log K = - 1.27) showing that the co-ordination in [CuAL] is from the imidazole and amino nitrogen of histidine, as in case of histamine.

It is observed that [CuA] co-ordinates with histidine from O^--N end in the lower pH range forming [CuA H.L] and from N-N end in the higher pH range forming [CuAL]. As in case of other amino acids having O^--N co-ordination, the value of Δ log K in case of LH co-ordination ($\log K^{CuA}_{CuALH} - \log K^{Cu}_{CuLH}$) is less negative. The value of Δ log K ($\log K^{CuA}_{CuAL} - \log K^{Cu}_{CuL}$) is more negative.

In the lower pH range the electronic spectrum of [CuAHistidineH] shows a d-d transition band at 610 nm comparable to that in [CuAphenylalanine] at 606 nm. This shows O^--N co-ordination from amino acid part of histidine, imidazole nitrogen being protonated, resulting in the species [CuAH.Hist]. In the higher pH range ~6.5 the spectrum of [CuAHist] shows a band at 666.7 nm comparable to that of [CuA Histamine] at 666.7 nm. This shows a co-ordination from imidazole and amino nitrogen of histidine in [CuAHist], carboxylate part remaining free, as Cu(II) does not prefer axial co-ordination.

It is observed in fig. IVA that in case of Ni(II) complexes, [NiA] is formed at lower pH (4.5) and there is formation of [NiAHist] with Histidine coordinating from imidazole nitrogen and amino nitrogen. As in the case of binary complex, there is no formation of the ternary complexes species [NiA Hist.H] with histidine coordinating from aminoacid end and imidazole nitrogen remaining protonated.

It is observed that the stabilization of the ternary complexes [M5-nitro-1,10-phenanthroline L] or [MdpkL] are more than [M1,10-phenanthrooine L] or [M2,2'-dipyridyl L]. This can be explained by considering that the electron withdrawing nitro or carboxyl group makes them stronger π acids and hence π interaction is more, resulting in greater stabilization of the ternary complexes.

The stabilization of [MdpkL] is not as much as expected from the electron withdrawing $>C=O$ group. This is because there is equilibrium between keto and geminal diol form (equation 4 of chapter 3). The equilibrium is shifted more towards keto form in 50% dioxan medium.

In the case of [MdpaL] complexes the value of Δ log K is similar to that of [MdipyL] complexes as explained in chapter 3.

Normally it is observed that Δ log K value for Cu(II) complexes are more positive or less negative than Δ log K value of Ni(II) complexes for the same ligand L. This is explained to be due to Jahn-Teller distortion. But in the present study it has been observed that Δ log K for Ni(II) complexes are less negative than that of Cu(II) complexes (Table 1 to 4), in the cases where L = Histamine or histamine like co-ordinated Histidine.

The probable reason could be that as in case of $[Cu(bipy)_2(H_2O)_2]$[172] complexes, $[CubipyL(H_2O)_2]$ has

a cis distorbed structure. Hence in the formation of $[CubipyL]$ from $[Cubipy(H_2O)_4]$ the ligand L gets co-ordinated to one equatorial and one axial position. Due to Jahn-Teller distortion, L is strained in the formation of $[CubipyL(H_2O)_2]$. However there is no strain felt by the ligand in occupying equatorial and axial positions in $[NibipyL(H_2O)_2]$. Hence Δ log K of Ni(II) complexes is less negative than in case of Cu(II) complexes.

"Ternary Complexes containing tertiaryamines and Ambivalent Secondary Ligands".

L-3,4-dihydroxyphenylalanine (L-dopa) is neurotransmitter and is important from both biochemical and therapeutic aspects.[136,172-174] Extensive studies have been made on the proton ligand, metal ligand formation constants of L-dopa to understand its biological activity and its application in therapy. Besides the biological significance, it is also a ligand of interest to co-ordination chemists because of its ambidentate character dependent on pH in binary complexes and its co-ordinating tendency in the ternary complexes,[127,175-181] depending on the nature of the second ligand.

Dopa has potentially four co-ordinating sites and thus possibility exists for the formation of $N\text{-}O^-$ complex with the alanine side chain or $O^-\text{-}O^-$ co-ordination with orthophenolate hydroxy groups. It has been shown[180-184] that with all the metal ions, species involving a mixed bonding mode are formed containing amino acid type ($N\text{-}O^-$) or($O^-\text{-}O^-$) phenolate type bonds.[182-185]

Due to the different basicity of the co-ordinating groups, the types of species formed in solution are strongly pH-dependent. This behaviour has been well shown by the study of the L-dopa complexes with Cu(II), Zn(II) or Ni(II).[178,183,186]

In efforts to clarify the bonding modes in the complexes formed, spectral procedures like visible;[175,177,178,182] UV;[190] CD[182] and ESR[180,181,187]

have been employed. From all these observation it has been concluded that with Ni(II) or Cu(II) as central metal ions, the amino acid type complexes are formed in significant concentration. The CD,[182] visible[175,177,178,182] spectral and cyclic voltametric[177,182] studies proved that with a metal ion dopa ratio of 1 : 2 upto pH ~ 5.4, only N-O^- bonded complexes are formed in the Cu(II)-dopa system. Kustin and coworkers[187,188] assumed that in the case of amino acid type dopa complexes of Cu(II) and Ni(II) one of the phenolic hydroxy group is linked to the metal ion via a hydroxy bond with the water molecule.

In case of Cu(II) complex, it has been observed that above pH 6, both aminocarboxylate and pyrocatecholate groups are involved in binding with Cu(II) and each dopa is bound to two Cu(II) resulting in polymeric species.[176,182] Above pH 8, two dopa molecules are predominently bound as catecholate.

However, tyrosine contains three donor groups, and there being only one -OH group with no possibility of chelate formation, only the amino acid side chain forms a five membered chelate ring. Therefore, the ambidentate character of tyrosine is not manifested in practice. The bidentate nature of tyrosine has been proved in many ways.[189-192]

It was shown by Rajan and Mainer[1,2] that in the mixed ligand complex [Cudpydopa] the chelation of dopa is from aminocarboxylate end upto higher pH. It has

been further confirmed by us that in [CuAdopa] complexes where A = 2,2'-dipyridyl or 1,10-phenanthroline, L-dopa co-ordinates from aminocarboxylate end only. The chelation is similar to that in phenylalanine, tyrosine and tryptophan. Though the co-ordination is from $\bar{O}$-N, the value of Δ log K has been found to be positive in Cu(II) complexes and less negative in Ni(II) complexes.

In view of the preference of the non-co-ordinated hydrophobic phenyl or substituted phenyl group of a ligand for a position near to the metal ion, as suggested by Martin and coworkers[193,194] and to see the effect of the substitution on the heteroaromatic N-base A on the ternary complex stability, in the present chapter mixed ligand complexes where M = Cu(II) or Ni(II), A = A^1 to A^3 and L = phenylalanine (L^{21}), tyrosine (L^{22}), L-dopa (L^{23}) or tryptophan (L^{24}) have been studied in aqueous-dioxan medium at initially constant ionic strength 0.2M $NaClO_4$ and temperature 30°C.

Experimental

Standardization of all the required solution of metal perchlorates, sodium hydroxide, perchloric acid were done in the same way as detailed in chapter IIA. The primary ligands A^1 to A^3 were of A.R. grade (Merck pure). The secondary ligands were also A.R. grade (BDH pure). The caliberation of microburette, pipettes, etc. and pH meter was done in the same way as detailed in chapter IIA.

Simple titration for the buffer region m = 0 to 3 is shown in Figs. 27, 28, 29. The titration data for aqueous-dioxan medium are given in Figures IVB 1 to IVB 24, where the concentrations of various reagents taken have also been shown.

The concentration of the species, as percentage of total M(II) at different pH have been plotted from the computer output for $[CuA^1dopa]$ and $[NiA^1dopa]$ shown in Figs. IV 25 and IV 26, respectively.

The preliminary values of the formation constants of the mixed ligand complexes obtained by using Irving-Rossotti titration technique were subjected to refinement by using computer program SCOGS. For the refinement of $[M.A.dopa]$, K^H values of dopa and log K^M_{ML} (dopa co-ordinating from amino carboxylate end) were kept as fixed parameters and log K^{MA}_{MAL} values (dopa co-ordinating from carboxylate end) were refined, considering the titration data in the pH range from

2.9 to 8.0. It was considered that -OH groups are not co-ordinated and hence, -OH protons are not dissociated and the co-ordinated ligand has two free -OH groups. The mixed ligand complex considered was [MAL], though it is really [$MALH_2$] with catechol protons remaining undissociated.

Calculations were further repeated using K_1H, K_2H, K_3H values of L^3, considering the possibility of one catechol proton dissociation at higher pH. In the second case, the species considered were [MALH] and [MAL] (with one phenolic hydrogen of dopa dissociated). However, there are no significant differences in the values of the formation constant of [MALH] obtained in two cases, showing that the formation of the species [MAL] is not significant upto pH 8. It should be noted that [MALH] is actually [$MALH_2$], but is represented as [MALH], as the fourth proton i.e. second undissociated phenolic OH proton of dopa has not been considered.

As discussed in previous chapters, the reaction was presumed to be proceeding in steps, M + A $\rightleftharpoons$ [MA]; [MA] + L $\rightleftharpoons$ [MAL] and hence the computer method was used in two ways :

(1) By considering the species present in the solution to be LH_2, LH, L, [MA] and [MAL].

(2) By considering all the possible species present in the solution to be LH_2, LH, L, AH_2, AH, A, M^{+2}, [ML], [ML_2], [MA], [MA_2] and [MAL].

The formation constant of [MAL] where L = phenylalanine, tyrosine or tryptophan were also refined in the above two ways, considering co-ordination from aminocarboxylate end in all the three cases and phenolic protons remaining undissociated in the co-ordinated tyrosinate (HL^{22}). The computer calculations were repeated using the titration data of M : A : L taken in the ratio (1 : 1 : 1, 1 : 1 : 5 and 1 : 1 : 10). The log K^{MA}_{MAL} values obtained in different computer runs are very close to each other. The refined values of the mixed ligand formation constants obtained by computer technique have been presented in Table IVb 1 and IVb 2. These tables also include standard deviation $\sigma\beta$ and Δ log K.

Spectral Measurement

The spectra were recorded in the same way as detailed in chapter IIA. The observed absorption peaks in free ligands, binary and ternary complexes have been reported in Table IVb 3.

Table IVB 1

Ternary complex stability constants of Copper(II) in dioxan-water medium (1 : 1, v/v) and 0.2M $NaClO_4$ at 30°C, with standard deviation $\sigma\beta$ in parentheses

Ligands	$\log K^{CuA}_{CuAL}$					
	A^1	$\Delta \log K$	A^2	$\Delta \log K$	A^3	$\Delta \log K$
L^{23}	8.76 (± 0.08)	+ 0.21	9.0 (± 0.07)	+ 0.43	8.45 (± 0.03)	- 0.12
L^{24}	8.87 (± 0.1)	+ 1.28	8.7 (± 0.09)	+ 1.11	8.29 (± 0.12)	+ 0.70
L^{25}	9.68 (± 0.08)	+ 1.76	9.63 (± 0.1)	+ 1.71	8.96 (± 0.06)	+ 1.04
L^{26}	9.49 (± 0.1)	+ 1.53	9.6 (± 0.14)	+ 1.64	8.92 (± 0.08)	+ 0.96

Table IVB 2

Ternary complex stability constants of Nickel(II) in dioxan-water medium (1 : 1, v/v) and 0.2M $NaClO_4$ at 30°C, with standard deviation $\sigma\beta$ in parentheses

Ligands	$\log K^{NiA}_{NiAL}$					
	A^1	$\Delta \log K$	A^2	$\Delta \log K$	A^3	$\Delta \log K$
L^{23}	5.91 (± 0.12)	- 0.09	5.88 (± 0.01)	- 0.14	5.46 (± 0.15)	- 0.56
L^{24}	5.33 (± 0.14)	- 0.5	5.46 (± 0.08)	- 0.37	5.03 (± 0.12)	- 0.8
L^{25}	5.42 (± 0.1)	- 0.49	5.47 (± 0.1)	- 0.44	5.12 (± 0.1)	- 0.79
L^{26}	6.13 (± 0.11)	+ 0.23	6.05 (± 0.08)	+ 0.19	5.71 (± 0.07)	- 0.15

Table I/B 3

Absorption spectra (λ_{max} nm) of Free Ligands, Binary and Mixed Ligand Complexes in dioxan-water medium (1 : 1, v/v)

	λmax
5-nitro-1,10-phen (A^1)	207.5, 227.8, 263.2
Phenylalanine (L^{23})	208.3
Tyrosine (L^{24})	222.2, 277.8
Dopa (L^{25})	261.7
$[Cu(I)A_2^1]$	216.5, 279.3, 719.4
$[Cu(II)L_2^{23}]$	223.5, 275.9, 625
$[Cu(II)L_2^{24}]$	208.3, 238.1, 625
$[Cu(II)L_2^{25}]$	222.2, 283.3, 312.5, 434, 625
$[Cu(II)A^1L^{23}]$	261.7, 277.7, 340.1, 588.2
$[Cu(II)A^1L^{24}]$	222.2, 279.3, 344.8, 588.2
$[Cu(II)A^1L^{25}]$	222.2, 279.3, 342.4, 588.2

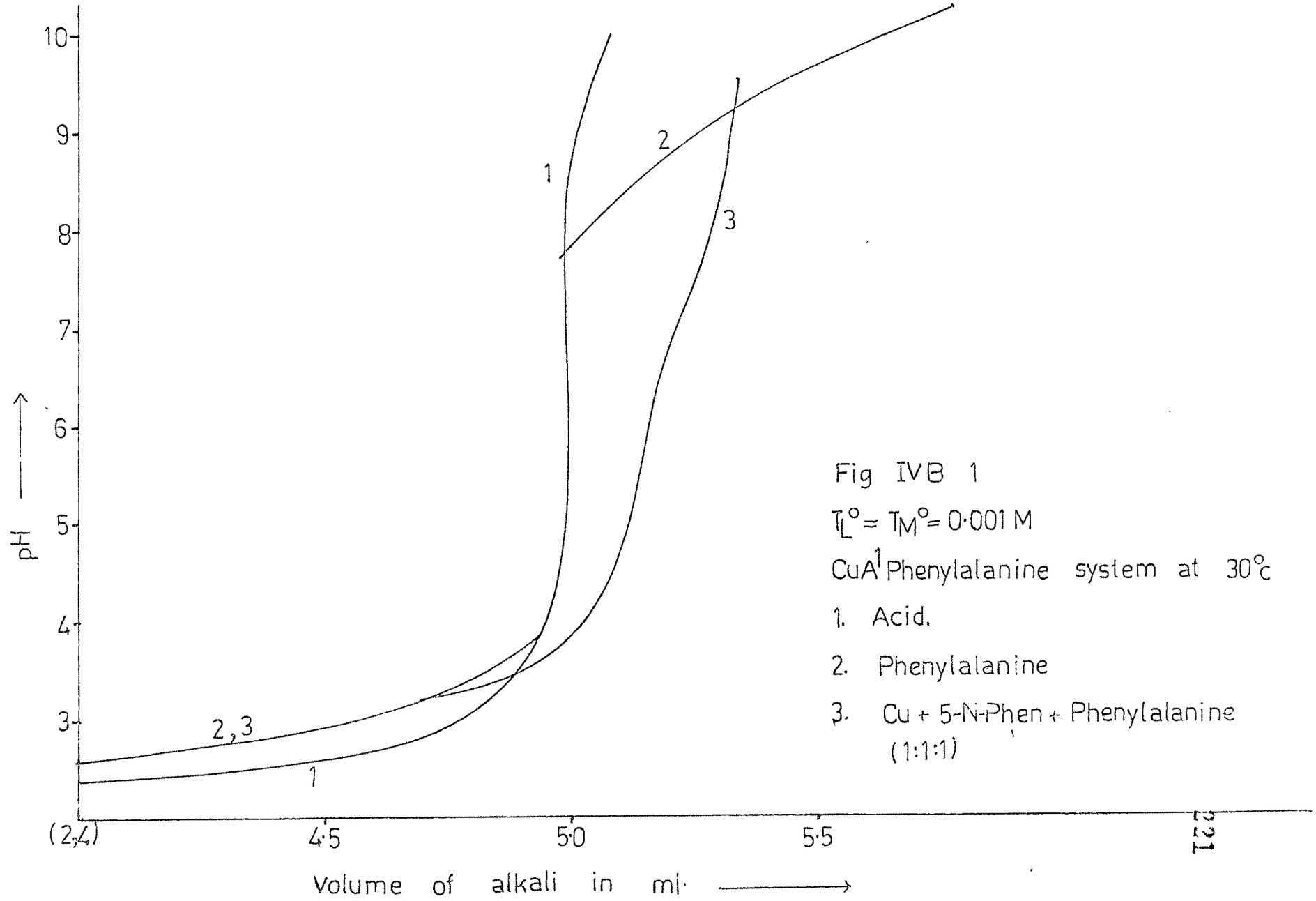


Fig IVB 1

$T_L^\circ = T_M^\circ = 0.001$ M

CuA^1 Phenylalanine system at 30°C

1. Acid.
2. Phenylalanine
3. Cu + 5-N-Phen + Phenylalanine (1:1:1)

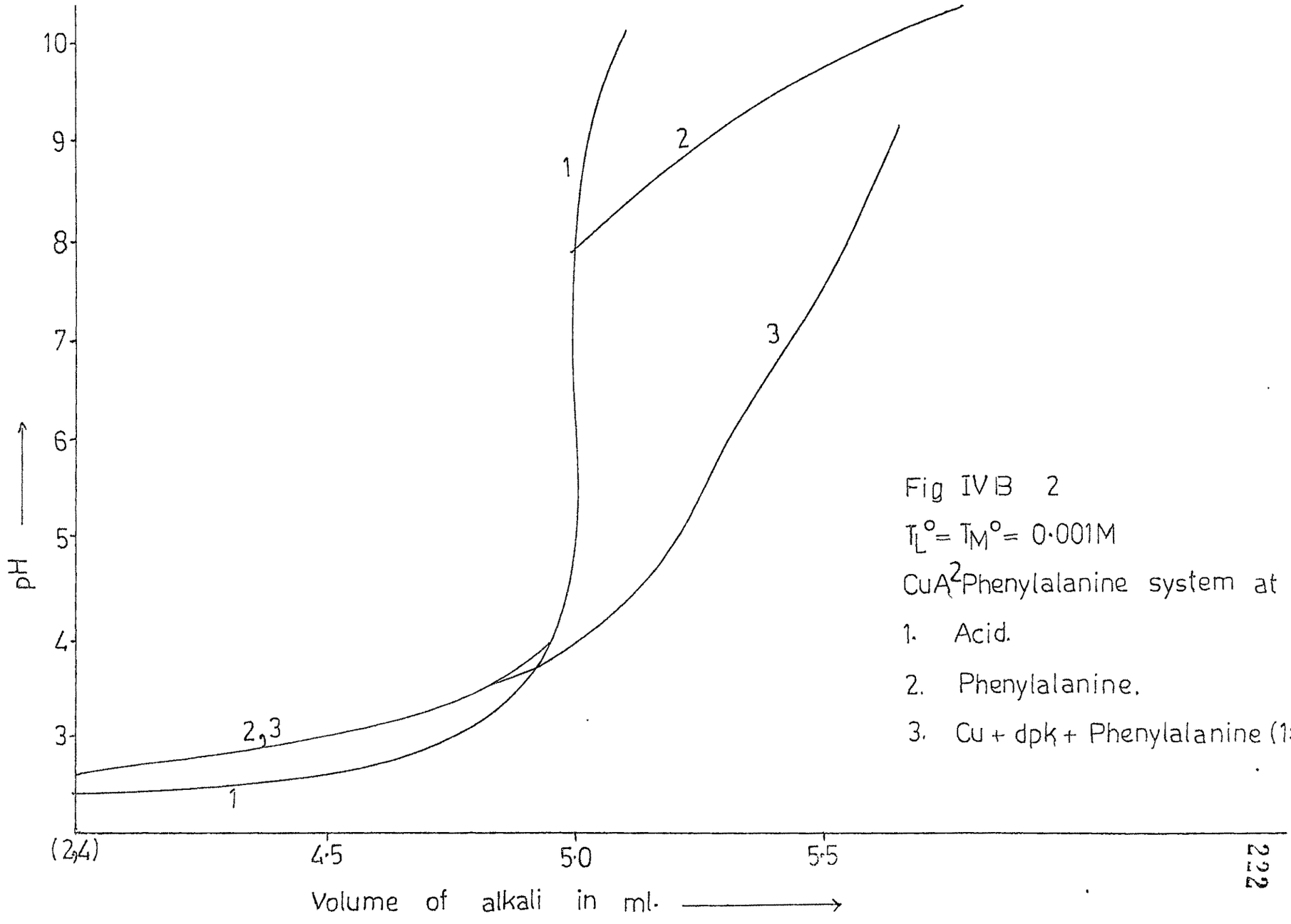


Fig IV B 2

$T_L^\circ = T_M^\circ = 0{\cdot}001M$

CuA^2 Phenylalanine system at 30°c

1. Acid.
2. Phenylalanine.
3. Cu + dpk + Phenylalanine (1:1:1)

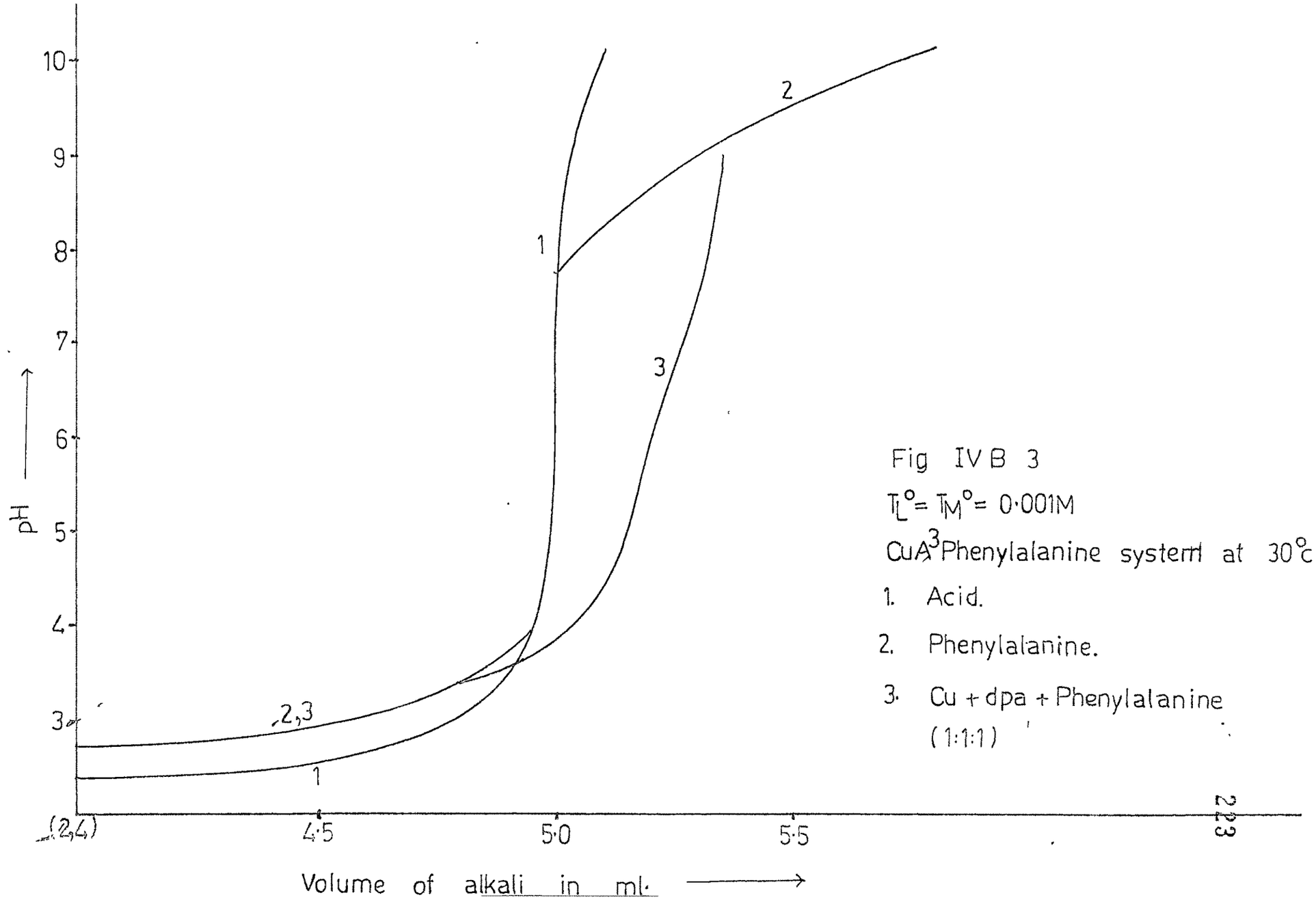


Fig IV B 3

$T_L^o = T_M^o = 0{\cdot}001M$

CuA^3 Phenylalanine system at 30°C

1. Acid.
2. Phenylalanine.
3. Cu + dpa + Phenylalanine (1:1:1)

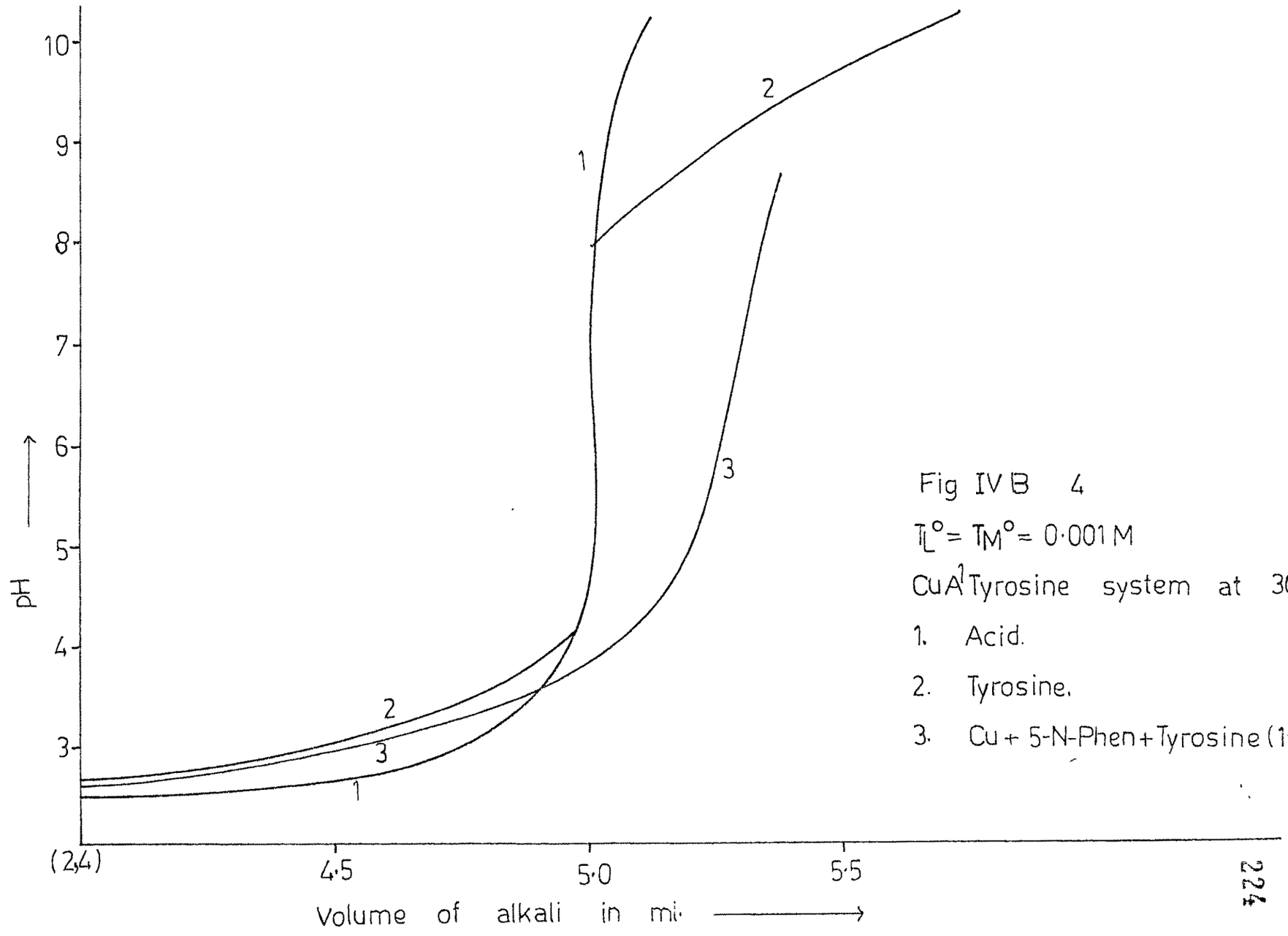


Fig IV B 4

$T_L^\circ = T_M^\circ = 0{\cdot}001$ M

Cu Tyrosine system at 30°c

1. Acid.
2. Tyrosine.
3. Cu + 5-N-Phen + Tyrosine (1:1:1)

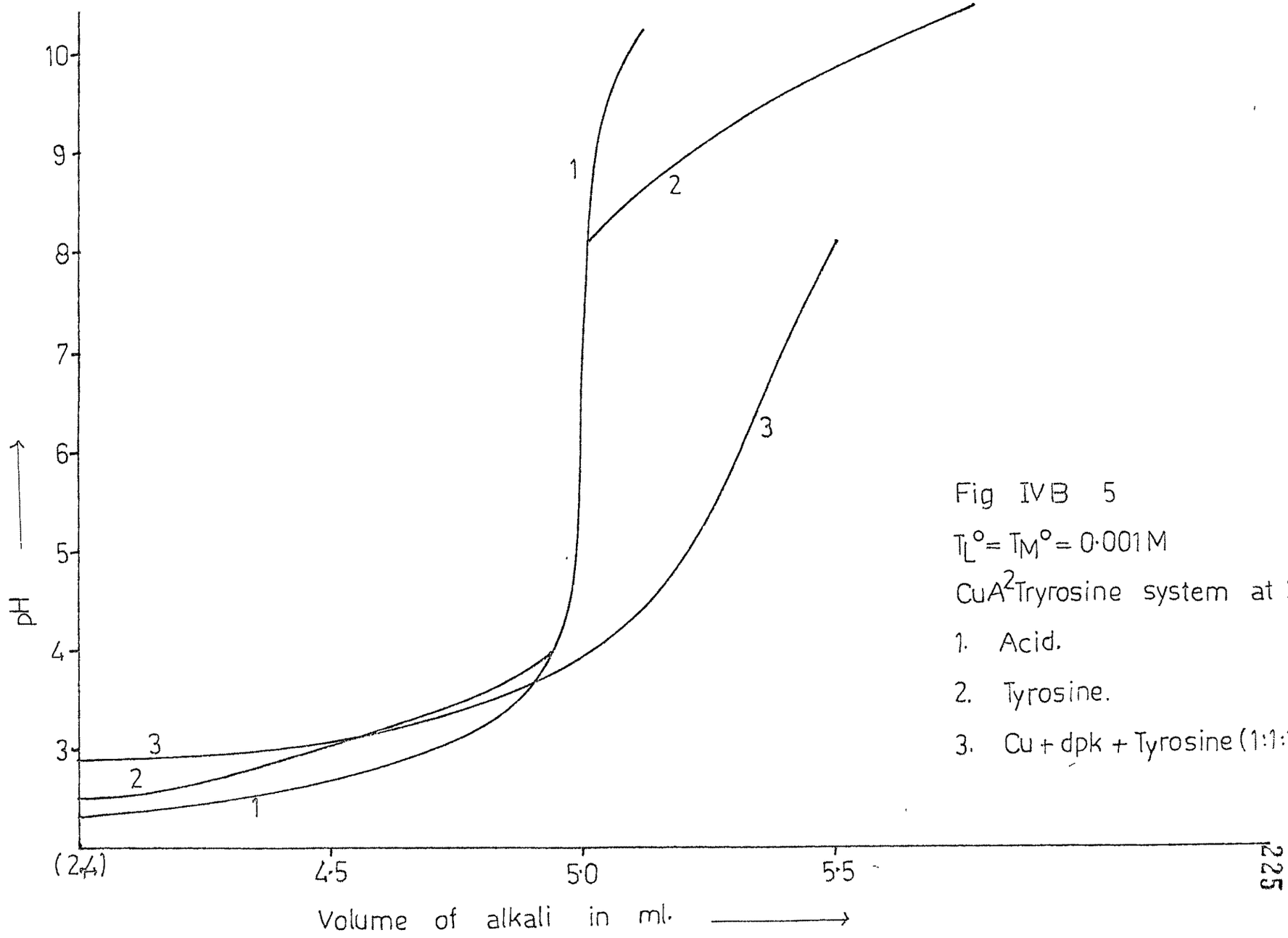


Fig IV B 5

$T_L^\circ = T_M^\circ = 0{\cdot}001\,M$

CuA^2 Tryrosine system at 30°c

1. Acid.
2. Tyrosine.
3. Cu + dpk + Tyrosine (1:1:1)

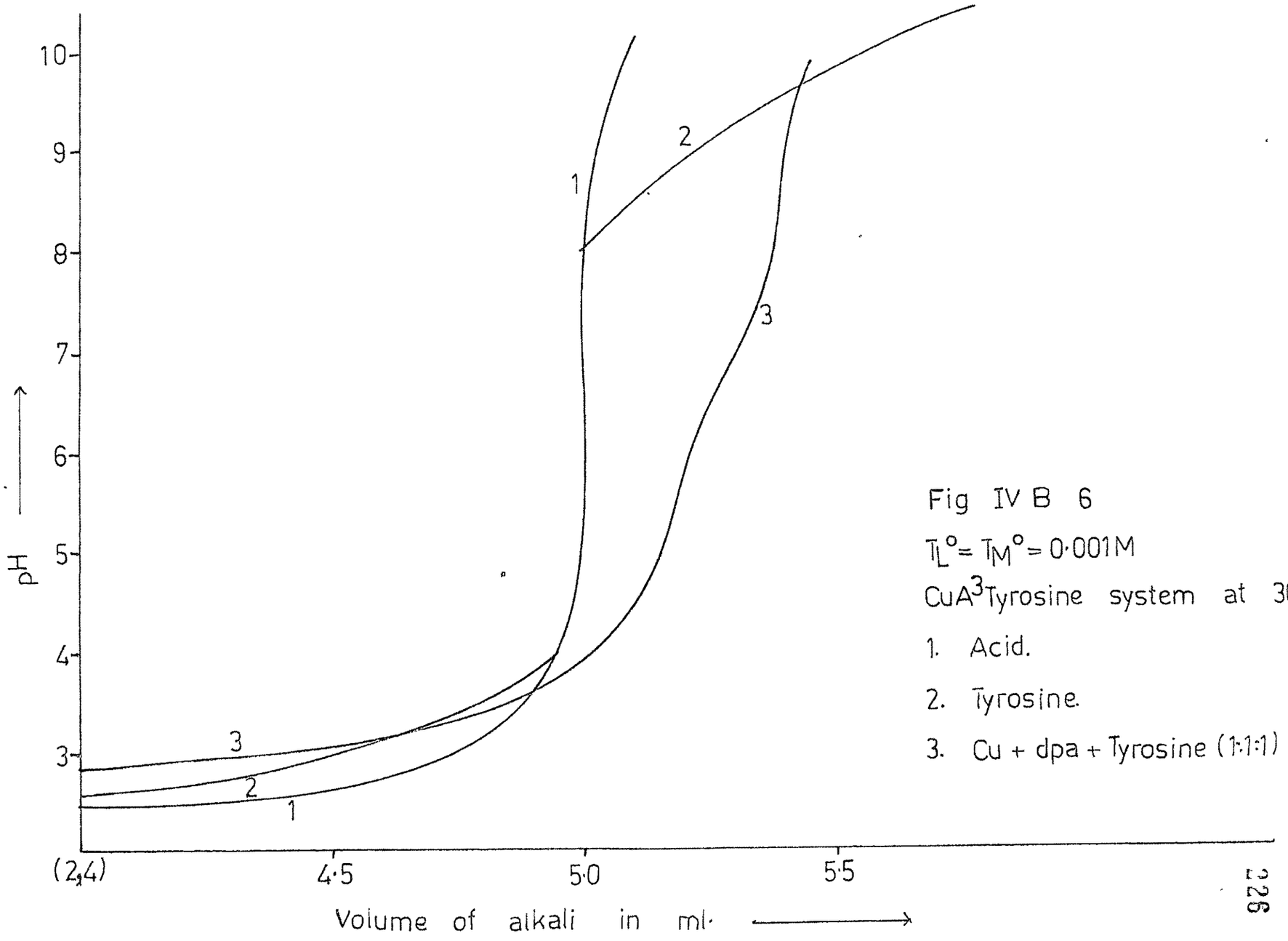


Fig IV B 6

$T_L^o = T_M^o = 0.001M$

CuA^3Tyrosine system at 30°c

1. Acid.
2. Tyrosine.
3. Cu + dpa + Tyrosine (1:1:1)

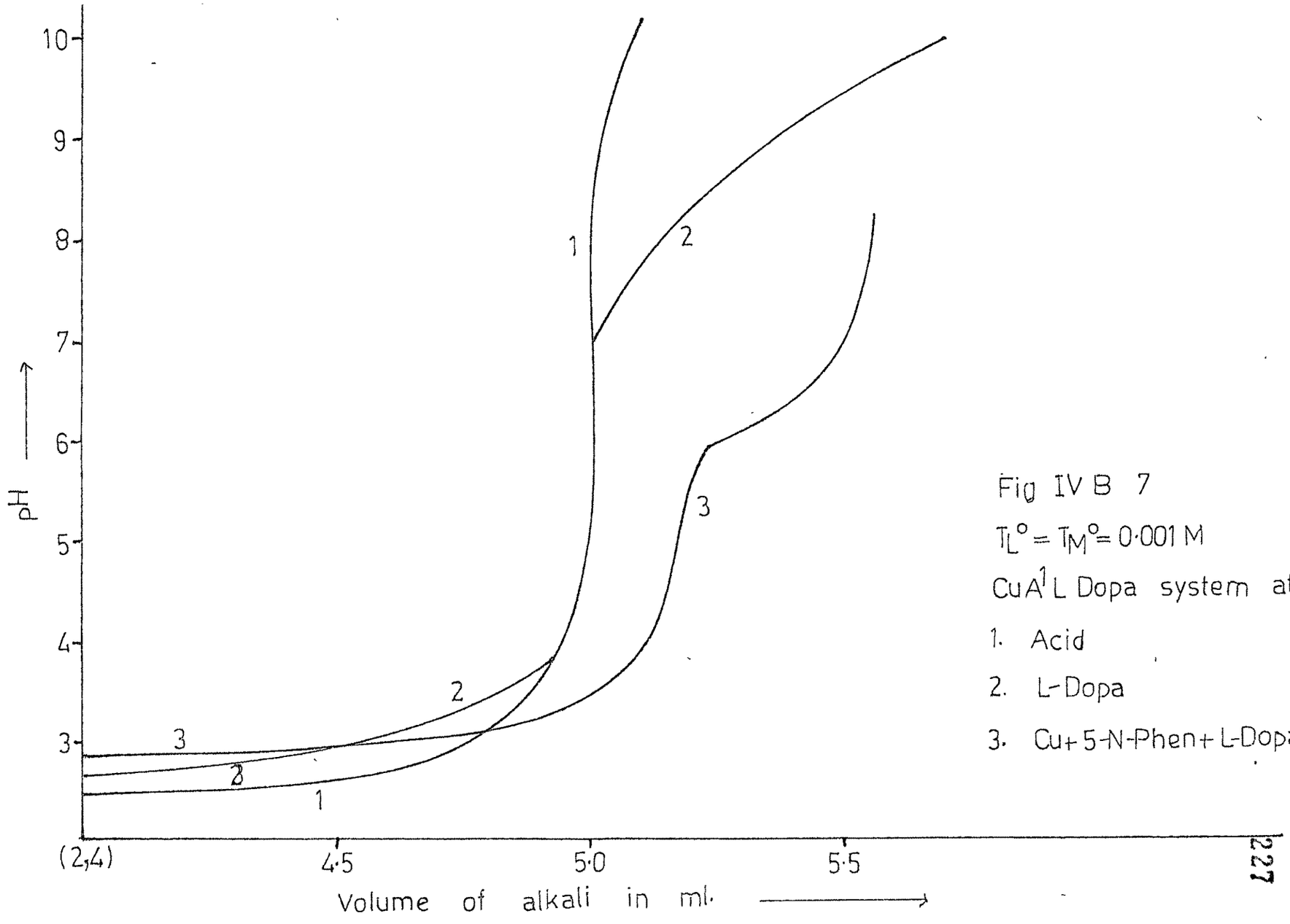


Fig IV B 7

$T_L^\circ = T_M^\circ = 0{\cdot}001$ M

CuA^1 L Dopa system at 30°c

1. Acid
2. L-Dopa
3. Cu+5-N-Phen+L-Dopa(1:1:1)

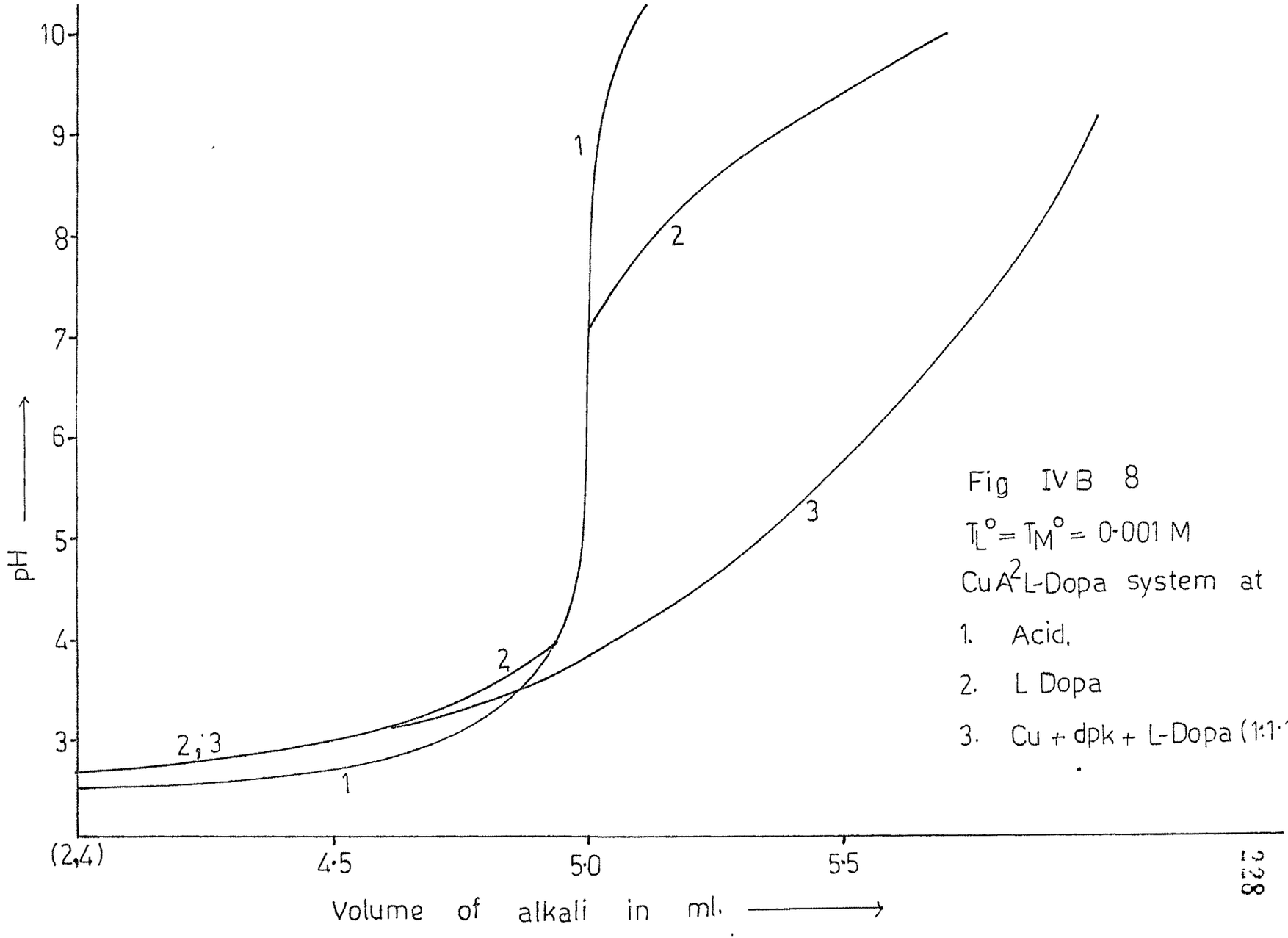


Fig IV B 8

$T_L^\circ = T_M^\circ = 0{\cdot}001$ M

CuA^2 L-Dopa system at 30°c

1. Acid.
2. L Dopa
3. Cu + dpk + L-Dopa (1:1:1)

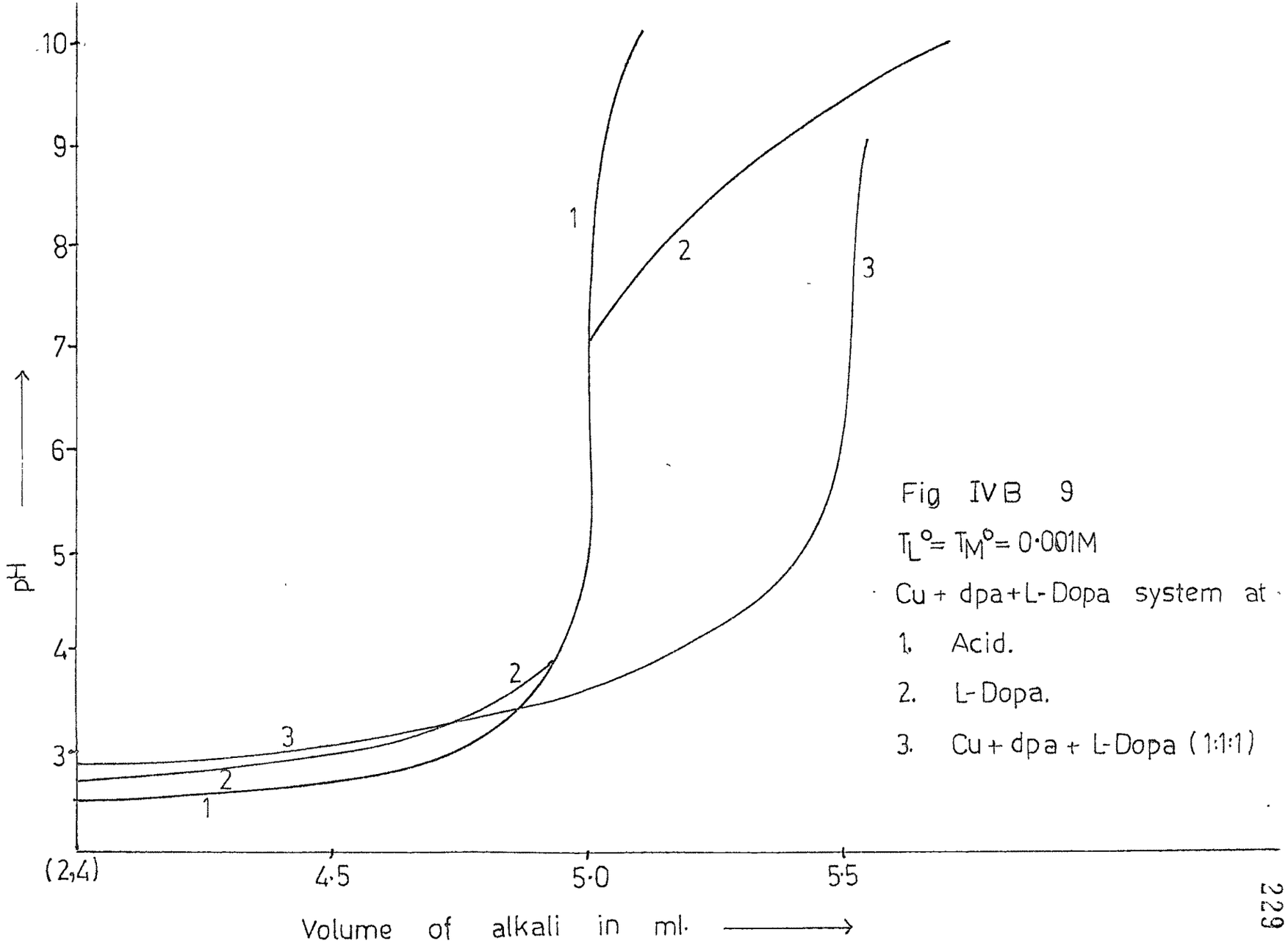


Fig IV B 9

$T_L^\circ = T_M^\circ = 0{\cdot}001M$

Cu + dpa + L-Dopa system at 30°c

1. Acid.
2. L-Dopa.
3. Cu + dpa + L-Dopa (1:1:1)

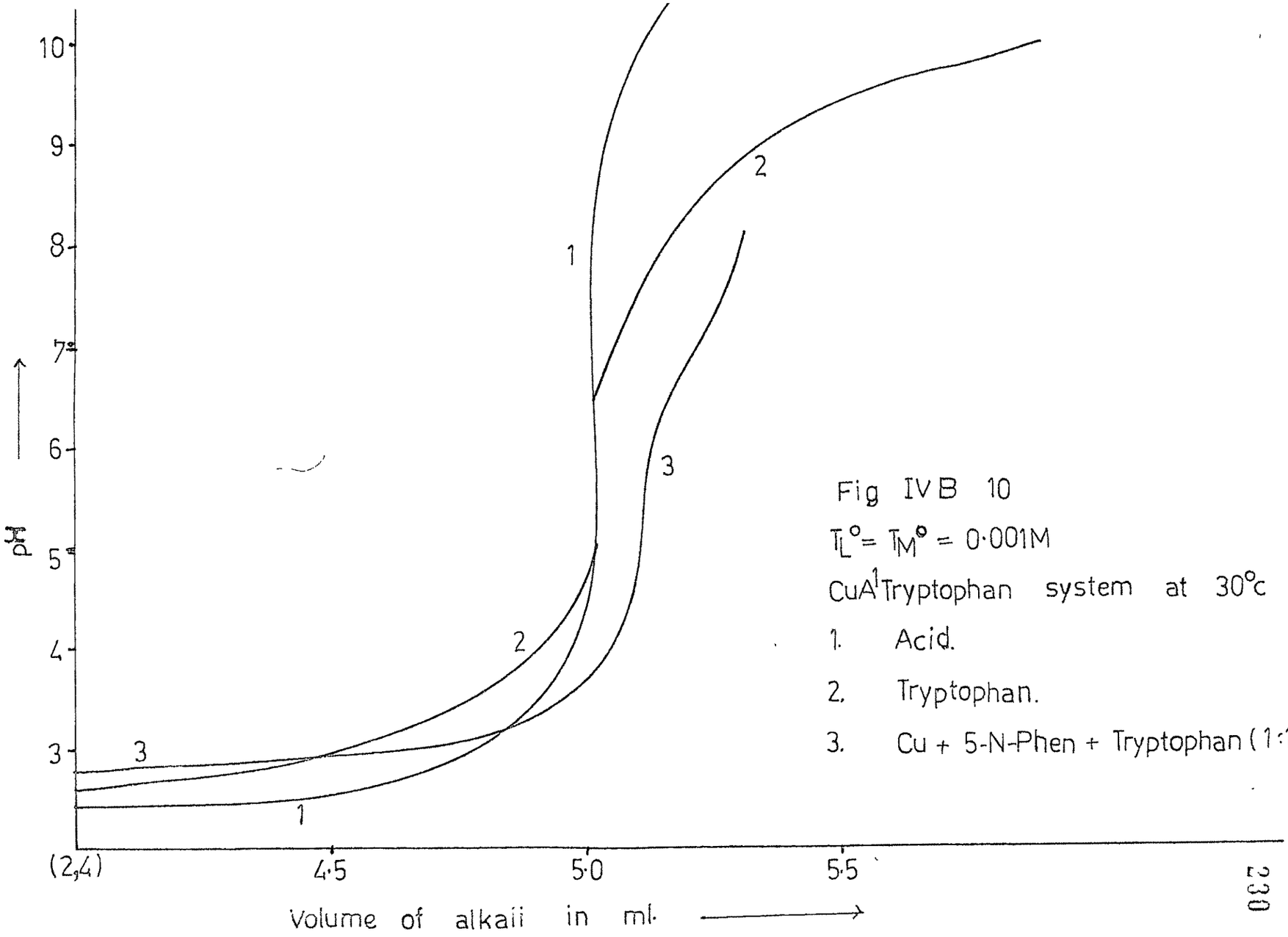


Fig IV B 10

$T_L^\circ = T_M^\circ = 0{\cdot}001M$

CuA^1 Tryptophan system at 30°c

1. Acid.
2. Tryptophan.
3. Cu + 5-N-Phen + Tryptophan (1:1:1)

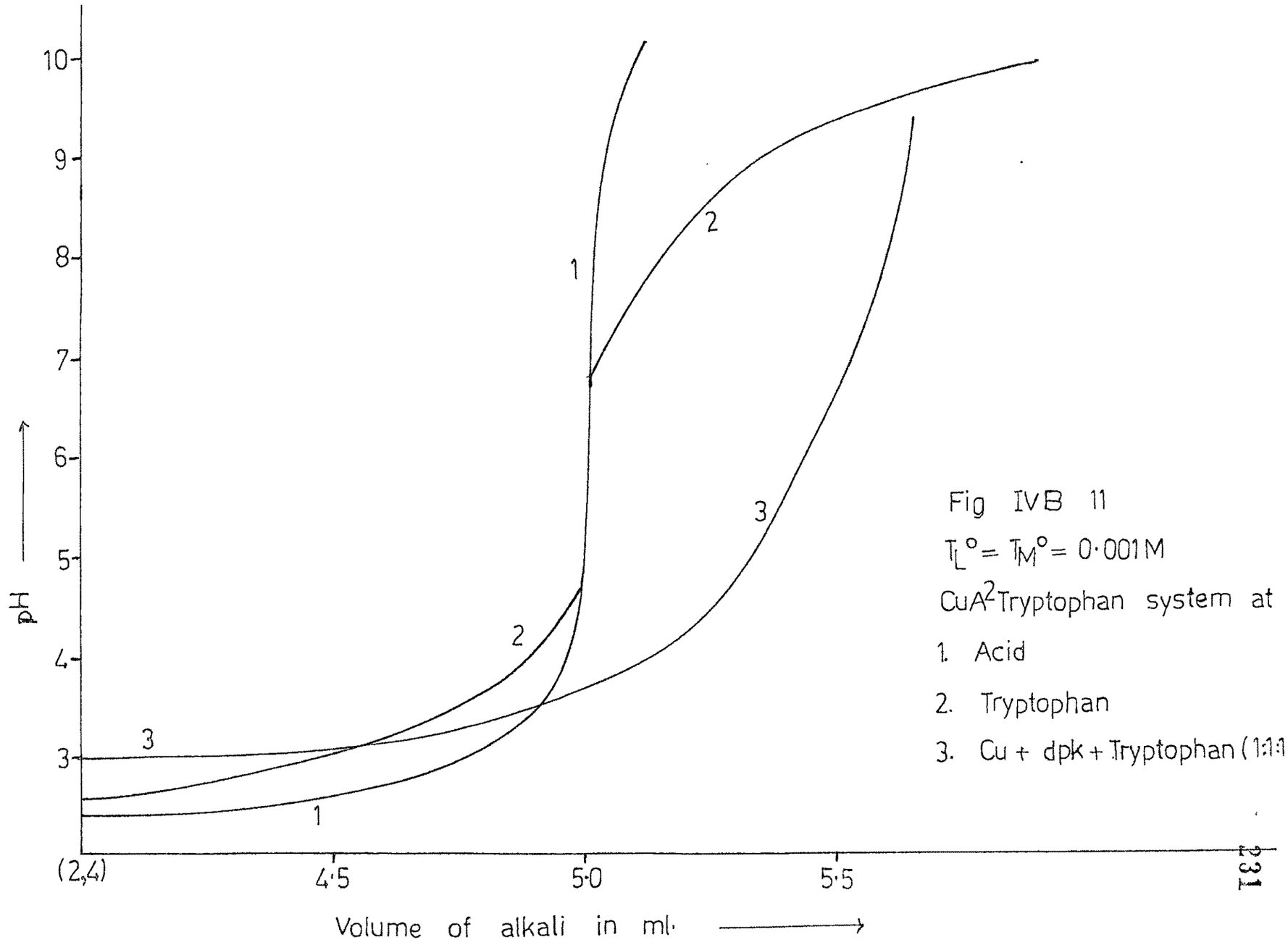


Fig IVB 11

$T_L^\circ = T_M^\circ = 0{\cdot}001\,M$

CuA^2 Tryptophan system at 30°c

1. Acid
2. Tryptophan
3. Cu + dpk + Tryptophan (1:1:1)

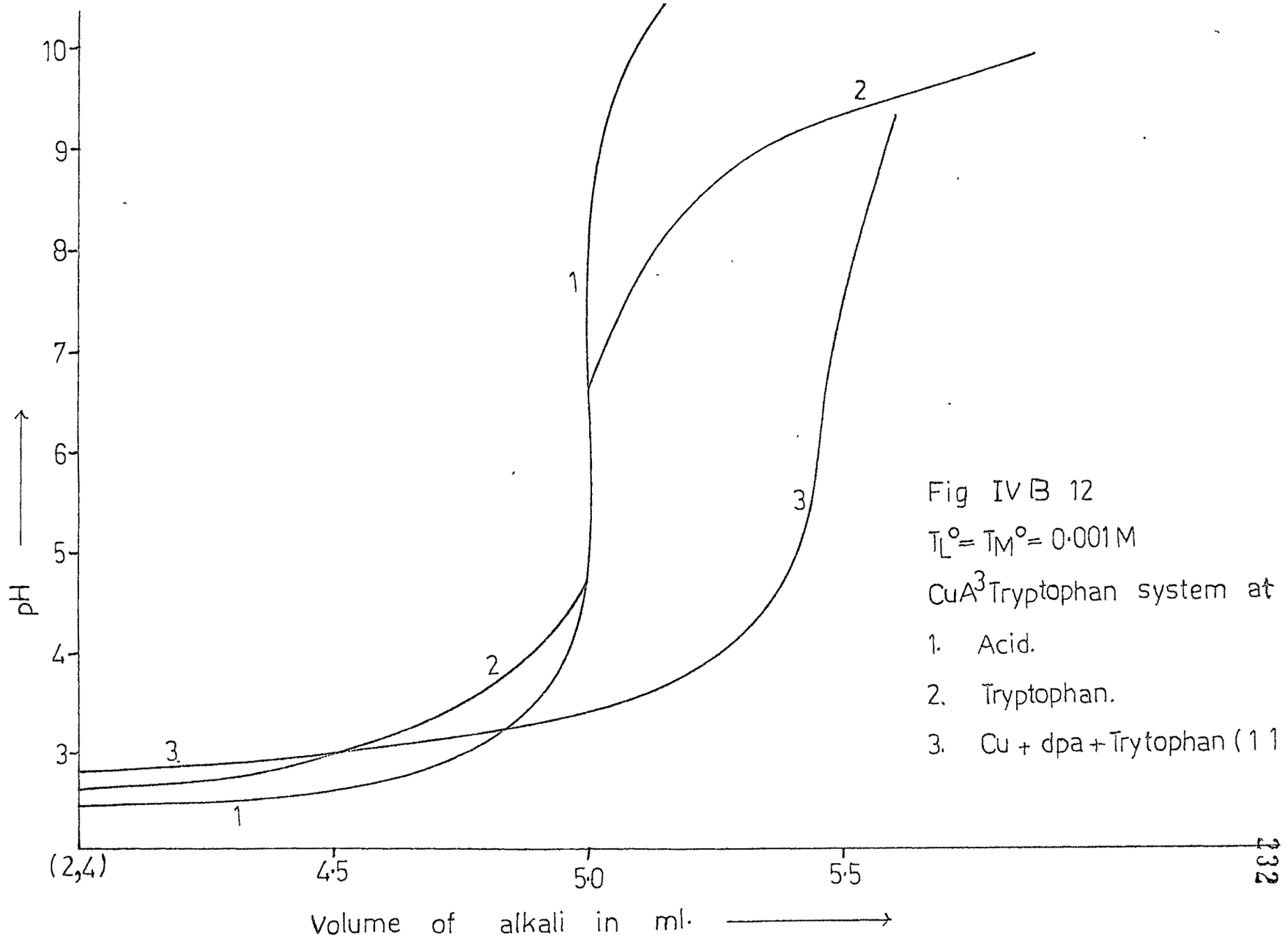


Fig IV B 12

$T_L^\circ = T_M^\circ = 0{\cdot}001$ M

CuA^3 Tryptophan system at 30°c

1. Acid.
2. Tryptophan.
3. Cu + dpa + Trytophan (1 1 1)

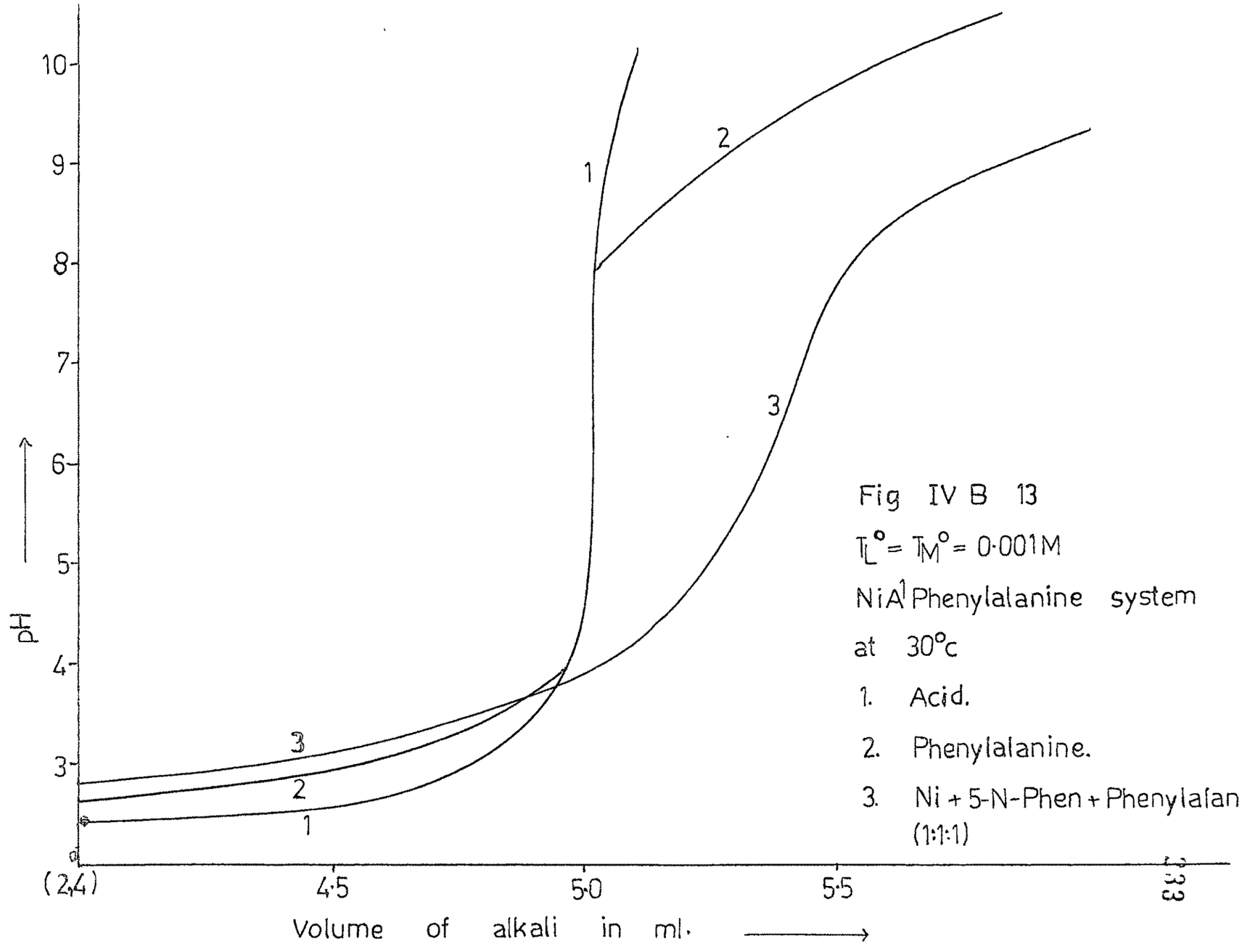


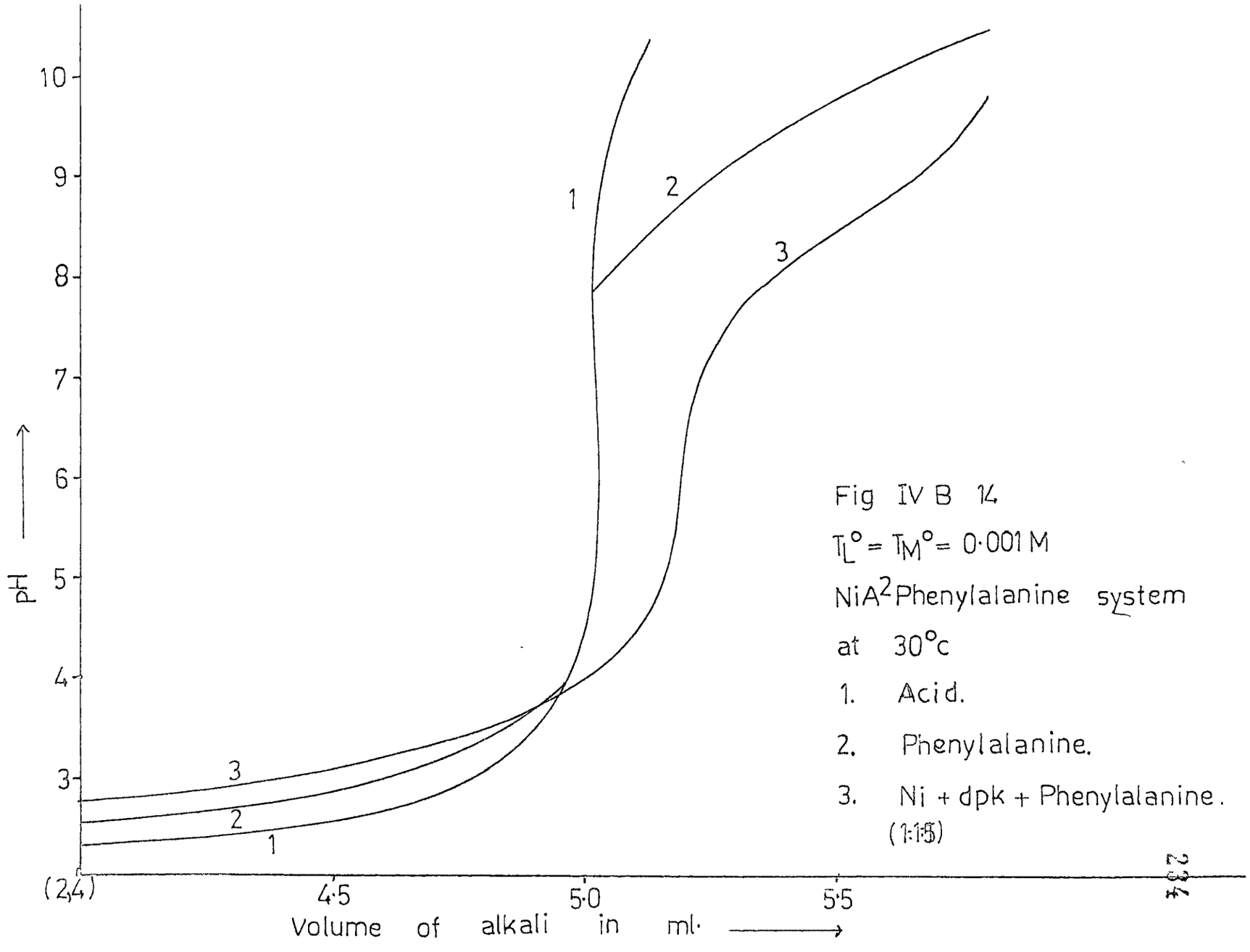
Fig IV B 13

$T_L^\circ = T_M^\circ = 0.001M$

Ni A[1] Phenylalanine system

at 30°c

1. Acid.
2. Phenylalanine.
3. Ni + 5-N-Phen + Phenylalanine (1:1:1)


10
9
8
7
6
5
4
3
pH
1
2
3
3
2
1
(2.4)
4·5
5·0
5·5
Volume of alkali in ml.
Fig IV B 14
$T_L^\circ = T_M^\circ = 0.001$ M
NiA^2 Phenylalanine system
at 30°c
1. Acid.
2. Phenylalanine.
3. Ni + dpk + Phenylalanine.
(1:1:5)

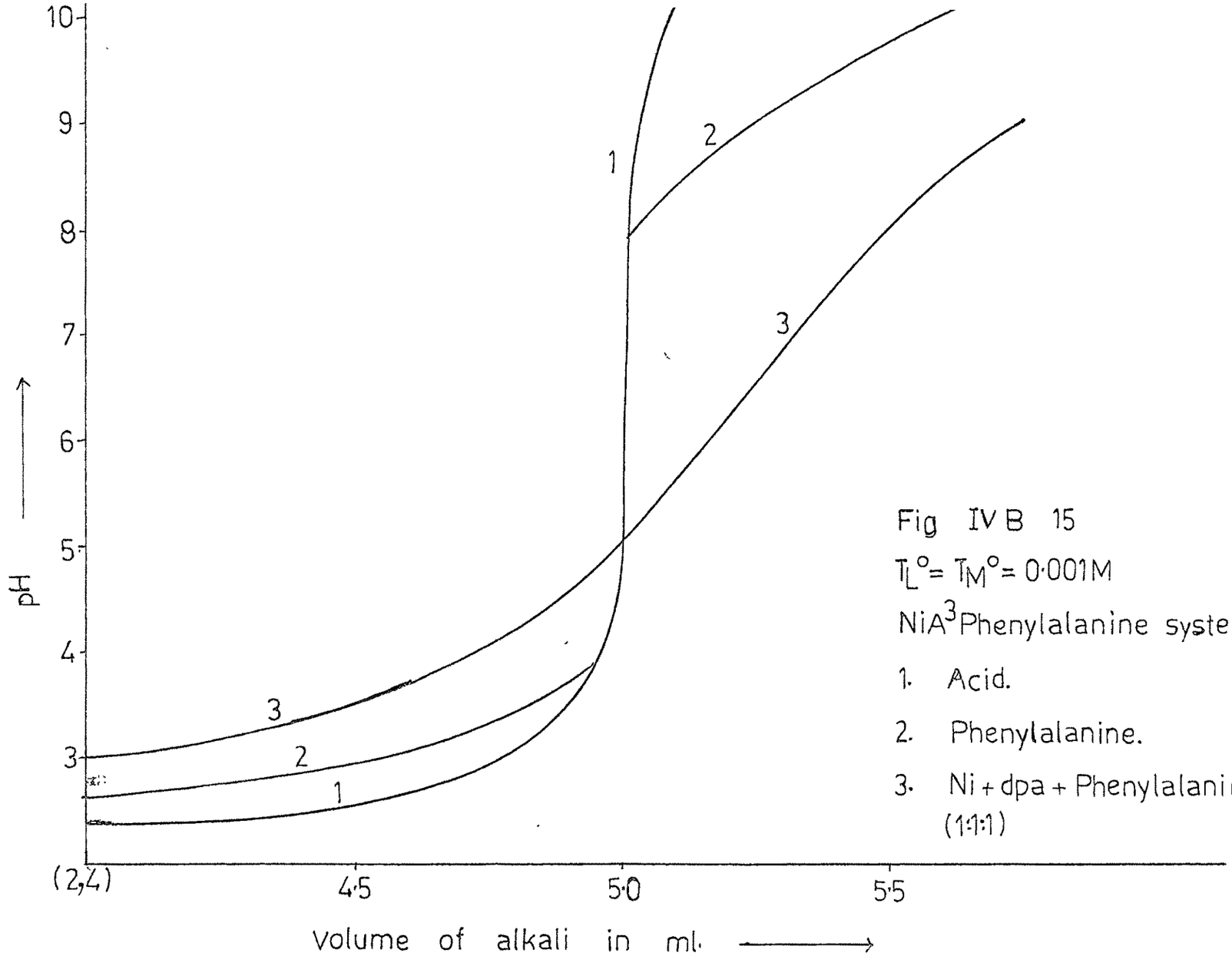


Fig IV B 15

$T_L^\circ = T_M^\circ = 0{\cdot}001M$

NiA^3 Phenylalanine system at 30°c

1. Acid.
2. Phenylalanine.
3. Ni + dpa + Phenylalanine. (1:1:1)

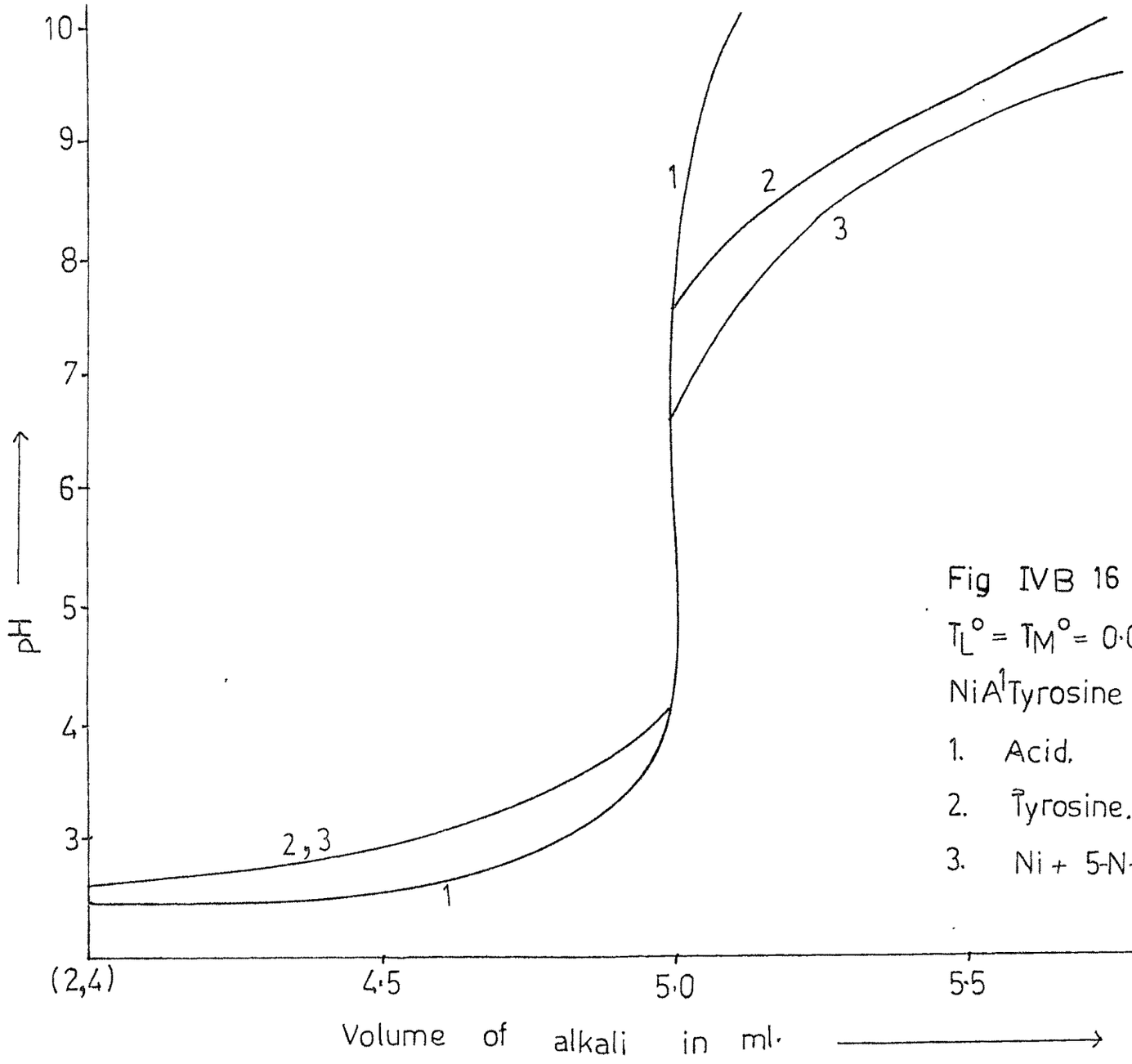


Fig IVB 16

$T_L^\circ = T_M^\circ = 0.001\,M$

NiA^1Tyrosine system at 30°c

1. Acid.
2. Tyrosine.
3. Ni + 5-N-Phen + Tyrosine (1:1:1)

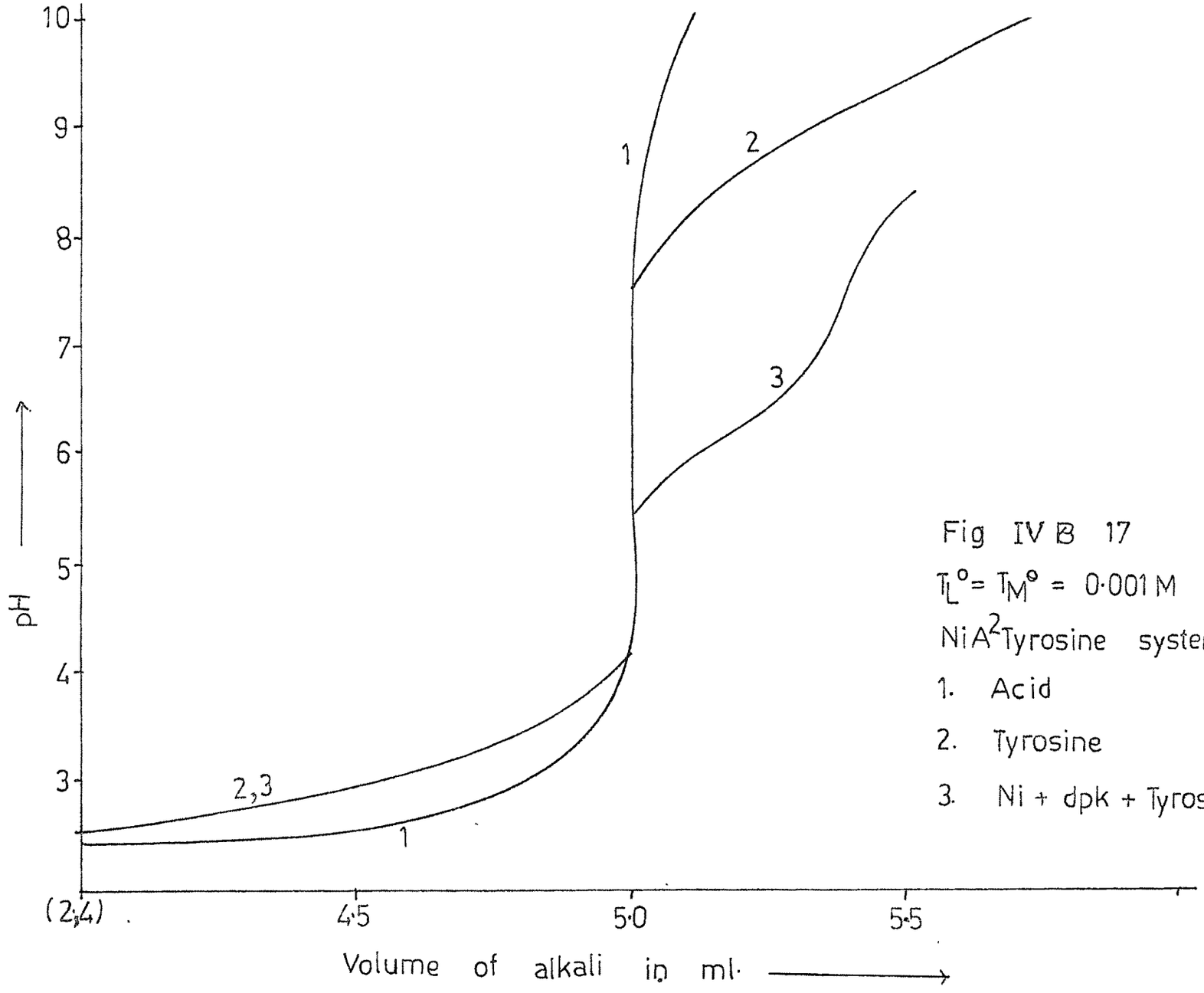


Fig IV B 17

$T_L^o = T_M^o$ = 0·001 M

Ni A^2 Tyrosine system at 30°c

1. Acid
2. Tyrosine
3. Ni + dpk + Tyrosine (1:1:1)

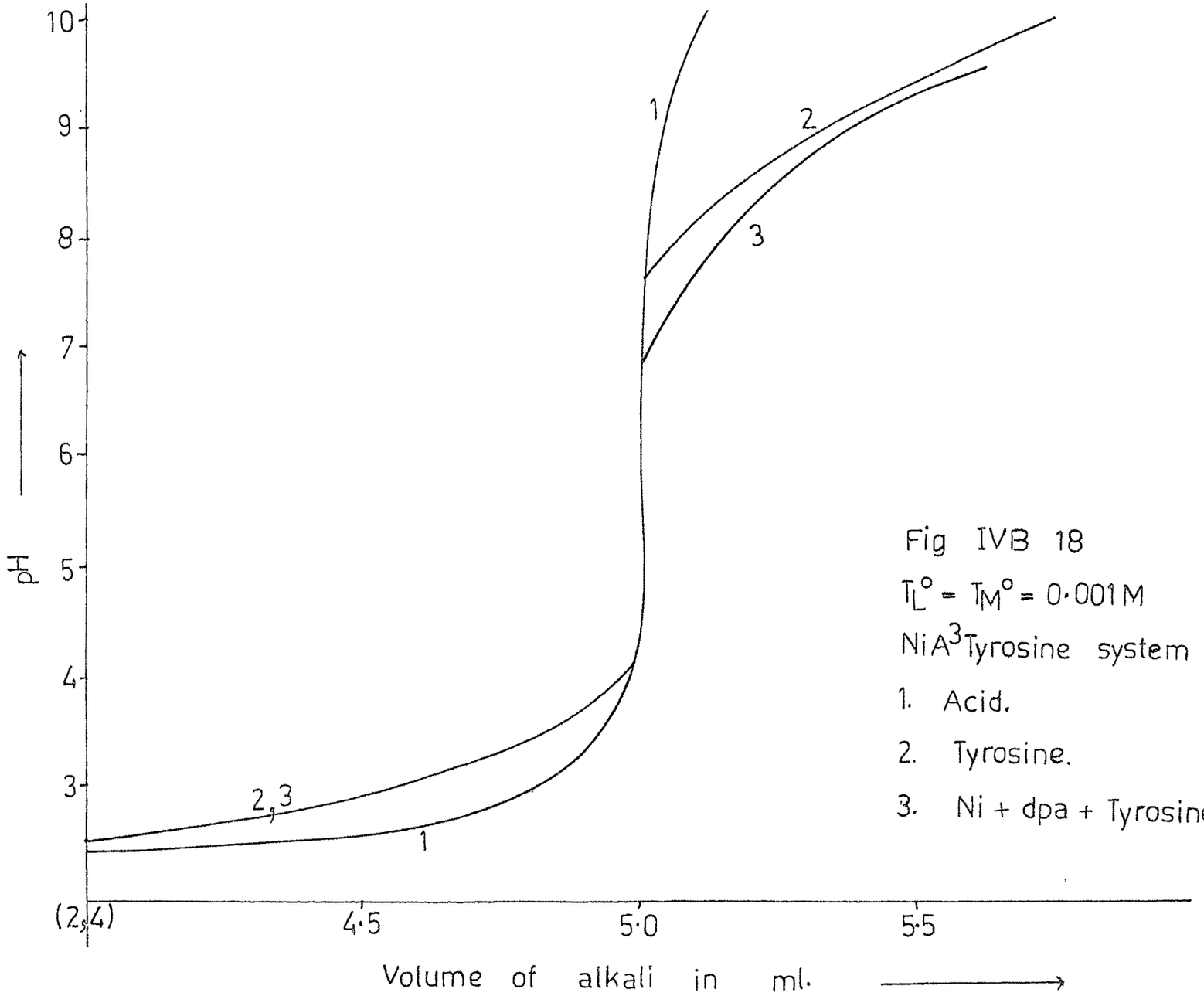


Fig IVB 18

$T_L^\circ = T_M^\circ = 0{\cdot}001\,M$

NiA^3Tyrosine system at 30°c

1. Acid.
2. Tyrosine.
3. Ni + dpa + Tyrosine (1:1:1)

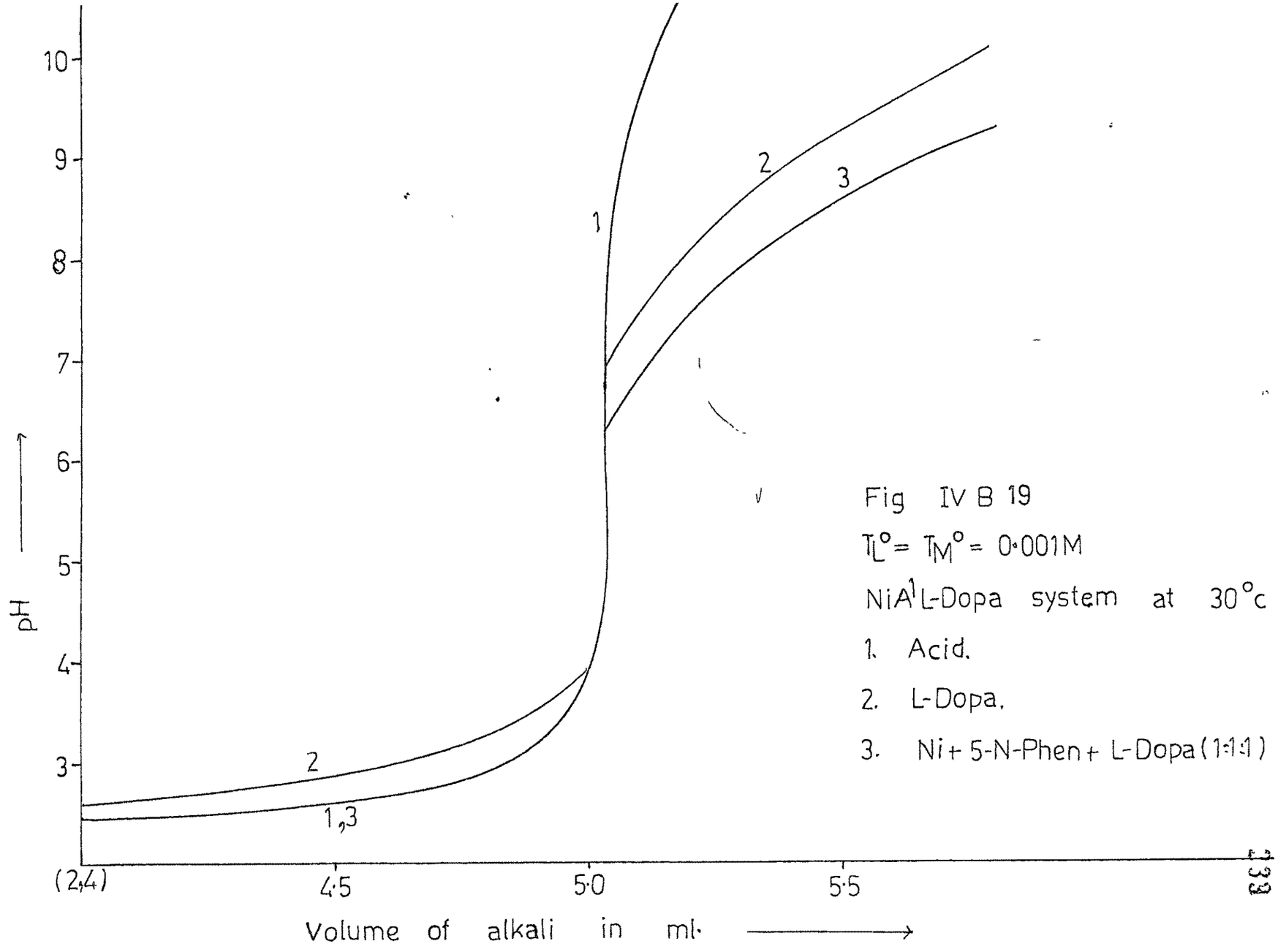


Fig IV B 19

$T_L^\circ = T_M^\circ = 0{\cdot}001M$

NiA[1] L-Dopa system at 30°c

1. Acid.
2. L-Dopa.
3. Ni + 5-N-Phen + L-Dopa (1:1:1)

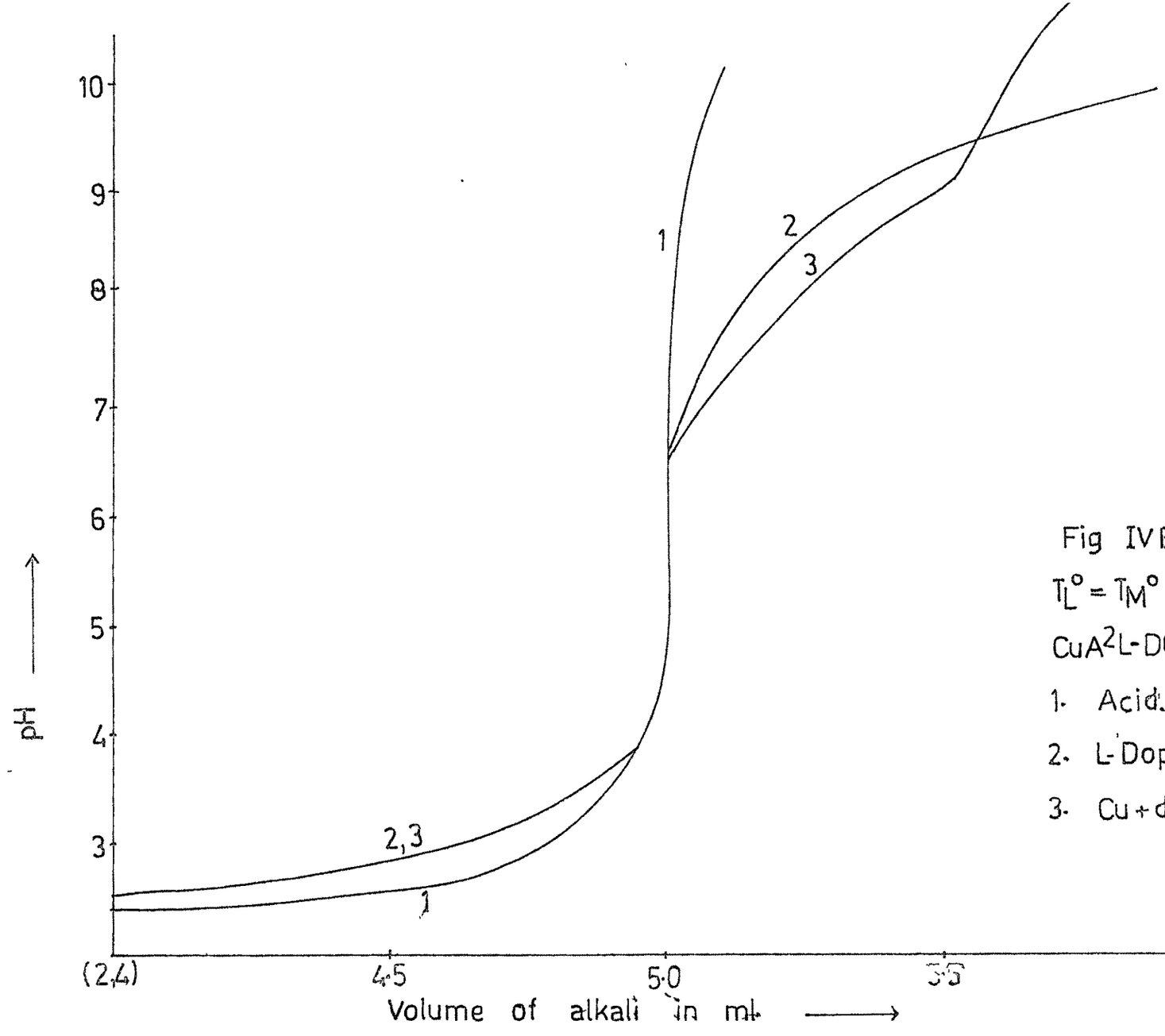


Fig IVB 20

$T_L^\circ = T_M^\circ$ = 0·001M

CuA^2L-DOPA system at 30°c

1. Acid.
2. L-Dopa
3. Cu + dpk + L-Dopa (1:1:1)

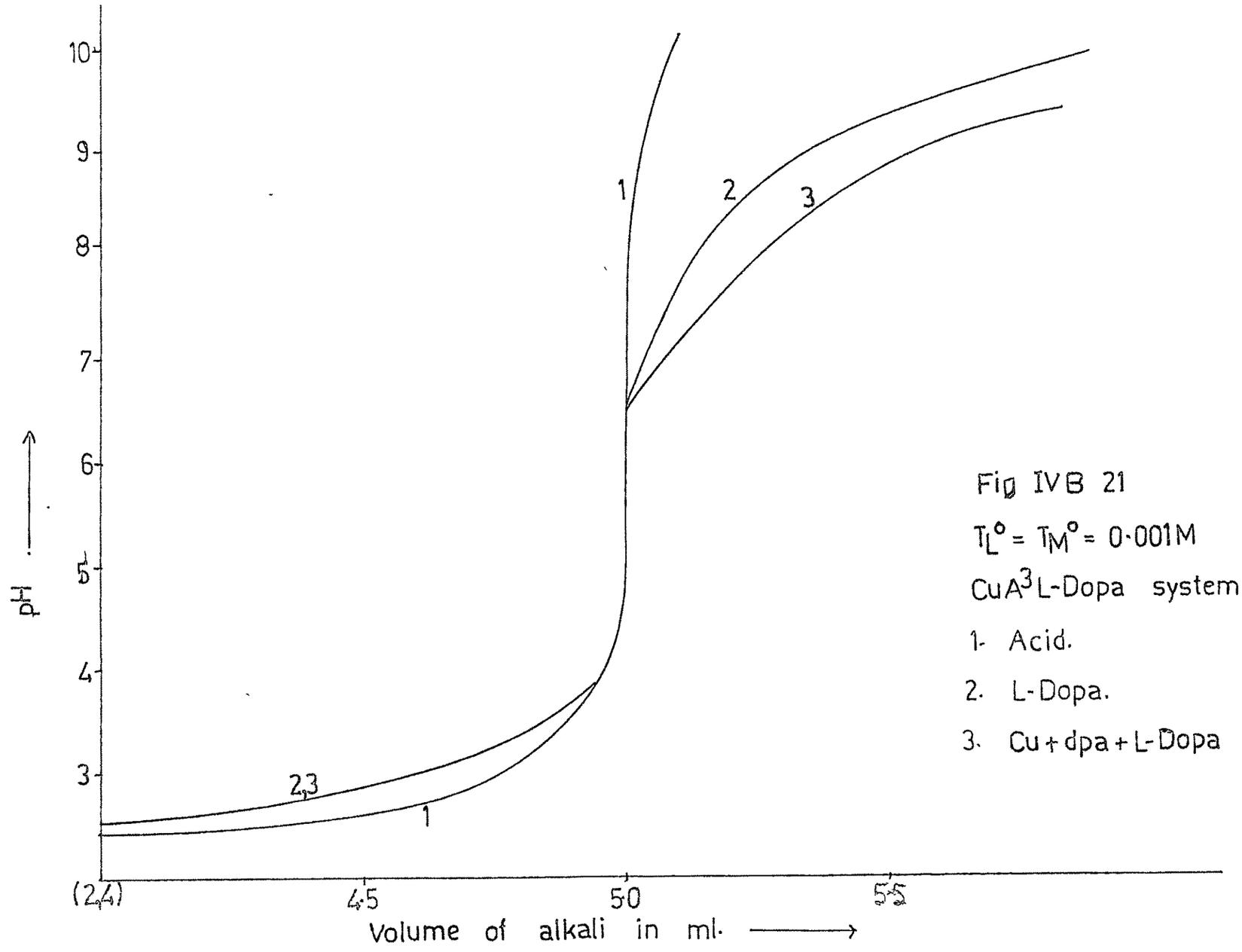


Fig IVB 21

$T_L^\circ = T_M^\circ = 0.001M$

CuA^3 L-Dopa system at 30°c

1. Acid.
2. L-Dopa.
3. Cu + dpa + L-Dopa

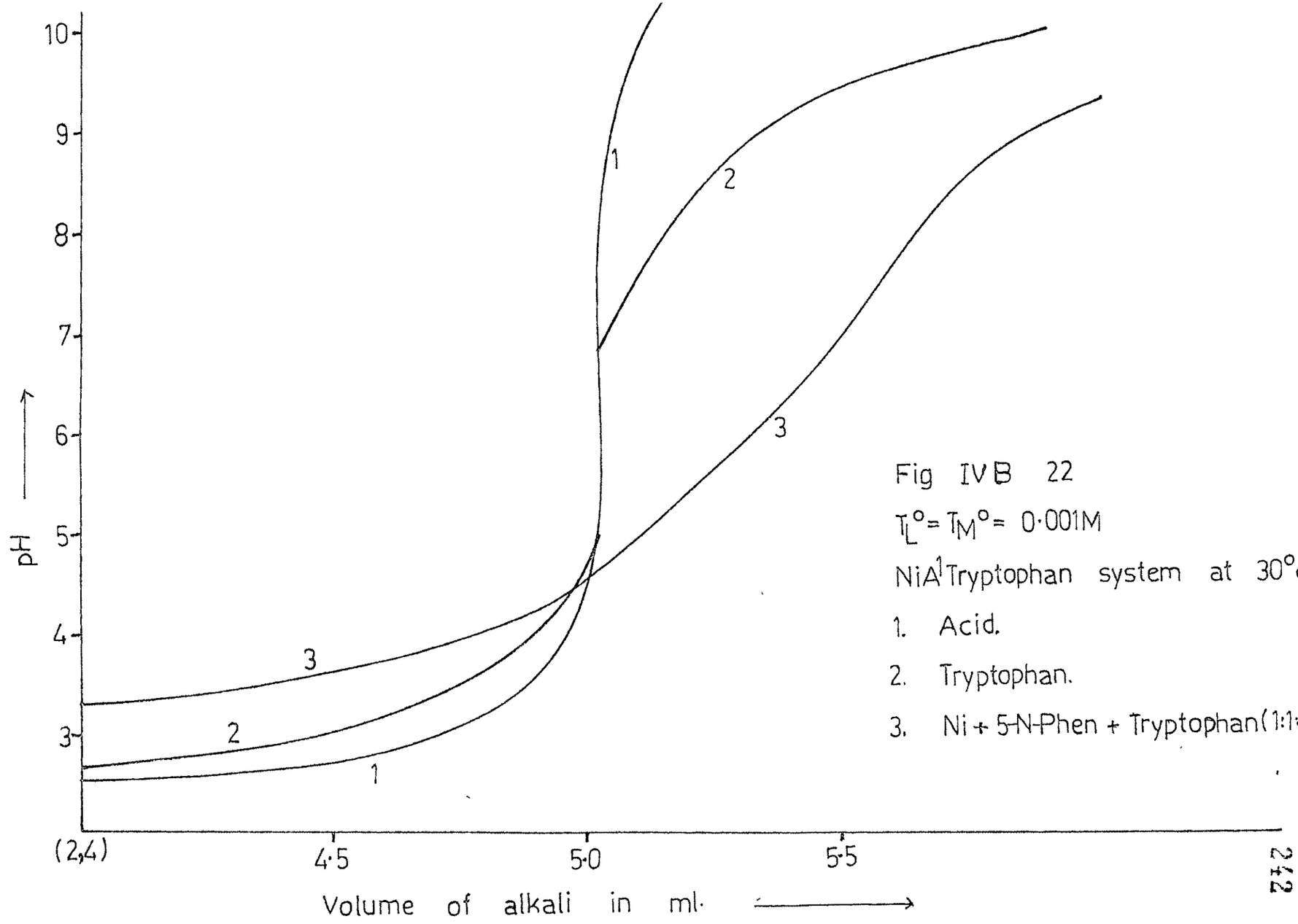


Fig IV B 22

$T_L^o = T_M^o = 0.001M$

NiA^1 Tryptophan system at 30°c

1. Acid.
2. Tryptophan.
3. Ni + 5-N-Phen + Tryptophan (1:1:1)

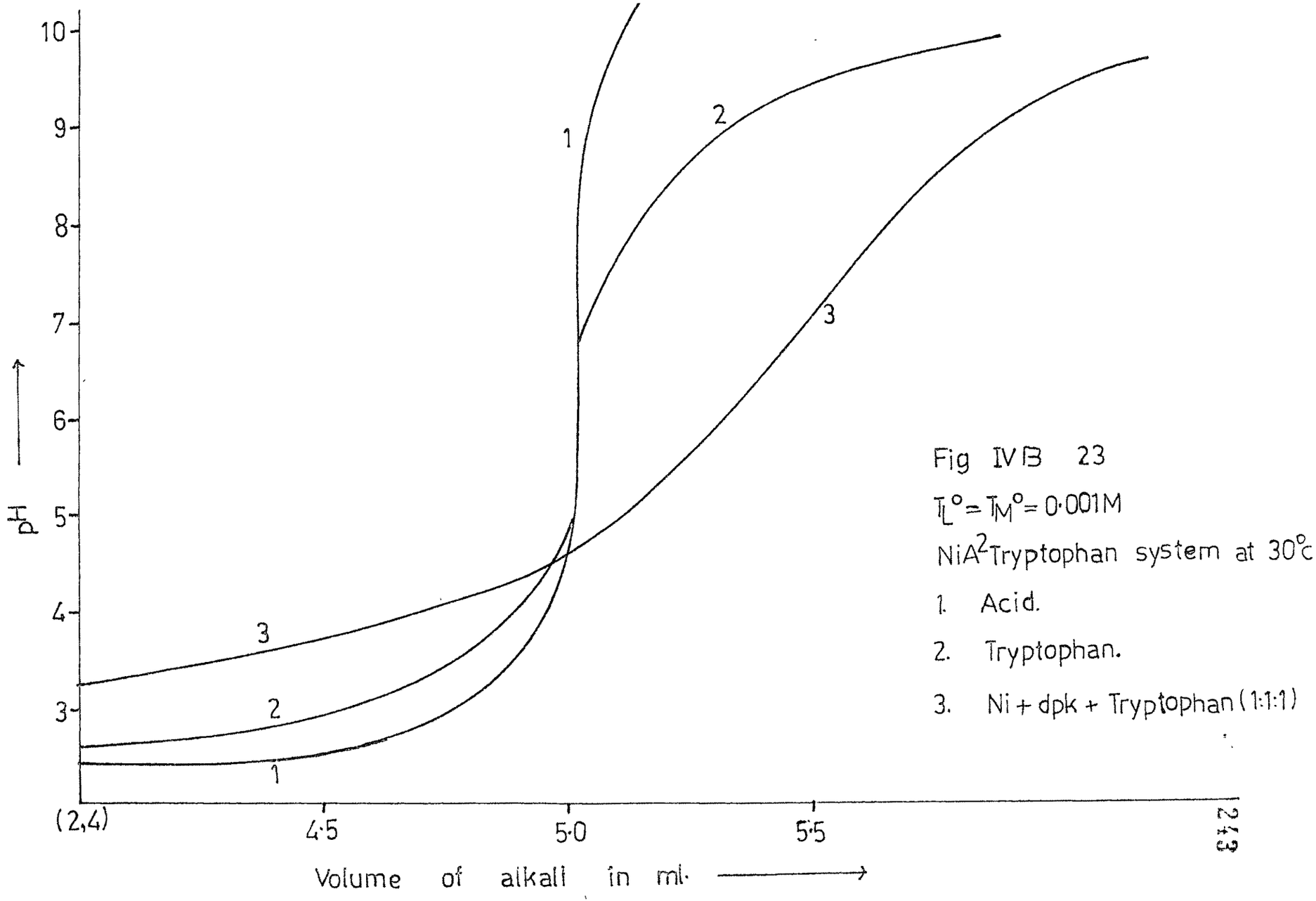


Fig IV B 23

$T_L^\circ = T_M^\circ = 0.001M$

NiA^2 Tryptophan system at 30°c

1. Acid.
2. Tryptophan.
3. Ni + dpk + Tryptophan (1:1:1)

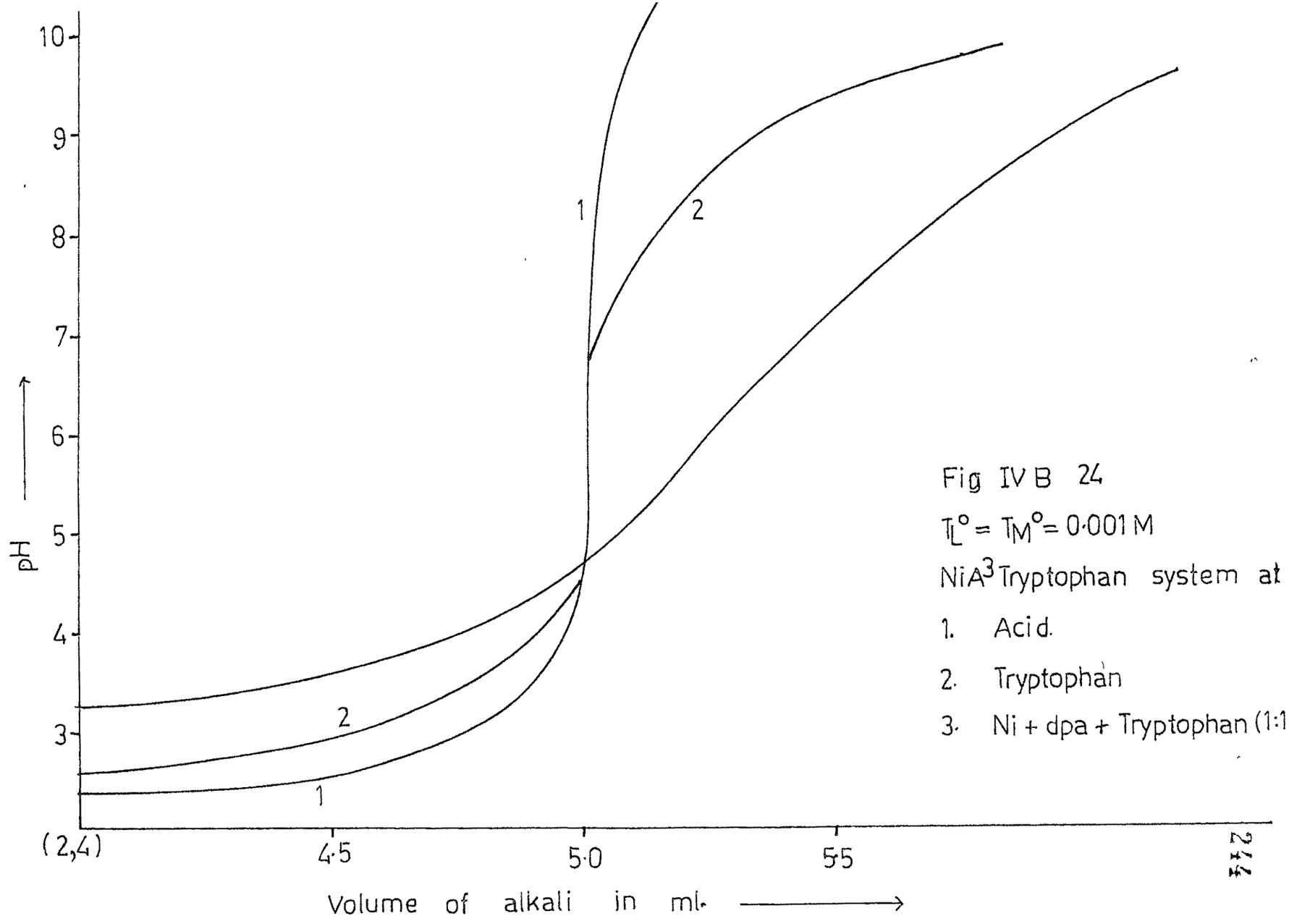


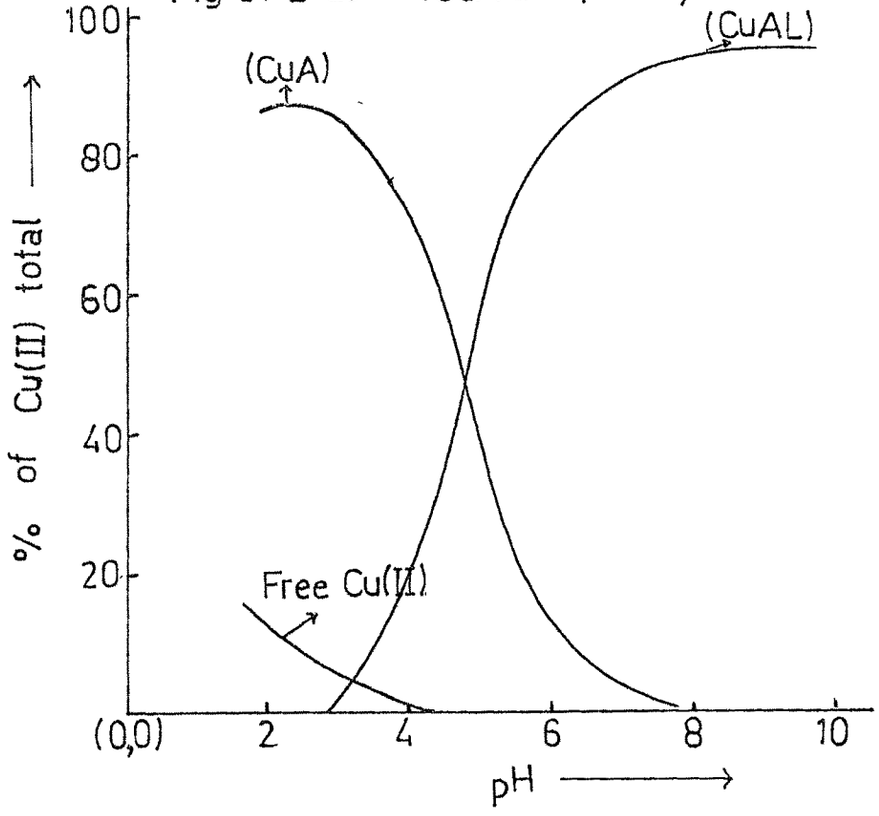
Fig IV B 24

$T_L^\circ = T_M^\circ = 0.001$ M

NiA^3 Tryptophan system at 30°C

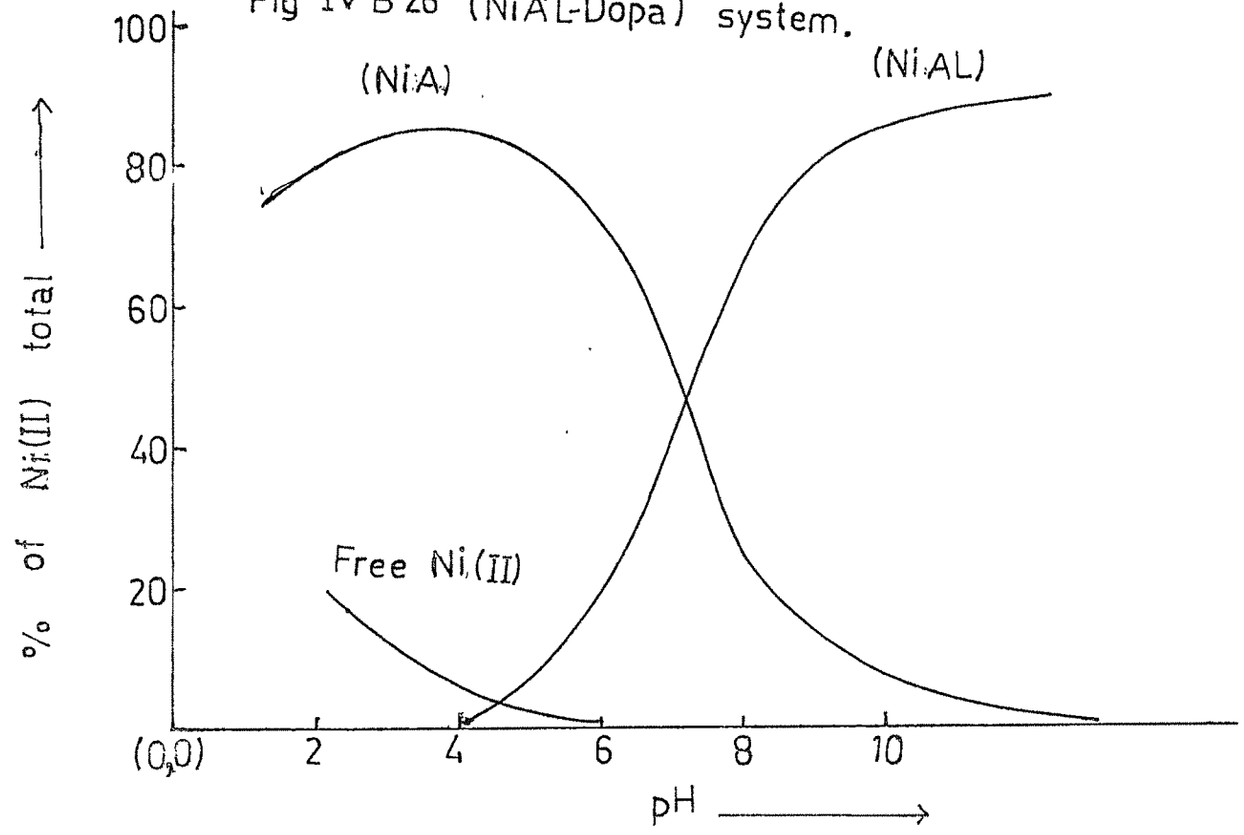
1. Acid.
2. Tryptophan
3. Ni + dpa + Tryptophan (1:1:1)

Fig IV B 25 (CuA[1]L-Dopa) system



Variation of concentrations of different species with pH ⟶

Fig IV B 26 (NiAL-Dopa) system.



Variation of concentrations of different species with pH

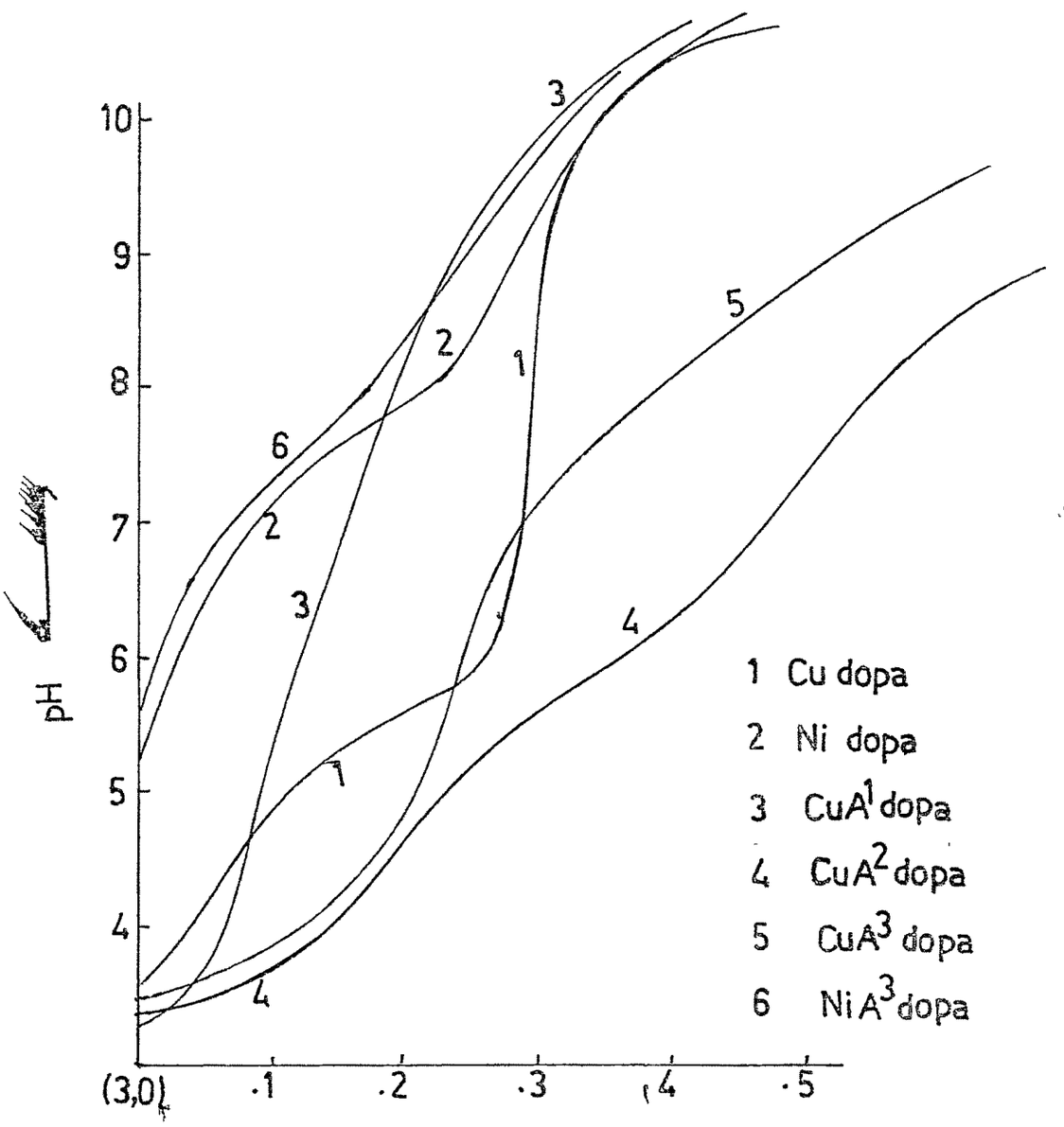


Fig IV B 27 Interaction of dopa with M(II) and [MA], M = Cu(II) or Ni (II)

Results & Discussions

In cases of phenylalanine (L^{21}), tyrosine (L^{22}) and tryptophan (L^{24}) co-ordination takes place from aminocarboxylate end of the ligand (L) both in [ML] and [MAL] complexes. The single phenolic -OH group of tyrosine is less co-ordinating than the bidentate aminocarboxylate, and hence remains unco-ordinated. As observed earlier by Rajan and coworkers[136,172] in case of [Cu(II)dopa], the present computer calculations also show that upto pH 5.0, the co-ordination of dopa is from aminocarboxylate end. But at higher pH dopa co-ordinates from the catechol end. This is confirmed by seeing the titration curve 5 of Fig. IV827.

In [Cu L-dopa] (1 : 1), two buffer regions are observed. One corresponding to amino carboxylate co-ordination between m = 0 to m = 1, where m is the number of mole of base added per mole of total metal ion, due to liberation of NH_3^+ proton and second due to catechol co-ordination between m = 1 to m = 3. In case of Ni : dopa (1 : 1) solution, only one buffer region was observed between m = 0 to m = 1, over the whole pH range 4.0 to 8.0 showing co-ordination of dopa only from aminocarboxylate end.

However, as observed earlier in case of [Cubipydopa][195] in the present [CuAdopa] complexes also, L-dopa is observed to co-ordinate from amino acid end only over the whole pH range. It is seen from the titration curve of both [CuAdopa] and [NiAdopa] where

A = 5-nitro-1,10-phenanthroline and dpa against alkali (Fig. 27), only one buffer region is observed between m = 0 - 1 upto pH 5.5. This shows that the co-ordination is only from the aminocarboxylate end over the whole pH range. Any co-ordination from the catechol end should have shown a break at higher pH in [CuAdopa].

In the case of [CudpkL-dopa], in the buffer region 0 to 1, the titration curve run parallel to [Cudipy L-dopa] upto pH 5.5 indicating that the co-ordination is only from from aminocarboxylate end of L-dopa and dpk is co-ordinated from N-N end. The second buffer region at pH 5.5, from m = 1 to 2 indicates that dpk changesits co-ordinating site from N-N to $N\text{-}O^{-}$ but L-dopa is co-ordinated from the amino carboxylate end only.

This has been further confirmed by the study of the absorption spectra of [CuAphenylalanine], [CuA tyrosine], [CuA dopa], [CuA tryptophan] and comparing with that of [CuA glycine]. It is observed that in all three complexes the d-d band occuring at 590 nm is similar to that in [CuA glycine] occuring at 609 nm. This shows that the co-ordination is from the aminocarboxylate end. Further in case of [CuA dopa] no charge transfer band at 435 nm, characteristics of phenolic $-OH^{195}$ co-ordination was observed upto pH 8.

Hence, in the refinement of the formation constant values of log $K_{Cu\ Adopa}$ by the computer program, dopa

has been considered to co-ordinate with [CuA] from the aminocarboxylate end throughout. The ternary complex species considered was $[CuAH_2L^3]$, unco-ordinated -OH group being undissociated, and reproducible results were obtained in each case. No convergence of results were obtained when species with catechol co-ordination was considered. In case of [CudpkL], the calculations were confined to pH 5.

It can be explained as follows.[195] In the lower pH range, dopa co-ordinates with [CuA] from amino-carboxylate end. The formation of dimeric species through catechol co-ordination cannot take place, because the other two equatorial co-ordination positions are occupied by A. Phenolate O^- cannot displace the co-ordinated aminocarboxylate even at higher pH because the substitution of electron withdrawing group over the ring reduces co-ordinating tendency of dopa phenolate O^- with [CuA]. Hence, the $[CuA(H_2L)]$ complex with aminocarboxylate co-ordination is retained upto higher pH. The co-ordination of phenolate O^- with Cu(II) of another molecule at the fifth and sixth position does not not take place, probably because Cu(II) does not favour axial co-ordination.

An interesting aspect that must be pointed out is the higher stability of phenylalanine, tyrosine, tryptophan and L-dopa ternary complexes as compared to the corresponding complexes of glycine. Normally in [CuAL]

complexes where L co-ordinates through N-O^-, value of Δ log K is negative.[26] However, in all the present complexes studied, though the co-ordination of L is from aminocarboxylate end, the value of Δ log K is more positive in case of Cu(II) complexes and only small negative in case of Ni(II) complexes.

The higher formation constants for these complexes is explained by considering that the aminocarboxylate end of phenylalanine, tyrosine, tryptophan or L-dopa co-ordinates with [CuA] and the phenyl, phenol or catechol part remains free. It may be expected to spread over the heteroaromatic N-base part of A leading to an intramolecular stacking interaction between the tertiary amines and the aromatic ring of the secondary ligand as suggested by Sigel in case of [Cu(II)(ophen) phenylacetate] complex.[196] However, construction of model shows that the aromatic ring of secondary ligand can spread only over the axial region of Cu(II) and not beyond. This rules out intramolecular interligand interaction.

The enhanced stability of these complexes can be explained by considering that the phenyl, hydroxyphenyl or indole moiety being hydrophobic seeks a position near to the metal ion and away from the bulk of the dipolar solvents as shown by Martin and coworkers.[193,194] A possibility of hydrophobic interaction between metal ion neighbourhood and the hydrophobic ring has also been suggested by them. Best known example of

hydrophobicity in the metal ion environment is in haemoglobin. It can be expected that the hydrophobicity of the metal environment increases on co-ordination with an aromatic N-base. Hence the interaction of [CuA] with the phenyl or hydroxyphenyl group is more, consequently, the ligand L are more strongly bound with [CuA] than $[Cu(H_2O)_n]$ resulting in more stable ternary complex. This leads to positive Δ log K in Cu(II) complex and less negative Δ log K in Ni(II) complexes.

Odani and Yamauchi[197] have considered shift of electron from metal ion to the aromatic ring of the amino acid. This facilitates the co-ordination of the second ligand stabilizing the ternary complex. If there is electron shift from metal ion to the aromatic part of the amino acid, it should facilitate the attachment of a σ bonding aliphatic diamine more than σ and π bonding aromatic diamines. However, in the present study it is seen that Δ log K is positive in [CuAaromatic$\overset{\text{amino}}{\wedge}$acid] whereas it is negative in [Cuen aromatic amino acid] as observed by Odani and Yamauchi. This indicates that the co-ordination of aromatic diamine with Cu(II) makes the environment more hydrophobic and helps in bringing the aromatic part of the amino acid closer to the metal ion in the ternary complex, resulting in greater stability of the ternary complex.

The stability of the complex $[CuA^1L]$ and $[CuA^2L]$ is found to be much greater[198] than

[Cu 1,10-phenanthroline L] due to the presence of the electron withdrawing nitro and carboxyl groups over A^1 and A^2, respectively. This depletes the electron density over the ring, making it a stronger π acid than 1,10-phenanthroline and hence stabilizes the ternary complexes. In case of dpa, an electron donating imino group (-NH group) attached between the two pyridine moieties enhances the electron density on the ring due to the presence of a lone pair of electrons on the nitrogen atom. However, the delocalization of electron density in dpa is over a larger area than in 2,2'-dipyridyl. Hence the values of the ternary complex stability are comparable for [CuAL] with A = dipyridyl or dipyridylamine.