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Juanita Williams Allison
Iowa State University

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Equilibrium studies of N-methyl and N-ethyl substituted diethylenetriamine complexes of copper(II) with amino acids

by

Juanita Williams Allison

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INTRODUCTION

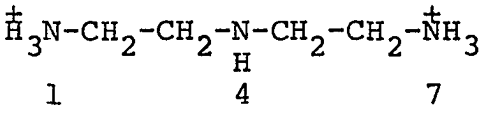
Diethylenetriamine, $H_2N(CH_2)_2N(H)(CH_2)_2NH_2$, has presented a long and controversial history. Although it was a known compound and some complexes were made almost twenty years earlier, it was only in 1950 that an investigation of its basic properties was made. At this time Schwarzenbach (1) developed a general method for calculating the association constants for polyamines and, in particular, a graphical method for the resolution of two constants which are very close together. Using this method, Prue and Schwarzenbach (2) obtained the values in Table 1 for the association constants of diethylenetriamine, hereafter known as dien. The constants given are defined by the following reactions:

$$\text{dien} + H^+ \overset{K_1}{\rightleftarrows} (\text{H dien})^+$$

$$(\text{H dien})^+ + H^+ \overset{K_2}{\rightleftarrows} (H_2\text{dien})^{2+}$$

$$(H_2\text{dien})^{2+} + H^+ \overset{K_3}{\rightleftarrows} (H_3\text{dien})^{3+}$$

Prue and Schwarzenbach felt that the first proton had an equal probability of being on the central nitrogen as on one of the terminal nitrogens of the molecule, but, from electrostatic grounds, the only possible structure of the di-cation is:



$$\underset{1}{\overset{+}{H_3N}}\text{-}CH_2\text{-}CH_2\text{-}\underset{4}{\underset{H}{N}}\text{-}CH_2\text{-}CH_2\text{-}\underset{7}{\overset{+}{NH_3}}$$

The distance between the 1- and 7-nitrogen accounts for the small differences in K_1 and K_2. The two ammonium groups must then contribute to the sharp weakening of the basicity of the central nitrogen.

At about the same time, Jonassen et al. (3) determined the association constants of dien using Bjerrum's method at two different temperatures to obtain the values in Table 1. The values they obtained for the heats of reaction are listed in Table 2.

McIntyre (4), in an attempt to remove the ambiguities caused by varying conditions, such as ionic strength, titrated dilute solutions of dien at several temperatures. From this data, he calculated the heats of reaction and said that the first two protons are bound to dien with about equal strength, while the third is much weaker. In a later publication based on this work, McIntyre et al. (5) report somewhat different values for ΔH. The decline they observe in ΔH for successive steps is explained by increased coulombic repulsions as more protons are added to the molecule. The quantities ΔG and ΔS are also reported, although they commented that ΔS is not very reliable since it is calculated from numbers of the same magnitude.

In 1961, interest in diethylenetriamine was revived when Ciampolini and Paoletti (6) investigated calorimetrically the heats of neutralization and compared them to those of ethylenediamine (en). The values are reported in Table 2.

The observation that ΔH_2(dien) > ΔH_2(en) indicates lower repulsions and the presence of the 1,7-di-cation, $H_3\overset{+}{N}(CH_2)_2NH(CH_2)_2\overset{+}{N}H_3$. They felt that the presence of the two ions, $H_2NCH_2CH_2\overset{H_2}{\overset{|}{N}}{}_{+}\text{-}CH_2CH_2NH_2$ and $H_2N\text{-}CH_2\text{-}CH_2\text{-}\overset{H}{N}\text{-}CH_2CH_2\overset{+}{N}H_3$, is responsible for $\Delta H_2 > \Delta H_1$. If they hypothesize that a secondary nitrogen has a lower ΔH of neutralization than a primary nitrogen, then the extra heat in the second step arises from the passage of the proton from the secondary to the primary nitrogen. The low value of ΔH_3 they feel is due to the repulsive action of the two adjacent charges to the secondary central nitrogen. The large ΔS of the first step is attributed to the release of water. A decrease is expected in successive steps and may also be due to a stiffening of the molecule by repulsion of the hydrocarbon portion by the positive nitrogen, which increases in the di- and tri-cations.

In 1968, Zarinskii and Kotov (7) attempted to clarify the sequence of protonation of the dien nitrogens. They investigated the reaction between sulfuric acid and dien by a high frequency conductometric titration and found two end points corresponding to a 2:1 ratio of added acid. The results suggested to them that the titration involved first the neutralization of the two primary amino groups, then the secondary amine, although this is not the expected result by analogy with the basicity of these groups and that of the individual ethylamines, where the order is 2°>3°>1°. They calculated the electronic charges according to the method of Del Re (8), an MO-LCAO method adapted to localized charges and sigma bonds, of the neutral and protonated forms of dien and found for the neutral form that the primary nitrogen has the higher negative charge and should therefore react first with a proton. In a saturated molecule where the electrons are localized, the inductive effect should fall off rapidly with increasing distance. The two primary amino groups should therefore protonate simultaneously.

Recently, the association constants of dien have been redetermined at different ionic strengths. Scharff and Pâris (9) determined the values in 0.5 M $NaNO_3$ at 25°C. Evtimova, Scharff and Pâris (10) repeated the determination in 1 M NH_4NO_3 and Evtimova and Pâris (11) changed to 1 M KNO_3 for yet another determination. These values are reported in Table 1. The variations seen in the constants obtained by various workers can be attributed partly to differences in ionic strength and temperature. Comparisons are best made between values obtained under similar conditions. Also, calorimetrically determined values of ΔH are considered more reliable than potentiometric values for similar reasons.

Little work has been done on the N-substituted diens. Marxer and Miescher (12) investigated the di- and triquaternary derivatives of pentamethyl-, 1,1,7,7-tetraethyl-, and 4-methyl-1,1,7,7-tetraethyldien and found they had a

Table 1. Proton stability constants of the diethylenetriamines

Amine	Log K_1	Log K_2	Log K_3	Ionic Strength	Temp, °C	Ref.
dien	9.94	9.13	4.34	0.1 N (KCl)	20	2
	9.98	9.21	4.61	0.5 N (KCl)	20	2
dien	9.94	8.88	3.74	∿0	20	4,5
	9.64	8.59	3.58		30	
	9.38	8.29	3.44		40	
dien	10.03	9.36	4.87	1 M (KNO_3)	25	11
dien	10.03	9.36	4.87	1 M (NH_4NO_3)	25	10
dien	9.94	9.23	4.78	1.0 M (KNO_3,KCl)	30	3
	9.68	8.94	4.59		40	
dien	10.03	9.24	4.59	0.5 M ($NaNO_3$)	25	9
Me_5dien	9.4	8.4	2.4		22	13
Et_4 dien	9.66[a]	8.62[a]	3.55	0.10 M ($NaClO_4$ or KNO_3)	25	14

[a] These constants should be redefined as the proton instability constants (15).

Table 2. Thermodynamic data for the reactions of diethylenetriamines with protons

Amine	$-\Delta H_1$[a]	$-\Delta H_2$	$-\Delta H_3$	$-\Delta F_1$[a]	$-\Delta F_2$	$-\Delta F_3$	ΔS_1[b]	ΔS_2	ΔS_3	Method[c]	Ref.
dien	11.5	11.8	7.2							pot	4
dien	11.1	12.25	7.6	13.3(20°C)	11.9	5.0	8(20°C)	-1	-9	pot	5
				13.4(30°C)	11.9	5.0	8(30°C)	-1	-9		
dien	11.7	12.6	8.2							pot	3
dien	11.20	11.95	7.20	13.35	12.25	5.80	7.2	1.0	-4.7	cal	6
en	12.20	10.60		13.90	10.15		5.7	-1.5		cal	6

[a] kcal/mole.

[b] entropy units.

[c] pot=potentiometric; cal=calorimetric.

pronounced nerve-blocking activity. Pentamethyldien was found to form only a diquaternary salt under mild conditions. Rometsch et al. (13) determined the association constants for Me_5dien reported in Table 1.

Margerum, Powell, and Luthy (14) recently determined the association constants of 1,1,7,7-tetraethyldien (Et_4dien) and found them all to be lower than the corresponding constants of dien (Table 1). The decrease in K_1 and K_2 of Et_4dien from the values for dien are expected, based on the observed values for ammonia, 9.25, and methylamine, 10.62, dimethylamine, 10.77, and trimethylamine, 9.80, which have been explained by the competition of the inductive effect of additional alkyls, tending to make the nitrogen more basic, and a steric effect which decreases solvation and makes the ion more acidic. The large decrease in K_3 is felt to be mainly a result of a decrease in the effective dielectric constant between the centers of positive charge, thus increasing the coulombic repulsion of the terminal charges for the center proton.

The literature contains a considerable amount on the chemistry of dien with the transition elements; therefore this discussion will be limited to the reactions of dien with copper(II). Mann (16) reported the isolation of the complex [Cu(dien)SCN]SCN and a deep blue compound of composition $dien_3Cu_2I_4 \cdot 2H_2O$. Treatment of an aqueous solution with silver nitrate gave no precipitate of silver iodide, which led him to propose a structure containing a bridging dien.

Job and Brigando (17) from a spectrophotometric study found that an aqueous solution contained a species of the composition of 3 Cu^{++} per 4 dien. Haendler (18) later disputed these results and from a study of the system, copper(II) acetate-dien, by continuous variations, declared the solution contained a mixture of the species, $[Cu\ dien]^{2+}$ and $[Cu(dien)_2]^{2+}$. Breckenridge (19) isolated the halides of both species, $Cu\ dien_2X_2 \cdot H_2O$, $Cu\ dien_2Cl_2$, and $Cu\ dien\ Cl_2$, from alcohol solutions. Further evidence for the existence of a $[Cu(dien)_2]^{2+}$ complex came from a polarographic study by Laitinen et al. (20) who also calculated a dissociation constant of 1.4×10^{-21} for the species.

Schwarzenbach (1, 2) potentiometrically determined the formation constants of the complex, $[Cu\ dien]^{2+}$. He found that for equimolar quantities of Cu^{++} and $(H_3dien)^{3+}$, the titration curve showed first the neutralization of the first proton of $(H_3dien)^{3+}$. The other two protons are removed in one step to form the complex with an average log formation constant, K_f, of 15.9 (Table 3). He found a second buffer region after the formation of the complex which could only be attributed to the species, $[Cu\ dien(OH)]^+$, formed by the neutralization of a proton from a coordinated water molecule.

Table 3. Thermodynamic data and formation constants for the reaction of the diethylenetriamines with copper(II)

Amine	Log K_{f_1}	Log K_{f_2}	Log K_{OH}(pK)	$-\Delta H_1$[a]	$-\Delta H_2$	$-\Delta F_1$[a]
dien	15.9		4.5 (9.5)			
dien	16.11					
	15.63			21		
dien	15.85	4.80		26.6	6.0	21.3
	15.40	4.71				21.4
	14.98	4.47				21.5
dien	15.84	4.79		18.9	6.3	21.3
	15.43	4.68				21.4
dien			(9.03)			
dien				18.00	8.15	21.55
dien	16.17					
dien	16.17					
Et_4dien	10.11		6.04			

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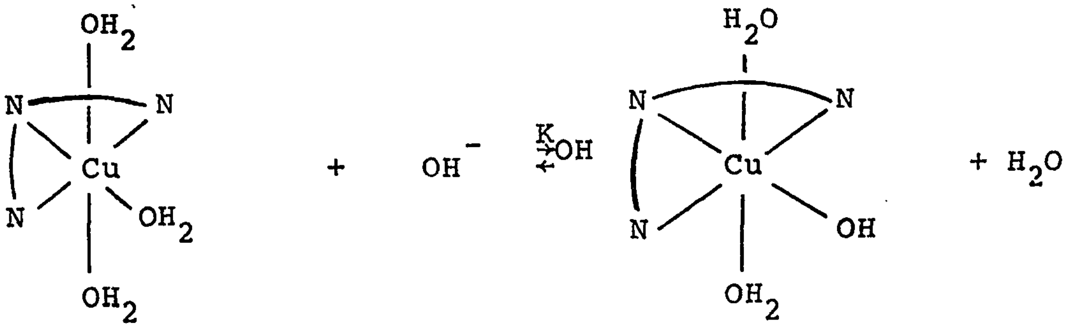
[a] kcal/mole.

[b] entropy units.

[c] pot=potentiometric; cal=calorimetric; spec=spectrophotometric.

$-\Delta F_2$	ΔS_1[b]	ΔS_2	Ionic strength	Temp., °C	Method[c]	Ref.
			0.1 M (KCl)	20°	pot	2
			1.0 M (KNO_3,KCl)	30°	pot	21
				40°		
6.4	-18	1	$\sim$0	20°	pot	4
6.5	-17	2		30°		
6.4	-16	1		40°		
6.4	8	1	$\sim$0	20°	pot	5
6.5	8	1		30°		
			0.1 M (KNO_3)	25°	pot	22
7.10	12.0	-3.5			cal	23
			1 M (KNO_3)	25°	pot,spec	11
			1 M (NH_4NO_3)	25°	pot	10
			0.1 M ($NaClO_4$ or KNO_3)	25°	pot,spec	14

$$Cu(H_2O)_6^{2+} + dien \overset{K_f}{\rightleftarrows} [Cu\ dien]^{2+}$$



The constant, K_f, was checked by a competition reaction of $(H_2dien)^{2+}$, $[Cu\ EDTA]^{2-}$, and excess Mg^{2+}.

Jonassen, Le Blanc, and Rogan (21) also determined the formation constant for the copper-dien complex. They found that $\bar{n}$, the average number of bound ligands per metal ion, did not approach the value of two asymptotically as is typical of a six-coordinate metal ion. They inferred from this that the second dien does not coordinate by all three nitrogens, and therefore K_f for the bis complex could not be calculated.

McIntyre (4) also determined the formation constants for the copper-dien system, reported in Table 3. In a later reference based on this work, McIntyre, Block and Fernelius (5) reported slightly different values for the enthalpy and entropy of reaction. They found that ΔH_1 was about fifty per cent greater for the reaction of dien with copper(II) than it was for diamines, which was expected for the formation of three copper-nitrogen bonds. But since ΔH_2 was only 6 kcal/mole, the average value for a copper-nitrogen bond, they concluded that only one further copper-nitrogen bond was formed and the second molecule of ligand was monodentate.

Courtney et al. (22) reinvestigated the titration curves for equimolar solutions of dien and copper(II). They found that three moles of acid per mole of chelate were liberated at low pH corresponding to the formation of the complex, $[\text{Cu dien}]^{2+}$. Between pH 8 and 10, a second buffer region occurred which required one mole of base per mole of chelate. Since no precipitation occurred and no excess ligand was present, the conclusion was that the complex $[\text{Cu dien(OH)}]^{+}$ was formed. Varying the concentration from 5×10^{-4} M to 1×10^{-2} M showed no irregularities which would suggest condensation to form other chelates of higher molecular weight.

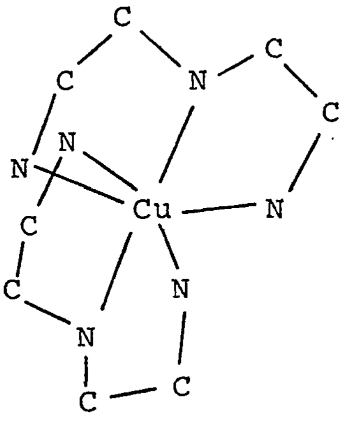
Ciampolini, Paoletti and Sacconi (23) looked at the heats of reaction of dien with copper(II) by a direct calorimetric technique on a solution buffered with hydrochloric acid to prevent formation of the hydroxo complex. They found that the overall heat of formation of a bis-dien complex is less than that observed for a tris-ethylenediamine complex. This lowering could be due either to ring strain on chelation or to the fact that bonds between a metal and a secondary nitrogen are weaker than those between a metal and a primary nitrogen. The latter hypothesis is felt to be true from data on alkylamines. The observed heats of reaction are listed in Table 3. The average value found for a copper-nitrogen bond is about 6.5 kcal/mole. Thus ΔH_1 has about the expected value. The value of ΔH_2 of 8 kcal/mole indicates more than one bond is forming between copper and the second ligand. However, ΔH_2 is low because the crystal field stabilization energy, CFSE, is less for the bis complex, $[Cu(dien)_2]^{2+}$, than for $[Cu\ dien]^{2+}$. The lowering of the CFSE is supported by the fact that the first absorption band of the bis complex shifts to lower frequencies.

Paoletti and Ciampolini (24) also investigated the interaction between hydroxide ion and the 1:1 complex of copper-dien by calorimetric, potentiometric, conductometric, and spectrophotometric methods in 0.1 M KCl. The conductometric titration showed a discontinuity for an $OH^-/[Cu\ dien]^{2+}$ ratio of 1:1, indicating the formation of the hydroxo complex.

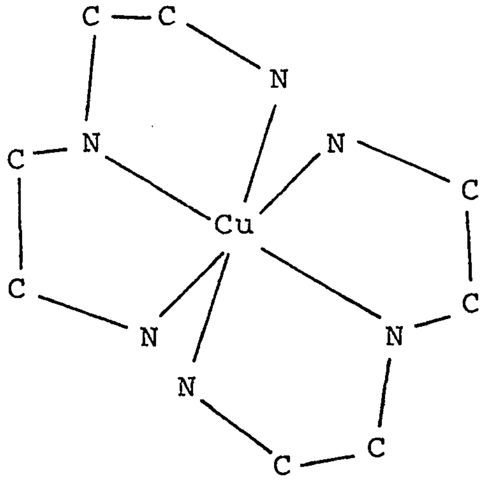
These results have been contradicted by a report of Evtimova and Pâris (11) who titrated solutions of 1:4 and 1:5 $Cu^{++}/(dien\ H_3)^{3+}$ with KOH while observing the spectral changes at 615 mμ. They found no complex was formed at pH values less than 2.5, but that the complex was completely formed at pH 4 and no further change occurred in the absorption with pH. From the titration of four different ratios of Cu^{++}/dien, they calculated $\bar{n}$, the average number of ligands bound per metal ion, and found that from pH 4 to 10, $\bar{n}$ did not vary from 1. Therefore, they excluded the formation of any protonated, hydroxo, or polynuclear species. Another study by Evtimova, Scharff and Pâris (10) of the same system in 1 M NH_4NO_3 gave the same value of K_f for the simple dien complex as in KNO_3. They found a mixed complex of $[Cu\ dien(NH_3)]^{2+}$ with an overall log formation constant of 19.32. In the pH range 5.5-7.5, they found only the simple species and the mixed complex and no hydroxo complex, the major components being $[Cu\ dien]^{2+}$ and $[Cu\ dien(NH_3)]^{2+}$. They speculated that the enhancement of the stability of the mixed species may be due to hydrogen bonding between the ligands or interaction with the solvent.

Despite the disagreements concerning the solution behavior of copper(II) and dien, some work has been done on the solid complexes. Curtis and Powell (25) looked at the infrared spectra and measured the magnetic susceptibilities of various copper-dien complexes. Zaslow and Ferguson (26) reported the X-ray structure of the double salt, $[(H_3NCH_2CH_2)_2NH_2]Cl[CuCl_4]$. Stephens (27, 28) determined the structures of the bis-dien complexes of the nitrate and halide salts of copper(II). In the structure of $[Cu(dien)_2]Br_2 \cdot H_2O$, he found the bonding of the ligands to be non-equivalent. Each dien was tridentate with the terminal nitrogens of the ligand trans to each other. The cation has approximate C_2 symmetry, the three nitrogens of one ligand and the central nitrogen of the other being almost coplanar. The terminal nitrogens of this second ligand have longer bond lengths, 2.35 and 2.46Å. The difference here suggested to him a possible distortion to a square pyramidal rather than a simple tetragonally elongated octahedral structure. He observed some weak hydrogen bonding between the bromides and the diens (Br-N distance 3.40-3.66Å).

In the nitrate salt, the ligands are equivalently bound, and in each ligand the central nitrogen-metal distance is shorter than that for the other nitrogens. The geometry then is a compressed form of a tetragonally distorted octahedron.



bromide



nitrate

Curtis (29) prepared the compound $\{[\mathrm{Cu\ dien}]_2C_2O_4\}(ClO_4)_2$ and studied its infrared spectrum. He found no band in the region which would indicate a non-coordinating or a weakly coordinating amine group. From the ir, he inferred the structure to be one having a bridging bichelate oxalate. There is no spin coupling in this compound and the measured μ_{eff} is 1.90 B.M.

Pflaum and Brandt (30) found that solutions of copper (II) and dien in a ratio of 1:3 could be reduced to coordination compounds of copper(I) by the action of hydroxylamine or sodium hyposulfite. The reaction occurred in acid solution.

The decomposition of hydrogen peroxide was found to be catalyzed by the complex of copper and dien by Kirson (31). The decomposition was found to stop, though, for dien/copper ratios of 1.25:1 and then begin again when a large excess, two-to threefold, of dien was present.

The reduction of the metal ion from copper(II) to copper(I) by the action of ultraviolet light on aqueous solutions containing the bis complexes of dien or en was observed by Il'yukevich and Shagisultanova (32). When only one molecule of amine was coordinated, no reduction occurred. The products other than copper(I) were ammonia and formaldehyde.

While the copper(II) complexes of dien have been studied extensively, only Me_5dien and Et_4dien of the substituted diens have been investigated. Ciampolini and Speroni (33) prepared a series of five-coordinate high spin complexes of M(II) of general formula $[M(Me_5dien)X_2]$, where M is Mn, Fe, Co, Ni, Cu, and Zn and X is a halogen. From molecular weight measurements in chloroform and nitroethane and conductivities, the complexes were generally found to be monomers and non-ionic species. Solids and solutions gave essentially the same spectra except for the chloro complex of copper. A band arose at 21-23,000 cm^{-1} in nitroethane which they felt was due to slight coordination of the solvent to form octahedral species. A review by Ciampolini et al. (34) indicates all the complexes are isomorphous with that of cobalt(II) chloride, whose geometry was determined to lie between that of a trigonal bipyramid and a square pyramid.

Paoletti and Ciampolini (35) later studied this series of complexes thermodynamically. Their results show that thermodynamically, the formation of the solid five-coordinate complex, $[Cu(Me_5dien)X_2]$, from the aquo species is favored, while, for example, nickel(II) prefers to remain as the aquo ion. Calculations were also made to determine the ease of formation of the five-coordinate species from reagents in the condensed and gaseous phases.

The interaction of Et_4dien with copper(II) has been examined potentiometrically and spectrophotometrically by Margerum, Powell and Luthy (14). They found only the mono-dien complex was formed in this case (Table 3). The pH dependence gave no evidence of a protonated complex, which would occur if only two nitrogens coordinated. Also, structures of other Et_4dien complexes showed all nitrogens coordinated. The lower stability of this complex has been attributed to the interactions of the N-ethyl groups and the axial coordination positions. Kinetic studies with the Pd-Et_4dien complex indicated the axial positions were blocked. Margerum et al. feel that the steric interaction of the ethyl groups and the axially coordinated water molecules causes these molecules to be released, lowering the stability of the complex. The hydroxo complex of Et_4dien has a higher log stability constant than dien due to the absence of these axial water molecules. The coordination of donors in the plane becomes stronger, thereby making the water more acidic.

The structure of the complex, [$CuEt_4$dien $Br(N_3)$] was determined by Dori (36). The dark green compound exhibits a distorted trigonal bipyramidal geometry about the copper with the azide in an axial position and the bromide occupying an equatorial position. The distortion from the trigonal bipyramid has been attributed to non-bonded repulsions and steric hindrance about the copper.

The study for which the results are reported here was undertaken for several reasons. The effects of alkyl substituents on the nitrogens on the complex stability and acidity of the remaining coordinated water were investigated. It was also desired to compare the catalysis, if any, of the dien complexes on the hydrolysis of amino acid esters to complexes where the ester group is part of the molecule which is first coordinated to the metal ion (37). Attempts to clarify the kinetics observed led to an investigation of the formation of mixed complexes of the type, $[\text{Cu dien AA}]^+$, where AA is an amino acid.

EXPERIMENTAL

Instrumentation

The principal instrument used was an automatic titrator, type TTT1C, manufactured by the Radiometer Corporation of Denmark. The instrument consists of three sections, a recorder, type SBR2c, the titrator, and a syringe burette, type SBU1a. Together they can be used for pH-stat work or automatic titrations. Disconnecting the recorder allows the titrator to be used as a pH meter.

These instruments were manufactured unfortunately before solid state electronics came into vogue. Thus with their increasing age and vacuum tubes, they are beset with many problems. The most common fault is an old glass electrode. Slow response to buffers and inaccurate readings are generally due to an aging glass electrode. It is possible sometimes to rejuvenate the surface according to instructions in the manufacturer's bulletin, but the electrode should always be checked on a working instrument before this is done or the Radiometer instrument is attacked.

If the meter is found to be at fault, it should first be checked by the tests given in the back of the manual for the instrument. These checks deal with three tubes and a chopper (vibrator) where most problems occur. Experience has shown the 12AT7 tube wears out before the other two, and this is a good place to start. The easiest way to find the faulty tube is to remove the back cover and one by one, then in combination, replace each of these three tubes and recheck the instrument. If there is no effect, return the original tubes and replace the vibrator, then recheck the tubes as above. It has been found to be prudent practice to maintain a supply of spare tubes, preferably Amperex brand, and one spare vibrator. These parts are not available here and long delays may be experienced otherwise. The normal lifetime of the reed type chopper has been about a year. Radiometer no longer supplies this type and the phototube replacements should have a longer lifetime. When first making this change, however, two resistors and a rectifier must be added to the circuit. The parts and instructions are normally supplied with the replacement chopper.

Another tube which has been found to wear out frequently is a 2D21. This is generally characterized by a large difference (0.4 or more units) between the end point setting when the valve is first activated and the actual pH reading of the meter.

When the first series of checks in the manual indicate problems with the instrument when switched to millivolts, but the three tubes, 12AT7, E80L, and EF86, and the vibrator do not appear to be the cause, one or more of the three 90C1 tubes, which are 90v regulators, may require replacement. Instability of the meter needle and buffer readings off by

0.2 pH units with a good glass electrode indicate a bad EZ80 tube, a power regulator. Faulty tubes in the recorder are indicated by non-correlation of the chart readings with the meter readings during automatic titrations.

There have also been problems of a more physical nature caused by age. The contact for the glass electrode is a strip of metal held in place by a plastic block attached to the chassis. This block can shear and take the metal contact out of reach of the electrode plug. This block cannot be put back together by glue or epoxy but must be replaced by a non-conducting material of similar size and shape. Replacement requires complete removal of the top section from the body of the instrument by unfastening some fourteen connections.

The bottom section of the recorder contains a relay which controls the addition of titrants by the syringe burette. The contact in the different positions of the relay is made by a metal strip. Age and fatigue caused this strip to break and keep the valve in the open position, though it could also have caused it to stay closed. This part is rather easily replaced once the bottom section of the recorder is removed.

<u>Titrant delivery system</u> The syringe burette was fitted with a 0.5 ml glass syringe which was calibrated by weighing the water delivered when the micrometer was manually

advanced. Several points are taken between zero and the full range of the micrometer, and the average of the volumes, calculated from these points and the density of the water at the measured temperature, was used as the volume of the burette. The volumes calculated from each point fell within a range of ± 0.0020 ml.

The system is also fitted with a glass delivery tube with a tip of 3-4 cm of 1/2 mm capillary to allow for easy observation of air bubbles. The bulk of the tube is 4 mm glass tubing. The successful operation of this system is dependent upon a good stopcock which is well lubricated. This burette is normally supplied with a polyethylene delivery tube and tip which has a very fine hole in it. The removal of insoluble materials clogging this tip requires the use of a wire. Too much of this practice will change the size of the hole in the tip, causing titrant to leak and giving inconsistent results.

<u>Meter calibration</u> The pH meter was standardized using Mallinckrodt Buffar solutions of pH 4.01 ± 0.01, 7.00 ± 0.01 and 10.00 ± 0.01 at 25.0°C. It was calibrated then in terms of hydrogen ion concentration by titrating a solution of 0.0100 M HCl and 0.100 M KNO_3. The hydrogen ion concentration was calculated assuming complete dissociation of hydrochloric acid. Calibration at high pH readings was

obtained using the added hydroxide ion concentration and $K_w=1.615 \times 10^{-14}$ (38). This value of K_w was calculated from the data given for KBr. No data was available for KNO_3.

The deviation between the meter readings and $-\log[H^+]$ in the acid region was less than 0.02 units. At pH 11.5, a total deviation of 0.10 units was found and was applied as a linear correction from pH 7 to 11.5.

Samples The sample solutions were kept under a nitrogen atmosphere by bubbling in prepurified nitrogen which has been passed through concentrated aqueous sodium hydroxide. The temperature was controlled by constant circulation of water through the jacket of the sample cell from an external bath kept at 25.00 ± 0.05°C by a mercury contact thermometer.

The reference electrode is a type K 101/3 liquid junction saturated calomel manufactured by Radiometer; the measuring electrode is a Beckman type E-2 miniature glass electrode with a silver-silver chloride internal element. The liquid junction calomel was used to minimize contamination of the reference by complex precipitates. The Beckman glass electrode was found to provide longer and more reliable service with the diethylenetriamines than Radiometer glass electrodes.

Materials

The substituted diethylenetriamines were supplied by The Ames Laboratories. Diethylenetriamine was supplied by J. T. Baker Chemical Company. All the amines were purified before use by vacuum distillation through a 10 cm glass column. The purity of the distilled product was checked by nmr or gas chromatography. When it was necessary, the amines were slowly redistilled over a Nester-Faust platinum spinning band column, using a drop ratio between 60:1 and 100:1. Distillation conditions for the amines are given in Table 4. Both vacuum systems were equipped with a Nester-Faust vacuum regulator to maintain constant pressures. Even after the second distillation, gas chromatography indicated similar boiling impurities in the 1,4,7-tri Me dien and it was not able to be used in this work. The distilled amines were stored away from light in a Dry Ice chest in tightly stoppered glass containers. No decomposition or other impurities were found even after several months of storage under these conditions.

Glycine, sarcosine hydrochloride, and glycine methyl ester were supplied by Mann Research Laboratories. The ester was recrystallized before use from methanol and stored in a desiccator. L-valine and p-nitrophenylacetate were obtained from Aldrich Chemical Company. The p-nitrophenylacetate was recrystallized from diethyl ether before use, m.p. 77-78°C

Table 4. Distillation conditions for the diethylenetriamines

Amine	Boiling Point, °C	Pressure, mm Hg	Ref.
1-Me dien	62	3	
1,4-di Me dien	84	15	
1,1-di Me dien	83	13	
	169-80	760	39
1,4,7-tri Me dien[a]	95	24-25	
Me_5dien[a]	82.5	13	
	85-86	12	12
1,1-di Et dien[a]	114	23	
	114-116	25	39
	108-110	19	39
1,4,7-tri Et dien	83-84	3.5	
1,1,7,7-tetra Et dien	120	10	
	117-119	12	12
4-Me-1,1,7,7-tetra Et dien	127	13	
	116	10	12

[a] Required distillation over spinning band column.

(lit. 79-80°C) (40). β-alanine was supplied by Matheson, Coleman and Bell. All the amino acids were analyzed for total hydrogen ion content by titration of a known amount with a standard solution of sodium hydroxide. The acids were dissolved in ten per cent aqueous formaldehyde to lower the pH of the end point for best results with a pH meter (41). All the amino acids were found to be within two per cent of the calculated hydrogen ion content.

β-alanine ethyl ester hydrochloride was prepared by treating 10g of β-alanine in 100 ml of absolute ethanol with hydrogen chloride gas for 25 minutes. The solution was initially yellow, but it changed to green and darkened during the two hours of refluxing. At the end of this time, the ethanol was removed by evaporation, leaving a pale yellow solid. The solid was recrystallized first from hot absolute ethanol, then from a room temperature mixture of absolute ethanol and diethyl ether. White crystals were obtained, m.p. 54-54.5°C (lit. 59°, 69-70°C) (42, 43). Analysis: Calc. for $C_5H_{11}NO_2 \cdot HCl$: C: 39.10; H: 7.87; N: 9.12; Cl: 23.08. Calc. for $C_5H_{12}NO_2Cl \cdot 0.5H_2O$: C: 36.93; H: 8.06; N: 8.61; Cl: 21.80; Found: C: 37.06; H: 8.02; N: 8.79; Cl: 21.84. The analysis of this compound indicates the presence of one-half molecule of water. Titration of this compound with standard sodium hydroxide does not show the presence of any water of hydration.

Carbonate-free sodium hydroxide was obtained by first making a fifty per cent solution, filtering the insoluble carbonates, and then diluting to the desired concentration. The base was standardized against dried potassium acid phthalate either by pH meter or to the phenolphthalein end point. The deviation in the normality calculated from either method was negligible.

All other chemicals were reagent grade. Copper(II) nitrate solutions were standardized by titration with EDTA using murexide as an indicator, according to the method of Schwarzenbach (44).

Doubly distilled water was used in making all solutions.

RESULTS AND DISCUSSION

Diethylenetriamines

The dissociation constants of the amines were measured on solutions approximately 9.5×10^{-3} M in amine, to which a known amount of standard nitric acid was added. Sufficient potassium nitrate solution was added so that the average ionic strength of the solution during the course of the titration was 0.11. Doubly distilled water was added to bring the volume to ten milliliters. The solution was titrated with 0.2 N carbonate-free sodium hydroxide. The first end point occurs after the addition of one equivalent of base. The second end point, as seen in Figures 1 to 3, is quite shallow and occurs after two additional equivalents of base have been delivered. The dissociation constants are calculated from six to ten points in each of the buffer regions lying between 0.3 to 0.7 and 1.3 to 2.7 equivalents of added base, according to the method of Schwarzenbach (1). For the reactions:

$$H^+ + A \rightleftarrows HA^+$$

$$H^+ + HA^+ \rightleftarrows H_2A^{2+}$$

$$H^+ + H_2A^{2+} \rightleftarrows H_3A^{3+}$$

the constants, K, are defined as:

$$K_1 = \frac{[HA^+]}{[H^+][A]}$$

$$K_2 = [H_2A^{2+}]/[H^+][HA^+] \qquad (1)$$

$$K_3 = [H_3A^{3+}]/[H_2A^{2+}][H^+]$$

The total amine concentration is defined as:

$$C_A = \sum_{j=0}^{m} [H_jA] = [A]+[HA]+[H_2A]+[H_3A] \qquad (2)$$

and the total acid concentration by

$$[H]_t = C_A(m-a) = [H]-[OH] + \sum_{j=1}^{m} j\cdot[H_jA] \quad \text{or} \qquad (3a)$$

$$C_A\cdot g = \sum_{j=1}^{m} j\cdot[H_jA] \qquad (3b)$$

where m is the maximum number of protons the molecule can accept, a is the apparent neutralization point of the acid and is defined as the number of moles of alkali hydroxide per mole of amine which have been added at that point in the titration. The quantity, [H], is directly measurable as the pH, and [OH] is obtained from it and the ion product for water, K_w. Rearrangement of Equation (3a) gives g the definition:

$$g = m-a + \frac{[OH]-[H]}{C_A} \tag{4}$$

Combining Equations (1), (2) and (3b) leads to:

$$g + (g-1)\cdot[H]\cdot K_1 + (g-2)\cdot[H]^2\cdot K_1\cdot K_2$$

$$+ (g-3)\cdot[H]^3\cdot K_1\cdot K_2\cdot K_3 = 0 \tag{5}$$

If one of the constants is separated sufficiently from the others, Equation (5) will reduce to only two significant terms, those involving the members, $[H]^j\overline{K}_j$ and $[H]^{j-1}\overline{K}_{j-1}$. Division of this result by $[H]^{j-1}\overline{K}_{j-1}$ gives:

$$(g-j+1) + (g-j)\cdot[H]\cdot K_j = 0 \tag{6}$$

Equation (6) can be reduced, when $g=j-1/2$, to $[H]\cdot K_j=1$, or the pK equals the pH at the half-neutralization point.

For the diethylenetriamines, the constant, K_3, is well separated from the others and its value was calculated according to Equation (6) with the aid of the computer program listed in the Appendix, page 148. The constants, K_1 and K_2, are not as readily obtained. Equation (5) for this case can be shown to contain only three significant terms, the term in $[H]^3\cdot K_1\cdot K_2\cdot K_3$ being small in comparison. Division of the result by K_1 allows the equation to be rearranged into the equation of a straight line when $y=K_2$ and $x=1/K_1$, Equation (7).

$$K_2 = \frac{(1-g)}{(g-2)[H]} - \frac{g}{(g-2)[H]^2} \cdot \frac{1}{K_1} \qquad (7)$$

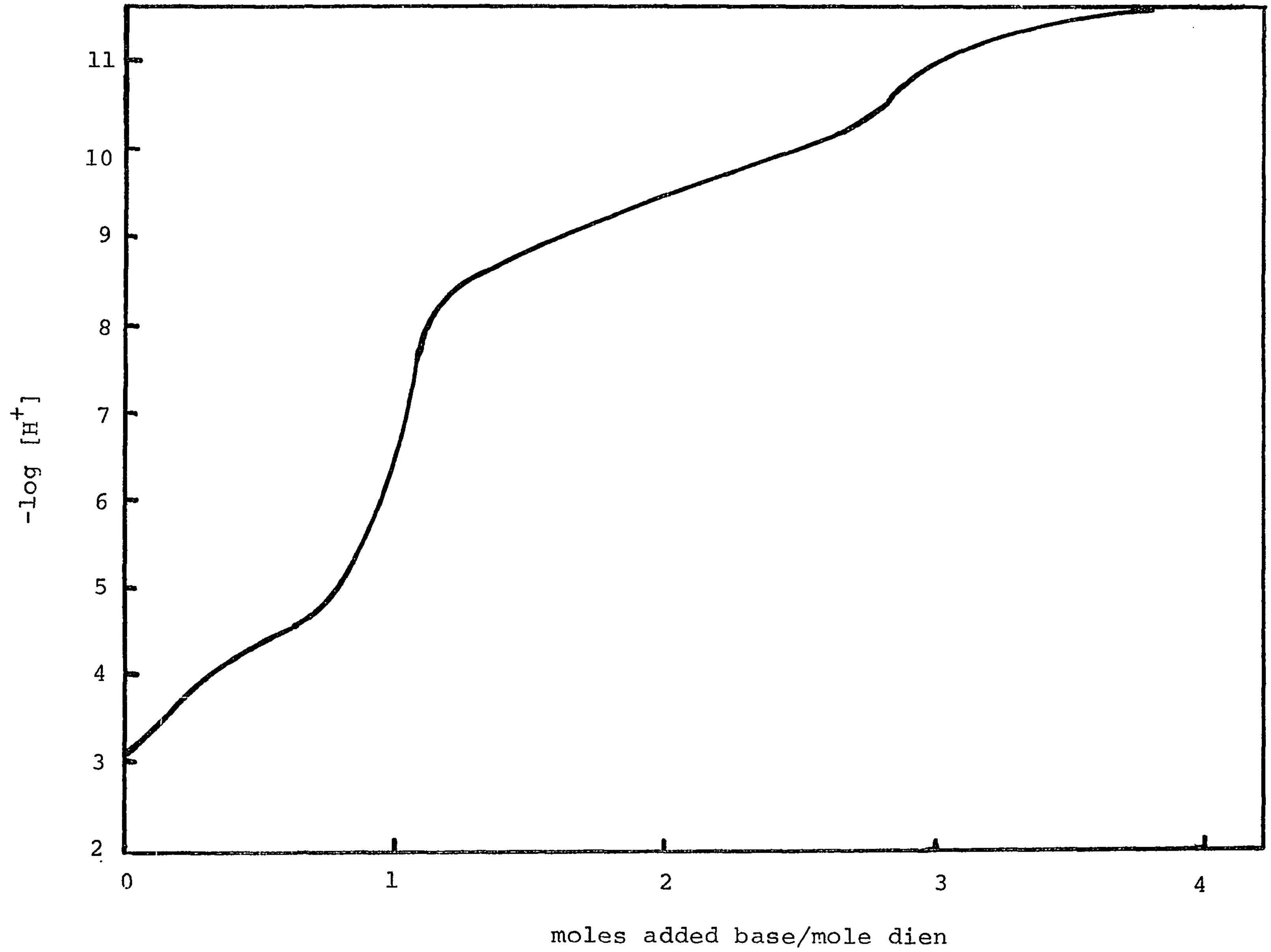
An ideal plot of these straight lines obtained from various values of g and [H] will have one common point of intersection which gives the constants, K_1 and K_2. Practically, small deviations are observed. For the diethylenetriamines, this series of simultaneous equations was solved for K_1 and K_2 with the aid of the computer program listed in the Appendix. The constants are reported in Table 5 with their standard deviations.

Qualitatively, the differences observed for the constants K_1 and K_2 are easily explained. The effects of ethyl groups versus methyl groups are clearly shown by 1,1-di Me dien and 1,1-di Et dien and Me_5dien and Et_4dien or 4-Me Et_4dien. In each case, the ethyl compound has the higher log K, as is observed for the corresponding alkylamines. Quantitatively, perhaps a bit more can be said about these two constants. From the corresponding alkylamines, it is known that tertiary and primary ethylamines have pK's within 0.2 log units, while trimethylamine is much less basic than monomethylamine or even monoethylamine. Therefore, one would expect the constants for Et_4dien, 1,1-di Et dien and 4-Me Et_4dien to be within 0.2 units of those of dien, which is what this author observes. Also, diethylamine is

Table 5. Observed values of the log association constants at 25.0 ± 0.1°C and $\mu=0.11(KNO_3)$

Amine	K_1	K_2	K_3
dien	9.89 ± 0.01	9.06 ± 0.01	4.27 ± 0.01
1-Me dien	9.86 ± 0.06	9.18 ± 0.02	3.30 ± 0.03
1,4-di Me dien	10.03 ± 0.02	9.35 ± 0.02	2.82 ± 0.03
1,1-di Me dien	9.62 ± 0.06	8.63 ± 0.05	3.62 ± 0.04
Me_5dien	9.22 ± 0.01	8.41 ± 0.03	2.09 ± 0.03
1,1-di Et dien	9.90 ± 0.08	9.10 ± 0.03	3.93 ± 0.05
1,4,7-tri Et dien	10.13 ± 0.02	9.37 ± 0.02	2.93 ± 0.02
1,1,7,7-tetra Et dien	9.78 ± 0.04	9.03 ± 0.02	3.39 ± 0.04
4-Me-1,1,7,7-tetra Et dien	9.71 ± 0.03	9.02 ± 0.01	2.29 ± 0.03

Figure 1. Titration curve of $H_3\overset{+}{N}CH_2CH_2\overset{+}{N}(H_2)CH_2CH_2\overset{+}{N}H_3$



-log [H$^+$]
11
10
9
8
7
6
5
4
3
2
0
1
2
3
4
moles added base/mole dien

Figure 2. Titration curve of $H_3\overset{+}{N}CH_2CH_2\overset{+}{N}(H)(CH_3)CH_2CH_2\overset{+}{N}(CH_3)H_2$

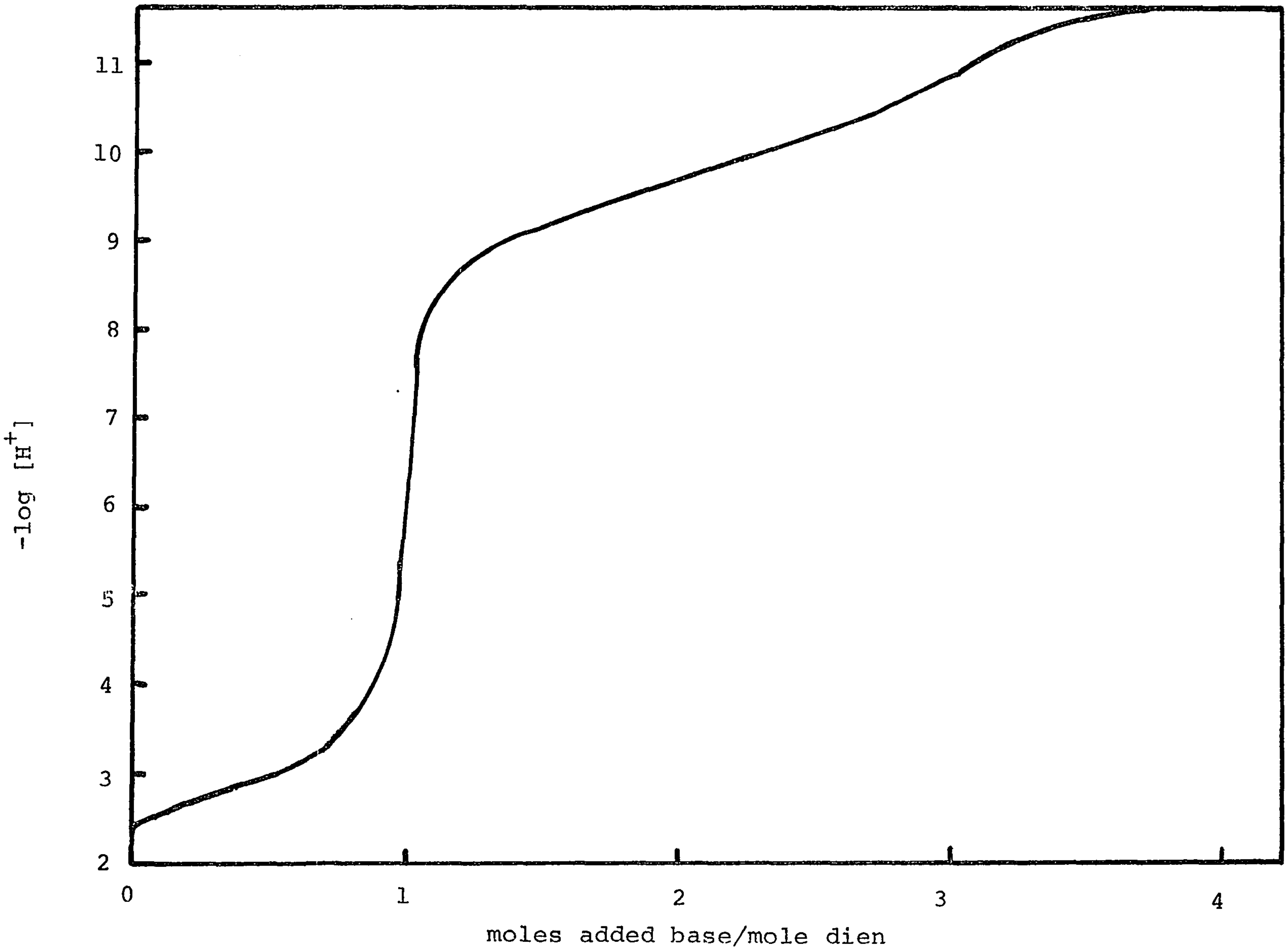
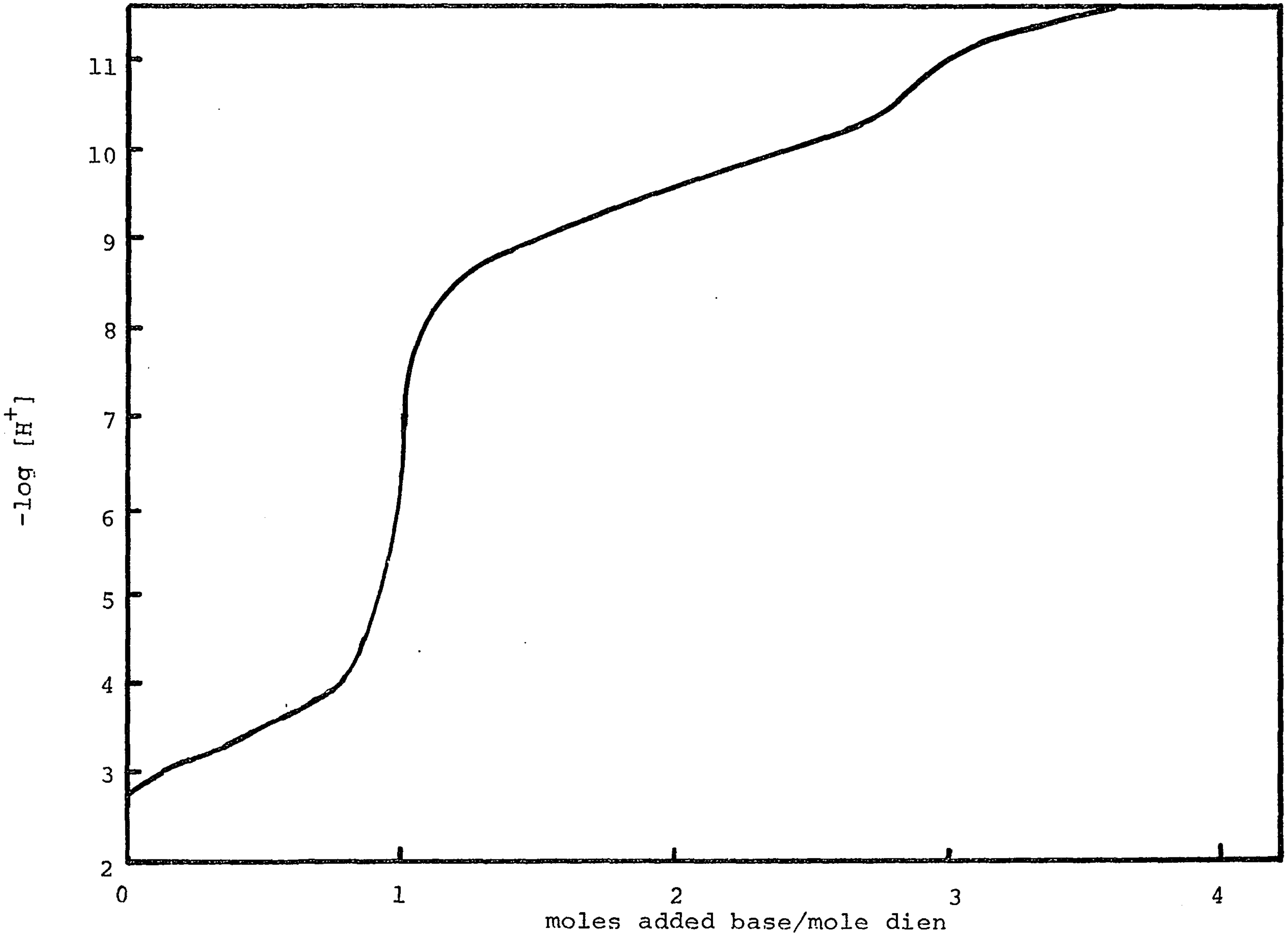

-log [H$^+$]
11
10
9
8
7
6
5
4
3
2
0
1
2
3
4
moles added base/mole dien

Figure 3. Titration curve of $(CH_3CH_2)_2(H)\overset{+}{N}CH_2CH_2\overset{+}{N}(H)_2CH_2CH_2\overset{+}{N}(CH_2CH_3)_2H$


-log [H+]
11
10
9
8
7
6
5
4
3
2
0
1
2
3
4
moles added base/mole dien

considerably more basic than mono- or triethylamine. Therefore, the secondary amine, 1,4,7-tri Et dien, is expected to have, and is observed to have, larger values of K_1 and K_2 than dien or the other ethyl-substituted diens.

The constant K_3 is most likely associated with the central nitrogen atom of the dien molecule. There are several reasons for this assignment, the most obvious being that it is most affected by alkyl substitution on this nitrogen. The observed trends in K_3 are a bit more difficult to explain. Although in many cases the central nitrogen has the same substituents as in the parent dien, the value of K_3 is significantly lower. One of the arguments put forth by Margerum et al. (14) for this decrease is the lowering of the dielectric constant by the alkyl groups between the centers of positive charge, causing the coulombic repulsion of the terminal charges for the central proton to increase. Though this may be a contributing factor, it does not appear to be the primary one. If it were, 1-Me dien should exhibit a K_3 similar to that of dien and not within experimental error of that of Et_4dien. In the cases of the 4-substituted diens, the value of K_3 would be expected to be lower, though perhaps not by as much as one order of magnitude or more which is observed. The fact that the ethyl-substituted is more basic than the methyl-substituted is not surprising. Where the substituent is the same, such as in 1,4-di Me dien and Me_5dien, the large difference in K_3 is not expected and may in part be due to an increase in hydrocarbon and a decrease in effective dielectric constant. The reasons for the decrease of K_3 in the terminally substituted diens are not immediately obvious. Inductive effects may cause it to be higher in similarly substituted diens with ethyl groups than with methyl groups, such as in 1,1-di Et dien and 1,1-di Me dien.

In an attempt to clarify some of the above statements and perhaps to determine the sequence of protonation of the nitrogens in the diens, the method of Clark and Perrin (45) for the prediction of organic base strengths was applied to these molecules. It consists of assuming a typical value of the pK of the amine, in this instance, values for the series of ethyl- and methylamines, and adjusting the pK with the average ΔpK values for the substituents. The effect of the substituent is assumed to halve for each additional atom in the chain between it and the basic center. The appropriate substituent effects, all of which are base-weakening, and the typical values for the amines are listed in Table 6, as well as the calculated and observed values for the diens. The number of the predicted site of protonation is given in parenthesis.

Table 6. Application of the method of Clark and Perrin to the diethylenetriamines

dien	Calculated			Observed		
a) Calculated and observed pK values for N-methyl and N-ethyl substituted diens						
	K_1	K_2	K_3	K_1	K_2	K_3
dien	10.10(1,7)	9.15(7,1)	3.95(4)	9.89	9.06	4.27
1-Me	10.30(1);9.99(7)	9.45(7);9.65(1)	3.95(4)	9.86	9.18	3.30
1,4-di Me	10.00(1);9.79(7);9.76(4)	9.45(7);9.65(1)	3.26(4)	10.03	9.35	2.82
1,1-di Me	9.80(7);9.45(4)	8.81(1)	3.95(4)	9.63	8.63	3.62
Me_5	9.45(1,7)	8.51(7,1)	3.26(4)	9.22	8.41	2.09
1,1-di Et	9.80(7);9.72(1)	9.37(1);9.46(7)	3.95(4)	9.91	9.11	3.93
1,4,7-tri Et	10.44(1,7)	9.50(7,1)	3.52(4)	10.13	9.37	2.93
Et_4	10.01(1,7)	9.07(7,1)	3.95(4)	9.78	9.03	3.39
4-Me Et_4	10.01(1,7)	9.07(7,1)	3.26(4)	9.71	9.02	2.29

b) ΔpKa of substituents and typical pKa values of amines

amine	pKa	substituent[a]	-ΔpKa
Et NH_2	10.81	NH_2	0.8
Et_2NH	11.15	NHR, NR_2	0.9
Et_3N	10.72	NH_3^+, NR_3^+	3.6
Et_2Me N	10.46		
$EtMe_2N$	10.16		

[a] 2C atoms from basic center.

Where the calculated pK values were less than 0.3 units apart, some mixing may occur as far as the position of the first proton. In these cases, both values and positions are given. The values of ΔpK of Clark and Perrin are at 20°C. The change in these values over five degrees is assumed to be small and they are used without correction to predict the basicities of the diethylenetriamines at 25°C. Examples of the calculations are given in Table 7. For some reason, this method is not applicable to the calculation of K_3, although it does indicate when large deviations may be expected. The agreement for K_1 and K_2 is reasonably good, within 0.4 log units. Clark and Perrin (45) reported results on some amino-polycarboxylic acids which were predicted to within 0.4 pK units. Where it is indicated that the central nitrogen may be protonated initially, the disposition of the di-cation is always assumed to be the 1,7-diprotonated species. Rearrangement is assumed to occur to ease the coulombic repulsions of like charges.

As these calculations show, Et_4dien is expected to have K_1 and K_2 values similar to those of dien. Margerum and co-workers (14) observe a large decrease in the value of K_2. This worker has been unable to derive their equation (2), which they used to calculate K_1 and K_2, by the method they have cited. It also does not agree with the equation of Schwarzenbach cited here (1). The values reported for K_1 and

Table 7. Examples of calculations according to the method of Clark and Perrin to predict the basicity of the diethylenetriamines

$CH_3CH_2\underset{1}{N}(H)CH_2CH_2\underset{4}{N}(CH_2CH_3)CH_2CH_2\underset{7}{N}(H)CH_2CH_3$

	Assumed position of protonation		
	1	4	7
a) Addition of first proton			
Typical value of pK from Table 6	11.15	10.72	11.15
Statistical correction	+0.30		+0.30
Effect of NR_2 group, 2 carbons distant	-0.9		-0.9
Effect of NHR group, 2 carbons distant		-1.8	
Effect of NHR group, 4 carbons and 1 nitrogen distant	-0.11		-0.11
Predicted value of pK	10.44	8.92	10.44

$Et\underset{1}{N}(H)CH_2CH_2\underset{4}{N}(Et)CH_2CH_2\underset{7}{\overset{+}{N}}(Et)H_2$

	1	4
b) Addition of second proton		
Typical value of pK	11.15	10.72
Statistical correction	-0.30	
Effect of NR_2 group, 2 carbons distant	-0.9	
Effect of NHR group, 2 carbons distant		-0.9
Effect of $\overset{+}{N}H_2R$ group, 2 carbons distant		-3.6
Effect of $\overset{+}{N}H_2R$ groups, 4 carbons and 1 nitrogen distant	-0.45	
Predicted value of pK	9.50	6.22

Table 7 (Continued)

$Et\underset{1}{\overset{+}{N}}(H_2)CH_2CH_2\underset{4}{N}(Et)CH_2CH_2\underset{7}{\overset{+}{N}}(Et)H_2$

	Assumed position of protonation		
c) Addition of third proton	1	4	7
Typical value of pK		10.72	
Effects of $\overset{+}{N}H_2R$ group, 2 carbons distant		-7.2	
Predicted value of pK		3.52	

K_2 should be considered as acid instability constants (15). However, when the data obtained by this author were recalculated by the equation of Margerum et al., the results did not agree. The value calculated for log K_1 was 9.4 compared to the value reported by Margerum et al. of 9.66. The calculated value of K_2 was negative in sign, but the log of the absolute value was 8.1, compared to the value reported of 8.62.

Calculations by Zarinskii and Kotov (7), according to the method of Del Re (8), on the electron density of the atoms in diethylenetriamine indicate the terminal, or primary, nitrogens should be the more basic and the central, or secondary nitrogen, the least basic. Repeating these calculations on the monoprotonated dien, they found little change in the calculated density for the central nitrogen. Also, in a saturated molecule such as this, the inductive effects of the protonated nitrogen will fall off rapidly with distance. Therefore, the other terminal nitrogen will still be more basic than the central nitrogen and will be protonated next, leaving the central nitrogen to accept the third proton. The coulombic repulsion of like charges would also predict that the diprotonated species will exist as: $H_3\overset{+}{N}(CH_2)_2\overset{H}{N}(CH_2)_2\overset{+}{N}H_3$. Further they calculated the charges on the atoms in the triprotonated species. The central nitrogen had a higher positive charge than the terminal nitrogens, which seems to say this nitrogen would be expected to be the most acidic. The calorimetric investigation of the individual heats of neutralization of diethylenetriamine by Ciampolini and Paoletti (6) adds to this argument. The observed values are listed below for dien and ethylenediamine.

	dien			en		
	$-\Delta G$ (kcal/mole)	$-\Delta H$ (kcal/mole)	ΔS (e.u.)	$-\Delta G$ (kcal/mole)	$-\Delta H$ (kcal/mole)	ΔS (e.u.)
$+ 1H^+$	13.35	11.20	7.2	13.90	12.20	5.7
$+ 2H^+$	12.25	11.95	1.0	10.15	10.60	-1.5
$+ 3H^+$	5.80	7.20	-4.7			

Here it has been argued that lower repulsions are indicated by ΔH_2(dien) > ΔH_2(en) and therefore the ion must be $H_3\overset{+}{N}CH_2CH_2N(H)CH_2CH_2\overset{+}{N}H_3$. But the possibility of tautomers in the first step was suggested by ΔH_2(dien) > ΔH_1(dien). This hypothesis may be supported by the calculations made earlier to predict the base strength and order of protonation in the substituted diens. The large decrease in ΔH_3 was felt to be due to the repulsive actions of the two adjacent charges toward the addition of the proton on the central nitrogen.

Copper complexes

The determination of the stability constants of the copper(II) complexes of the diethylenetriamines was done potentiometrically on a solution of 9 x 10^{-3} M copper(II) nitrate, 9 x 10^{-3} M dien, sufficient standard nitric acid to completely protonate the dien, and sufficient distilled water and potassium nitrate solution to bring the initial volume to ten milliliters and the average ionic strength to 0.11 at 25.0 ± 0.1°C. The nitrate salts were used to minimize interferences caused by anion coordination. The solution was titrated with 0.2 N carbonate-free sodium hydroxide. The curves, Figures 4 through 12, typically show an initial region where the pH rises, until about one equivalent of base is added. This region has been attributed in dien (2) to the neutralization of the proton from the central nitrogen. Since all the amines show this region, it may be stated that they all behave in the same way. Beyond this point, the curve has the relatively flat buffer region until pH 5 or 6. Here corresponding to the addition of two further equivalents of base, the first end point is reached and the solution is deep blue in color. This end point corresponds to the formation of the 1:1 complex of copper(II) and the dien. Concentration studies on dien (22) have shown that species such as $[Cu(dienH_2)]^{4+}$ and $[Cu(dien\ H)]^{3+}$ are not to be considered. Also along this line, experimental conditions are such that species as $[Cu(dien)_2]^{2+}$, if they can be formed, will be very minor constituents. After the formation of the complex, another very short buffer region occurs and at the addition of one further equivalent of sodium hydroxide, another end point is found. Beyond this point, the curve is essentially flat to about pH 12, the extent of the observation. This second end point has generally been attributed to the formation of the monohydroxo species, $[Cu(OH)dien]^{+}$ (2, 14, 22, 24). Some doubt has recently been cast on these conclusions (11). In the following report, no excess dien was present and the only possible species which could be forming at this point is the hydroxo complex, $[Cu(OH)dien]^{+}$. Concentration studies (22) again indicate that polymeric and dihydroxo species are not important. These studies were made on the parent diethylenetriamine and they are assumed to hold for the N-alkylated derivatives, although no studies were made to confirm it.

The formation constants of the copper(II) complexes were calculated from data in the region of 1.3 to 2.7 equivalents of added base, according to the method of Prue and Schwarzenbach (2). Examples of the titration curves are shown in Figures 4-12.

Figure 4. Titration curve of (dien $H_3)^{3+}$ in the presence of copper(II)

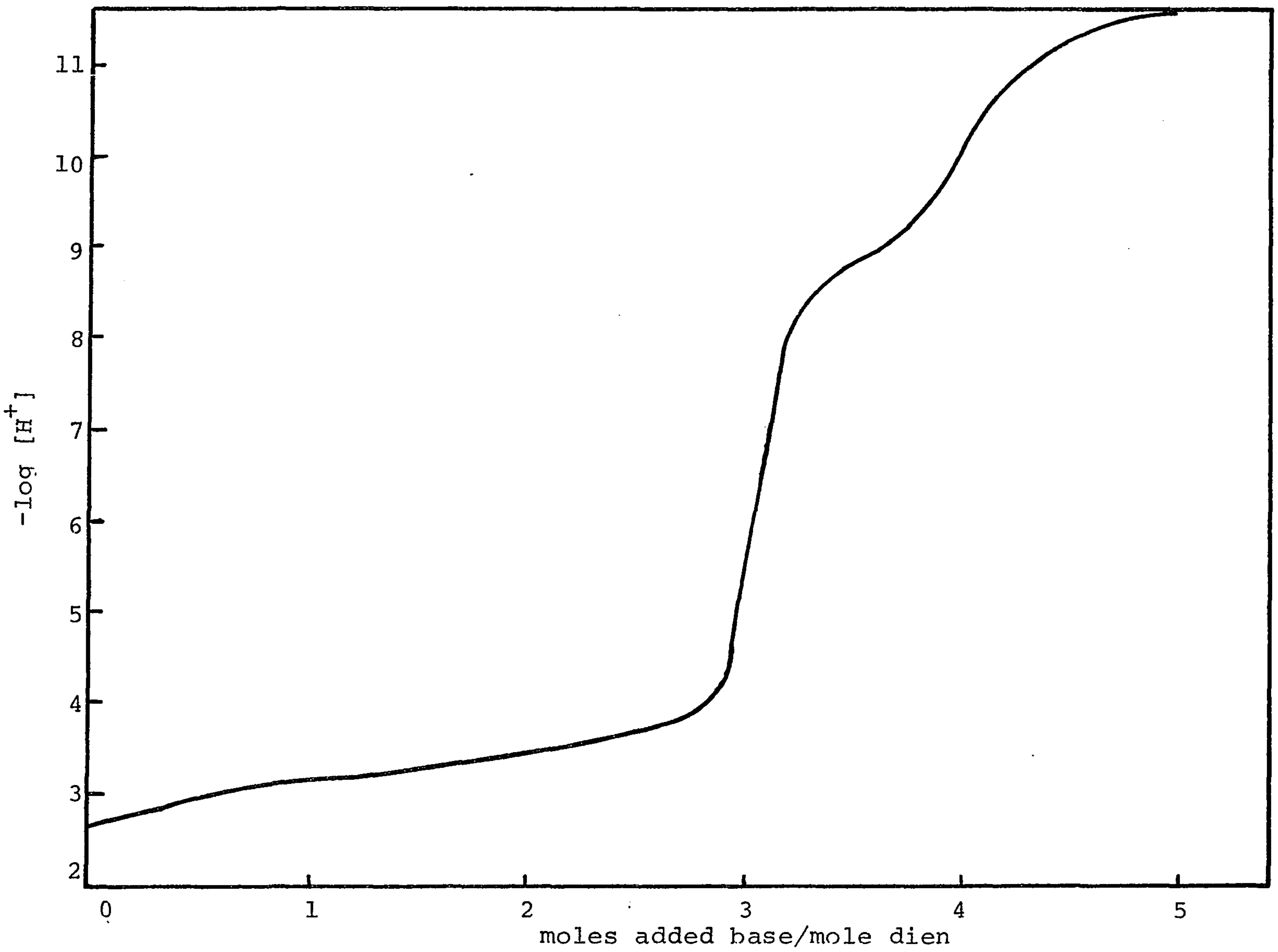

-log [H$^+$]
11
10
9
8
7
6
5
4
3
2
0
1
2
3
4
5
moles added base/mole dien

Figure 5. Titration curve of (1-Me dien H_3)$^{3+}$ in the presence of copper(II)

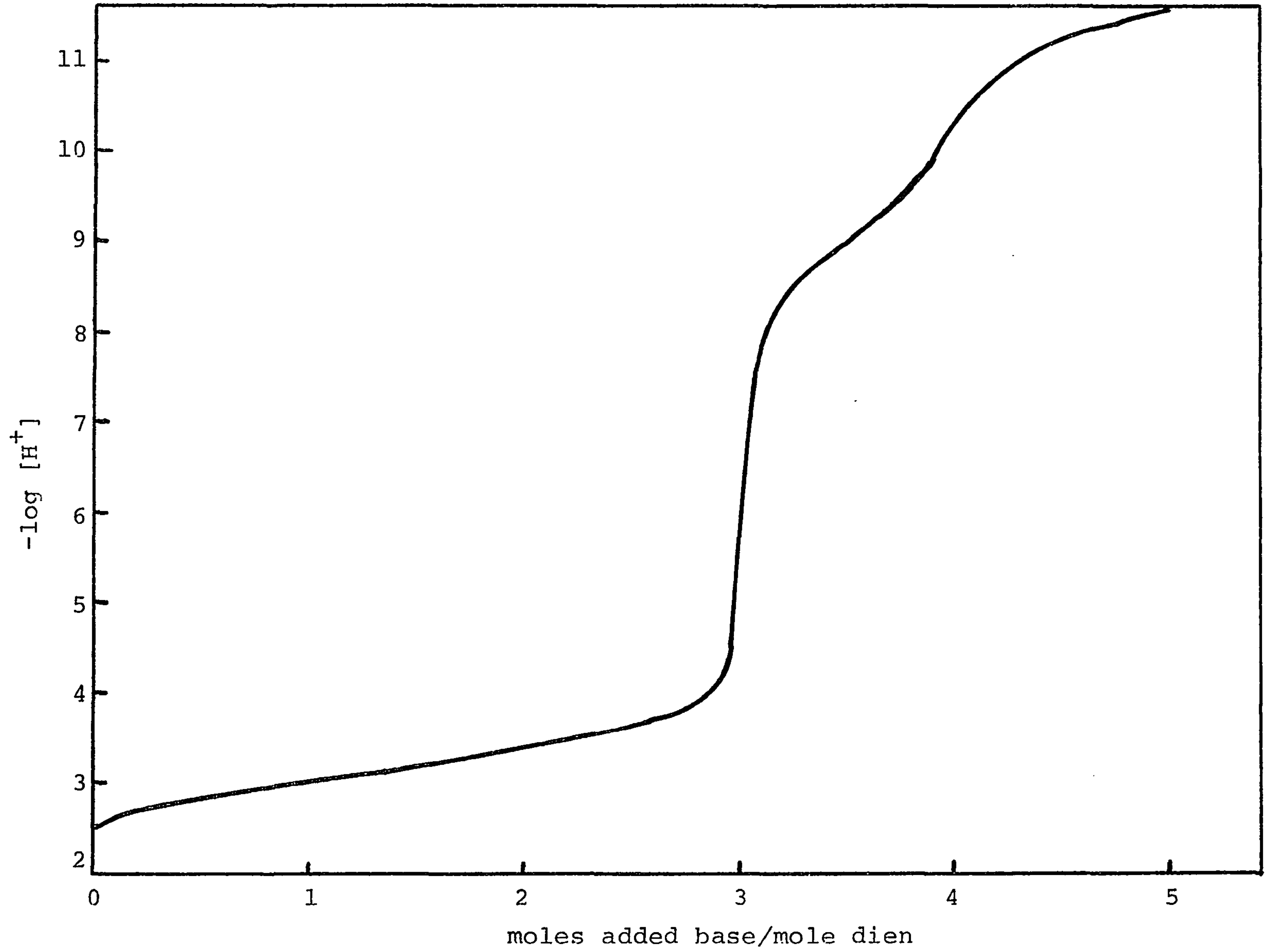
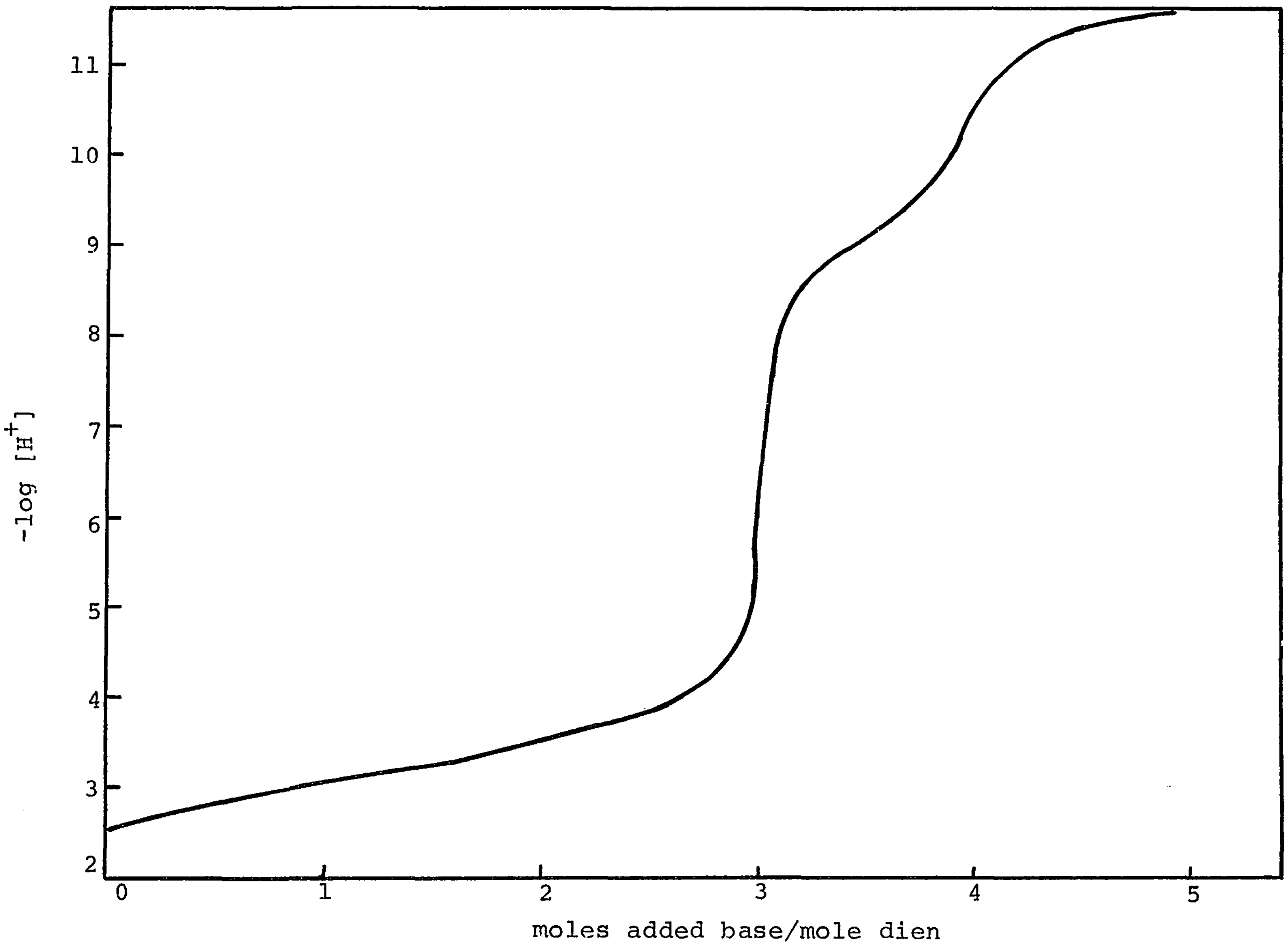
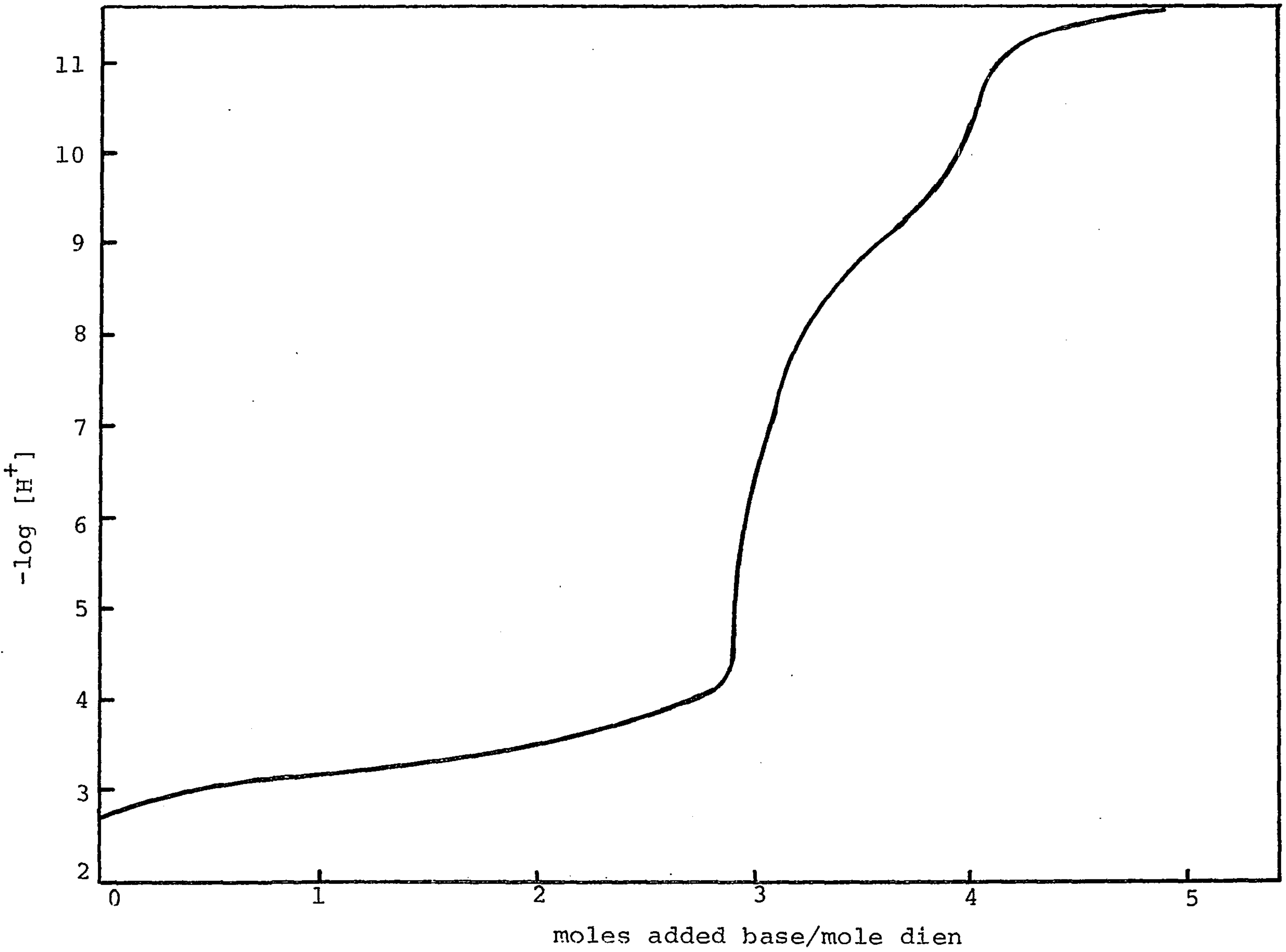

-log [H$^+$]
2
3
4
5
6
7
8
9
10
11
0
1
2
3
4
5
moles added base/mole dien

Figure 6. Titration curve of (1,4-di Me dien H_3)$^{3+}$ in the presence of copper(II)



-log [H$^+$]
11
10
9
8
7
6
5
4
3
2
0
1
2
3
4
5
moles added base/mole dien

Figure 7. Titration curve of (1,1-di Me dien H_3)$^{3+}$ in the presence of copper(II)



2
3
4
5
6
7
8
9
10
11
-log [H$^+$]
0
1
2
3
4
5
moles added base/mole dien

Figure 8. Titration curve of $(Me_5dien\ H_3)^{3+}$ in the presence of copper(II)

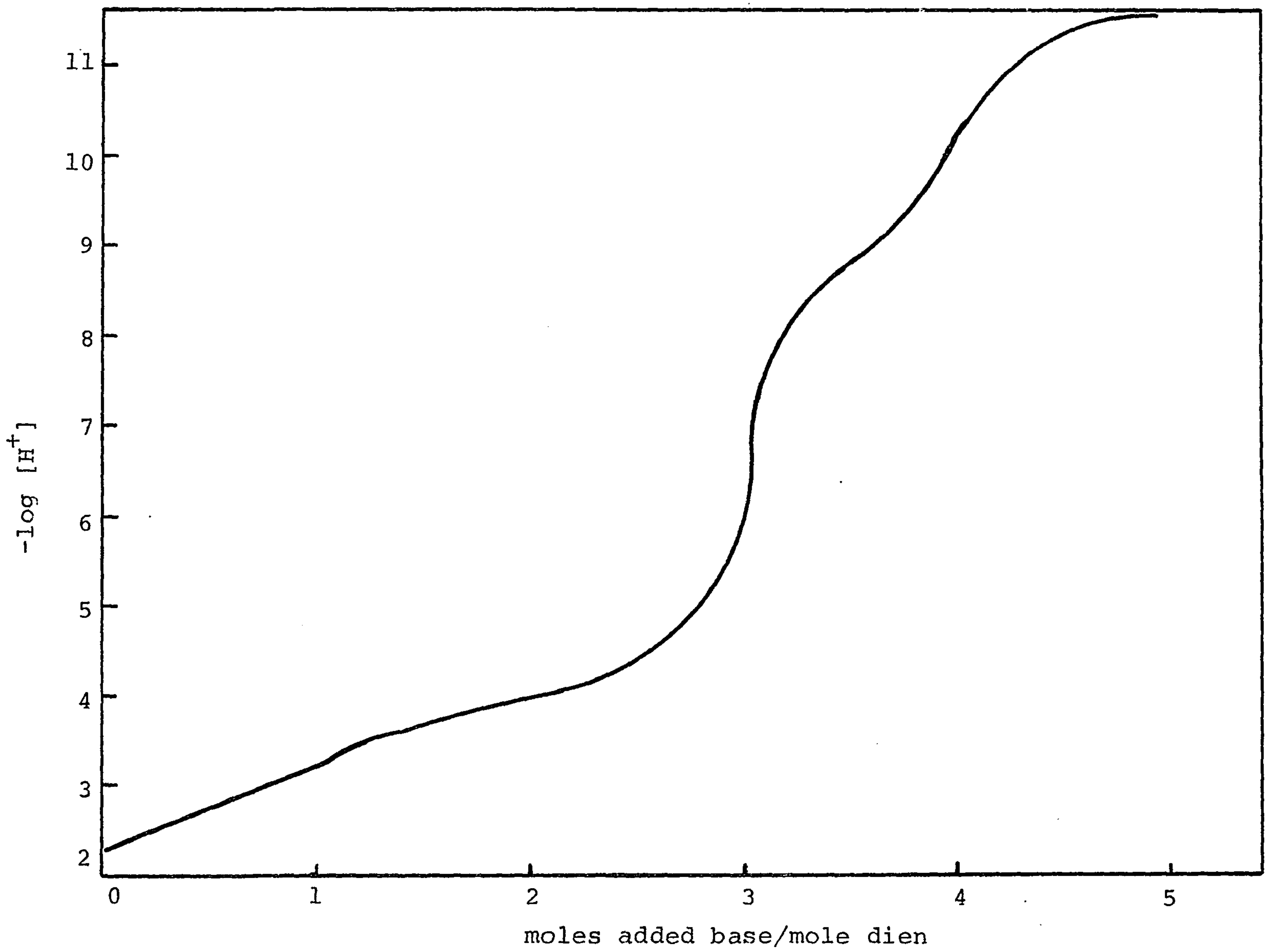

-log [H^+]
11
10
9
8
7
6
5
4
3
2
0
1
2
3
4
5
moles added base/mole dien

Figure 9. Titration curve of (1,1-di Et dien H_3)$^{3+}$ in the presence of copper(II)

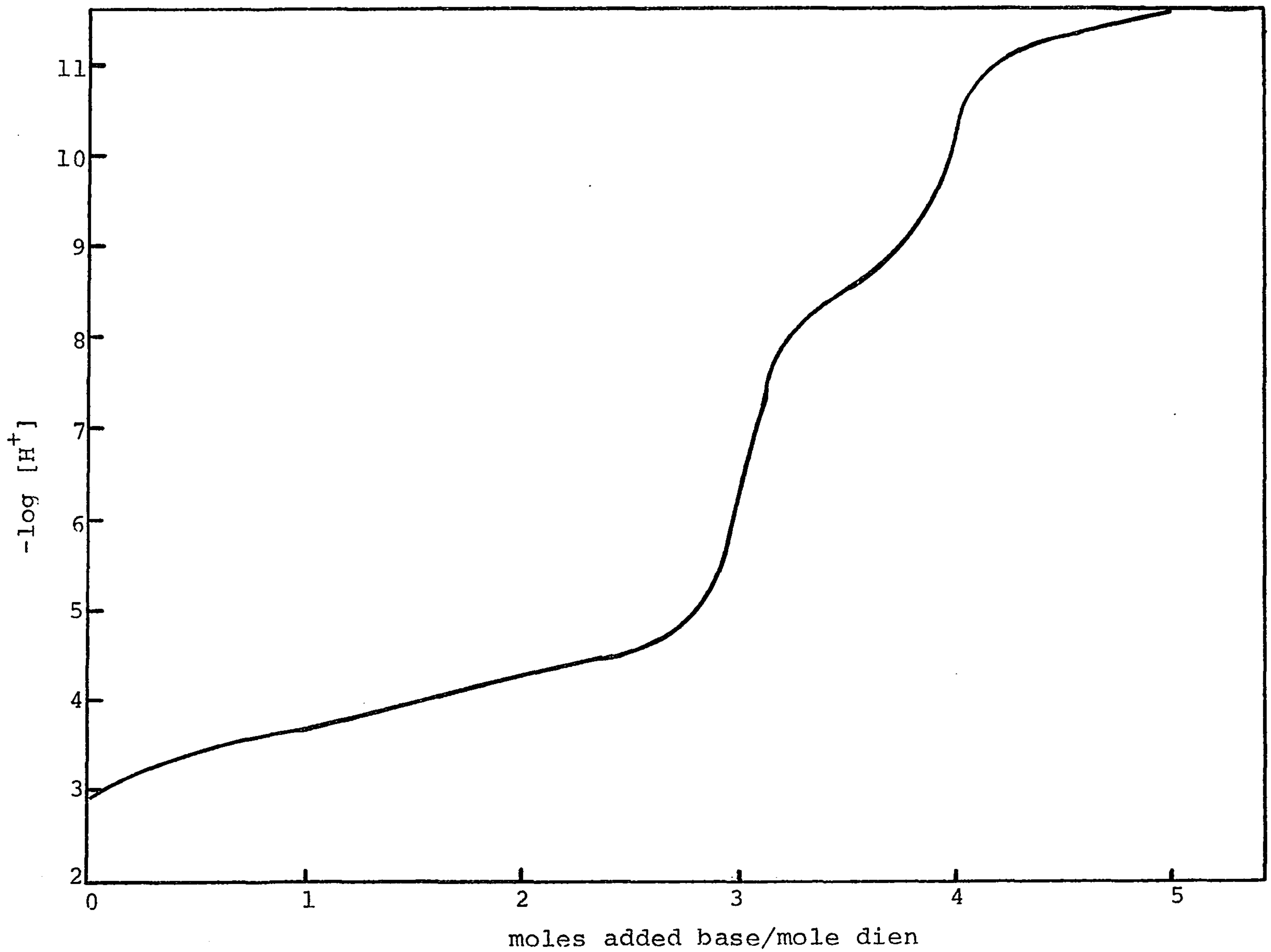

-log [H$^+$]
11
10
9
8
7
6
5
4
3
2
0
1
2
3
4
5
moles added base/mole dien

Figure 10. Titration curve of (1,4,7-tri Et dien H_3)$^{3+}$ in the presence of copper(II)

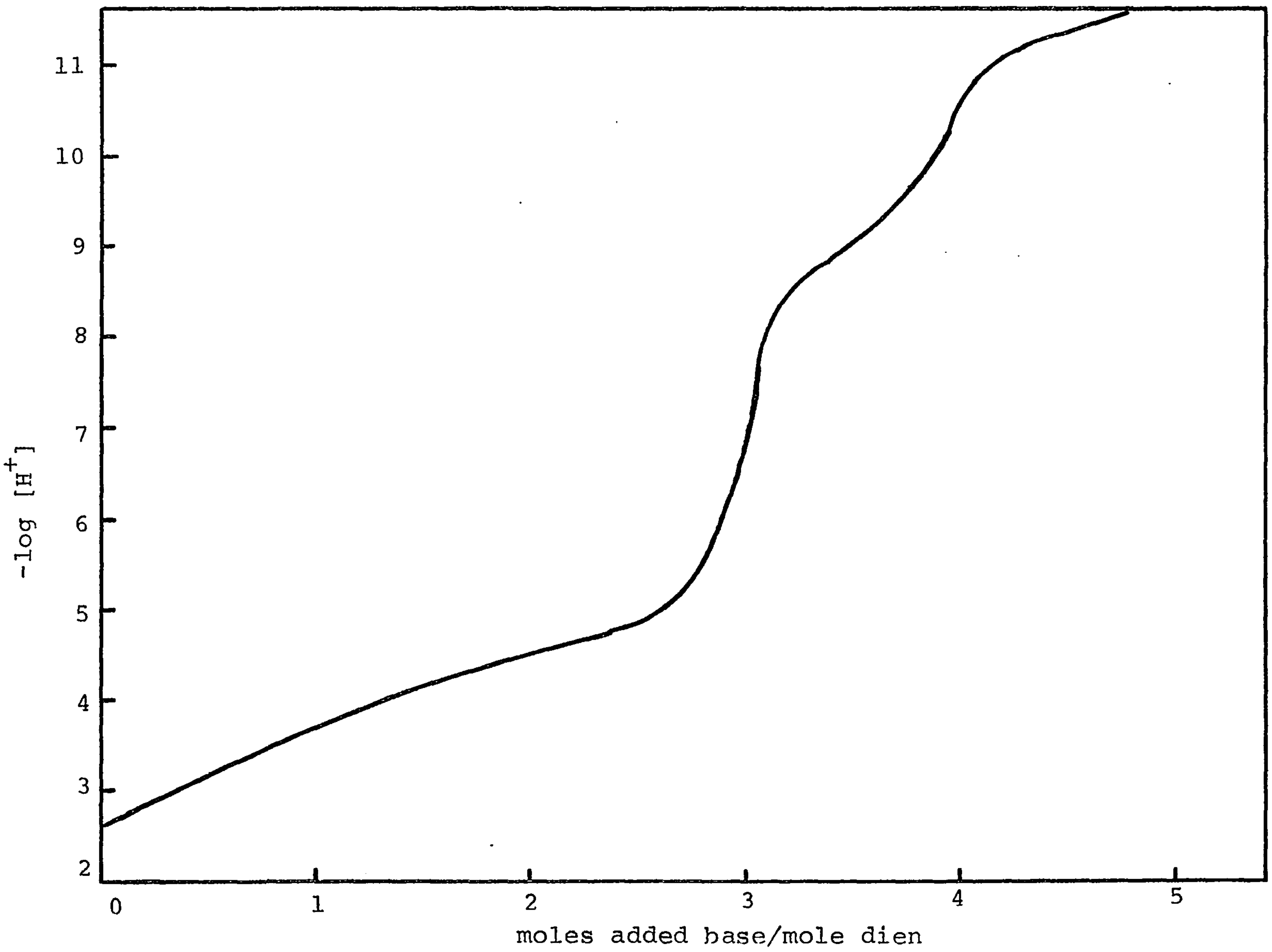

11
10
9
8
7
6
5
4
3
2
-log [H$^+$]
0
1
2
3
4
5
moles added base/mole dien

Figure 11. Titration curve of $(1,1,7,7\text{-tetra Et dien } H_3)^{3+}$ in the presence of copper(II)

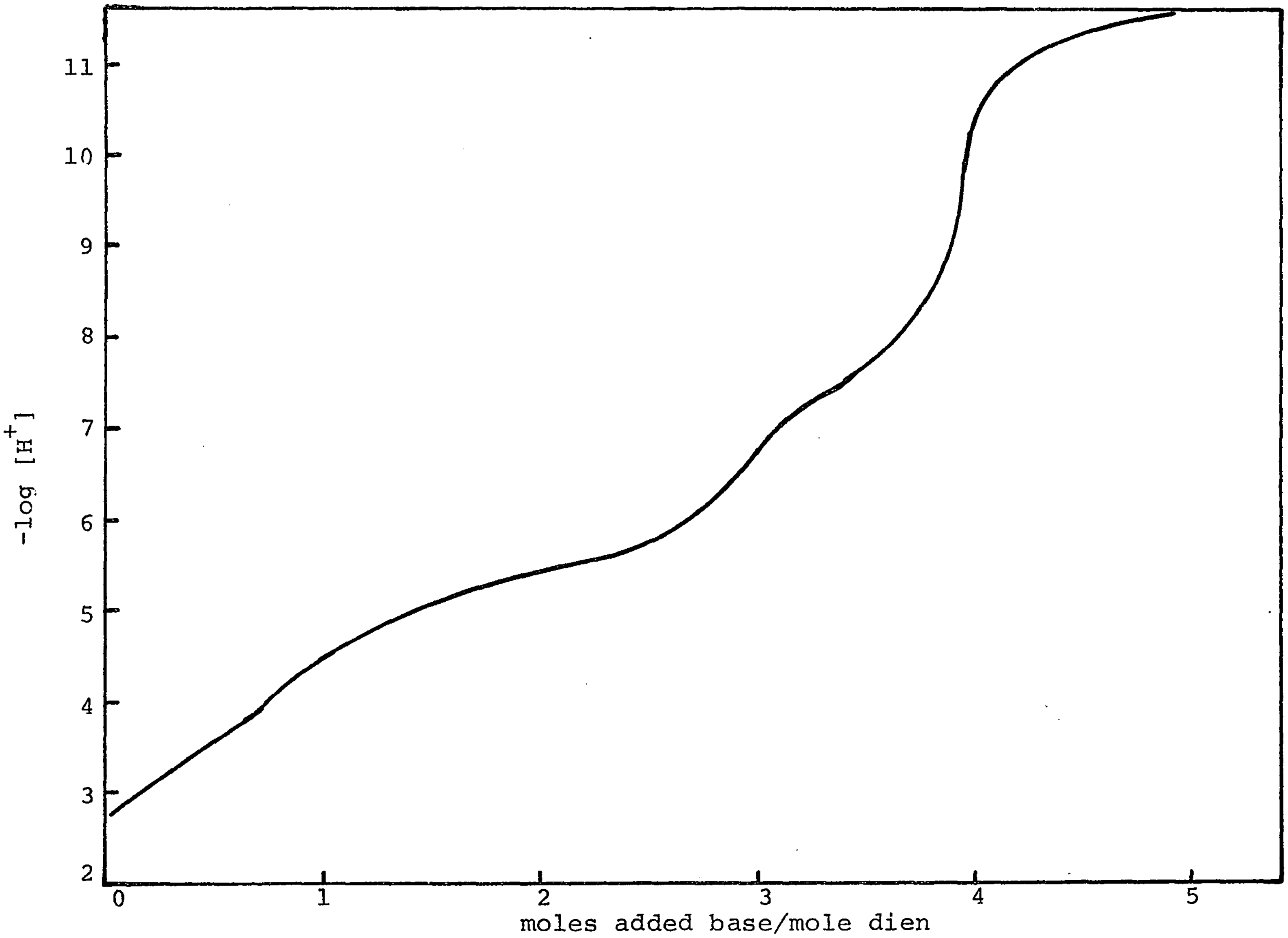
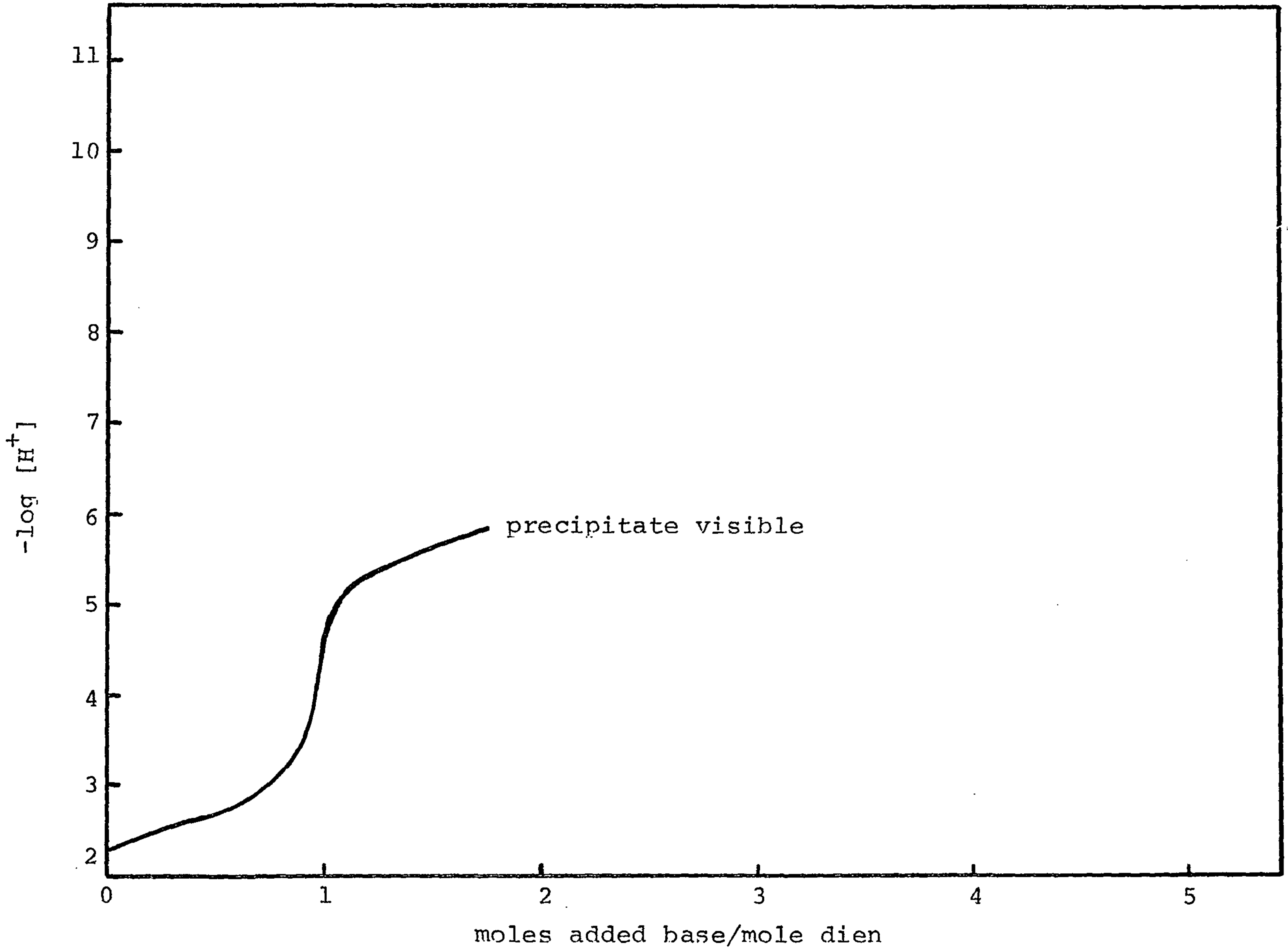

-log [H$^+$]
11
10
9
8
7
6
5
4
3
2
0
1
2
3
4
5
moles added base/mole dien

Figure 12. Titration curve of (4-Me-tetra Et dien H_3)$^{3+}$ in the presence of copper(II)


-log [H$^+$]
11
10
9
8
7
6
5
4
3
2
0
1
2
3
4
5
moles added base/mole dien
precipitate visible

The following set of equations was used to obtain K_e for the reaction:

$$Cu^{2+} + H_2dien^{2+} \overset{K_e}{\rightleftarrows} [Cu\ dien]^{2+} + 2H^+ \qquad (8)$$

$$Cu_{TOT} = c = (Cu)^{2+} + (CuA)^{2+} \qquad (9a)$$

$$A_{TOT} = c = \alpha(H_2A)^{2+} + (CuA)^{2+} \qquad (9b)$$

$$H_{TOT} = c.g = \beta(H_2A)^{2+} \qquad (9c)$$

where

$$\alpha = 1/(H)^2K_1K_2 + 1/(H)K_2 + 1 + (H)K_3$$

and

$$\beta = 1/(H)K_2 + 2 + 3(H)K_3$$

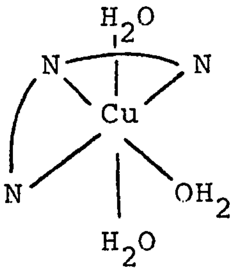
and g is defined by Equation (4). From Equations (9), the unknowns (H_2A), $(Cu)^{2+}$, and $(CuA)^{2+}$ can be calculated as $c.g/\beta$, $\alpha.c.g/\beta$, and $c - \frac{\alpha.c.g}{\beta}$ respectively. These quantities, together with the appropriate $[H^+]$, can be combined to obtain K_e of Equation (8).

$$K_e = \frac{[H^+]^2\{c - \frac{\alpha.c.g}{\beta}\}}{(\frac{\alpha.c.g}{\beta})(\frac{c.g}{\beta})} = \frac{[H^+]^2[CuA^{2+}]}{[Cu^{2+}][H_2A^{2+}]} \qquad (10)$$

Multiplication of K_e by the acid stability constants, K_1 and K_2, of the appropriate amine will yield the value of the formation constant, K_f, for the reaction:

$$Cu^{2+} + A \overset{K_f}{\rightleftarrows} [CuA]^{2+}$$

The calculations were performed by computer with program 3 listed in the Appendix, page 152. The results are given in Table 8. Structures by Stephens (27, 28) on the bis complexes of dien and copper(II) have shown dien to coordinate with the terminal nitrogens trans. The complexes studied here are presumed to have a similar structure in solution.



The value of K_f appears to be dependent on the substituent groups of the ligand. Unless the ligands are completely substituted, an alkyl group in the 4-position seems to have little effect on K_f. Otherwise, K_f decreases linearly with the number of N-alkyl substituents, as illustrated in Figure 13. The number of ethyl groups appears to have a greater effect on K_f than the number of methyl groups. The different steric requirements of the two groups may account for some of the change in slope observed. Other workers have found similar behavior for N-substituted ethylenediamines. Basolo and Murmann (46) found that for a series of N-N'-dialkyl ethylenediamine complexes, K

Figure 13. Relationship of log K_f and N-alkyl substitution

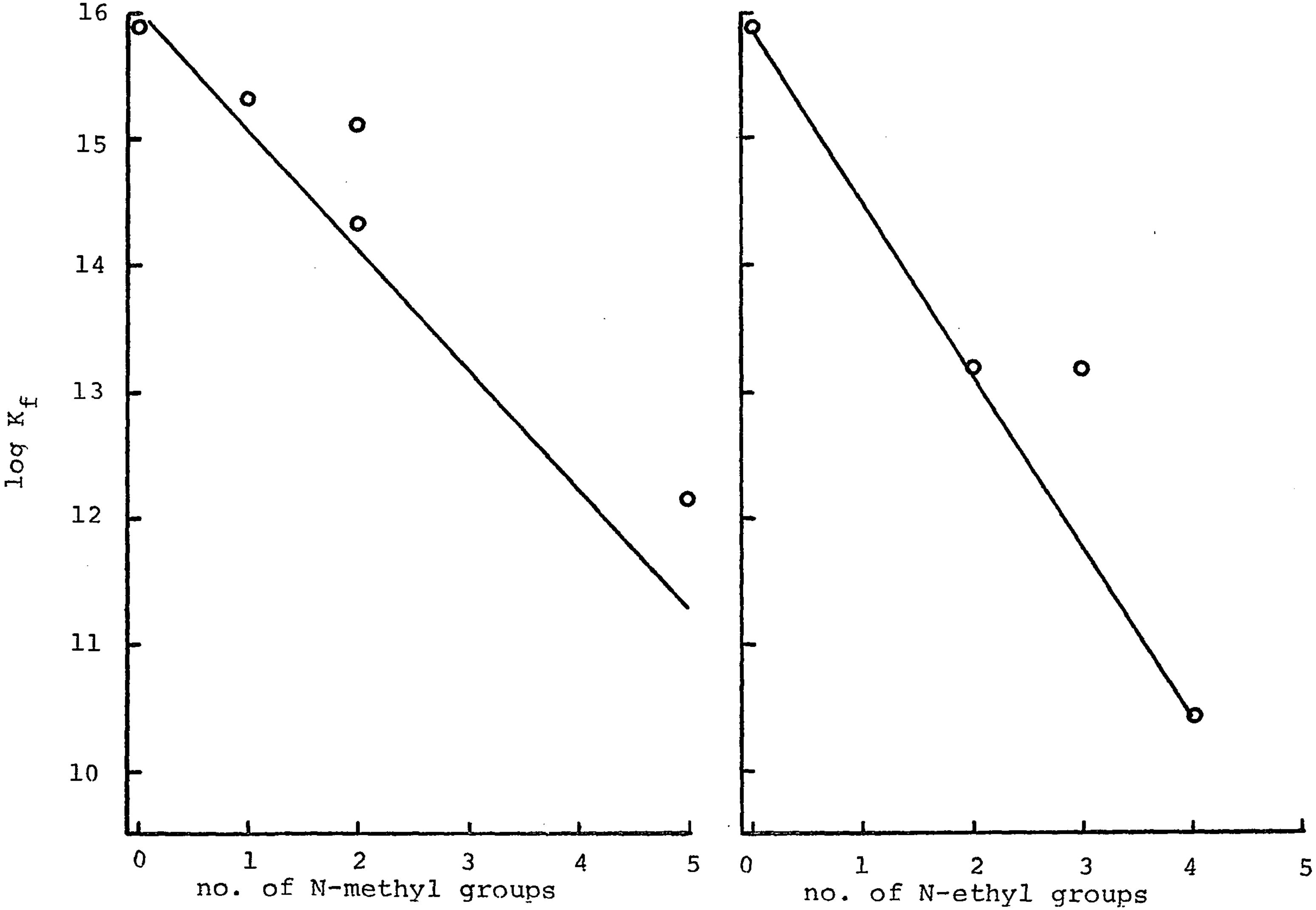

log K$_f$
16
15
14
13
12
11
10
0
1
2
3
4
5
no. of N-methyl groups
0
1
2
3
4
5
no. of N-ethyl groups

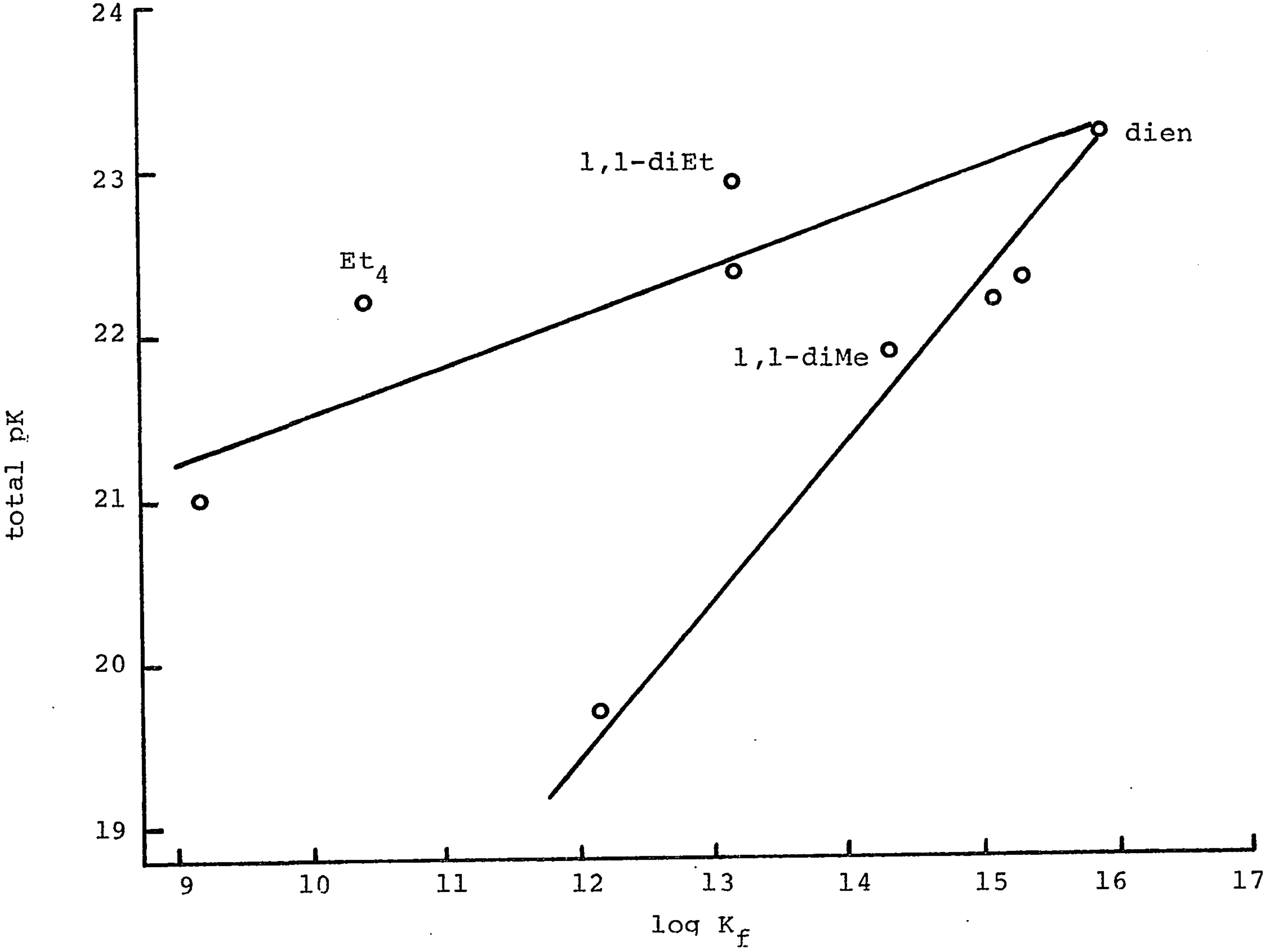
Table 8. Logs of the equilibrium constant, K_e, and the formation constant K_f, for the diens with copper(II) at 25.0°C and $\mu_{avg} = 0.13$ (KNO_3)

Amine	K_e	K_f
dien	-3.03 ± 0.02	15.91 ± 0.03
1-Me dien	-3.71 ± 0.03	15.32 ± 0.03
1,4-di Me dien	-4.27 ± 0.02	15.11 ± 0.02
1,1-di Me dien	-3.92 ± 0.04	14.33 ± 0.04
Me_5dien	-5.47 ± 0.03	12.16 ± 0.03
1,1-di Et dien	-5.84 ± 0.13	13.17 ± 0.11
1,4,7-tri Et dien	-6.33 ± 0.08	13.17 ± 0.08
1,1,7,7-tetra Et dien	-8.39 ± 0.03	10.43 ± 0.03
4-Me-1,1,7,7-tetra Et dien	-9.58 ± 0.02	9.15 ± 0.20

followed the order Me > Et > n-Pr > n-Bu. Näsänen and coworkers (47) later studied a series of symmetrically and unsymmetrically substituted N-ethyl and N-methylethylenediamines and developed an equation for the prediction of the values of K_f from the number and position of the substituents. The present study does not include a sufficient number of compounds to make a correlation of this type. However, it can be seen that the effect of an ethyl group is roughly twice that of a methyl group on the value of K_f.

Generally, the stability of a complex can be related to the basicity of the ligand (48). Where the donor atoms and structures are similar, as in this study, a linear relationship is expected between the stability of the complex and the basicity of the ligands. Figure 14 shows a plot of log K_f as a function of the log of the total proton affinity of the ligand, that is, the sum of the logs of K_1, K_2, and K_3. Although the correlation is not as good as expected, some trends can be seen. The stability of the complexes does decrease with basicity, but Et_4dien and 1,1-di Et dien form weaker complexes than expected from their total pKa values. The basicity of the N-methyl diens decreases faster than the N-ethyl diens, but log K_f does not follow. Steric requirements of the ethyl groups appear to be greater and predominate over the inductive increase in stability anticipated for an N-ethyl ligand over an N-methyl

Figure 14. Dependence of log K_f on total ligand basicity


24
23
22
21
20
19
total pK
9
10
11
12
13
14
15
16
17
log K_f
dien
1,1-diEt
Et_4
1,1-diMe

ligand. The best example is for the 1,1-di Et dien, which is ten times more basic, but which forms a ten times less stable complex, than 1,1-di Me dien. Both of these compounds, however, seem to deviate from the behavior predicted by the other ligands. The lower stability of the unsymmetrically substituted complex from the symmetrically substituted was also observed for some ethylenediamines. One of the reasons in this case may be the interference of the alkyl groups with the water molecules remaining on the metal ion, particularly in the plane of the ligand. Models of the 1,1-di Et dien complex and the 1,4,7-tri Et dien complex demonstrate that the ethyl groups of the 1,1-di Et dien crowd the ligands in the other coordination positions, while the ethyl groups of 1,4,7-tri Et dien can be directed away from the metal ion.

Margerum and co-workers (14) have studied the formation of the Et_4dien complex, reporting K_f as 10.1 ± 0.1. As stated previously, the values of K_1 and K_2 they obtained differ from those in the present work. The sum of the differences in the logs of these quantities is nearly equal to the difference observed in K_f. They attribute the decrease in stability of this complex to a steric interaction between two water molecules coordinated above and below the square plane and the alkyl groups. If this steric repulsion were the major reason, the complex of

4-Me-1,1,7,7-tetra Et dien should be only slightly less stable than the complex of Et_4dien. Perhaps other factors should be considered such as the destruction of the secondary hydration sphere when the metal ion is inside the hydrophobic alkyl groups. The entropy change for the complex formation reaction may be a good measure of this effect.

The value of K_f for the complex of 4-Me-1,1,7,7-tetra Et dien is an approximation of the uppermost value. The measurement was complicated by precipitation around pH 5.8, and only a few points were available for calculations.

An attempt was made to extend the study of the complexes of the diens to nickel(II) and zinc(II), which were measured by Prue and Schwarzenbach (2) for dien as 10.7 and 8.9, respectively. Solutions of zinc(II) of the same concentration as the copper(II) gave visible white precipitates before reaching the first end point when titrated in the presence of $(H_3Et_4dien)^{3+}$ or $(H_3Et_2dien)^{3+}$. When the concentration was decreased ten-fold, no precipitates were visible, but after the addition of an aliquot of sodium hydroxide, the pH would drift downward. Nickel (II) behaved similarly with both ligands. Both metal ions are known to form complexes with Et_4dien and Me_5dien in nonhydroxylic solvents (49, 33).

Hydroxo complexes

As stated previously, the second end point observed in the titrations of copper(II) with the diens is due to the formation of the complex, $[\text{Cu dien(OH)}]^+$. Particularly in this study, where the ratio of the ligand to metal ion is kept as close to unity as possible, the formation of this complex is the only explanation for this second end point. Conductometric measurements (24) and concentration studies (22) have shown it to be a monohydroxo complex and monomeric.

The calculation of the acid dissociation constant, K_d, for the reaction:

$$[\text{Cu dien}(H_2O)]^{2+} \overset{K_d}{\rightleftarrows} [\text{Cu dien(OH)}]^+ + H^+$$

was adapted from the method of Courtney et al. (22).

$$[\text{Cu(OH)A}]^+ = [\text{OH}]_{\text{TOT}} + (\text{H}) - (\text{OH}) \qquad (11a)$$

$$A_{\text{TOT}} = [\text{CuA}]^{2+} + [\text{Cu(OH)A}]^+ \qquad (11b)$$

$$K_d = [\text{Cu(OH)A}]^+(\text{H})^+/[\text{CuA}]^{2+} \qquad (11c)$$

where $[\text{OH}]_{\text{TOT}}$ is the amount of added hydroxide, adjusted to the volume of the solution and (OH) is the amount of hydroxide arising from the dissociation of water, calculated from K_w and the pH. Appropriate substitutions from Equations (11a) and (11b) in Equation (11c) yield K_d in terms of known or measurable quantities:

$$K_d = \frac{\{[OH]_{TOT} + (H) - (OH)\}(H)}{A_{TOT} - [OH]_{TOT} - (H) - [OH]}$$

The stability constant, K_{OH}, defined by the reaction:

$$[\text{Cu dien } H_2O]^{2+} + (OH)^- \overset{K_{OH}}{\rightleftarrows} [\text{Cu dien}(OH)]^+ \qquad (12)$$

is obtained by dividing K_d by K_w, the ionization constant of water. The stability constant, K_{OH}, was also calculated using Equation (6) first to obtain K_d. The constants obtained by these methods are identical. The calculations were performed by computer with the subroutine of program 3, page 156 of the Appendix. The results are given in Table 9.

The factors which influence the acidity of a coordinated water molecule are still unknown. Although several series of compounds have been investigated, the trends observed have not always been easily explained. A recent investigation of some terdentate chelates, including such varied ligands as 4-amino-5-hydroxyacridine, glycylglycine, and iminodiacetic acid with copper(II) determined the pK_d values of the coordinated water to lie within the range of 9 to 10 (50). Martell and co-workers (51) have studied the acidity of a number of copper(II) complexes of bidentate and tridentate ligands. They found that for ethylenediamine,

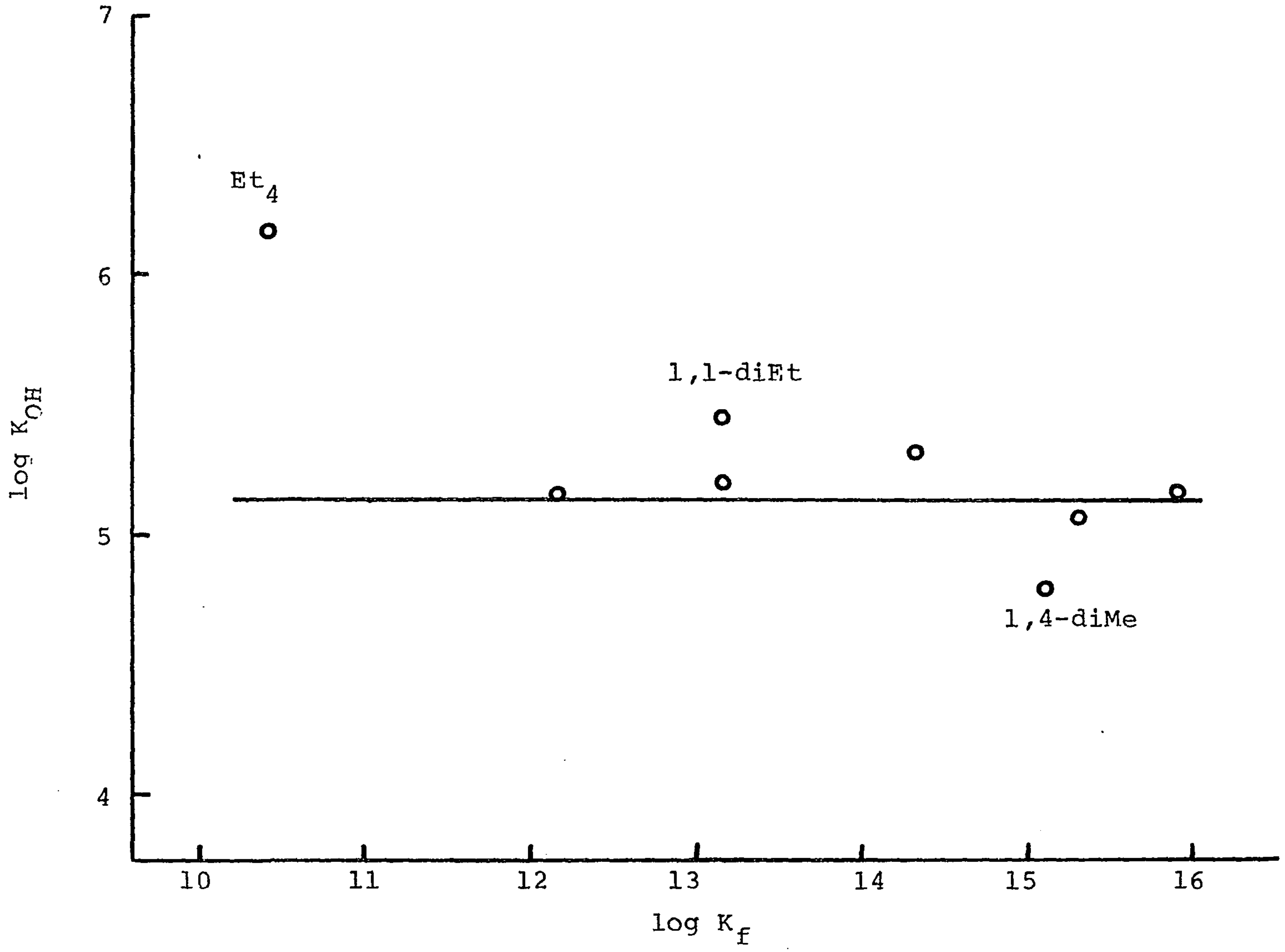
Table 9. Dissociation constants, K_d, and hydroxo stability constants, K_{OH}, of the copper-dien complexes

Amine complex	Log K_d	Log K_{OH}
dien	-8.63 ± 0.06	5.17 ± 0.06
1-Me dien	-8.72 ± 0.08	5.07 ± 0.08
1,4-di Me dien	-9.00 ± 0.04	4.79 ± 0.04
1,1-di Me dien	-8.47 ± 0.12	5.32 ± 0.11
Me_5 dien	-8.65 ± 0.04	5.14 ± 0.04
1,1-di Et dien	-8.35 ± 0.11	5.44 ± 0.11
1,4,7-tri Et dien	-8.59 ± 0.13	5.21 ± 0.14
1,1,7,7-tetra Et dien	-7.61 ± 0.03	6.18 ± 0.03

with widely varying substituents on carbon and nitrogen, the pK_d values fell within the range of 7.1 to 7.5. The higher pK_d values they observed for tridentate chelates were taken as indications of the greater electron donor effects of a tridentate ligand on the remaining waters, and the effect of decreasing the number of molecules available for hydrolysis.

The plot in Figure 15 shows that here also the pK_d is virtually independent of the formation constant of the complex. Also, the values lie within a narrow range, 8.3 to 9.0, slightly below that reported for other terdentate chelates, with the exception of the pK_d for the Et_4dien complex, which is much lower at 7.6. Margerum et al. (14) attribute the high value of K_{OH} for this complex to the absence of water in the axial coordination positions, which would tend to strengthen the in-plane bonds and make the water molecule there more acidic. This explanation is reasonable if the basic assumption, the lack of axial coordination, is true. Beaumont (52) has studied a series of cobalt(III) amine complexes and has proposed that the acidity of coordinated water may be influenced by two different things. In some instances, the nature of the ligand *trans* to the water molecule would affect the acidity of the water, and the observed acidities, or pK_d values, should vary inversely as the *trans* effect of the ligand. The nature

Figure 15. Dependence of log K_{OH} on log K_f


7
6
5
4
log K_{OH}
Et$_4$
1,1-diEt
1,4-diMe
10
11
12
13
14
15
16
log K_f

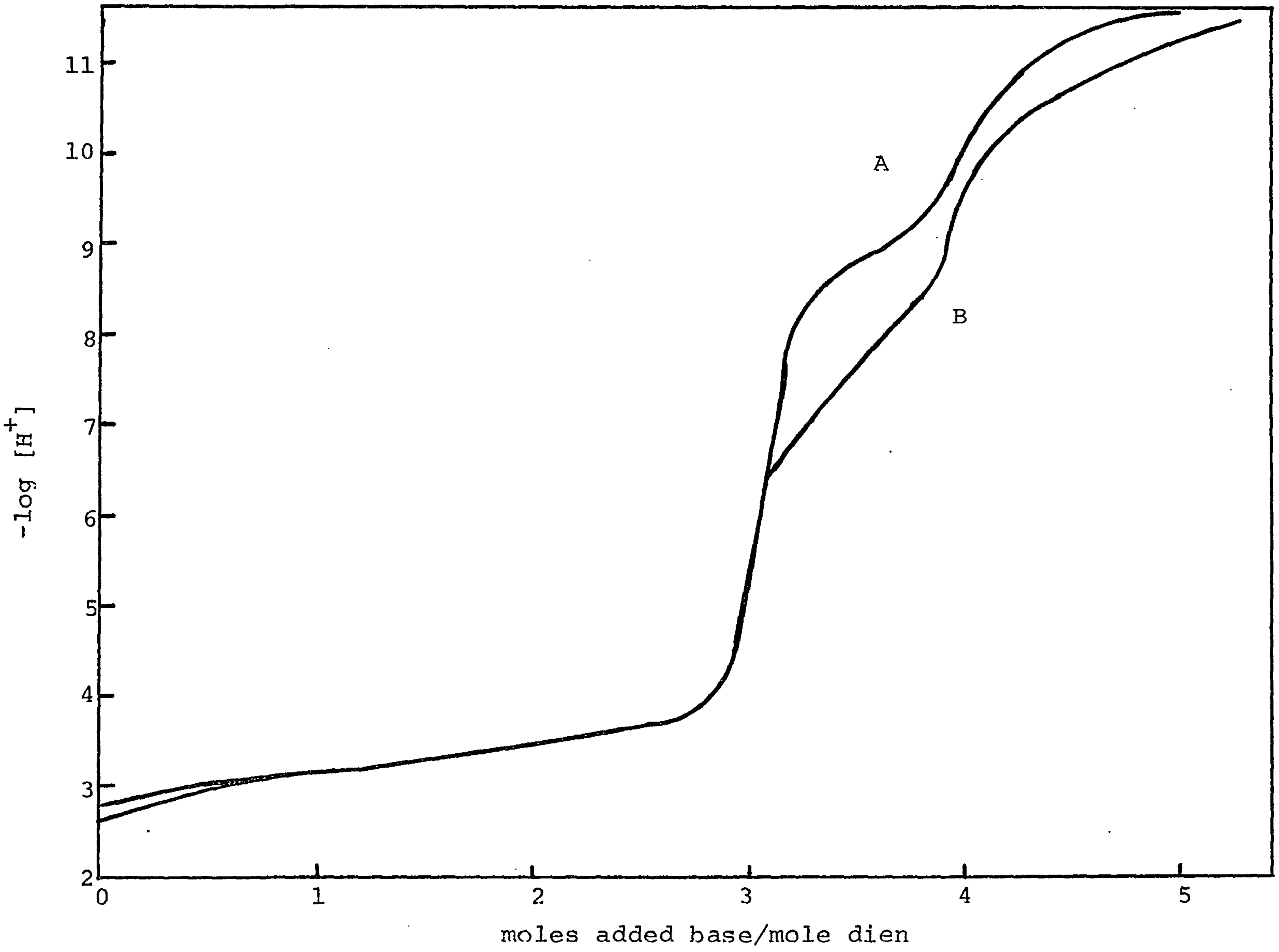
of the ligands cis to the water may also be taking part. Steric effects of the cis substituents may increase the acidity of the water.

The observations on the series of dien complexes may be explained in terms of these two different phenomena. If dien is taken as a point of reference, then the trans nitrogen, the 4-nitrogen, in 1,4-di Me dien seems to donate more electron density to cause the acidity of the coordinated water molecule to decrease. The acidity increases in 1,1-di Me dien and 1,1-di Et dien, possibly due to increased steric repulsions of the alkyls on the cis nitrogen for the water molecule. The constants for Me_5dien and 1,4,7-tri Et dien could be explained as a combination of both effects, resulting in no net change from dien. The sharp increase in acidity of the Et_4dien complex may be due to steric crowding of the in-plane water molecule, as well as weak or non-existent axial coordination which might strengthen the in-plane bonds.

Mixed ligand complexes

The investigation of the stability of the mixed ligand complexes of diens and amino acids, or amino acid ester hydrochlorides, with copper(II) was done potentiometrically on a solution of 9×10^{-3} M copper(II) nitrate, 9×10^{-3} M dien, 9×10^{-3} M amino acid, sufficient standard nitric acid to completely protonate the dien, and sufficient distilled water and potassium nitrate solution to bring the initial volume to ten milliliters and the average ionic strength to 0.11 at 25.0 ± 0.1°C. For the titration of the amino acid esters, the procedure was varied slightly to minimize hydrolysis of the ester during the course of the measurements. The initial volume of the solution was nine milliliters and the ester solution was added after the dien complex was formed, and the titration was then continued from this point to obtain the formation constant for the mixed species. The solutions were titrated with 0.2 N carbonate-free sodium hydroxide. The typical curve, Figure 16, shows that the titration follows that of the dien complex closely until near the first end point. The dien complex is therefore formed first with no interference from the amino acid. The calculations are simplified considerably because of this behavior. From the first end point, the titration curve in the presence of amino acid lies below that for the dien complex. A competition between the hydroxo complex and the amino acid complex is assumed, and it is data from this region between a=3 and a=4 which are used in the calculations. In this region the following equilibria are to be considered:

Figure 16. Titration curve of an equimolar mixture of (dien H_3)$^{3+}$ and copper(II) (a) no amino acid, (b) with an equimolar amount of glycine added


A
B
11
10
9
8
7
6
5
4
3
2
0
1
2
3
4
5
-log [H$^+$]
moles added base/mole dien

$$\mathrm{HA} \overset{K_a}{\rightleftarrows} \mathrm{H}^+ + \mathrm{A}^- \qquad (13)$$

$$\begin{array}{llll}
[\mathrm{Cu\ dien}]^{2+} & + \mathrm{HA} \overset{K_n}{\rightleftarrows} \mathrm{H}^+ & & (14) \\
\quad + & & & \\
\quad \mathrm{OH}^- & & + [\mathrm{Cu\ dien(A)}]^+ & \\
\quad \uparrow\downarrow K_{OH} & & & \\
[\mathrm{Cu\ dien(OH)}]^+ & + \mathrm{HA} \overset{K'_n}{\rightleftarrows} \mathrm{H_2O} & & (15)
\end{array}$$

The equilibrium constant desired is for the reaction:

$$[\mathrm{Cu\ dien}]^{2+} + \mathrm{A}^- \overset{K_x}{\rightleftarrows} [\mathrm{Cu\ dien\ (A)}]^+ \qquad (16)$$

Combining Equations (13) and (14) leads to the definition

$$K_x = K_n/K_a \qquad (17)$$

Likewise K'_n can be expressed in terms of other constants and its determination is not necessary in the following treatment to obtain K_x.

$$[\mathrm{Cu_{TOT}}] = [\mathrm{Cu\ dien}]^{2+} + [\mathrm{Cu(dien)(OH)}]^+ + [\mathrm{Cu\ dien(A)}]^+ \qquad (18a)$$

$$[\mathrm{A_{TOT}}] = [\mathrm{A}]^- + [\mathrm{Cu\ dien(A)}]^+ + [\mathrm{HA}] \qquad (18b)$$

$$[\mathrm{OH}]_{add} = [\mathrm{OH}]^- - [\mathrm{H}]^+ + [\mathrm{Cu\ dien(OH)}]^+ + [\mathrm{Cu\ dien(A)}]^+ + [\mathrm{A}]^- \qquad (18c)$$

Substitution into Equation (18) from Equations (12), (13), and (16) will reduce the number of variables in the expressions to $[\mathrm{Cu\ dien}]^{2+}$, $[\mathrm{A}]^-$ and K_x.

$$[Cu_{TOT}] = [Cu\ dien]^{2+}\{1 + K_{OH}[OH] + K_x[A]\} \qquad (19a)$$

$$[A_{TOT}] = [A]^{-}\{1 + K_x[Cu\ dien]^{2+} + [H]^{+}/K_a\} \qquad (19b)$$

$$[OH]_{add} = [OH] - [H] + K_{OH}[Cu\ dien][OH]$$
$$+ K_x[Cu\ dien][A] + [A] \qquad (19c)$$

Let $[OH]_{add'} = [OH]_{add} + [H]$. Then Equation (19c) can be solved for [Cu dien] in terms of K_x and [A]:

$$[Cu\ dien] = \frac{[OH]_{add'} - [OH] - [A]}{K_{OH}[OH] + K_x[A]} \qquad (20)$$

Equation (20) is now substituted in Equations (19a) and (19b). The resulting expressions are solved for K_x and set equal to each other. The result, after considerable simplification, is a quadratic in [A] of the form:

$$[A]^2\{K_{OH}[OH] - K_w/(K_b[OH])\} + [A]\{[Cu_{TOT}]K_{OH}[OH]$$
$$+ \frac{K_w\{[OH]_{add'} - [OH]\}}{[OH]K_b} - [OH]_{add'} + [OH]$$
$$+ [A_{TOT}] - 2\cdot K_{OH}\cdot[OH]\cdot[OH]_{add'}$$
$$+ 2\cdot K_{OH}[OH]^2\}$$
$$+ \{[Cu_{TOT}]K_{OH}[OH]^2 - [Cu_{TOT}]K_{OH}[OH][OH]_{add'}$$
$$+ [OH]_{add'}\{[OH]_{add'} - [OH]\}$$

$$- [OH]\{[OH]_{add'} - [OH]\} - [A_{TOT}]\{[OH]_{add'} - [OH]\}$$

$$- K_{OH}[OH]^2[OH]_{add'} + K_{OH}[OH][OH]_{add'}^2$$

$$- K_{OH}[OH]^2\{[OH]_{add'} - [OH]\}\} = 0 \qquad (21)$$

Only one of the two roots of Equation (21) is positive and less than $[A_{TOT}]$. This root is returned to either expression for K_x obtained from Equations (19a) and (19b) to obtain a value for K_x. The method outlined above was written into program 4, page 159 of the Appendix, and the calculations were performed by computer. The results obtained are listed in Table 10. The proton stability constants of the amino acids and esters were redetermined under the experimental conditions used here. The constants, K_b, calculated according to Equation (6) and reported in Table 11, agree well with the literature values under similar conditions.

It is easier, perhaps, to discuss the obvious exceptions before any explanations for the trends observed are attempted. First, the titration curve of the Et_4dien complex in the presence of glycine, Figure 17, does not behave as the other complexes do initially in the presence of amino acids. Glycine forms a complex with copper(II) of

Table 10. Log of the formation constants, K_x, of the mixed ligand complexes of copper(II) at 25.0°C and μ_{avg}=0.11 (KNO_3)

Dien Complex	Gly	Val	Me Gly	Sarc	β-ala	Et-β-ala
dien	4.42±0.05	3.79±0.09	2.52±0.08	3.98±0.12	3.65±0.19	NC[a]
1-Me dien	4.65±0.07	3.99±0.09		3.98±0.12	3.15±0.16	NC
1,4-di Me dien	4.68±0.01	4.22±0.04		3.79±0.19	3.29±0.08	
1,1-di Me dien	4.38±0.04	3.96±0.03		3.10±0.30	2.89±0.12	
Me_5dien	5.04±0.05[b]	4.79±0.04[b]		3.23±0.13[c]	3.23±0.06[c]	
1,1-di Et dien	4.16±0.04	3.46±0.17		3.05±0.18	3.43±0.10	
1,4,7-tri Et dien	4.25±0.07	3.84±0.02		NC	NC	
Et_4dien	D[d]					

[a] Presumed to be non-coordinating, see text.

[b] Undergo a color change during formation.

[c] No color change.

[d] Displaces dien ligand.

Table 11. Proton stability constants of the amino acids and esters at 25.0°C and μ_{avg}=0.11 (KNO_3)

Amino Acid	Log K_{b_2} [a]	Log K_{b_1} [a]
glycine	2.35 ± 0.02	9.54 ± 0.01
L-valine	2.25 ± 0.02	9.47 ± 0.02
sarcosine	2.17 ± 0.02	9.98 ± 0.01
β-alanine	3.55 ± 0.01	10.08 ± 0.02
methyl glycinate		7.68 ± 0.01
ethyl-β-alaninate		9.23 ± 0.02

[a] $K_b = 1/K_a$ as defined by Equation (13).

similar stability, 10^8, to the Et_4dien. It appears that the basicity of the dien takes over and it is displaced from the metal by the glycine.

The titration curves for 1,4,7-tri Et dien with valine and β-alanine and dien with β-alanine ethyl ester hydrochloride are shown respectively in Figures 18, 19, and 20. The common feature of Figures 19 and 20 is that after the first end point, the pH continues to increase on addition of base, but no inflection is observed which would indicate coordination. The calculation of K_x by the method described resulted in negative values for K_x. The expected

Figure 17. Titration curves of $(Et_4dien\ H_3)^{3+}$ and copper(II) (a) no amino acid, (b) in the presence of an equimolar amount of glycine

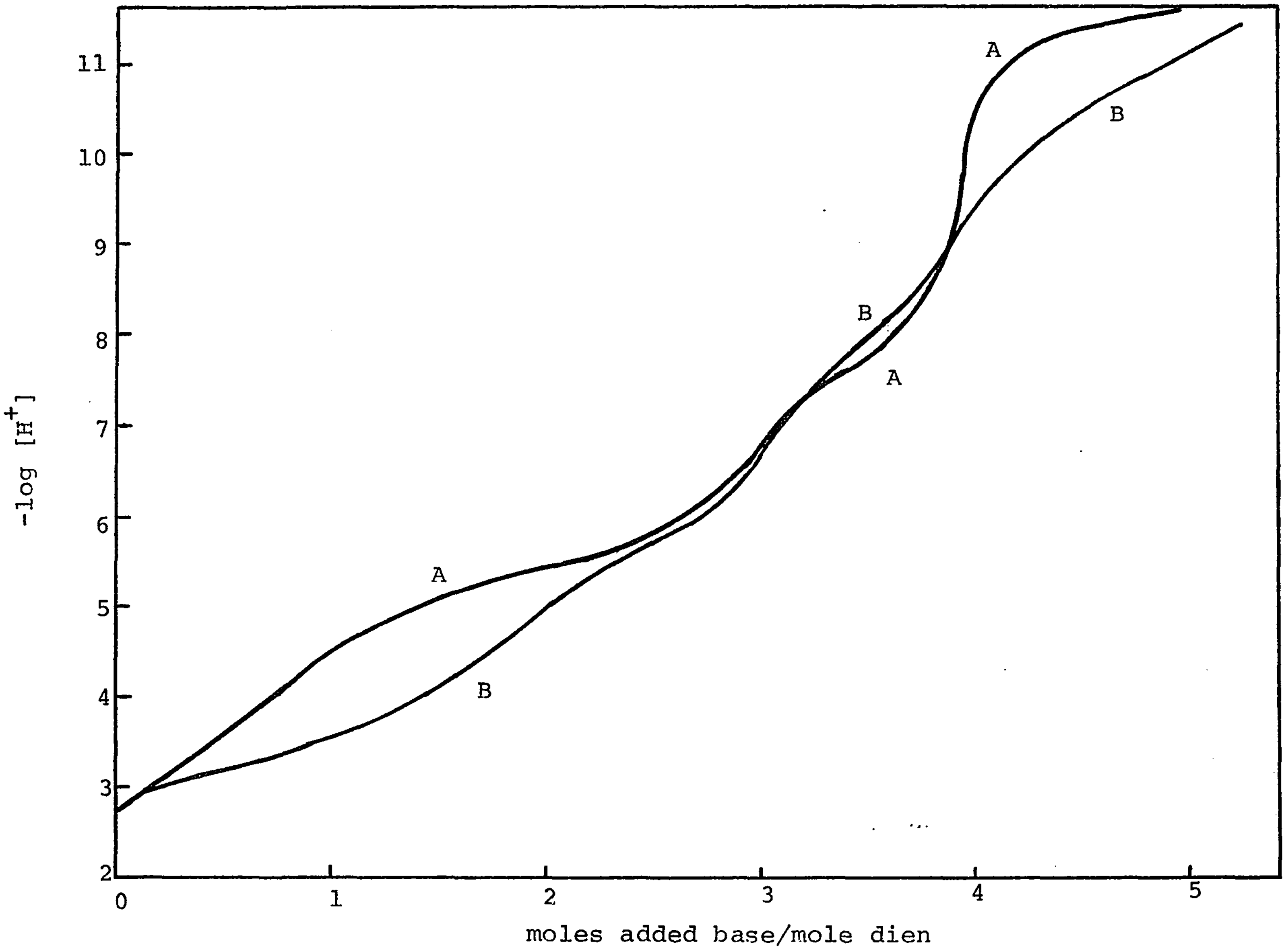
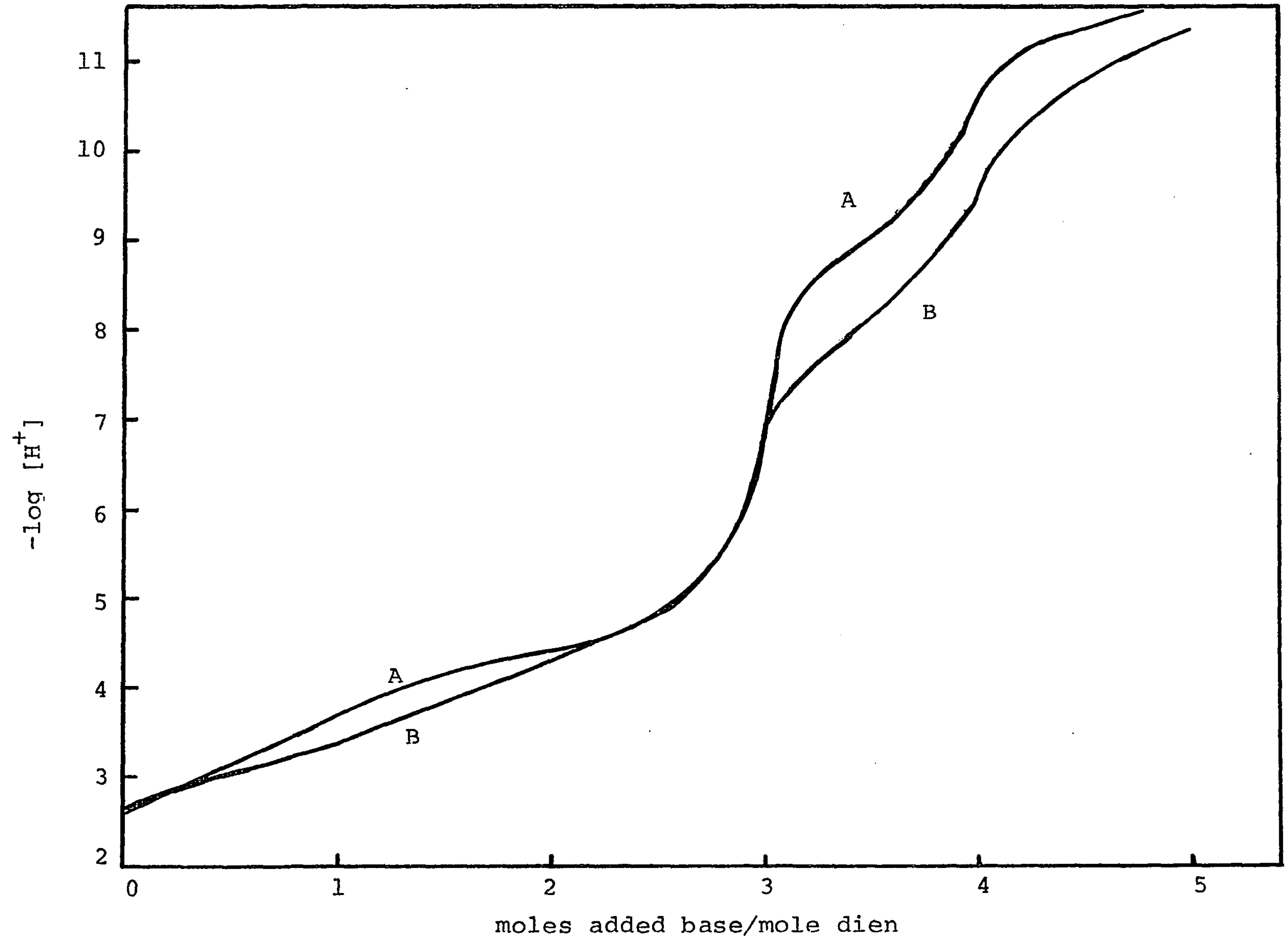

11
10
9
8
7
6
5
4
3
2
-log [H$^+$]
0
1
2
3
4
5
moles added base/mole dien
A
B
B
A
A
B

Figure 18. Titration curves of (1,4,7-tri Et dien H_3)$^{3+}$ and copper(II) (a) no amino acid, (b) in the presence of an equimolar amount of L-valine



-log [H$^+$]
2
3
4
5
6
7
8
9
10
11
0
1
2
3
4
5
moles added base/mole dien
A
B
A
B

Figure 19. Titration curves of $(1,4,7\text{-tri Et dien }H_3)^{3+}$ and copper(II) (a) no amino acid, (b) in the presence of an equimolar amount of β-alanine

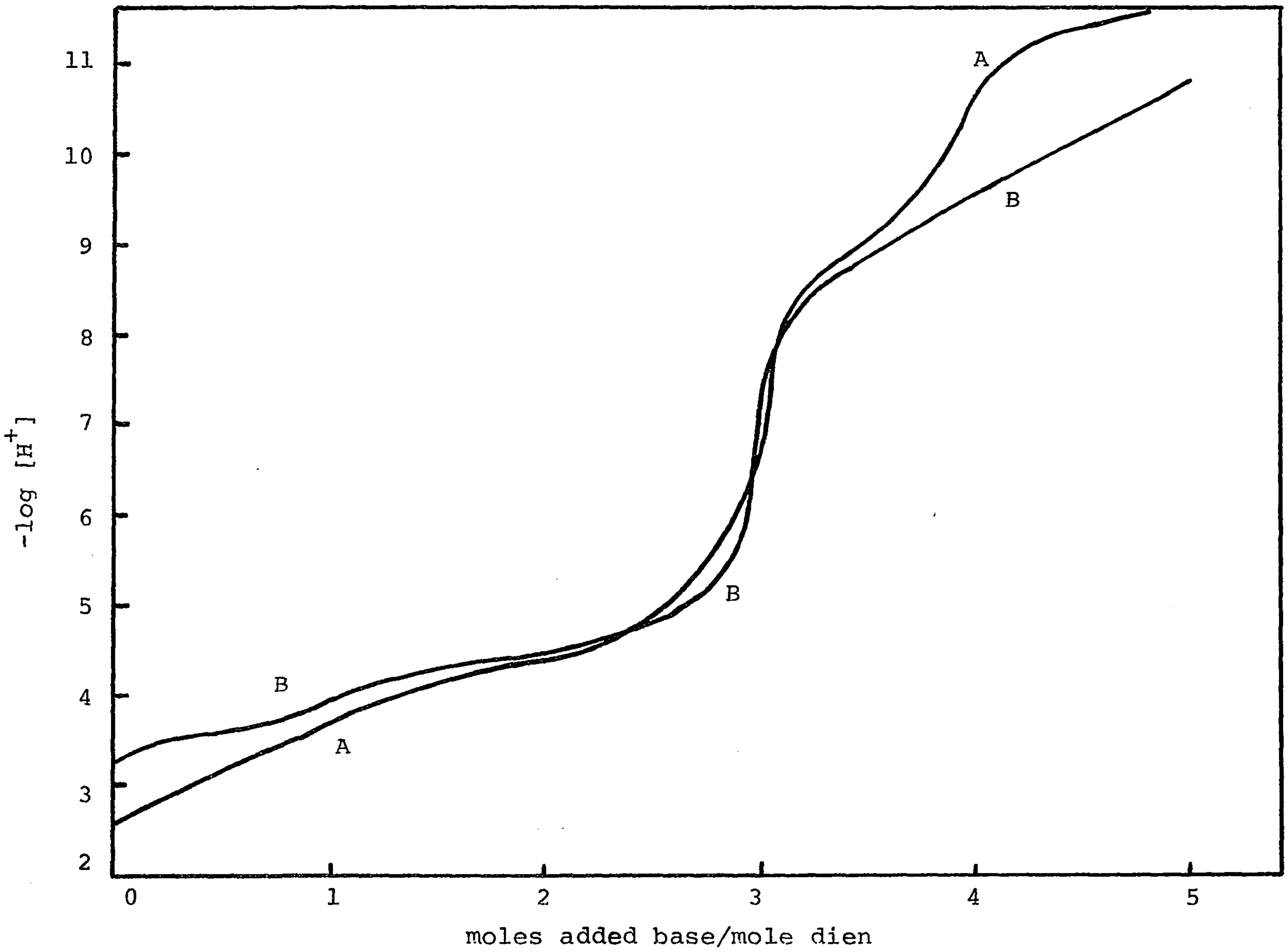
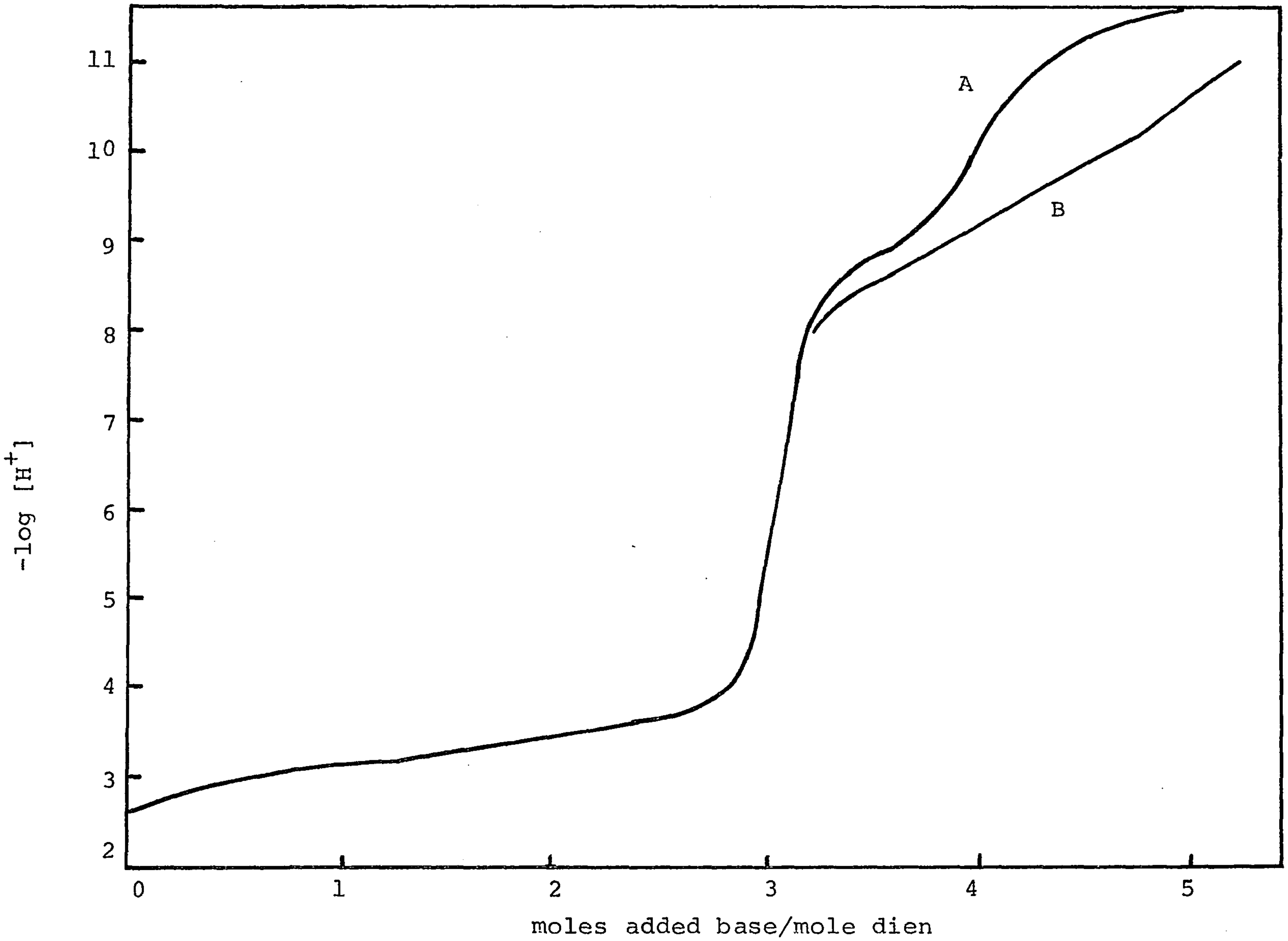

-log [H^+]
11
10
9
8
7
6
5
4
3
2
0
1
2
3
4
5
moles added base/mole dien
A
B
B
A
B
A

Figure 20. Titration curves of (dien H_3)$^{3+}$ and copper (II) (a) no amino acid ester, (b) containing an equimolar amount of β-alanine ethyl ester hydrochloride


-log [H$^+$]
2
3
4
5
6
7
8
9
10
11
0
1
2
3
4
5
moles added base/mole dien
A
B

value of log K_x for β-alanine ethyl ester and the dien complex is about 3.1, and for β-alanine and the triethyl dien complex, 3.3, both of which should be measurable quantities. The only explanation for this behavior is that no coordination is occurring. For the β-alanine ethyl ester with dien and 1-Me dien, this result was particularly surprising and it strongly suggests that with the other diens, β-alanine acts as a monodentate ligand. Although β-alanine is a stronger base than glycine, the stability of its complex with copper(II), log K_f is 7.2, is less than that of glycine, log K_f is 8.1, (53) because of the formation of a six-membered chelate ring. This difference is observed by Hopgood and Angelici (54) in the formation of glycine and β-alanine complexes of $[Cu(NTA)]^-$, log K_x is 5.44 and 4.56, respectively, Table 12. In the dien complexes, the differences in log K_x of the glycine and β-alanine complexes would be expected to be 0.8 to 1.0 log units. Only for dien and 1,1-di Et dien is the difference this small. For the other dien complexes, the difference in log K_x is 1.4 to 1.5 log units, suggesting a change in denticity of the ligand. However, β-alanine is probably monodentate in all cases. The ethyl ester of β-alanine is more basic than the methyl ester of glycine. Hopgood and Angelici (54) found that the β-alanine ester therefore forms a stronger complex with $[Cu(NTA)]^-$, log K_x of 3.65, than the glycine ester, log K_x of 3.06. This does not occur with the dien complex, thereby providing further evidence that β-alanine itself is only monodentate.

The different behavior of the tri Et dien complex toward valine and β-alanine and sarcosine was not expected. The titration curve of this complex in the presence of L-valine appears to have the same features as the other complexes, saying that no steric problems were encountered with the isopropyl group of the amino acid. Sarcosine would be expected to coordinate only weakly because of the N-methyl group interfering with the dien N-ethyl groups. The apparent non-coordination of β-alanine to this complex has no ready explanation.

Figures 21 and 22 show the titration curves for the Me_5dien complex with glycine and β-alanine, respectively. The curves show no unusual behavior which might explain the sharp rise in stability observed for the mixed complexes of Me_5dien and glycine or valine. However, during the course of the titrations, some color changes occurred between a=3 and a=4 which did not take place with any of the other dien complexes in the presence of valine or glycine. Normally, the solution is dark blue at this time with some purple from the hydroxo complex. In these two titrations with the Me_5dien complex, the solution got lighter blue in color until a reached 4 and then darkened again. No

Figure 21. Titration curve of $(Me_5dien\ H_3)^{3+}$ and copper(II) (a) no amino acid, (b) in the presence of an equimolar amount of glycine

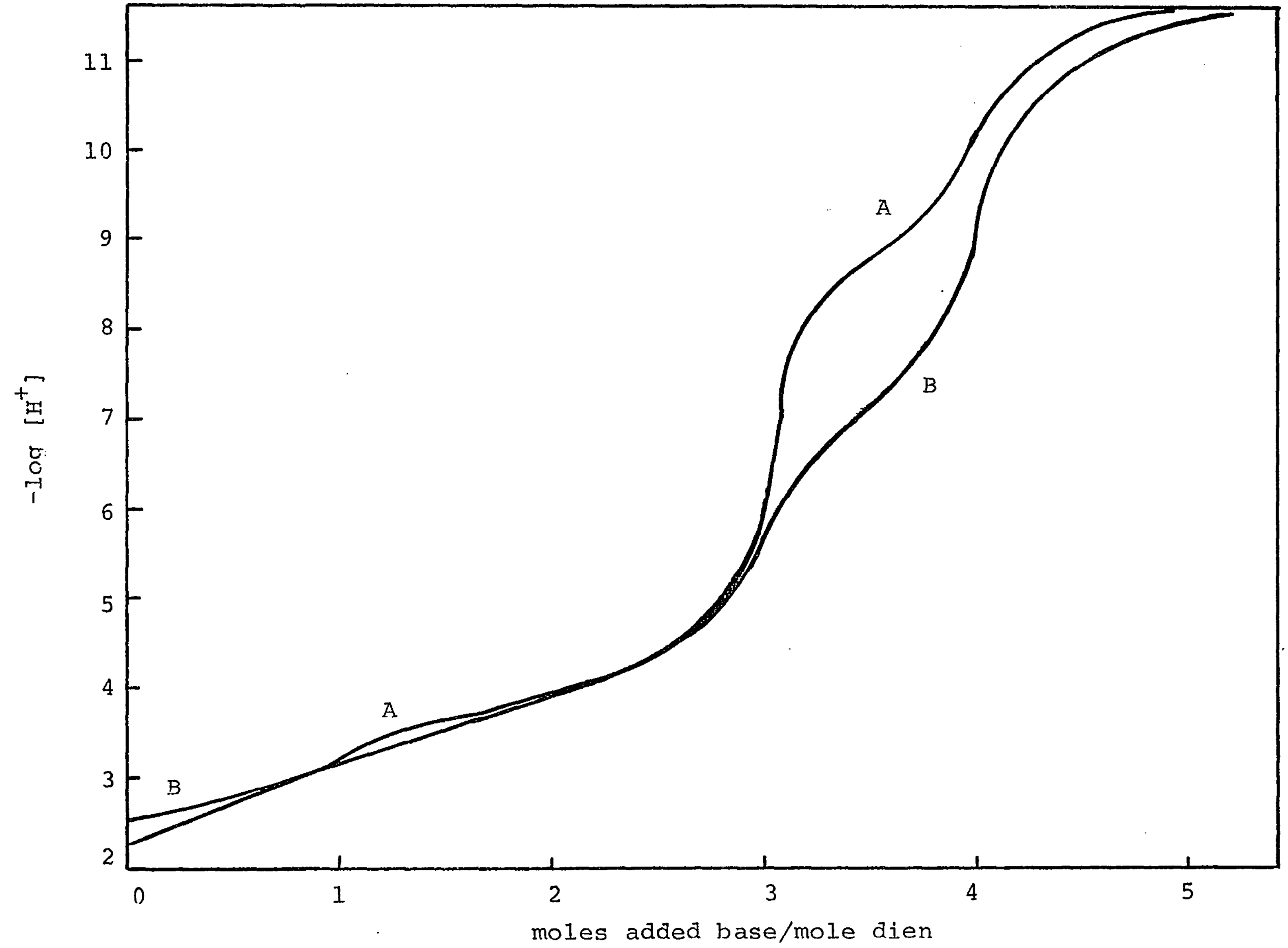
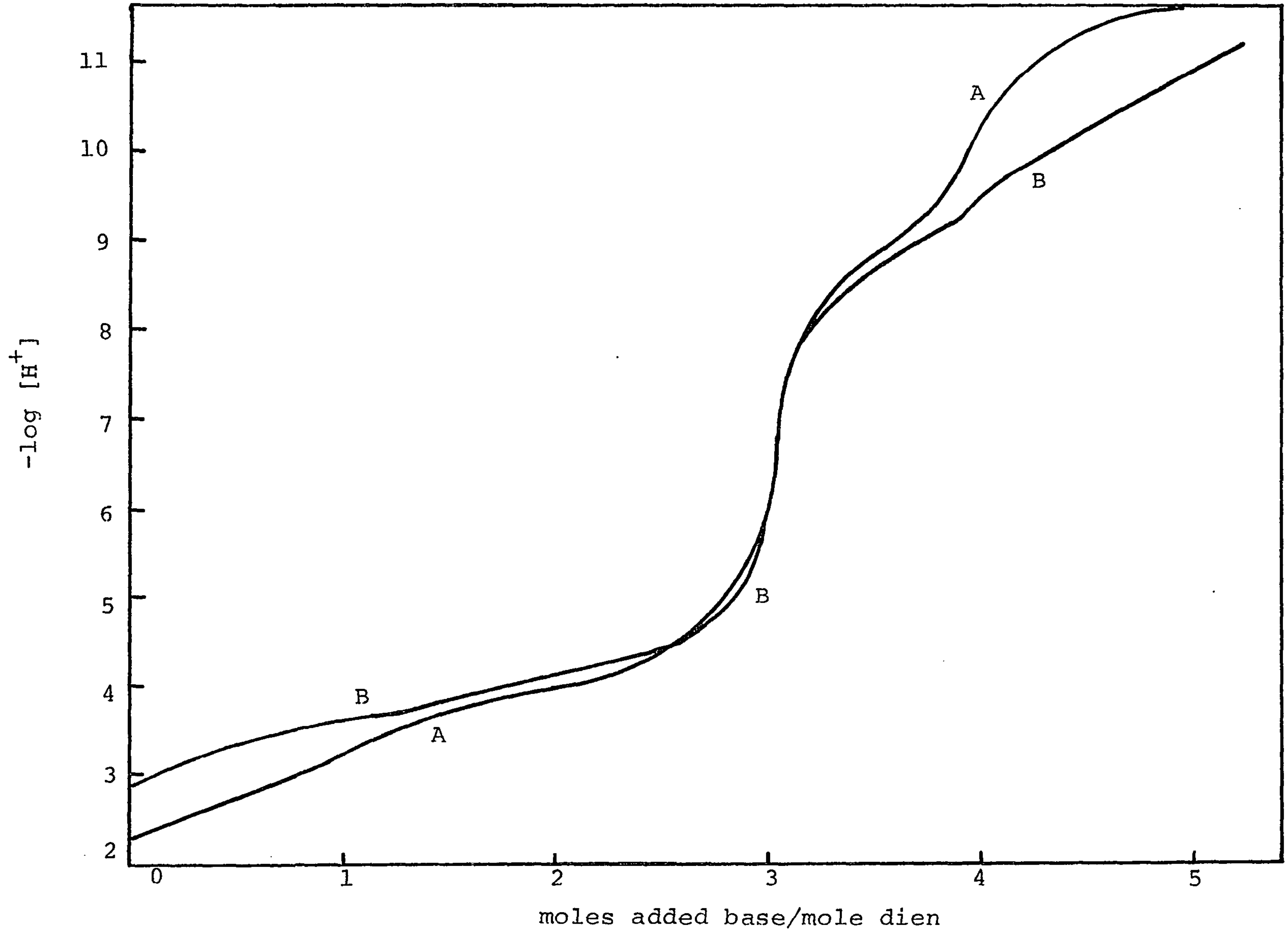

-log [H$^+$]
11
10
9
8
7
6
5
4
3
2
0
1
2
3
4
5
moles added base/mole dien
A
A
B
B

Figure 22. Titration curve of $(Me_5dien\ H_3)^{3+}$ and copper(II) (a) no amino acid, (b) in the presence of an equimolar amount of β-alanine


-log [H$^+$]
11
10
9
8
7
6
5
4
3
2
0
1
2
3
4
5
moles added base/mole dien
A
B
B
A
B

unusual color behavior was observed with the Me_5dien complex in the presence of sarcosine or β-alanine. The answer to the questions posed here is not immediately obvious, although it may mean that a change in geometry has taken place. This explanation comes to mind first since five-coordinate distorted trigonal bipyramidal copper(II) complexes of Me_5dien have been isolated and they have low energy, low intensity absorption bands (33).

Evidence to support the bidentate nature of glycine and valine in the dien complexes has been given by infrared and circular dichroism studies on the interactions of L-alanine and L-alaninamide with the complexes, $[Cu(dien)]^{2+}$ and $[Cu\ en]^{2+}$ (55). Murokami and co-workers inferred from their results that alanine and alaninamide were bidentate and coordinated in the axial position with square pyramidal geometry in the dien complex, and bidentate but in the equatorial plane with the en complex.

The trends observed in the stability constants for an amino acid as the dien is varied are difficult to explain, particularly the increase in stability of the substituted dien-amino acid mixed complexes over that observed for dien. In cases where the stability decreases, it might be attributed to partial blocking of the open equatorial position by the alkyl groups on the terminal nitrogens of the dien. Likewise, the reasons for the decrease of

Table 12. Formation constants of some amino acids and esters with some copper(II) complexes

Complex	Acid or ester	log K_x
$[Cu\ NTA]^-$	Gly	5.44[a]
$[Cu\ NTA]^-$	Me Gly	3.06[a]
$[Cu\ NTA]^-$	β-Ala	4.56[a]
$[Cu\ NTA]^-$	Et-β-Ala	3.65[a]
$[Cu\ NTA]^-$	Val	5.10[a]
[Cu IMDA]	Gly	6.42[b]
[Cu IMDA]	Val	6.17[b]
$[Cu\ en]^{2+}$	Ser	6.70[c]
$[Cu(Bipy)]^{2+}$	Gly	7.92[d]

[a] Reference 54.

[b] Reference 58.

[c] Reference 57.

[d] Reference 56.

0.4 to 0.6 log K in the stability of the valine complexes from the corresponding glycine complexes is unexpected. They are equal in basicity and form complexes with the aquo ion of copper(II) to the same extent (53).

Sarcosine is more basic than glycine or valine and would be expected to form stronger complexes. However, because of the N-methyl group of sarcosine, the stability of the complex would be expected to vary as the number and size of the substituents on the terminal nitrogens of the diens varies due to steric interactions. Actually, the diens form two groups, one containing dien, 1-Me dien, and 1,4-di Me dien whose stability constants are around 3.9, the other containing 1,1-di Me dien, 1,1-di Et dien, and Me_5 dien whose stability constants are about 3.1. The addition of one methyl group apparently is not enough to interfere with the coordination of sarcosine, but the number or size of the groups after two methyl groups are added does not seem to have much effect on the stability of the complex either. Perhaps a change from bidentate to monodentate coordination occurs between the two groups of complexes. Another possibility is a change in the position of coordination of the sarcosine nitrogen from the plane of the dien molecule in the first group to one of the axial positions in the second group.

The stability of the complex of methyl glycinate with

$[Cu(dien)]^{2+}$ is another indication of the bidentate character of glycine in these mixed complexes.

In general, the mixed complexes studied here are less stable than other mixed complexes with similar systems. The complex of glycine with the 2,2'-bipyridyl complex of copper(II) is the most stable, log K_x of 7.92, perhaps due to π-acceptor ability of the bipyridyl ligand and the fact that coordination is in the square plane (56). The complex of $[Cu\ en]^{2+}$ with serine is also more stable (57). The complexes of [Cu IMDA] and $[Cu\ NTA]^-$ with glycine are also more stable than the dien complexes (58, 54), indicating that the attraction of dissimilar charges in the system of dien complex and glycine anion does not play an important part in determining the stability of these complexes.

A review of the factors which have been found to affect the stability of mixed ligand complexes has recently been published (59). There is, however, insufficient data available to make some of the quantitative comparisons mentioned in this article as to the relative stabilities of the ternary and binary complexes. Sigel and McCormick have also discussed the formation of ternary complexes and their role in biological processes (60).

Ester hydrolysis

The hydrolysis of methyl glycinate as catalyzed by the dien complex of copper(II) was studied by pH-stat techniques in the pH range of 7.7 to 8.9 at 25.0°C and ionic strength of 0.11 M (KNO_3). The solutions were 9 x 10^{-3} M in copper (II), and 9 x 10^{-4} M in methyl glycinate. A ten per cent excess of dien was used in these studies after results with equimolar amounts of copper(II) and dien were found to give inconsistent values. Excess dien, by as much as fifty per cent, did not affect the observed rate of hydrolysis. The solutions of complex were equilibrated first at 25°C while a stream of nitrogen was passed through the solution. The ester solution was then added and the hydrolysis at constant pH followed by the addition of 0.04 N carbonate-free sodium hydroxide. The pseudo-first order rate constants were obtained according to techniques described previously (37). Particularly at the higher pH values, the amount of hydroxide consumed was always less than the theoretical amount, based on the total ester present. The order of the reaction in total copper(II) was determined at pH 8.0. The results are listed in Table 13. A plot of k_{obs} versus the pH, Figure 23, shows the reaction to be first order in hydroxide ion concentration, the slope of the line being 0.89. Since the rate constants are only known to ± 10 per cent, this slope indicating the hydroxide dependence is within experimental error of 1.0. Inclusion of the data at pH 8.9 decreases the slope slightly, but this may be due to bad reproducibility. The

Table 13. Observed pseudo first order rate constants for the hydrolysis of methyl glycinate catalyzed by $[Cu\ dien]^{2+}$ at 25.0°C and μ=0.11 M (KNO_3)

(a) Total metal ion concentration is 9.54 x 10^{-3} M

$-\log [H^+]$	k_{obs} x 10^3 sec^{-1}	Average k_{obs} x 10^3 sec^{-1}
7.69	0.417	0.437
	0.457	
7.79	0.550	0.597
	0.574	
	0.667	
7.89	0.569	
8.00	0.781	0.870
	0.881	
	0.948	
8.10	0.900	0.918
	0.937	
8.20	1.28	1.29
	1.30	
8.30	1.30	1.63
	1.65	
	1.71	
	1.87	
8.40	1.21	1.76
	1.75	
	1.81	
	1.86	
	2.17	
8.50	2.13	2.39
	2.39	
	2.67	
8.90	4.00	4.66
	4.50	
	4.81	
	5.33	

Table 13 (Continued)

(b) Dependence on metal ion concentration

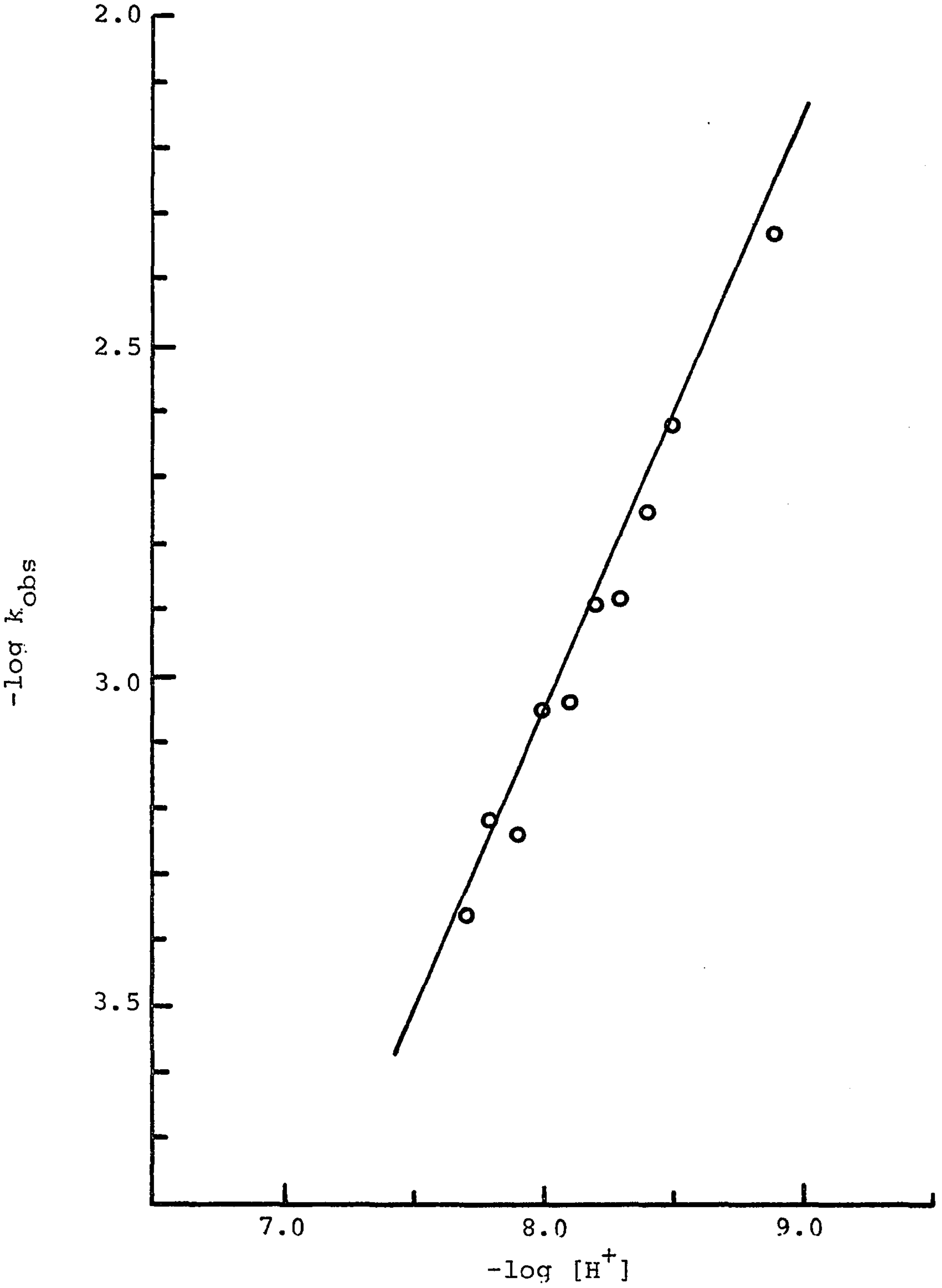
$-\log[H^+]$	$k_{obs} \times 10^3$ sec^{-1}	Average $k_{obs} \times 10^3$ sec^{-1}	$[Cu^{2+}]_{TOTAL}$
8.00	1.26 1.41 1.48	1.38	1.43×10^{-2}
8.00	1.77 1.83 1.90 2.06 2.17	1.95	1.91×10^{-2}

reaction was also found to be first order in copper(II), so that the general rate expression is:

$$\text{Rate} = k[OH][Cu_{TOT}][Ester_{TOT}] \qquad (22)$$

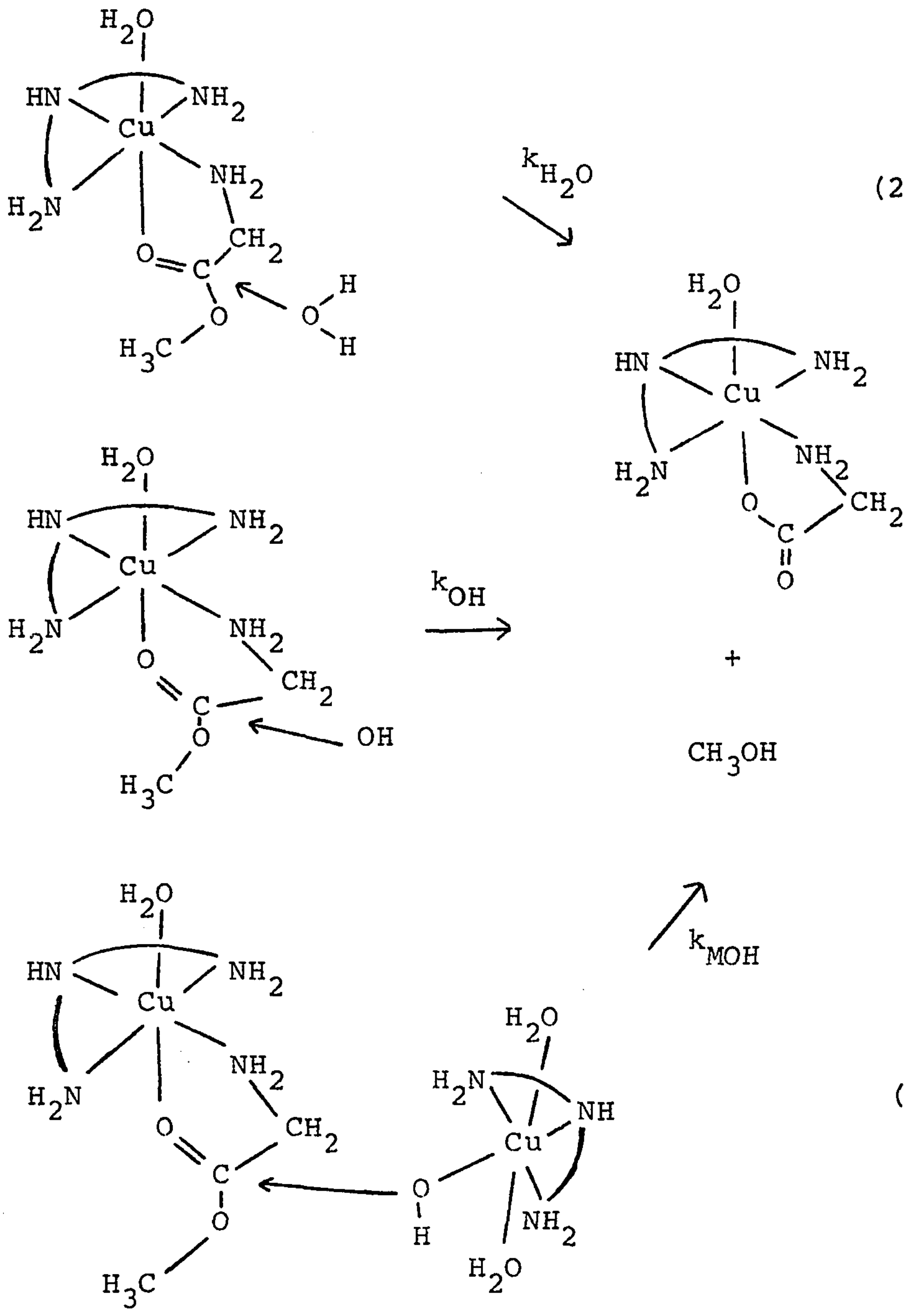
The products of this reaction were identified by nmr. A solution of four hundred fifty milliliters of 0.04 M copper(II) nitrate, 0.05 M dien, and slightly less than 0.04 M methyl glycinate was allowed to react at room temperature for two and one-half hours with the pH maintained between 7.9 and 8.1 by the addition of sodium hydroxide. At the end of this time, the pH remained constant indicating the reaction had gone to completion. Slightly more than one equivalent of sodium sulfide, $Na_2S \cdot 9H_2O$, was added to precipitate the copper(II). The solution was filtered and the volume of the filtrate reduced from 0.5ℓ

Figure 23. Dependence of k_{obs} on $[H^+]$ to determine the order of the reaction with respect to [OH]


-log k_{obs}
2.0
2.5
3.0
3.5
7.0
8.0
9.0
-log [H^+]

to 0.02ℓ, yielding a white precipitate. The precipitate and water were extracted twice with forty milliliter portions of methylene chloride. An nmr of this extract showed the same number of peaks, at the same positions and in the same ratios, as a known sample of dien in deuteriochloroform. A small amount of the precipitate was dissolved in deuterium oxide, and the nmr of this solution indicated that not all of the dien was extracted. A single sharp peak was observed about 0.75 ppm upfield from the water resonance. A known sample of dien and glycine in D_2O exhibited the same features, although the positions of the peaks differed by about 0.2 ppm. The peak positions may be different due to slight variations in pH or the large amount of inert salt from the reaction mixture. From this analysis of the ligands, the products of the reaction can be formulated as $[Cu(dien)gly]^+$ and methanol, and not the amide, $H_2NCH_2CH_2N(H)CH_2CH_2N(H)C(O)CH_2NH_2$.

The mechanism of the reaction is not entirely clear. From the dependence on the copper ion concentration, the active species must be the complex, $[Cu(dien)(Me\ Gly)]^{2+}$. From the known equilibrium constant and the concentrations used, it is found that as much as one-fourth of the ester is not coordinated to the dien complex under the conditions of the kinetic studies. However, the hydrolysis of this uncoordinated ester should not contribute appreciably to the observed rate under these conditions (61). Therefore, the following possible mechanisms need to be considered:



(23)

(24)

(25)

Each of the proposed mechanisms is dependent on the prior equilibrium of the dien complex with the ester, whose equilibrium constant was measured in a separate experiment. The mechanism of Equation (23), involving water attack on the coordinated ester, can be ruled out of consideration immediately. By plotting the values of k_{obs} as a function of hydroxide ion concentration and extrapolating to zero hydroxide, one can determine k_{H_2O}, which for this system is negligible and in further calculations, it will be taken as equal to zero. The reactive species shown in the mechanism of Equation (25) is admittedly rather unusual. Only recently have mechanisms similar to this one been proposed, one involving the catalysis of the hydrolysis of p-nitrophenylacetate by the hydroxo complex of glycylglycine and copper(II) (62), one where the catalytic species is the hydroxo complex of mercury(II) and dien in the hydrolysis of p-nitrophenylacetate (63), and another involving the species $[MgOH]^+$ and $[CaOH]^+$ in the hydrolysis of acetyl phosphate (64). For a first approximation, then, only the mechanism of Equation (24) will be considered. The rate equation becomes:

$$\text{Rate} = k_{OH}(OH)[Cu(dien)Me\ Gly]$$

or, knowing that all the ester is not coordinated to the dien complex:

$$\text{Rate} = k_{OH}(OH)\{\frac{[Cu(dien)Me\ Gly]}{(Me\ Gly)_{tot}}\}(Me\ Gly)_{tot} \qquad (26)$$

It is desirable to evaluate k_{OH} in order to compare the catalysis of this complex with others. To make this evaluation, it is necessary to express [Cu(dien)Me Gly] in terms of known quantities.

From Equation (16):

$$[Cu\ (dien)Me\ Gly] = K_x[Cu\ dien][Me\ Gly] \qquad (27)$$

By definition:

$$(Me\ Gly)_{tot} = (Me\ Gly) + (Me\ Gly\ H)^+ + [Cu(dien)Me\ Gly]^{2+} \qquad (28)$$

and

$$(Cu)_{tot} = [Cu\ dien]^{2+} + [Cu\ dien(OH)]^+$$

$$= [Cu\ dien]^{2+}\ (1+K_{OH}(OH)) \qquad (29)$$

Equations (27, 28 and 29) can be combined to express the rate Equation (26), in terms of the known quantities, $(Cu)_{tot}$, (OH), K_{OH} and K_x:

$$\text{Rate} = \frac{k_{OH}(OH)K_x(Cu)_{tot}}{K_x(Cu)_{tot}+(K_b(H)+1)(1+K_{OH}(OH))}(Me\ Gly)_{tot}$$

or

$$k_{obs} = \frac{k_{OH}(OH)K_x(Cu)_{tot}}{K_x(Cu)_{tot}+(K_b(H)+1)(1+K_{OH}(OH))} \qquad (30)$$

Equation (30) can be rearranged to this linear form:

$$\frac{1}{k_{obs}} = \frac{1}{(Cu)_{tot}} \cdot \frac{(K_b(H)+1)(1+K_{OH}(OH))}{k_{OH}(OH)K_x} + \frac{1}{k_{OH}(OH)} \qquad (31)$$

From a plot of $1/k_{obs}$ _versus_ $1/Cu_{tot}$ at pH 8.0, the intercept yields k_{OH}, 9.5×10^4 sec^{-1} M^{-1}, and the slope can be used to check the agreement with K_x, which is determined here to be 17.4, considerably lower than the value obtained potentiometrically. Therefore, the mechanism of Equation (24) is not correct alone.

By similarly considering only the mechanism of Equation (25), the following expression for k_{obs} is obtained:

$$k_{obs} = \frac{k_{MOH}K_xK_{OH}(OH)(Cu)^2_{tot}}{(1+K_{OH}(OH))\{K_x(Cu)_{tot}+(K_b(H)+1)(1+K_{OH}(OH))\}} \qquad (32)$$

which can be linearly plotted as:

$$\frac{(Cu)_{tot}}{k_{obs}} = \frac{1}{(Cu)_{tot}} \frac{\{(K_b(H)+1)(1+K_{OH}(OH))\}(1+K_{OH}(OH))}{k_{MOH}K_xK_{OH}(OH)}$$

$$+ \frac{(1+K_{OH}(OH))}{k_{MOH}K_{OH}(OH)} \qquad (33)$$

The intercept of Equation (33) yields a k_{MOH} of 0.17 sec^{-1} M^{-1}, and the slope gives a log K_x of 2.45, which is within experimental error of the potentiometric value of 2.52.

This mechanism was subjected to one further test, the prediction of k_{obs} at a different pH. When the appropriate numbers were put in Equation (32), k_{obs} at pH 8.4 was calculated to be 3.5×10^{-4} sec^{-1}, quite different from the observed value, 1.76×10^{-3} sec^{-1}. Therefore, this mechanism is also not the only one acting in the hydrolysis.

The combination of the mechanisms of Equations (24) and (25) is next assumed. Analysis of the rate expression as in the two preceding cases leads to the following expression for k_{obs}:

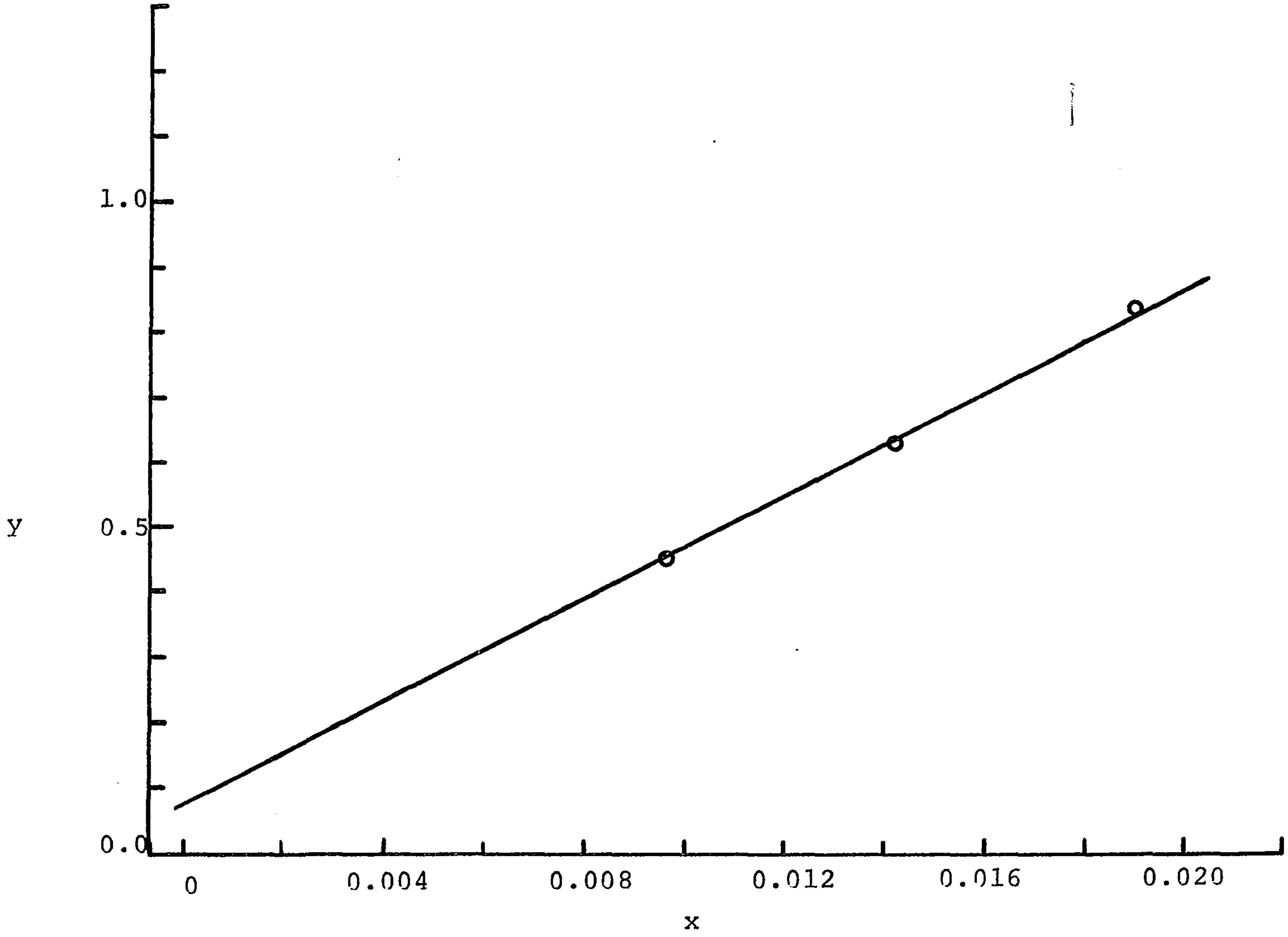
$$k_{obs} = \frac{K_x(Cu)_{tot}}{K_x(Cu)_{tot}+(K_b(H)+1)(1+K_{OH}(OH))}\{k_{OH}(OH) + \frac{k_{MOH}K_{OH}(OH)(Cu)_{tot}}{1+K_{OH}(OH)}\} \qquad (34)$$

which can be rearranged to:

$$k_{obs}K_x + \frac{k_{obs}(K_b(H)+1)(1+K_{OH}(OH))}{(Cu)_{tot}} = (Cu)_{tot}\{\frac{K_xk_{MOH}K_{OH}(OH)}{1+K_{OH}(OH)}\} + k_{OH}K_x(OH) \qquad (35)$$

Plotting the left side of Equation (35) versus $(Cu)_{tot}$, Figure 24, gives a line with a slope of 39.2 and an intercept of 0.075, using the value of K_x. From the intercept k_{OH} was determined to be 139 sec^{-1} M^{-1} and the slope gave a

Figure 24. Plot of Equation (35) with $y = k_{obs}K_x + \frac{k_{obs}(K_b(H)+1)(1+K_{OH}(OH))}{(Cu)_{tot}}$ and $x = (Cu)_{tot}$


1.0
y
0.5
0.0
0
0.004
0.008
0.012
0.016
0.020
x

value for k_{MOH} of 0.614 sec^{-1} M^{-1}. The values of k_{OH} and k_{MOH}, and the mechanism, were verified by calculating the pseudo first-order rate constant, k_{obs}, from Equation (34) at pH 8.2 which was found to be 1.26×10^{-3} sec^{-1}, the experimental value being 1.29×10^{-3} sec^{-1}. The average k_{obs}, 1.76×10^{-3} sec^{-1}, k_{MOH} and k_{OH} were used to calculate K_x at pH 8.4 from Equation (34). The calculated value of log K_x is 2.54, the observed is 2.52. A value of log K_x of 2.76 was calculated from the average k_{obs}, 4.37×10^{-4} sec^{-1}, k_{MOH} and k_{OH} at pH 7.7. This value of log K_x is still within the ten percent experimental error of the kinetic data.

The rate of hydrolysis of methyl glycinate in the presence of neutral complexes of copper(II) has been studied by Leach and Angelici (58). The second order rate constants for hydroxide ion attack varied from 2×10^3 M^{-1} sec^{-1} to 3×10^4 M^{-1} sec^{-1}, depending upon the N-substituent of the iminodiacetate ligand. Angelici and Hopgood (65) found the rate constant decreased to 460 M^{-1} sec^{-1} for the tetradentate, negatively charged complex of copper(II) and nitrilotriacetic acid. The decrease was attributed partially to the negative charge of the complex, which would be expected to inhibit the attack of the hydroxide ion. Following this line of reasoning, the positively charged dien complexes should have an attraction for the hydroxide and therefore k_{OH} would be expected to be larger than that for the iminodiacetate complexes of copper(II). In reality the hydrolysis of the ester by hydroxide attack in the presence of the dien complex is only increased one-hundred fold over the rate of ester hydrolysis without any metal ion present, the rate constants being 139 M^{-1} sec^{-1} and 1.32 M^{-1} sec^{-1}, respectively. The reasons for this behavior are not clear.

In the studies of Leach and Angelici (58) and Angelici and Hopgood (65), the donor atoms of the ligands are mainly oxygens. The nitrogen donor ligands here decrease the catalytic ability of copper(II) as compared to that of the oxygen donor ligands. The system requires further study to determine which of these effects, if either, is operating in this system. It would be particularly interesting to study the hydrolysis of the ester in the presence of some of the substituted dien complexes. Preliminary investigations along this line with the complex of 1,1-di Me dien show that the observed rates of hydrolysis are slightly faster at the same pH than for the dien complex, although the value of k_{OH} cannot be determined at this point.

Table 14. Rate constants, k_{OH}, for the hydrolysis of methyl glycinate in the presence of complexes of copper(II) at 25.0° C

Complex	$10^{-4}k_{OH}$, M^{-1} sec^{-1} [a]
Cu IMDA	3.21
Cu(D-PhglyMA)	2.3
Cu(Cy IMDA)	1.97
Cu(Ph IMDA)	1.41
Cu(t-Bu IMDA)	0.838
Cu(Me IMDA)	0.329
Cu(L-Val MA)	0.317
Cu(Fur IMDA)	0.208
$Cu(Ur\ IMDA)^-$	0.056
$Cu(NTA)^-$	0.046[b]
$Cu(dien)^{2+}$	0.014[c]

[a] Values taken from reference (58).

[b] Reference (65).

[c] This work.

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VITA

The author was born in Sewickley, Pennsylvania, on December 11, 1943, to Mr. and Mrs. Joseph J. Williams. She received her elementary and secondary education in the Aliquippa, Pennsylvania, public schools. She attended Juniata College in Huntingdon, Pennsylvania, graduating with a B.S. degree in chemistry in 1965. Her chemistry studies were interrupted during this time by a year of study in the Brethren College program at Phillips-Universitat in Marburg, Germany.

The author attended Bucknell University, Lewisburg, Pennsylvania, graduating with a M.S. degree in chemistry, under the direction of Dr. Charles A. Root, in 1967. She entered the Graduate College at Iowa State University in 1967 and majored in Inorganic Chemistry. Here, she met and married David A. Allison, son of Mr. and Mrs. W. Leroy Allison, Tarentum, Pennsylvania, on June 29, 1968.

After graduation, she will accompany her husband to Uppsala, Sweden, where she will work in the group of Professor K. Siegbahn, with whom her husband has accepted a post-doctoral fellowship.

APPENDIX

The following computer programs were written in the FORTRAN IV language. The computations were executed on the IBM 360/65 system at the Iowa State University Computation Center.

Proton stability constants K_1 and K_2

The constants K_1 and K_2 were calculated with the aid of the general non-linear least squares program originally written by Moore and Zeigler and revised by Birk (66). The iterative least square method of Gauss is used. In this adaptation of the program, the function to be fitted was Equation (7) where the dependent variable is now $\frac{(g-1)}{(g-2)[H]}$ and the independent variable is $\frac{g}{(g-2)[H]^2}$. The parameters are K_1 and K_2. The variables, x and y, were initially entered as zero, and in the YP subroutine, page 146, the appropriate pH values and concentration terms were entered and x and y recalculated. All the points were weighted as unity. The iterations, to a maximum of twenty-five, were continued until a convergence value of 10^{-6} was reached. In most cases, less than ten iterations were necessary to solve the problem.

```
C     GENERAL NONLINEAR LEAST SQUARES ROUTINE
C     MAIN ROUTINE TO CALL SUBROUTINES (MPAKAG)
      DIMENSION Y(50 ),X(5,50 ),W(50 ),IX(40),PG(40),DUM(50),P(40),
     1SP(40),YC(50 ),DY(50 ),BM(40,1),ALAB(18),PART(40),Z(5),AM(40,40),
     2PH(50 ),TURNS(50 )
       COMMON Y,W,IX,PG,DUM,P,SP,YC,DY,BM,ALAB,PART,Z,AM,IM,TEST,X,VOLB,
     1WK,CA,CONBAS,PH,TURNS
C     CLEAR STORAGE OF OLD INFORMATION
    1 IM=0
      IK=0
      IDF=0
      DET=0.0
      M=0
      N=0
      SSQ=0.0
      WVAR=0.0
      VOLB = 0.0
      CONBAS = 0.0
      WK = 0.0
      CA = 0.0
      READ (1,222)N,M
  222 FORMAT(2I3)
      DO 2 I=1,N
      PH(I) =0.0
      TURNS(I) =0.0
      Y(I)=0.0
      W(I)=0.0
      YC(I)=0.0
    2 DY(I)=0.0
      DO 3 I=1,40
      IX(I)=0
      PG(I)=0.0
      P(I)=0.0
    3 SP(I)=0.0
      DO 4 I=1,50
    4 DUM(I)=0.0
      DO 5 I=1,40
```

```
      DO 5 J=1,40
    5 AM(I,J)=0.0
      DO 6 I=1,M
      DO 6 J=1,N
    6 X(I,J)=0.0
      CALL IPAKAG(N,IK,M,NDUM,IPR,IFG)
      IF (N)8,8,7
    7 CALL PPAKAG(N,IK,M,WVAR,SSQ,IDF,DET,NDUM,IPR,IFG,ASUM)
      IF (IM-IK)13,10,13
   13 IF (DET)10,11,10
   10 CALL RPAKAG(N,IK,M,WVAR,SSQ,IDF,ASUM)
      GO TO 1
   11 WRITE (3,12)
   12 FORMAT(55H0PROGRAM QUIT BECAUSE MATRIX WAS SINGULAR            )
      GO TO 1
    8 STOP
      END


      SUBROUTINE IPAKAG(N,IK,M,NDUM,IPR,IFG)
C     IPAKAG READS IN DATA AND CONTROL CARDS
      DIMENSION Y(50 ),X(5,50 ),W(50 ),IX(40),PG(40),DUM(50),P(40),
     1SP(40),YC(50 ),DY(50 ),BM(40,1),ALAB(18),PART(40),Z(5),AM(40,40),
     2PH(50 ),TURNS(50 )
       COMMON Y,W,IX,PG,DUM,P,SP,YC,DY,BM,ALAB,PART,Z,AM,IM,TEST,X,VOLB,
     1WK,CA,CONBAS,PH,TURNS
   10 FORMAT(6E12.7)
   11 FORMAT(24I3)
   12 FORMAT(6F12.0)
   13 FORMAT(18A4)
      READ (1,13)(ALAB(I),I=1,18)
      READ (1,11)N,IK,IW,M,IB,ITEST,IDUM,NDUM,IPR,IFG,IFOR
  131 IF (N)43,43,132
  132 IF (M-1)14,15,15
   14 M=1
   15 READ (1,11)IM
      IF (IM) 400,400,401
```

```
  401 READ (1,11)(IX(I),I=1,IM)                                   0073
  400 IF (IFOR-1)151,151,152                                      0074
  151 READ (1,10)(PG(I),I=1,IK)                                  00075
      GO TO 153                                                  00076
  152 READ (1,12)(PG(I),I=1,IK)                                  00077
  153 IF (IB-1)154,271,271                                       00078
  154 IF (IFOR-1)16,261,261                                      00079
   16 READ (1,10)(Y(I),I=1,N)                                   I00080
      DO 17 J=1,M                                               I00081
   17 READ (1,10)(X(J,I),I=1,N)                                 I00082
      IF (IW)24,24,18                                           I00083
   18 IF (IW-1)26,26,19                                         I00084
   19 IF (IW-2)22,22,20                                         I00085
   20 DO 21 I=1,N                                               I00086
   21 W(I)=1./(Y(I)**2)                                         I00087
      GO TO 34                                                  I00088
   22 DO 23 I=1,N                                               I00089
   23 W(I)=1./Y(I)                                              I00090
      GO TO 34                                                  I00091
   24 DO 25 I=1,N                                               I00092
   25 W(I)=1.                                                   I00093
      GO TO 34                                                  I00094
   26 READ (1,10)(W(I),I=1,N)                                   I00095
      GO TO 34                                                  I00096
  261 READ (1,12)(Y(I),I=1,N)                                     0097
      DO 2611 J=1,M                                               0098
 2611 READ (1,12)(X(J,I),I=1,N)                                   0099
      IF (IW)268,268,262                                         00100
  262 IF (IW-1)270,270,263                                       00101
  263 IF (IW-2)266,266,264                                       00102
  264 DO 265 I=1,N                                               00103
  265 W(I)=1.0/(Y(I)**2)                                         00104
      GO TO 34                                                   00105
  266 DO 267 I=1,N                                               00106
  267 W(I)=1.0/Y(I)                                              00107
      GO TO 34                                                   00108
  268 DO 269 I=1,N                                               00109
```

```
 269 W(I)=1.0                                                           00110
     GO TO 34                                                           00111
 270 READ (1,12)(W(I),I=1,N)                                            00112
     GO TO 34                                                           00113
 271 IF (IFOR-1)27,331,331                                              00114
  27 DO 33 I=1,N                                                       I00115
     IF (IW-1)31,32,28                                                 I00116
  28 IF (IW-2)30,30,29                                                 I00117
  29 READ (1,10)Y(I),(X(J,I),J=1,M)                                    I00118
     W(I)=1./(Y(I)**2)                                                 I00119
     GO TO 33                                                          I00120
  30 READ (1,10)Y(I),(X(J,I),J=1,M)                                    I00121
     W(I)=1./Y(I)                                                      I00122
     GO TO 33                                                          I00123
  31 READ (1,10)Y(I),(X(J,I),J=1,M)                                    I00124
     W(I)=1.0                                                          I00125
     GO TO 33                                                          I00126
  32 READ (1,10)Y(I),(X(J,I),J=1,M),W(I)                               I00127
  33 CONTINUE                                                          I00128
     GO TO 34                                                           00129
 331 DO 337 I=1,N                                                       00130
     IF (IW-1)335,336,332                                               00131
 332 IF (IW-2)334,334,333                                               00132
 333 READ (1,12)Y(I),(X(J,I),J=1,M)                                     00133
     W(I)=1.0/(Y(I)**2)                                                 00134
     GO TO 337                                                          00135
 334 READ (1,12)Y(I),(X(J,I),J=1,M)                                     00136
     W(I)=1.0/Y(I)                                                      00137
     GO TO 337                                                          00138
 335 READ (1,12)Y(I),(X(J,I),J=1,M)                                     00139
     W(I)=1.0                                                           00140
     GO TO 337                                                          00141
 336 READ (1,10)Y(I),(X(J,I),J=1,M),W(I)                                00142
 337 CONTINUE                                                           00143
  34 IF (IDUM-1)36,35,35                                               I00144
  35 READ (1,10)(DUM(I),I=1,NDUM)                                      I00145
  36 IF (ITEST-1)37,38,38                                              I00146
```

```
   37 TEST=0.000001                                                       L00147
      GO TO 39                                                            L00148
   38 READ (1,10)TEST                                                     L00149
   39 READ (1,40)VOLB,WK,CONBAS                                             0150
   40 FORMAT (E10.2,E10.3,E10.3)                                            0151
      READ (1,41)(PH(I),I=1,N)                                              0152
   41  FORMAT (6F12.2)                                                      0153
      READ (1,42)(TURNS(I),I=1,N)                                           0154
   42  FORMAT (6F12.0)                                                      0155
   43 RETURN                                                                0156
      END                                                                 L00157


      SUBROUTINE PPAKAG(N,IK,M,WVAR,SSQ,IDF,DET,NDUM,IPR,IFG,ASUM)          0158
C     PPAKAG PERFORMS THE LEAST SQUARES COMPUTATIONS                      P00159
      DIMENSION Y(50 ),X(5,50 ),W(50 ),IX(40),PG(40),DUM(50),P(40),         0160
     1SP(40),YC(50 ),DY(50 ),BM(40,1),AM(40,40),DP(40),PC(40),AN(40),ALA    0161
     2B(18),PART(40),Z(5),INDEX1(40),INDEX2(40),IPIVOT(40),PH(50 ),TURNS    0162
     3(50 )                                                                 0163
       COMMON Y,W,IX,PG,DUM,P,SP,YC,DY,BM,ALAB,PART,Z,AM,IM,TEST,X,VOLB,    0164
     1WK,CA,CONBAS,PH,TURNS                                                 0165
    1 FORMAT(///115H   K                                        A(K,L)    P00166
     1                                                           B(K)///) P00167
    2 FORMAT(I5,1P5E17.7/(1PE21.7,1P4E17.7))                              P00168
    3 FORMAT(1H+1P1E119.7//)                                              P00169
    4 FORMAT(24HOVALUE OF DETERMINANT = 1P1E14.7///)                      P00170
    5 FORMAT(56H   K                                   INVERSE OF A(K,L)  P00171
     1//)                                                                 P00172
    6 FORMAT(1H0)                                                         P00173
    8 FORMAT(///I6,  11H ITERATIONS)                                        0174
      CALL IONICS(ASUM)                                                     0175
      ITS=0                                                               P00176
      IHSP=0                                                              P00177
      M25C=0                                                              P00178
      CALL SLITE (0)                                                      P00179
      VAR=0.0                                                             P00180
      SS=0.0                                                              P00181
```

```
      LIES=0                                                            P00182
    9 DO 10 I=1,IK                                                      P00183
      DP(I)=0.0                                                         P00184
      PC(I)=PG(I)                                                       P00185
      BM(I,1)=0.0                                                       P00186
      SP(I)=0.0                                                         P00187
   10 P(I)=PG(I)                                                        P00188
      LIE=0                                                             P00189
      IF (IPR)18,18,11                                                  P00190
   11 WRITE (3,12)(ALAB(J1),J1=1,18)                                    P00191
   12 FORMAT(18A4)                                                      P00192
      WRITE (3,13)NDUM                                                  P00193
   13 FORMAT(//10H THERE ARE I4, 38H ENTRIES FOR THE VARIABLE CALLED -DU P00194
     1M-)                                                               P00195
      IF (NDUM)16,16,14                                                 P00196
   14 WRITE (3,15)(I,DUM(I),I=1,NDUM)                                   P00197
   15 FORMAT(1H0,4(8H    DUM(I3, 3H) =1PE14.7))                         P00198
   16 WRITE (3,17)TEST                                                  P00199
   17 FORMAT(//8H TEST = 1PE15.7///)                                    P00200
   18 LICK=0                                                            P00201
      K=IK-IM                                                           P00202
   19 IT=0                                                              P00203
      KP=K+1                                                            P00204
      IF (K)115,20,21                                                   P00205
   20 LIES=1                                                            P00206
      GO TO 27                                                          P00207
   21 DO 22 I=1,K                                                       P00208
      BM(I,1)=0.0                                                       P00209
      DO 22 J=1,K                                                       P00210
   22 AM(I,J)=0.0                                                       P00211
      H=1.0                                                             P00212
      IT=IT+1                                                           P00213
   27 DO 44 L=1,N                                                       P00214
      DO 28 J=1,M                                                       P00215
   28 Z(J)=X(J,L)                                                       P00216
   29 CALL YP(YT,L,N,M,IK,ASUM)                                           0217
   30 IF (LIES)31,31,37                                                 P00218
```

```
31 JACK=0                                        P00219
   DO 36 JUK=1,IK                                P00220
   IF (IM)115,34,32                              P00221
32 DO 33 JOKE=1,IM                               P00222
   IF (JUK-IX(JOKE))33,35,33                     P00223
33 CONTINUE                                      P00224
34 JAKE=JUK-JACK                                 P00225
   AN(JAKE)=PART(JUK)                            P00226
   GO TO 36                                      P00227
35 JACK=JACK+1                                   P00228
36 CONTINUE                                      P00229
37 YC(L)=YT                                      P00230
   DY(L)=Y(L)-YC(L)                              P00231
   IF (LIES)39,39,38                             P00232
38 VAR=VAR+W(L)*DY(L)**2                         P00233
   SS=SS+DY(L)**2                                P00234
   GO TO 44                                      P00235
39 IF (K)115,44,40                               P00236
40 DO 43 I=1,K                                   P00237
   DO 43 J=I,KP                                  P00238
   IF (J-KP)41,42,42                             P00239
41 AM(I,J)=AM(I,J)+AN(I)*AN(J)*W(L)              P00240
   GO TO 43                                      P00241
42 BM(I,1)=BM(I,1)+AN(I)*DY(L)*W(L)              P00242
43 CONTINUE                                      P00243
44 CONTINUE                                      P00244
   V=0.0                                         P00245
   DO 45 L=1,N                                   P00246
45 V=V+W(L)*DY(L)**2                             P00247
   IF (LIES)46,46,101                            P00248
46 IF (K-1)49,49,47                              P00249
47 DO 48 J=2,K                                   P00250
   JIG=J-1                                       P00251
   DO 48 I=1,JIG                                 P00252
48 AM(J,I)=AM(I,J)                               P00253
49 IF (K)115,51,50                               P00254
50 CALL SLITET (1,LCP$$$)                        P00255
```

```
      GO TO (51,55      ),LCP$$$                                    0256
   51 CALL SLITE (1)                                              P00257
      WRITE (3,12)(ALAB(J1),J1=1,18)                              P00258
      IF (K)115,100,52                                            P00259
   52 IF (IPR)55,55,53                                            P00260
   53 WRITE (3,1)                                                 P00261
      DO 54 I=1,K                                                 P00262
      WRITE (3,2)I,(AM(I,J),J=1,K)                                P00263
   54 WRITE (3,3)BM(I,1)                                          P00264
   55 IF (LIE)115,56,57                                           P00265
   56 KT=1                                                        P00266
      GO TO 58                                                    P00267
   57 KT=KP                                                       P00268
   58 IF (K)115,100,60                                            P00269
   60 CALL MATINV(AM,K,BM,40,1,DET,INDEX1,INDEX2,IPIVOT,PIVOT)    P00270
      IF (DET)61,115,61                                           P00271
   61 CALL SLITET (1,LCP$$$)                                      P00272
      GO TO (62,63      ),LCP$$$                                    0273
   62 WRITE (3,4)DET                                              P00274
      CALL SLITE (1)                                              P00275
   63 JUK=0                                                       P00276
      DO 77 I=1,IK                                                P00277
   64 IF (IM)115,67,65                                            P00278
   65 DO 66 JOKE=1,IM                                             P00279
      IF (I-IX(JOKE))66,76,66                                     P00280
   66 CONTINUE                                                    P00281
   67 JAKE=I-JUK                                                  P00282
      IF (IFG-1)68,78,69                                          P00283
   68 IF (IT-5)69,69,78                                           P00284
   69 DP(I)=BM(JAKE,1)                                            P00285
   70 PC(I)=P(I)+H*DP(I)                                          P00286
      CALL SLITET (1,LCP$$$)                                      P00287
      GO TO (73,71      ),LCP$$$                                    0288
   71 IF (IFG-1)72,77,74                                          P00289
   72 IF (IT-5)74,74,77                                           P00290
   73 CALL SLITE (1)                                              P00291
      GO TO 77                                                    P00292
```

```
74 IF (P(I)*PC(I))75,77,77                                      P00293
75 H=H/2.0                                                      P00294
   IF (H-1.0E-10)82,70,70                                       P00295
76 JUK=JUK+1                                                    P00296
   GO TO 77                                                     P00297
78 IF (IT-25)69,69,79                                           P00298
79 ITS=IT                                                       P00299
80 IF (ABS(DP(I))-ABS(BM(JAKE,1)))81,81,69                      P00300
81 H=H/2.0                                                      P00301
   IF (H-1.0E-10)82,69,69                                       P00302
82 IHSP=1                                                       P00303
   GO TO 115                                                    P00304
77 CONTINUE                                                     P00305
83 CALL SLITET (1,LCP$$$)                                       P00306
   GO TO (92,84      ),LCP$$$                                     0307
84 IF (IPR)88,88,85                                             P00308
85 WRITE (3,86)IT,H,V                                           P00309
86 FORMAT(1HOI3,1P2E17.7)                                       P00310
   DO 87 I=1,IK                                                 P00311
87 WRITE (3,2)I,PG(I),P(I),PC(I),DP(I)                          P00312
88 JERK=0                                                       P00313
   DO 91 I=1,IK                                                 P00314
   IF (P(I))89,90,89                                            P00315
89 IF (ABS((PC(I)-P(I))/P(I))-TEST)91,91,93                     P00316
90 JERK=JERK+1                                                  P00317
91 CONTINUE                                                     P00318
   IF (JERK-IK)92,93,93                                         P00319
92 CALL SLITE (1)                                               P00320
   LIE=1                                                        P00321
   M25C=1                                                       P00322
93 DO 94 I=1,IK                                                 P00323
94 P(I)=PC(I)                                                   P00324
   IF (LICK)115,95,100                                          P00325
95 CALL SLITET (1,LCP$$$)                                       P00326
   GO TO (96,97      ),LCP$$$                                     0327
96 CALL SLITE (1)                                               P00328
   LICK=1                                                       P00329
```

```
   97 IF (M25C)98,98,21                                                 P00330
   98 IF (IT-25)21,99,21                                                P00331
   99 CALL SLITE (1)                                                    P00332
      IT=0                                                              P00333
      ITS=26                                                            P00334
      GO TO 92                                                          P00335
  100 VAR=0.0                                                           P00336
      SS=0.0                                                            P00337
      LIES=1                                                            P00338
      GO TO 27                                                          P00339
  101 DF=N-K                                                            P00340
      IDF=N-K                                                           P00341
      IF (K)115,108,102                                                 P00342
  102 IF (IPR)105,105,103                                               P00343
  103 WRITE (3,5)                                                       P00344
      DO 104 I=1,K                                                      P00345
      WRITE (3,2)I,(AM(I,J),J=1,K)                                      P00346
  104 WRITE (3,6)                                                       P00347
  105 IF (ITS)106,107,106                                               P00348
  106 IT=ITS                                                            P00349
  107 WRITE (3,8)IT                                                     P00350
  108 WVAR=VAR/DF                                                       P00351
      SSQ=SS                                                            P00352
      JACK=0                                                            P00353
      DO 114 I=1,IK                                                     P00354
      IF (IM)115,111,109                                                P00355
  109 DO 110 J=1,IM                                                     P00356
      IF (I-IX(J))110,113,110                                           P00357
  110 CONTINUE                                                          P00358
  111 JAKE=I-JACK                                                       P00359
  112 SP(I)=SQRT(AM(JAKE,JAKE)*WVAR)                                    P00360
      GO TO 114                                                         P00361
  113 JACK=JACK+1                                                       P00362
  114 CONTINUE                                                          P00363
  115 CALL SLITE (0)                                                    P00364
      IF (IHSP)116,118,116                                              P00365
  116 WRITE (3,117)                                                     P00366
```

```
  117 FORMAT(75H0THE PROGRAM QUIT ITERATING SINCE THE PARAMETER(S) INSIS  P00367
     1T ON CHANGING SIGNS)                                                P00368
  118 RETURN                                                              P00369
      END                                                                 P00370


      SUBROUTINE RPAKAG(N,IK,M,WVAR,SSQ,IDF,ASUM)                           0371
C     RPAKAG PROVIDES RECORD OF DATA AND RESULTS                          R00372
      DIMENSION Y(50 ),X(5,50 ),W(50 ),IX(40),PG(40),DUM(50),P(40),         0373
     1SP(40),YC(50 ),DY(50 ),BM(40,1),ALAB(18),PART(40),Z(5),RP(40),        0374
     2AN(40),AM(40,40),PH(50 ),TURNS(50 )                                   0375
       COMMON Y,W,IX,PG,DUM,P,SP,YC,DY,BM,ALAB,PART,Z,AM,IM,TEST,X,VOLB,    0376
     1WK,CA,CONBAS,PH,TURNS                                                 0377
      WRITE (3,1)(ALAB(J1),J1=1,18)                                       R00378
    1 FORMAT(18A4)                                                        R00379
      ITCHY=0                                                             R00380
      DO 2 I=1,IK                                                         R00381
      IF (IX(I)-I)3,2,3                                                   R00382
    2 CONTINUE                                                            R00383
      ITCHY=1                                                             R00384
    3 I=-1                                                                R00385
      CALL YP(YT,I,N,M,IK,ASUM)                                             0386
    4 IF (IM)5,5,6                                                        R00387
    5 IM=0                                                                R00388
    6 WRITE (3,7)N,M,IK,IM,WVAR,SSQ                                       R00389
    7 FORMAT(////23H THIS PROBLEM CONTAINS I3,14H DATA POINTS, I2,        R00390
     130H INDEPENDENT VARIABLE(S), AND I2,15H PARAMETER(S) (I2,           R00391
     224H OF THEM HELD CONSTANT).//                                       R00392
     326H THE WEIGHTED VARIANCE IS 1PE14.7,                               R00393
     456H AND THE UNWEIGHTED SUM OF SQUARES OF THE DEVIATIONS IS 1PE14.7  R00394
     5,1H./////)                                                          R00395
      WRITE (3,25)                                                        R00396
      JACK=0                                                              R00397
      DO 23 I=1,IK                                                        R00398
      IF (IM)10,10,8                                                      R00399
    8 DO 9 J=1,IM                                                         R00400
      IF (I-IX(J))9,12,9                                                  R00401
```

```
  9 CONTINUE                                                            R00402
 10 JAKE=I-JACK                                                         R00403
    J=JAKE+1                                                            R00404
 11 CONTINUE                                                            R00405
    GO TO 13                                                            R00406
 12 JACK=JACK+1                                                         R00407
 13 WRITE (3,24)I,PG(I),P(I),SP(I)                                      R00408
    IF (ITCHY)14,14,17                                                  R00409
 14 IF (IM)17,17,15                                                     R00410
 15 DO 16 J=1,IM                                                        R00411
    IF (I-IX(J))16,22,16                                                R00412
 16 CONTINUE                                                            R00413
 17 A=0.0                                                               R00414
    B=0.0                                                               R00415
    DO 20 JOE=1,N                                                       R00416
    DO 18 JUMP=1,M                                                      R00417
 18 Z(JUMP)=X(JUMP,JOE)                                                 R00418
 19  CALL YP(YT,JOE,N,M,IK,ASUM)                                          0419
    A=A+W(JOE)*YC(JOE)*PART(I)                                          R00420
 20 B=B+W(JOE)*Y(JOE)*PART(I)                                           R00421
    WRITE (3,21)A,B                                                     R00422
 21 FORMAT(1H+1PE102.7,1PE17.7)                                         R00423
    IF (ITCHY)23,23,22                                                  R00424
 22 WRITE (3,26)                                                        R00425
 23 CONTINUE                                                            R00426
 24 FORMAT(I4,1P5E17.7/(1PE21.7,1P4E17.7))                              R00427
 25 FORMAT(118H       GUESSTIMATE OF   FINAL VALUE OF      S.D.  OF     R00428
  1                                   EXACT LEAST SQUARES EQUATIONS/    R00429
  2118H    K   K-TH PARAMETER   K-TH PARAMETER   K-TH PARAMETER         R00430
  3                            FITTED FUNCTION    INPUT DATA//)         R00431
 26 FORMAT(90H+                                                       T R00432
  1HIS PARAMETER WAS HELD FIXED.       )                                R00433
    WRITE (3,27)                                                        R00434
 27 FORMAT(/////47H MATRIX OF CORRELATIONS BETWEEN FREE PARAMETERS/)    R00435
    K=IK-IM                                                             R00436
    IF (K)50,301,271                                                    R00437
271 DO 29 I=1,K                                                         R00438
```

```
      DO 28 J=1,K                                                       R00439
   28 RP(J)=AM(I,J)/SQRT(AM(I,I)*AM(J,J))                               R00440
   29 WRITE (3,30)I,(RP(J),J=1,K)                                       R00441
   30 FORMAT(1H0,I4,14F8.3/(F12.3,13F8.3))                              R00442
  301 WRITE (3,1)(ALAB(J1),J1=1,18)                                     R00443
      WRITE (3,31)                                                      R00444
   31 FORMAT(119H0                           INDEPENDENT       DEPENDEN  R00445
     1T       CALCULATED                                PCT. DEV. OF/     0446
     2120H     I       WEIGHT          VARIABLE              VARIABLE   R00447
     3  FUNCTION        DEVIATION                CALC. FUNCTION)          0448
      DO 49 I=1,N                                                       R00449
      DO 32 J=1,M                                                       R00450
   32 Z(J)=X(J,I)                                                       R00451
      CALL YP(YT,I,N,M,IK,ASUM)                                           0452
      A=0.0                                                             R00453
      JACK=0                                                            R00454
      DO 37 JUK=1,IK                                                    R00455
      IF (IM)35,35,33                                                   R00456
   33 DO 34 JOKE=1,IM                                                   R00457
      IF (JUK-IX(JOKE))34,36,34                                         R00458
   34 CONTINUE                                                          R00459
   35 JAKE=JUK-JACK                                                     R00460
      AN(JAKE)=PART(JUK)                                                R00461
      GO TO 37                                                          R00462
   36 JACK=JACK+1                                                       R00463
   37 CONTINUE                                                          R00464
      K=IK-IM                                                             0465
      IF (K)50,371,371                                                    0466
  371 DO 38 J=1,K                                                         0467
      DO 38 JJ=1,K                                                      R00468
   38 A=A+AN(J)*AN(JJ)*AM(J,JJ)                                         R00469
      A=100*DY(I)/Y(I)                                                    0470
      IF (A)51,52,52                                                      0471
   51 A=-A                                                                0472
   52 J=1                                                                 0473
      IF (M-2)39,41,41                                                  R00474
   39 WRITE (3,40)I,W(I),X(1,I),Y(I),YC(I),DY(I),A                      R00475
```

```
   40 FORMAT(1HOI5,1PE17.7,1PE18.7,1P3E17.7,1PE27.7)                     R00476
      GO TO 46                                                          R00477
   41 WRITE (3,42)I,W(I),J,X(1,I),Y(I),YC(I),DY(I),A                    R00478
   42 FORMAT(1HOI5,1PE17.7,I3,1PE15.7,1P3E17.7,1PE27.7)                  R00479
   43 DO 44 J=2,M                                                       R00480
   44 WRITE (3,45)J,X(J,I)                                              R00481
   45 FORMAT(I26,1PE15.7)                                               R00482
   46 IF (ITCHY)49,49,47                                                R00483
   47 WRITE (3,48)(PART(J),J=1,IK)                                      R00484
   48 FORMAT(9H PARTIALS 1PE14.7,1P4E17.7/(1PE23.7,1P4E17.7))            R00485
   49 CONTINUE                                                          R00486
   50 RETURN                                                            R00487
      END                                                               R00488


      SUBROUTINE MATINV (A,N,B,NMAX,M,DET,INDEX1,INDEX2,IPIVOT,PIVOT)  MATV0489
      DIMENSION INDEX1(1),INDEX2(1),IPIVOT(1),A(1),B(1)                MATV0490
      EQUIVALENCE (IROW,JROW),(ICOLUM,JCOLUM),(AMAX,T,SWAP),(NL1,NROW) MATV0491
C                                                                      MATV0492
C     INITIALIZATION                                                   MATV0493
C                                                                      MATV0494
   10 DET=1.0                                                          MATV0495
   15 DO 20 J=1,N                                                      MATV0496
   20 IPIVOT(J)=0                                                      MATV0497
   30 DO 550 I=1,N                                                     MATV0498
C                                                                      MATV0499
C     SEARCH FOR PIVOT ELEMENT                                         MATV0500
C                                                                      MATV0501
   40 AMAX=0.0                                                         MATV0502
   45 DO 105 J=1,N                                                     MATV0503
   50 IF (IPIVOT(J)-1) 60,105,60                                       MATV0504
   60 DO 100 K=1,N                                                     MATV0505
   70 IF (IPIVOT(K)-1) 71,100,740                                      MATV0506
   71 LL=(K-1)*NMAX+J                                                  MATV0507
   80 IF (ABS(AMAX)-ABS(A(LL))) 85,100,100                             MATV0508
   85 IROW=J                                                           MATV0509
   90 ICOLUM=K                                                         MATV0510
```

```
   95 AMAX=A (LL)                                                      MATV0511
  100 CONTINUE                                                         MATV0512
  105 CONTINUE                                                         MATV0513
      IF (AMAX) 110,111,110                                            MATV0514
  111 DET=0.0                                                          MATV0515
      GO TO 740                                                        MATV0516
  110 IPIVOT(ICOLUM)=IPIVOT(ICOLUM)+1                                  MATV0517
C                                                                      MATV0518
C     INTERCHANGE ROWS TO PUT ELEMENT ON DIAGONAL                      MATV0519
C                                                                      MATV0520
  130 IF (IROW-ICOLUM) 140,260,140                                     MATV0521
  140 DET=-DET                                                         MATV0522
  150 DO 200 L=1,N                                                     MATV0523
  151 JCON=(L-1)*NMAX                                                  MATV0524
  152 NROW=JCON+IROW                                                   MATV0525
  153 NCOL=JCON+ICOLUM                                                 MATV0526
  160 SWAP=A(NROW)                                                     MATV0527
  170 A(NROW)=A(NCOL)                                                  MATV0528
  200 A(NCOL)=SWAP                                                     MATV0529
  205 IF (M) 260,260,210                                               MATV0530
  210 DO 250 L=1,M                                                     MATV0531
  211 JCON=(L-1)*NMAX                                                  MATV0532
  212 NROW=JCON+IROW                                                   MATV0533
  213 NCOL=JCON+ICOLUM                                                 MATV0534
  220 SWAP=B(NROW)                                                     MATV0535
  230 B(NROW)=B(NCOL)                                                  MATV0536
  250 B(NCOL)=SWAP                                                     MATV0537
  260 INDEX1(I)=IROW                                                   MATV0538
  270 INDEX2(I)=ICOLUM                                                 MATV0539
  271 LL=(ICOLUM-1)*NMAX+ICOLUM                                        MATV0540
  310 PIVOT=A(LL)                                                      MATV0541
  320 DET=DET*PIVOT                                                    MATV0542
C                                                                      MATV0543
C     DIVIDE PIVOT ROW BY PIVOT ELEMENT                                MATV0544
C                                                                      MATV0545
  330 A(LL)=1.0                                                        MATV0546
  340 DO 350 L=1,N                                                     MATV0547
```

```
  341 NCOL=(L-1)*NMAX+ICOLUM                                            MATV0548
  350 A(NCOL)=A(NCOL)/PIVOT                                             MATV0549
  355 IF(M) 371,371,360                                                 MATV0550
  360 DO 370 L=1,M                                                      MATV0551
  361 NCOL=(L-1)*NMAX+ICOLUM                                            MATV0552
  370 B(NCOL)=B(NCOL)/PIVOT                                             MATV0553
C                                                                       MATV0554
C     REDUCE NON-PIVOT ROWS                                             MATV0555
C                                                                       MATV0556
  371 JCON=(ICOLUM-1)*NMAX                                              MATV0557
  380 DO 550 L1=1,N                                                     MATV0558
  390 IF (L1-ICOLUM) 391,550,391                                        MATV0559
  391 LL=JCON+L1                                                        MATV0560
  400 T=A(LL)                                                           MATV0561
  420 A(LL)=0.0                                                         MATV0562
  430 DO 450 L=1,N                                                      MATV0563
  431 NCON=(L-1)*NMAX                                                   MATV0564
  432 NL1=NCON+L1                                                       MATV0565
  433 NCOL=NCON+ICOLUM                                                  MATV0566
  450 A(NL1)=A(NL1)-A(NCOL)*T                                           MATV0567
  455 IF (M) 550,550,460                                                MATV0568
  460 DO 500 L=1,M                                                      MATV0569
  461 NCON=(L-1)*NMAX                                                   MATV0570
  462 NL1=NCON+L1                                                       MATV0571
  463 NCOL=NCON+ICOLUM                                                  MATV0572
  500 B(NL1)=B(NL1)-B(NCOL)*T                                           MATV0573
  550 CONTINUE                                                          MATV0574
C                                                                       MATV0575
C     INTERCHANGE COLUMNS                                               MATV0576
C                                                                       MATV0577
  600 DO 710 I=1,N                                                      MATV0578
  610 L=N+1-I                                                           MATV0579
  620 IF (INDEX1(L)-INDEX2(L)) 630,710,630                              MATV0580
  630 JROW=INDEX1(L)                                                    MATV0581
  640 JCOLUM=INDEX2(L)                                                  MATV0582
  641 JCON=(JROW-1)*NMAX                                                MATV0583
  642 NCON=(JCOLUM-1)*NMAX                                              MATV0584
```

```
650 DO 705 K=1,N                                                       MATV0585
651 NROW=JCON+K                                                        MATV0586
652 NCOL=NCON+K                                                        MATV0587
660 SWAP=A(NROW)                                                       MATV0588
670 A(NROW)=A(NCOL)                                                    MATV0589
700 A(NCOL)=SWAP                                                       MATV0590
705 CONTINUE                                                           MATV0591
710 CONTINUE                                                           MATV0592
740 RETURN                                                             MATV0593
    END                                                                    0594


     SUBROUTINE YP(YT,L,N,M,IK,ASUM)                                       0595
    DIMENSION Y(50 ),X(5,50 ),W(50 ),IX(40),PG(40),DUM(50),P(40),          0596
   1SP(40),YC(50 ),DY(50 ),BM(40,1),ALAB(18),PART(40),Z(5),AM(40,40),      0597
   2PH(50 ),TURNS(50 )                                                     0598
     COMMON Y,W,IX,PG,DUM,P,SP,YC,DY,BM,ALAB,PART,Z,AM,IM,TEST,X,VOLB,     0599
   1WK,CA,CONBAS,PH,TURNS                                                  0600
C    YP SUBROUTINE FOR K1, K2 OF DIEN SYSTEMS                              0601
C   Y=(G-1)/((G-2)*PROT AND Y = -P(2) - (G/(G-2)*PROT**2)/P(1)             0602
    PROTL = -PH(L)
    PROT = 10.**PROTL                                                      0605
    VOLCOR = (TURNS(L)/50.0)*VOLB                                          0606
    CDIEN = (CA*2.0)/(10.0+VOLCOR)                                         0607
    AVBAS = (VOLCOR*CONBAS)/(CA*2.0)                                       0608
    G = 3.0 -AVBAS + (WK   /PROT - PROT)/CDIEN                             0609
    Y(L) = (G-1.0)/((G-2.0)*PROT)                                          0610
    Z(1) = G/((G-2.0)*PROT**2)                                             0611
    X(1,L) = Z(1)                                                          0612
    YT = -P(2) - (Z(1))/P(1)                                               0613
    PART(1) = Z(1)/P(1)**2                                                 0614
    PART(2) = -1.0                                                         0615
    RETURN                                                                 0616
    END                                                                    0617


     SUBROUTINE IONICS(ASUM)                                               0618
```

```
      DIMENSION Y(50 ),X(5,50 ),W(50 ),IX(40),PG(40),DUM(50),P(40),
     1SP(40),YC(50 ),DY(50 ),BM(40,1),ALAB(18),PART(40),Z(5),AM(40,40),
     2PH(50 ),TURNS(50 )
      COMMON Y,W,IX,PG,DUM,P,SP,YC,DY,BM,ALAB,PART,Z,AM,IM,TEST,X,VOLB,
     1WK,CA,CONBAS,PH,TURNS
C     SUBROUTINE IONICS CALCULATES MEAN IONIC STRENGTH
      SUM1 = 0.0
      SUM2 = 0.0
      DO 1 J =1,4,1
       READ (1,2)A,V,C,ZCHGI
    2 FORMAT (F3.0,F4.1,E9.2,F3.0)
      SION = (A*(V*C/10.0)*ZCHGI**2)/2.0
      SUM1 = SUM1 + SION
    1 CONTINUE
      READ (1,4)TURNF,CA
    4  FORMAT (F6.0,E10.3)
      VOLCO1 = (TURNF/50.0)*VOLB
      DO 3  K = 1,4,1
      READ (1,5)B,D,YCHGI,V2
    5  FORMAT(F3.0,E9.2,F3.0,F4.1)
      IF (K-4) 7,6,7
    6 S2ION= (CONBAS*VOLCO1)/(VOLCO1+10.0)*B*YCHGI  /2.0
      GO TO 8
    7 S2ION = (B*((V2*D)/(VOLCO1+10.0))*YCHGI**2)/2.0
    8  SUM2 = SUM2+S2ION
    3  CONTINUE
      ASUM = (SUM1+SUM2)/2.0
      WRITE (3,9) ASUM, SUM1, SUM2
    9 FORMAT (1H0,10HAVG MU =  E12.3,2X,8HMU 1 =  E12.3,2X,8HMU 2 =  E1
     12.3)
      RETURN
      END
```

Proton stability constant K_3

The constant K_3 was calculated from Equation (6) by the following program. The variables are initialized first and then the average ionic strength calculated. The program then reads the data, pH, TURNS or volume increments, and CA, initial acid concentration. Volume corrections are made at each point before the stability constant, EQK3, is calculated. The logarithm of EQK3 is taken at each point, and a standard deviation is computed. The program prints the average ionic strength, EQK3, the log and average value of the log of EQK3, the deviations, and the standard deviation.

```
      DIMENSION PH(25),TURNS(25),EQK3(25),X(25),R(25) ,ANAME(18)
       COMMON VOLB,CONBAS,WK,CA, PH,TURNS,EQK3,X,R,ANAME
      READ (1,17)ITER
   17 FORMAT (I5)
C      CALCULATION OF K3 FOR DIEN SYSTEMS
   18 VOLB =0.0
      CONBAS =0.0
      CA = 0.0
      WK = 0.0
      SUM1=0.0
      SUM2=0.0
      DO 21 I=1,25
      PH(I)=0.0
      TURNS(I)=0.0
       EQK3(I)=0.0
      X(I)=0.0
   21 R(I)=0.0
      DO 20 I=1,18
   20 ANAME(I) = 0.0
      READ (1,25)(ANAME(I),I=1,18)
   25 FORMAT (18A4)
C     CALCULATION OF MEAN IONIC STRENGTH
      DO 1 J=1,4,1
      READ (1,2)A,V,C,ZCHGI
    2 FORMAT (F3.0,F4.1,E9.2,F3.0)
      SION = (A*(V*C/10.0)*ZCHGI**2)/2.0
      SUM1 = SUM1 + SION
    1 CONTINUE
      READ (1,4)TURNF,CA,VOLB,CONBAS,WK,L
    4 FORMAT (F6.0,4E10.3,I5)
      VOLCO1 = (TURNF/50.0)*VOLB
      DO 3 K=1,4,1
      READ (1,5)B,D,YCHGI,V2
    5 FORMAT (F3.0,E9.2,F3.0,F4.1)
      IF (K-4)7,6,7
    6 S2ION= (CONBAS*VOLCO1)/(VOLCO1+10.0)*B*YCHGI  /2.0
      GO TO 8
```

```
    7 S2ION =(B*((V2*D)/(VOLCO1+10.0))*YCHGI**2)/2.0
    8 SUM2 = SUM2+S2ION
    3 CONTINUE
      ASUM = (SUM1+SUM2)/2.0
      WRITE (3,25)(ANAME(I),I=1,18)
      WRITE (3,9)ASUM,SUM1,SUM2
    9 FORMAT (1H0,7HAVG MU E12.3,2X,5HMU 1 E12.3,2X,5HMU 2 E12.3)
C       CALCULATION OF K3 AND STANDARD DEVIATION
      READ (1,10)(PH(N),N=1,L)
   10 FORMAT (6F12.2)
      READ (1,11)(TURNS(N),N=1,L)
   11 FORMAT (6F12.0)
      DO 12 N=1,L
      PROTL = -PH(N)
      PROT = 10.**PROTL
      VOLCOR = (TURNS(N)/50.0)*VOLB
      CDIEN = CA/(10.0 + VOLCOR)
   50 AVBAS = (VOLCOR*CONBAS)/CA
      G = 3.0 -AVBAS + (WK   /PROT - PROT)/CDIEN
       EQK3(N) = - ((G-2.0)/(G-3.0))/PROT
   12 CONTINUE
       SUMX=0.0
      DO 13 N=1,L
      X(N)=ALOG10(EQK3(N))
      SUMX = X(N)+SUMX
   13 CONTINUE
      T=L
       S=0.0
      SUMLOG =SUMX/T
      DO 14 N=1,L
      R(N)=X(N)-SUMLOG
      S=R(N)**2+S
   14 CONTINUE
      SIGMA =SQRT(S/(T-1.0))
       WRITE (3,15)(EQK3(J),X(J),R(J),J=1,L)
   15 FORMAT (1H0,11HEQ CONST K3,5X,13HLOG EQ CONST ,5X,12HDEV FROM AVG,
     1/(2X,E11.5,7X,F8.5,11X,F10.6)/)
```

```
    WRITE (3,16)SUMLOG,SIGMA
 16 FORMAT (1H0,13HAVG LOG K3 = F8.5,4X,10HSTD DEV = F10.6)
    ITER =ITER-1
     IF (ITER)19,19,18
 19 STOP
    END
```

Diethylenetriamine and hydroxo complex stability constants

The stability constants of the dien complexes were calculated from Equation (10) by the following program. The variables were initialized and the average ionic strength calculated. The pH, volume increments and initial concentrations were then read in. Volume corrections were made at each point. The logarithm of the formation constant, CPLXK, was determined for each point and the standard deviation computed which are then printed. On page 156, the part of the program dealing with the calculation of the hydroxo complex stability constants begins. The computations are based on Equations (11) and (6). The results are treated in the manner above.

```
      DIMENSION PH(25),TURNS(25),ANAME(18),EKONST(25),CPLXK(25),
     1XEKONK(25),XCPXK(25),REKONK(25),RCPXK(25),PHO(25),TURNSO(25),
     2DISSK(25),EXPDK(25),STABK(25),EXPSK(25),RLDK(25),RLSK(25)
      DIMENSION GKOH(25),DISSKG(25),EXDKG(25),STABKG(25),EXSKG(25),
     1RLDKG(25),RLSKG(25)
      COMMON PH,TURNS,ANAME,EKONST,CPLXK,XEKONK,XCPXK,REKONK,RCPXK,VOLB,
     1CONBAS,CA,WK,CCU,EK1,EK2,EK3
      READ (1,17)ITER
   17 FORMAT (I5)
   18 VOLB =0.0
      CONBAS =0.0
      CA = 0.0
      WK = 0.0
      SUM1=0.0
      SUM2=0.0
      EK1 = 0.0
      EK2 = 0.0
      EK3 = 0.0
      CCU = 0.0
      SUMDK=0.0
      SUMSK=0.0
      RDK =0.0
      RSK=0.0
      RSKG = 0.0
      RDKG = 0.0
       SUMLSG = 0.0
      SUMLDG = 0.0
       SUMSKG = 0.0
      SUMDKG = 0.0
      DO 20 I=1,18
   20 ANAME(I) = 0.0
      DO 21 I=1,25
      PH(I)=0.0
      TURNS(I)=0.0
      EKONST(I) = 0.0
       CPLXK(I) = 0.0
      XEKONK (I) = 0.0
```

```
      XCPXK(I) = 0.0
      REKONK(I) =0.0
      PHO(I)=0.0
      TURNSO(I)=0.0
      DISSK(I)=0.0
      EXPDK(I)=0.0
      STABK(I)=0.0
      EXPSK(I)=0.0
      RLDK(I)=0.0
      RLSK(I)=0.0
      RLSKG(I) = 0.0
      RLDKG(I) =0.0
      EXSKG(I) = 0.0
      STABKG(I) = 0.0
      EXDKG(I) = 0.0
      DISSKG(I) = 0.0
       GKOH(I) = 0.0
   21 RCPXK(I) =0.0
      READ(1,25)(ANAME(I),I=1,18)
   25 FORMAT(18A4)
C     CALCULATION OF MEAN IONIC STRENGTH
      DO 1 J=1,6,1
      READ (1,2)A,V,C,ZCHGI
    2 FORMAT (F3.0,F4.1,E9.2,F3.0)
      SION = (A*(V*C/10.0)*ZCHGI**2)/2.0
      SUM1 = SUM1 + SION
    1 CONTINUE
      READ(1,4)TURNF,CA,VA,CCU,VCU,VOLB,CONBAS,WK,L
    4 FORMAT(F4.0,E10.3,F4.0,E10.3,F4.0,3E10.3,I5)
      VOLCO1 = (TURNF/50.0)*VOLB
      DO 3 K=1,6,1
      READ (1,5)B,D,YCHGI,V2
    5 FORMAT (F3.0,E9.2,F3.0,F4.1)
      IF(K-6)7,6,7
    6 S2ION= (CONBAS*VOLCO1)/(VOLCO1+10.0)*B*YCHGI  /2.0
      GO TO 8
    7 S2ION =(B*((V2*D)/(VOLCO1+10.0))*YCHGI**2)/2.0
```

```
    8 SUM2 = SUM2+S2ION
    3 CONTINUE
      ASUM = (SUM1+SUM2)/2.0
      WRITE(3,25)(ANAME(I),I=1,18)
      WRITE (3,9)ASUM,SUM1,SUM2
    9 FORMAT (1H0,7HAVG MU E12.3,2X,5HMU 1 E12.3,2X,5HMU 2 E12.3)
C     CALCULATION OF FORMATION CONSTANTS FOR M + DIEN
      READ (1,10)(PH(N),N=1,L)
   10 FORMAT (6F12.2)
      READ (1,11)(TURNS(N),N=1,L)
   11 FORMAT (6F12.0)
       READ(1,24)EK1,EK2,EK3
   24 FORMAT(3E12.4)
      DO 12 N=1,L
      PROTL = -PH(N)
      PROT = 10.**PROTL
      VOLCOR = (TURNS(N)/50.0)*VOLB
      CLIG = (CA*VA)/(10.0+VOLCOR)
      CMET = (CCU*VCU)/(10.0+VOLCOR)
      AVBAS = (VOLCOR*CONBAS)/(CA*VA)
       G = 3.0 - AVBAS + (WK/PROT - PROT)/CLIG
      ALPHA = 1.0/((PROT**2)*EK1*EK2) + 1.0/(PROT*EK2) + 1.0 + PROT*EK3
      BETA = 1.0/(PROT*EK2) + 2.0 + 3.0*PROT*EK3
      DENH2 = (CLIG*G)/BETA
      COMMET = CLIG - ALPHA*DENH2
      FREMET = CMET - COMMET
C     EKONST IS FORMATION CONSTANT FOR M + H2DIEN = MDIEN + 2H
      EKONST(N) = ((PROT**2)*COMMET)/(FREMET*DENH2)
C     CPLXK IS FORMATION CONSTANT FOR M + DIEN = MDIEN
      CPLXK(N) = EKONST(N)*EK1*EK2
   12 CONTINUE
       SUMX=0.0
      SUMY = 0.0
      DO 13 N=1,L
      XEKONK(N) = ALOG10(EKONST(N))
      XCPXK(N) = ALOG10(CPLXK(N))
      SUMX = XEKONK(N) + SUMX
```

```
      SUMY = XCPXK(N) + SUMY
   13 CONTINUE
      T=L
      XEK = 0.0
      XCK = 0.0
      SUMXLG = SUMX/T
      SUMYLG = SUMY/T
      DO 14 N=1,L
      REKONK(N) = XEKONK(N) - SUMXLG
      RCPXK(N) = XCPXK(N) - SUMYLG
      XEK = REKONK(N)**2 + XEK
      XCK = RCPXK(N)**2 + XCK
   14 CONTINUE
      SIGEK = SQRT(XEK/(T-1.0))
      SIGCK = SQRT(XCK/(T-1.0))
      WRITE (3,30)(EKONST(N),XEKONK(N),REKONK(N),N=1,L)
   30 FORMAT(1H0,8HEQ CONST,10X,12HLOG EQ CONST,10X,12HDEV FROM AVG,/
     1(1X,E12.6,10X,F10.6,12X,F12.7)/)
      WRITE (3,31)SUMXLG,SIGEK
   31 FORMAT(1H0,19HAVG LOG EQ CONST = F10.6,6X,10HSTD DEV = F12.6)
      WRITE (3,32)(CPLXK(N),XCPXK(N),RCPXK(N),N=1,L)
   32 FORMAT(1H0,15HCPLX FORM CONST,5X,19HLOG CPLX FORM CONST,6X,12HDEV
     1FROM AVG,/(1X,E12.6,12X,F10.6,12X,F12.7)/)
      WRITE (3,33)SUMYLG,XCK
   33 FORMAT(1H0,26HAVG LOG CPLX FORM CONST = F10.6,8X,10HSTD DEV = F12.
     16)

C     CALCULATION OF HYDROXO COMPLEX CONSTANTS
      READ(1,48) M
   48 FORMAT(I5)
      READ(1,46)(PHO(N),N=1,M)
   46 FORMAT(6F12.2)
      READ(1,47)(TURNSO(N),N=1,M)
   47 FORMAT(6F12.0)
      YZ=M
      DO 40 N=1,M
```

```
      PROTL = -PHO(N)
      PROT = 10.**PROTL
      VOLCOR= (TURNSO(N)/50.0)*VOLB
      CUOHA=((CONBAS*VOLCOR)-(3.*CCU*VCU))/(10.0+VOLCOR) + PROT- WK/PROT
      CUA = (CCU*VCU)/(10.0+VOLCOR) - CUOHA
      DISSK(N) = CUOHA*PROT/CUA
C     DISSK IS DISSOCIATION CONSTANT FOR MDIENH2O = MDIENOH + H
      EXPDK(N) =ALOG10(DISSK(N))
      SUMDK = SUMDK + EXPDK(N)
      STABK(N) = DISSK(N)/WK
      EXPSK(N) = ALOG10(STABK(N))
C     STABK IS STABILITY CONSTANT FOR MDIEN + OH = MDIENOH
      SUMSK = SUMSK + EXPSK(N)
      CMETO = (CCU*VCU)/(10.0 + VOLCOR)
      AVBASO = (VOLCOR*CONBAS)/(CCU*VCU)
      GO = 4.0 - AVBASO + (WK/PROT  - PROT)/CMETO
      GKOH(N) = -GO/((GO - 1.)*PROT)
       DISSKG(N) = 1.0/GKOH(N)
      EXDKG(N) = ALOG10(DISSKG(N))
       SUMDKG = SUMDKG + EXDKG(N)
      STABKG(N) = DISSKG(N)/WK
      EXSKG(N) = ALOG10(STABKG(N))
      SUMSKG = SUMSKG + EXSKG(N)
   40 CONTINUE
      SUMLDK =SUMDK/YZ
       SUMLDG = SUMDKG/YZ
      SUMLSK =SUMSK/YZ
      SUMLSG = SUMSKG/YZ
      DO 41 N=1,M
      RLDK(N)=EXPDK(N) -SUMLDK
      RLSK(N) = EXPSK(N) -SUMLSK
      RDK = RLDK(N)**2 +RDK
      RSK = RLSK(N)**2 +RSK
       RLDKG(N) = EXDKG(N) - SUMLDG
      RLSKG(N) = EXSKG(N) - SUMLSG
      RDKG = RLDKG(N)**2  +  RDKG
      RSKG = RLSKG(N)**2  +  RSKG
```

```
41 CONTINUE
   SIGDK = SQRT(RDK/(YZ-1.))
   SIGSK = SQRT(RSK/(YZ-1.))
   SIGDKG = SQRT(RDKG/(YZ - 1.))
   SIGSKG = SQRT(RSKG/(YZ - 1.))
   WRITE(3,42)(DISSK(N),EXPDK(N),RLDK(N),N=1,M)
42 FORMAT(1H0,10HDISS CONST,14X,14HLOG DISS CONST,10X,12HDEV FROM AVG
  1,/(1X,E14.7,10X,F12.7,11X,F12.7)/)
   WRITE(3,43)SUMLDK,SIGDK
43 FORMAT(1H0,21HAVG LOG DISS CONST = F12.7,8X,10HSTD DEV = F12.8)
   WRITE(3,44)(STABK(N),EXPSK(N),RLSK(N),N=1,M)
44 FORMAT(1H0,10HSTAB CONST,14X,14HLOG STAB CONST,10X,12HDEV FROM AVG
  1,/(1X,E14.7,10X,F12.7,11X,F12.7)/)
   WRITE(3,45)SUMLSK,SIGSK
45 FORMAT(1H0,21HAVG LOG STAB CONST = F12.7,8X,10HSTD DEV = F12.8)
    WRITE(3,61)(DISSKG(N),EXDKG(N),RLDKG(N),N=1,M)
61 FORMAT(1H0,14HSCHWARZ METHOD,/'0',10HDISS CONST,14X,14HLOG DISS CO
  1NST,10X,12HDEV FROM AVG,/(1X,E14.7,10X,F12.7,11X,F12.7)/)
    WRITE(3,43)SUMLDG,SIGDKG
   WRITE(3,44)(STABKG(N),EXSKG(N),RLSKG(N),N=1,M)
    WRITE(3,45)SUMLSG,SIGSKG
   ITER =ITER-1
    IF (ITER)19,19,18
19 STOP
   END
```

Mixed ligand stability constants

The computation of the stability constant, K_x, for the mixed species is done by the following program. The variables are initialized and the appropriate volume, pH and initial concentrations are read in. The value of free amino acid, AFREEA, from Equation (21) is first calculated, followed by the value of K_x, ALFK1A and ALFK2A, from each Equation (19a) and (19b). The logarithm of K_x and the average value of log K_x are calculated before a standard deviation is computed. The amount of free amino acid, both values of K_x and log K_x, the average value of log K_x, the deviations, and the standard deviation are printed.

```
      DIMENSION ANAME(18),RFKB(25),RFKA(25),RAKB(25),RAKA(25),SIKAA(25),
     1SIKFA(25),SIKAB(25),SIKFB(25),EXAK1A(25),EXAK1B(25),EXAK2A(25),EXA
     2K2B(25),EXFK1A(25),EXFK1B(25),EXFK2A(25),EXFK2B(25),ALFK2A(25),ALF
     3K2B(25),ALFK1A(25),ALFK1B(25),ALK2DB(25),ALK2DA(25),ALK2NB(25),ALK
     42NA(25),ALK1DB(25),ALK1DA(25),ALK1NB(25),ALK1NA(25),AFREEA(25),AFR
     5EEB(25),PH(25),TURNS(25)
      READ (1,10) ITER
   10 FORMAT (I5)
  400 SSAKA = 0.0
      SSAKB = 0.0
       SSFKA = 0.0
      SSFKB = 0.0
      SDAKA = 0.0
      SDAKB = 0.0
      SDFKA = 0.0
      SDFKB = 0.0
      READ (1,101) (ANAME(I),I=1,18)
  101 FORMAT (18A4)
      READ (1,13) ATOT, TOTMET,EK, AK
   13 FORMAT (2E12.4,2F12.4)
      READ (1,14) WK,VOLBUR,CONBAS
   14 FORMAT (E12.4,F8.4,F10.5)
      READ (1,18)L,K
   18 FORMAT (2I5)
      READ (1,15)(PH(N),N=1,L)
   15 FORMAT (8F9.2)
      READ (1,16)(TURNS(N),N=1,L)
   16 FORMAT (8F9.0)
      EQKONS = 10.**EK
       ACIDK = 10.**(-AK)
      DO 17 N = 1,L
      VOLCOR = (TURNS(N)/50.0)*VOLBUR
      VOLFIN = 10.0 + VOLCOR
      PROTL = -PH(N)
      PROT = 10.**PROTL
      BASE = WK/PROT
      IF (K.EQ.1) GO TO 300
```

```
      BADD = VOLCOR*CONBAS/VOLFIN - (TOTMET*3.0)/VOLFIN  + PROT
      GO TO 600
  300 BADD=VOLCOR*CONBAS/VOLFIN-(TOTMET*3.0)/VOLFIN +PROT -ATOT/VOLFIN
  600 AQUAD =EQKONS*BASE - (WK/(BASE*ACIDK))
      BQUAD = (TOTMET/VOLFIN)*EQKONS*BASE - BADD + BASE + ATOT/VOLFIN +
     1WK*(BADD - BASE)/(BASE*ACIDK) - 2.*EQKONS*BASE*BADD + 2.*EQKONS*(B
     2ASE**2)
      CQUAD = (TOTMET/VOLFIN)*EQKONS*(BASE**2) - (TOTMET/VOLFIN)*EQKONS*
     1BASE*BADD + BADD*(BADD-BASE) - BASE*(BADD-BASE) - (ATOT/VOLFIN)*(B
     2ADD - BASE) - EQKONS*BADD*(BASE**2) + EQKONS*BASE*(BADD**2) - EQKO
     3NS*(BADD-BASE)*(BASE**2)
      AFREEA(N) = (-BQUAD+SQRT(BQUAD**2 - 4.*AQUAD*CQUAD))/(2.*AQUAD)
      ALK1NA(N) = (TOTMET/VOLFIN)*EQKONS*BASE - BADD + BASE + AFREEA(N)
     1-(BADD-BASE-AFREEA(N))*EQKONS*BASE
      ALK1DA(N) = AFREEA(N)*(BADD-BASE-AFREEA(N))-AFREEA(N)*(TOTMET/VOLF
     1IN)
      ALFK1A(N) = ALK1NA(N)/ALK1DA(N)
      ALK2NA(N) = (ATOT/VOLFIN)*EQKONS*BASE/AFREEA(N)-EQKONS*BASE-EQKONS
     1*WK/ACIDK
      ALK2DA(N) = BADD-BASE-(ATOT/VOLFIN)+(AFREEA(N)*WK)/(BASE*ACIDK)
      ALFK2A(N) = ALK2NA(N)/ALK2DA(N)
      EXAK1A(N) = ALOG10(ALFK1A(N))
      EXAK2A(N) = ALOG10(ALFK2A(N))
      EXFK1A(N) = ALOG10(ALFK1A(N)*ACIDK)
      EXFK2A(N) = ALOG10(ALFK2A(N)*ACIDK)
      SIKAA(N) = (EXAK1A(N)+EXAK2A(N))/2.
      SIKFA(N) = (EXFK1A(N)+EXFK2A(N))/2.
       SSAKA = SSAKA + SIKAA(N)
      SSFKA = SSFKA + SIKFA(N)
   17 CONTINUE
      T = L
      TSSAKA = SSAKA/T
      TSSFKA = SSFKA/T
      DO 117 N = 1,L
      RAKA(N) = SIKAA(N) -TSSAKA
      RFKA(N) = SIKFA(N) - TSSFKA
      SDAKA = RAKA(N)**2  + SDAKA
```

```
      SDFKA = RFKA(N)**2 + SDFKA
  117 CONTINUE
      SIGAKA = SQRT(SDAKA/(T-1.))
      SIGFKA = SQRT(SDFKA/(T-1.))
      WRITE (3,101) (ANAME(I),I=1,18)
      WRITE (3,1001) (AFREEA(N),ALFK1A(N),ALFK2A(N),ALK1NA(N),ALK1DA(N),
     1ALK2NA(N),ALK2DA(N),N=1,L)
 1001 FORMAT (1H0,7HFREE A ,2X,7HK EQN 1,2X,7HK EQN 2,2X,5HNUM 1,4X,7HDE
     1NOM 1,2X,5HNUM 2,4X,7HDENOM 2,/(1X,E11.4,1X,2F10.3,4E10.4)/)
      WRITE(3,100)(AFREEA(N),EXAK1A(N),EXAK2A(N),SIKAA(N),RAKA(N),N=1,L)
  100 FORMAT (1H0,12HFREE A, + RT,2X,12HLOG KA EQN 2,2X,12HLOG KA EQN 2,
     12X,10HSUM LOG KA 4X,10HDEV SUM KA,/(1X,E12.5,2X,F12.7,2X,F12.7,2X,
     2F12.6,2X,F12.6))
      WRITE(3,102)(EXFK1A(N),EXFK2A(N),SIKFA(N),RFKA(N),N=1,L)
  102 FORMAT(1H0,12HLOG KF EQN 1,2X,12HLOG KF EQN 2,2X,10HSUM LOG KF,4X,
     110HDEV SUM KF,/(1X,F12.7,2X,F12.7,2X,F12.6,2X,F12.6))
      WRITE (3,103) TSSAKA, SIGAKA, TSSFKA, SIGFKA
  103 FORMAT (1H0,13HAVG LOG KA = F12.6,10X,17HSTD DEV LOG KA = F12.6,/,
     11X,13HAVG LOG KF = F12.6,10X,17HSTD DEV LOG KF = F12.6)
      ITER = ITER - 1
      IF (ITER) 200,200,400
  200 STOP
      END
```