The Influence of Ring Size upon the Stability of Metal Chelates.

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Although the basic strength of the ligand is greater, the stability constants of the six-membered ring chelates of 1 : 3-diaminopropane with copper, nickel, and cadmium are lower than those of the corresponding five-membered ring chelate complexes of ethylene- or propylene-diamine. Similarly, β-alanine is found to form weaker metal complexes than α-alanine or glycine, despite its greater affinity for protons. The same behaviour characterises complexes of malonic and oxalic acid, and published data for a great variety of polydentate ligands support the generalisation that the stability of chelate complexes decreases with increasing ring size. Several factors which contribute to this behaviour are discussed.

ALTHOUGH the relation between ring size and stability in *cyclo*paraffins and similar systems has provided one of the classical problems of organic chemistry, the superficially analogous problems presented by chelate-ring formation among inorganic co-ordination compounds have excited little interest. Relatively few attempts have been made to correlate their stability with ring size, with the nature of the metal involved and the orbitals available, or with the electronegativities of the co-ordinating atoms and the basic strength and molecular geometry of the ligand molecules.

Evidence that stability diminished with ring size has been based upon the facts that Bailar and Work (*J. Amer. Chem. Soc.*, 1946, **68**, 233) experienced more difficulty in making cobaltic tris-complexes with 1 : 3-diaminopropane (" dmp "; $NH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot NH_2$) or *neo*pentanediamine ($NH_2 \cdot CH_2 \cdot CMe_2 \cdot CH_2 \cdot NH_2$) than with ethylenediamine (" en "; $NH_2 \cdot CH_2 \cdot CH_2 \cdot NH_2$), that Pfeiffer and Haiman (*Ber.*, 1903, **36**, 1064) experienced similar difficulties with copper, and that Drew and Tress (*J.*, 1933, 1335) found platinum would co-ordinate with ethylenediamine and " less readily " with 1 : 3-diaminopropane, while higher diamines formed only amorphous, ill-defined products. The value of such evidence, however, is vitiated because there is an obvious confusion here between the " ease of formation " of a ring-system and its stability when once obtained.

More satisfactory evidence is provided by Mann's demonstration (*J.*, 1926, 2681) that the complex formed by platinic chloride and 1 : 2 : 3-triaminopropane could be resolved; this proved that a five-membered ring was present in (I) and, by implication, that this must be more stable than the alternative structure (II) which could have contained a six-membered ring.

$$
\underset{\text{(I)}}{\overset{\displaystyle NH_2 \cdot CH_2 \cdot CH \cdot NH_2}{\underset{\displaystyle CH_2 \cdot NH_2}{\big|}}} PtCl_4
\qquad\qquad
\underset{\text{(II)}}{NH_2 \cdot CH} \Big\langle \begin{array}{c} CH_2 \cdot NH_2 \\ CH_2 \cdot NH_2 \end{array} PtCl_4
$$

The fundamental difference between chelate ring complexes in organic chemistry and, *e.g.*, polymethylene rings is that the reactions leading to ring formation are reversible in the former cases. Thus it becomes possible in principle to determine the equilibrium constant and free-energy change of the inorganic chelating reaction from measurements of the concentrations of metal, ligand, and chelated complex in equilibrium. Proceeding on these lines we have measured the stability constants of several inorganic complexes containing

five- and six-membered rings. Supplemented by data in the literature, the results confirm the hypothesis that increase in chelate ring size is accompanied by a decrease in stability.

From measurements at a series of temperatures it is possible to analyse the free-energy change of a chelation reaction into its component entropy and heat terms. The latter may also, with advantage, be determined by direct calorimetry. In a further paper (Irving and Dickens, in preparation) such thermodynamic data for many of the complexes referred to in this paper will be presented and discussed.

Chelate Rings formed by Aliphatic Diamines.—By the Calvin–Bjerrum technique as previously described (Irving and Griffiths, *J.*, 1954, 213; Irving and Rossotti, *J.*, 1954, 2904) the acid dissociation constants of 1 : 3-diaminopropane were found to be given by $pK_{BH+} = 10.72$ and $pK_{BH_2++} = 8.98$ in 0·1N-potassium chloride at 25°. Compared with that of ethylenediamine (Table 1) the increased chain length has caused a significant increase in basic strength while, as expected from statistical and other considerations, the difference between pK_{BH+} and pK_{BH_2++} is considerably reduced (cf. Schwarzenbach, Maissen, and Ackermann, *Helv. Chim. Acta*, 1952, **35**, 2333). With hexamethylenediamine the difference between the two thermodynamic constants at 25° is only 1·1 logarithmic units (Everett and Pinsent, *Proc. Roy. Soc.*, 1952, *A*, **215**, 417).

TABLE 1.

	Ethylene-diamine	Propylene-diamine	1 : 3-Di-amino-propane		Ethylene-diamine	Propylene-diamine	1 : 3-Di-amino-propane
Proton complexes				*Copper complexes*			
pK_{BH+}	10·17 [a]	9·83 [b]	10·72 [c, d]	$\log K_1$	10·73 [a]	10·58 [b]	9·77 [c]
pK_{BH_2++}	7·44	7·07	8·98	$\log K_2$	9·30	9·08	7·17
ΔpK	2·73	2·76	1·74	$\log \beta_2$	20·03 [e]	19·66 [e]	16·94 [c, f]
				$\log K_1/K_2$	1·43	1·50	2·60
Cadmium complexes				$\frac{1}{2} \log \beta_2/pK_{BH+}$	0·98	1·0	0·79
$\log \beta_2$	10·22 [g]	9·97 [b]	7·42 [h]				
$\log \beta_3$	12·29	12·12	8·03	*Nickel complexes*			
$\frac{1}{2} \log \beta_2/pK_{BH+}$	0·50	0·50	0·35	$\log K_1$	7·66 [g]	7·41 [b]	6·38 [i]
				$\log K_1/pK_{BH+}$	0·76	0·76	0·6

[a] Bjerrum and Nielsen, *Acta Chim. Scand.*, 1948, **2**, 297; glass-electrode measurements in N-potassium nitrate. [b] Carlson, McReynolds, and Verhoek, *J. Amer. Chem. Soc.*, 1945, **67**, 1334; glass-electrode measurements at 30° in 0·5M-neutral salt background. [c] Present authors; glass electrode at 25° in 0·1M-potassium chloride. [d] Schwarzenbach, Maissen, and Ackermann (*loc. cit.*) report 10·64, 8·88, and 1·76 for 0·1N-sodium nitrate at 20°. [e] Laitinen, Onstott, and Bailar, *J. Amer. Chem. Soc.*, 1949, **71**, 1550, obtained the values $\log \beta_2 = 19.72$ for ethylenediamine and 20.17 for propylenediamine by polarography in 0·1N-potassium nitrate at 25°. [f] Polarographic value (ref. h) = 16·67. [g] Bjerrum and Andersen, *Kgl. Danske Videnskab.*, 1945, **22**, 1773; glass-electrode measurements in N-potassium nitrate at 25°. [h] Present authors; polarography at 25° in 0·1M-potassium chloride. [i] Bjerrum, personal communication.

For the complex species ML_n the stability constant is defined by $K_n = [ML_n]/[ML_{n-1}][L]$, and $\beta_n = K_1 K_2 \ldots K_n$.

Difficulty was at first encountered in measuring the stability constants of the copper complexes of 1 : 3-diaminopropane owing to the separation of basic material during the titration. This was overcome by considerably reducing the concentration of metal used. For the same reason barium chloride was used in place of magnesium chloride when measuring the dissociation of the ligand itself. For free ligand exponents less than 4·5 (Fig. 1, inset) the degree of formation rose slightly above two. This might suggest the co-ordination of a third molecule of diamine, possibly through one nitrogen atom only, as Bjerrum and Nielsen (*loc. cit.*) have postulated in the case of ethylenediamine and copper. This possibility was not supported by spectrophotometric measurements, for no difference could be detected between the spectra in the visible region of solutions containing copper and diamine in the ratios 1 : 4 and 1 : 12. The discrepancy may arise from the effect of high diamine concentrations on the liquid–liquid junction potentials which are assumed to be constant throughout the titration. Independent determination of the stability of the copper–1 : 3-diaminopropane complex by a polarographic method gave the value $\log \beta_2 = 16.67$ in 0·1M-potassium nitrate at 25°, confirming the potentiometric measurements. The values

log β_2 = 7·42 and log β_3 = 8·03 obtained by this technique for cadmium and 1 : 3-diamino-propane are decidedly lower (Table 1) than the values for ethylenediamine.

It has been shown (Irving and Griffiths, *loc. cit.*) that methyl substitution at one or both of the nitrogen atoms of ethylenediamine increases the basic strength but, through the operation of steric factors, decreases the stability of the metal complexes. Table 1 shows that methyl substitution in the aliphatic chain has remarkably little effect on the dissociation constants of either proton or metal complexes of ethylenediamine (for further data, see Carlson, McReynolds, and Verhoek, *loc. cit.*). Increased chain length, by increasing ring size, brings about a notable decrease in stability notwithstanding the increased basicity of the ligand, *i.e.*, its affinity for protons. This is depicted quantitatively by the fall in the quotient $\frac{1}{2}$log $\beta_2/pK_{\mathrm{BH^+}}$. The steric hindrance to the co-ordination of a second molecule of diamine is measured by the value of log K_1/K_2 which increases on passing from " en " and " pn " to " dmp." With cadmium the effect of exchanging " dmp " for " en " can be seen in the ratio log β_3/β_2.

FIG. 1. *The formation curve for copper and* 1 : 3-*diaminopropane at* 25°
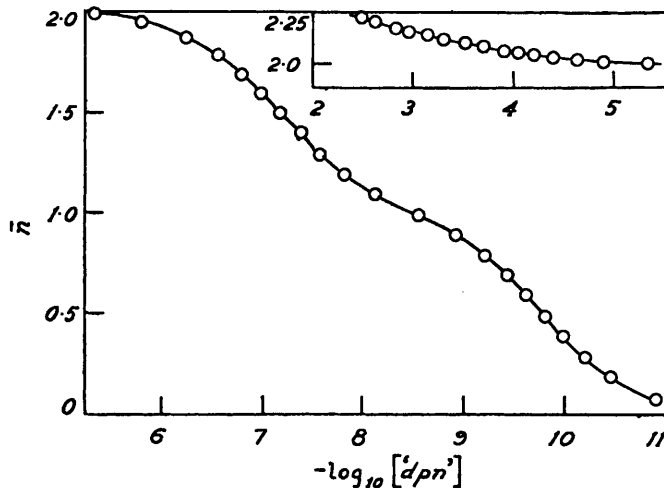
With water as solvent it does not appear to be possible to measure the stability constants of chelates of 1 : 3-diaminopropane with bivalent ions of complexing power appreciably lower than that of copper, nickel, or cadmium; with diamines capable of forming seven- or higher-membered rings, measurements are impossible even with copper. This can be explained as follows. As the separation between the terminal groups of a diamine is increased the tendency to chelate with metals decreases, but the tendency to bind protons increases. For any arbitrary values of C_M and C_L, the total concentrations of metal and ligand in the system, the first effect of increasing chain length will be to reduce the degree of formation, $\bar{n}$, of the system, since individual values of the stability constants K_n are decreased (Irving and Williams, *Analyst*, 1952, **77**, 257). This will cause an increase in the concentration [M] of uncomplexed cations, while the pH will rise owing to the increased interaction of ligand (no longer complexed to metal) with protons derived from the solvent. The effects are co-operative in favouring the formation of metal hydroxides or basic complexes. Furthermore, with increasing chain lengths the ends of a bidentate ligand, Z, can function increasingly as monodentate ligands. This favours the formation of bimetallic complexes, *e.g.*, M·Z·M, or binuclear complexes, *e.g.*, M$\overset{\diagup Z\diagdown}{\underset{\diagdown Z\diagup}{}}$M, and greatly increases the

difficulty of interpreting the experimental data (cf. Schwarzenbach, Maissen, and Ackermann, *loc. cit.*; Schwarzenbach, Ackermann, Maissen, and Anderegg, *Helv. Chim. Acta*, 1952, **35**, 2337).

When an aliphatic diamine is incorporated into a polydentate ligand the over-all stability may be increased sufficiently to permit the stability of five-, six-, and even seven-membered rings to be compared even when using ions of lower co-ordinating tendencies than those of the transition metals.

Table 2 shows that the homologues of ethylenediaminetetra-acetic acid, ($n = 1$) are almost identical in basic strength. However " Enta " (Fig. 2; $n = 1$, $m = 1$) derived from ethylenediamine gives five five-membered rings on chelation and forms complexes with magnesium, calcium, strontium, and barium which are more stable by some 4—5 kcal. than those formed by the homologue (Fig. 2; $n = 2$, $m = 1$) derived from 1 : 3-diamino-propane which forms one six- and four five-membered rings. In the exceptionally strong calcium complexes the further decrease in stability as seven- and eight-membered rings replace the five-membered chelate formed by " Enta " is convincingly shown. The diamine rings under discussion will certainly be strainless, and while this might also be
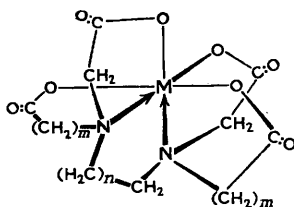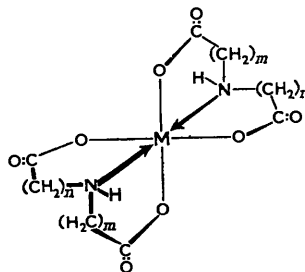
FIG. 2.

FIG. 3.

expected when the relevant nitrogen atoms are attached to a *cyclo*hexane ring as in the second group of compounds in Table 2, yet other stereochemical factors combine to produce a marked fall in stability when the five-membered ring formed by 1 : 2-diamino*cyclo*hexane-tetra-acetic acid with calcium and magnesium is replaced by the six- and seven-membered rings formed by its 1 : 3- and 1 : 4-isomers.

TABLE 2.

$A_2N\cdot[CH_2]_n\cdot CH_2\cdot NA_2$ [a] $(A = CH_2\cdot CO_2H)$	pK_1	pK_2	pK_3	pK_4	log K in 0·1N-KCl at 20° for			
					Mg	Ca	Sr	Ba
$n = 1$	2·0	2·67	6·16	10·26	8·69	10·59	8·63	7·76
$n = 2$	2·0	2·67	7·91	10·27	6·02	7·12	5·18	4·24
$n = 3$	1·9	2·66	9·07	10·45	—	5·05	—	—
$n = 4$	2·2	2·79	9·50	10·58	—	4·60	—	—
1 : 2-$C_6H_{10}(NA_2)_2$ [b,c] ...	2·4	3·5	6·1	11·7	10·3	12·50	—	8·0 [d]
1 : 3- ,, ...	1·8	2·6	8·6	10·9	4·64	4·77	—	—
1 : 4- ,, ...	2·1	2·5	9·0	10·9	4·30	4·19	—	—

[a] Schwarzenbach and Ackermann, *Helv. Chim. Acta*, 1947, **30**, 1798; 1948, **31**, 1029.   [b] C_6H_{10} = *cyclo*Hexylene residue.   [c] *Idem, ibid.*, 1949, **32**, 1682.   [d] Unpublished work by Schwarzenbach and Anderegg, quoted by Schwarzenbach (*loc. cit.*).

Chelate Rings formed by Amino-acids.—The most direct comparisons can be made between the five-membered chelates formed by glycine (" gl "; $NH_2\cdot CH_2\cdot CO_2H$) or α-alanine (" α-al "; $NH_2\cdot CHMe\cdot CO_2H$) and the six-membered chelates of β-alanine (" β-al "; $NH_2\cdot CH_2\cdot CH_2\cdot CO_2H$). Although β-alanine proves to be a stronger base than glycine (Table 3), titrations with the glass electrode and polarographic measurements establish that its copper, nickel, zinc, and cobalt complexes are appreciably weaker. This is best shown by the falling values of the quotient $\frac{1}{2}$ log $\beta_2/pK_{ZH}\pm$ (Table 3).

As with the diamines (see above) confirmatory evidence of the decrease of stability with increasing ring size is provided by complexes of polydentate amino-acids. Table 4 shows the fall in stability when the tridentate α-alaninediacetic acid ($NA_2\cdot CHMe\cdot CO_2H$; " Cim-α "), which forms three five-membered rings with an alkaline-earth metal, is replaced by β-alaninediacetic acid ($NA_2\cdot CH_2\cdot CH_2\cdot CO_2H$; " Cim-β ") which forms two five-membered and

one six-membered ring. The same phenomenon is shown by the phosphonic acids " Pim-α " and " Pim-β." In these instances the respective pairs of chelating partners are of much the same basicity, so the observed decrease in stability must be due predominantly to ring enlargement. Unambiguous proof follows from the data of Table 4 for the set of related compounds iminodiacetic acid (" Imda "), iminoaceticpropionic acid (" Impa ") and imino-dipropionic acid (" Imdp "), for although the basicities increase regularly in this order the

TABLE 3.

	Glycine (" gl ")	α-Alanine (" α-al ")	β-Alanine (" β-al ")
$pK_{ZH_2}+$	2·24 ^{a}	2·34 ^{b}	3·52 ^{a}
$pK_{ZH}±$	9·85	9·87	10·26

	Nickel complexes			Copper complexes		
	gl	α-al	β-al	gl	α-al	β-al
log K_1	5·73 ^{a}	5·96 ^{d}	4·63 ^{a}	8·12 ^{a}	8·18 ^{b}	7·13 ^{a}
log K_2	4·76	4·70	3·40	6·91	6·65	5·47
log K_1/K_2	0·97	1·26	1·23	1·21	1·53	1·66
log $β_2$	10·49	10·66	8·03	15·03	14·83	12·60
½ log $β_2$/p$K_{ZH}±$	0·53	0·54	0·39	0·76	0·75	0·61

	Zinc complexes			Cobalt complexes		
	gl	α-al	β-al	gl	α-al	β-al
log K_1	5·16 ^{a}	5·16 ^{b}	~4 ^{a}	4·95 ^{b}	4·83	—
log K_2	4·34	4·34	—	3·99	3·95	—
log $β_2$	9·50	9·50	—	8·94	8·78	~7
½ log $β_2$/p$K_{ZH}±$	0·48	0·48	<0·34	0·46	0·45	<0·33

^{a} A. E. Williams (this paper); glass-electrode measurements at 20°; additional measurements are quoted in ref. *b*. ^{b} Mellor and Maley, *Austral. J. Sci. Res.*, 1948, **2**, 579; potentiometric titrations at 25°. ^{c} Albert, *Biochem. J.*, 1950, **47**, 531; potentiometric titrations at 20°. ^{d} Monk, *Trans. Faraday Soc.*, 1951, **47**, 285, 297; values for 25°. ^{e} Ferrett (this paper) obtained log $β_2$ = 12·65 by polarography at 25° in 0·1M-potassium nitrate; Albert (ref. *c*) reports log $β_2$ = 12·90, which is reduced to 12·8 if the value p$K_{ZH}±$ = 10·3 is employed.

TABLE 4. *Stability constants of complexes formed by polydentate amino-acids.*

(*a*) Proton complexes

Formula	Trivial name	pK_1	pK_2	pK_3	pK_4	Ref.
NA$_3$ *	Cim-α	1·89	2·49	9·73	—	*a*
NA$_2$B †	Cim-β	2·06	3·69	9·66	—	*a*
NA$_2$·CH$_2$·PO(OH)$_2$	Pim-α	2·0	2·25	5·57	10·76	*a*
NA$_2$·CH$_2$·CH$_2$·PO(OH)$_2$	Pim-β	1·95	2·45	6·54	10·46	*a*
NHA$_2$	Imda	2·54	9·12	—	—	*b*
NHAB	Impa	3·61	9·46	—	—	*c*
NHB$_2$	Imdp	4·11	9·61	—	—	*b*
NH$_2$·CHA·CO$_2$H	Aspa	3·68	9·46	—	—	*c*
NA$_2$·CH$_2$·CH$_2$·NA$_2$	Enta	2·0	2·67	6·16	10·26	*e*
NAB·CH$_2$·CH$_2$·NAB	Endap	3·0	3·79	5·98	9·83	*d*

(*b*) Metal complexes

Ligand		Mg	Ca	Sr	Ba	Fe	Co	Ni	Cu	Zn	Cd	Pb	Ref.
Cim-α	log K_1	5·41	6·41	4·94	4·82	—	—	—	—	10·49	—	—	*a*
Cim-β	log K_1	5·28	5·04	3·87	3·40	—	—	—	—	10·07	—	—	*a*
Pim-α	log K_1	6·28	7·18	5·59	5·35	—	—	—	—	—	—	—	*a*
Pim-β	log K_1	6·33	5·44	4·10	3·64	—	—	—	—	11·24	—	—	*a*
Imda	log K_1	3·66	3·41	—	1·67	5·8 ^{f}	6·98	8·25	10·55	7·02 ^{f}	5·33	—	*b*
	log K_2	—	—	—	—	4·3	5·34	5·65	5·65	5·14	4·18	—	*b*
Impa	log K_1	—	—	—	—	—	6·15	7·34	10·48	6·21	4·53	—	*c*
	log K_2	—	—	—	—	—	4·20	5·23	4·45	4·31	3·16	—	*c*
Imdp	log K_1	—	—	—	—	—	4·94	6·16	9·44	4·95	3·55	—	*b*
	log K_2	—	—	—	—	—	3·25	3·77	3·68	precipitation when $n>0·5$			
Aspa	log K_1	—	—	—	—	—	5·87	7·10	8·54	5·81	4·37	—	*c*
	log K_2	—	—	—	—	—	4·28	5·27	6·78	4·31	3·11	—	*c*
Enta	log K_1	8·7	10·6	8·6	7·8	14·3 ^{g}	16·1	18·4	18·3	16·1	16·4	18·2	*e*
Endap	log K_1	6·9	—	—	—	—	14·9	15·5	16·3	14·5	11·8	13·2	*d*

* A = CH$_2$·CO$_2$H.   † B = CH$_2$·CH$_2$·CO$_2$H.

^{a} Schwarzenbach and Ruckstuhl, *Helv. Chim. Acta*, 1949, **32**, 1175. ^{b} Chabareck and Martell, *J. Amer. Chem. Soc.*, 1952, **74**, 5052. ^{c} *Idem, ibid.*, p. 6021. ^{d} *Idem, ibid.*, p. 6228. ^{e} Schwarzenbach and Freitag, *Helv. Chim. Acta*, 1951, **34**, 1503. ^{f} Schwarzenbach and Ruckstuhl, *ibid.*, 1952, **35**, 2346. ^{g} Schwarzenbach and Heller, *ibid.*, 1951, **34**, 576.

stabilities of the metal complexes decrease as the two five-membered rings found in complexes of Imda (Fig. 3; $n = m = 1$) are replaced successively by one five- and one six-membered ring in Impa (Fig. 3; $n = 1$, $m = 2$) and two six-membered rings in complexes formed by Imdp (Fig. 3, $n = m = 2$). The effect is clear cut with complexes of cobalt, nickel, zinc, and cadmium, and for the attachment of both the first and the second molecule of these bidentate ligands.

Values of log K_1 in the case of copper again demonstrate the fall in stability as first one and then the second five-membered is replaced by a six-membered ring. The anomalous low values of log K_2 arise from copper's lower maximum co-ordination number of four, in consequence of which only four chelate groups are present in the 1 : 2-complex in contrast to the six chelate rings formed by the neighbouring metals (Fig. 3). The abnormally small decrease in log K_2 in passing from Imda (16·20) to Impa (15·38) is similarly explained; for while the 1 : 1 complex of Impa possesses both a five- and a six-membered ring, since only two chelate rings are tolerated by copper, the formation of the 1 : 2 complex will probably involve two 5-rings formed from the α-amino-acid moiety of each ligand, the residual $-CH_2 \cdot CH_2 \cdot CO_2-$ being directed away form the central ion. On the assumption that $Cu(Imdp)_2$ is normally constructed from two six-membered rings, the effect of ring enlargement is clear. Comparisons of Aspa and Impa, both of which can form one five- and one six-membered ring, have been made by Chabarek and Martell (*loc. cit.*).

Data for the hexadentate ligands ethylenediaminetetra-acetic acid (Enta; Fig. 2; $n = 1$, $m = 1$) and ethylenediaminediaceticdipropionic acid (Endap; Fig. 2; $n = 1$, $m = 2$) illustrate again the fall in stability on ring enlargement in the complexes with magnesium, cobalt, zinc, copper, cadmium, and lead (Table 4). For all these polydentate ligands the stability order Fe < Co < Ni < Cu > Zn is strictly obeyed for values of log K_1, thus supplementing the results previously discussed by Irving and Williams (*J.*, 1953, 3192). Minor regularities in the case of copper (especially for log K_2) result from its lower co-ordination number and from changes in the type of rings formed when a second molecule of ligand becomes attached (Irving and Williams, *loc. cit.*; Chabarek and Martell, *loc. cit.*). Albert's results for polyaminocarboxylic acids (*Biochem. J.*, 1952, **50**, 690) afford further examples of decrease of stability accompanying ring enlargement, although the interpretation of the pH titrations is complicated by the many alternative possible modes of chelation whose relative probabilities will depend in a complicated way upon the pH of the solution, the dissociation constants of the ligands, the relative amounts of metal and ligand as well as their absolute concentrations, and the permitted or favoured stereochemistry (cf. Williams, *Nature*, 1953, **171**, 304).

Chelate Rings formed by Carboxylic Acids.—Attention has often been drawn to the general decrease in stability of complexes of certain metals when malonic acid replaces oxalic acid as the bidentate partner (cf. James and Peacock, *J.*, 1951, 2233; Schwarzenbach, *loc. cit.*; Irving, "Discussion on Co-ordination Chemistry," I.C.I. Report BRL/146, September 1950; Williams, *J.*, 1952, 3770). Table 5 summarises the available data for dicarboxylic acids and shows that the stability decrease persists for the 5-, 6-, and 7-membered rings formed by oxalate, malonate, and succinate ions with a wide variety of bivalent cations. That tervalent ions behave similarly is shown by the data for La^{3+} in Table 5, and by the values $[Mn(C_2O_4)_3{}^{3-}]/[Mn(C_2O_4)_2(H_2O)_2{}^-][C_2O_4{}^{2-}] = 260$, and $[Mn(C_3H_2O_4)_3{}^{3-}]/[Mn(C_3H_2O_4)_2(H_2O)_2{}^-][C_3H_4O_2{}^{2-}] = 18$ obtained spectrophotometrically at 0° for the oxalato- and malonato-complexes of Mn^{3+} by Cartledge and Ericks (*J. Amer. Chem. Soc.*, 1936, **58**, 2065) and Cartledge and Nichols (*ibid.*, 1940, **62**, 3057).

With further increase in chain length there appears some indication that the stability of metal complexes derived from carboxylic acids, $HO_2C \cdot [CH_2]_n \cdot CO_2H$, passes through a minimum when $n = 4$. Whether this effect is real or not cannot readily be established, for the values given in the last three rows of Table 5 are obtained as the differences between averaged stability constants, themselves obtained by a variety of methods and recalculated to a common basis (25° and $\mu = 0$) from the often widely different conditions prevailing in the original measurements. Although polydentate carboxylic acids of the type $HO_2C \cdot CH[(CH_2)_n \cdot CO_2H]_2$ have not been studied systematically, Schubert and Lindenbaum (*J. Amer. Chem. Soc.*, 1952, **74**, 3529) report for tricarballylic acid ($n = 1$) and carboxy-

pimelic acid ($n = 2$) the values $\log K_1$ (calcium) $= 1\cdot82$ and $1\cdot59$ and for $\log K_1$ (strontium) $= 1\cdot68$ and $1\cdot54$, confirming the lower stability associated with the larger ring.

TABLE 5.   *Stability constants of metal–dicarboxylate ion complexes.*

Ligand	pK_1	pK_2	Mg	Ca	Sr	Ba
Acetate	4·75	—	1·05	1·0	0·97	0·93
Oxalate	1·23	4·19	3·43, 3·25 [a]	3·00	2·54	2·33
Malonate	2·85	5·66	2·85, 2·60 [a]	2·50, 2·16 [a]		1·71, 1·93,[a] 2·13 [c]
Succinate	4·20	5·60	1·90, [a] 2·40 [f]	1·90 [a]	—	2·08,[c] 1·73,[a] 1·96 [f]
Glutarate	4·34	5·42	1·78 [a]	1·76 [a]	—	2·04 [c]
Adipate	4·43	5·42	—	2·19 [f]	—	1·92,[c] 1·85 [f]
Ligands exchanged						
Oxalate/malonate	—	—	0·6	0·7	—	0·4
Malonate/succinate	—	—	0·8	0·2	—	0·0
Succinate/glutarate	—	—	0·1	0·4	—	−0·1
Glutarate/adipate	—	—	—	−0·4	—	0·2

Ligand	Mn	Co	Ni	Cu	Zn	Cd	La^{3+}	Co(NH$_3$)$_6^{3+}$
Acetate	—	—	0·67 [h]	1·66 [i]	1·57	—	—	—
Oxalate	3·89	4·70	5·30	6·12 [b]	4·89 5·00	3·89 4·00 [e]	—	3·40 [c]
Malonate	3·29	3·72	4·01	5·80 [c] 5·73 [d]	3·68 3·75 [g]	3·25	4·89 [c]	3·54 [c]
Succinate	—	—	—	3·33 [c]	2·48 [a]	—	3·96 [c]	2·94 [c]
Glutarate	—	—	—	3·16 [c]	2·30 [a]	—	3·82 [c]	3·17 [c]
Adipate	—	—	—	3·38 [c]	—	—	4·10 [c]	3·35 [c]
Ligands exchanged								
Oxalate/malonate	0·6	1·0	1·3	0·4	1·2	0·7	—	−0·1
Malonate/succinate	—	—	—	2·4	1·2	—	0·9	0·6
Succinate/glutarate	—	—	—	0·2	0·2	—	0·1	−0·2
Glutarate/adipate	—	—	—	−0·2	—	—	−0·3	−0·2

Thermodynamic acid dissociation constants from Jeffery and Vogel (*J.*, 1935, 21) and Speakman (*J.*, 1940, 855).

[a] Cannan and Kibrick, *J. Amer. Chem. Soc.*, 1938, **60**, 2314.   [b] Ives, *J.*, 1933, 1360.   [c] Peacock and James, *J.*, 1951, 2233.   [d] Ives and Riley, *J.*, 1931, 1998.   [e] Vosburgh and Beb, *J. Amer. Chem. Soc.*, 1940, **62**, 1028.   [f] Topp and Davies, *J.*, 1940, 87.   [g] James, *J.*, 1951, 153.   [h] *Idem, Acta Chem. Scand.*, 1952, **6**, 1200.   [i] Fronaeus, *ibid.*, 1951, **5**, 859.

Unless stated to the contrary the metal stability constants are those quoted by Denny and Monk from many sources (*Trans. Faraday Soc.*, 1951, **47**, 992, and refs. therein).   Data from refs. *a, d,* and *f* have been corrected to $\mu = 0$ by Peacock and James (ref. *c*).

Discussion.—From the foregoing it may be concluded that the decrease in stability in replacing five- by six-membered rings of the same type is a general phenomenon shown by all metals and all polydentate ligands; further ring enlargement leads to still greater reduction in stability.   Complexes of silver with aliphatic diamines, NH$_2$·[CH$_2$]$_n$·NH$_2$ form a noteworthy exception to this generalisation as may be seen from the following values valid for 20° and $\mu = 0\cdot1$ (Schwarzenbach, *Helv. Chim. Acta*, 1953, **36**, 23) :

n	2	3	4	5
$\log K_1$	$4\cdot7 \pm 0\cdot1$	$5\cdot5 \pm 0\cdot07$	$5\cdot90 \pm 0\cdot1$	$5\cdot95 \pm 0\cdot1$

The anomaly is readily explicable, for, since silver tends to form linear complexes, *e.g.*, NH$_3$→Ag$^+$←NH$_3$ and NC–Ag$^-$–CN, considerable strain will accompany the attempt to bridge the coaxial co-ordination positions with ethylenediamine.   This strain will be reduced as n increases, but the consequent gain in stability will be offset to an increasing extent by the opposing effect of ring-enlargement already noted.

The " chelate effect," *i.e.*, the gain in stability when n molecules of a monodentate ligand are replaced by a single molecule of an n-dentate ligand, has been interpreted by Schwarzenbach (*ibid.*, 1952, **35**, 2344) as essentially an entropy effect.   His semi-quantitative treatment, based on the volume, J, swept out by a ligand (*e.g.*, a diamine) co-ordinated to a metal only by one end, correctly predicts the observed decrease in stability with ring enlargement—but it underestimates its magnitude.   Thus for the change from ethylenediamine to 1 : 3-diaminopropane the calculated increase in J (*loc. cit.*, p. 2354) is from 200 to 460 Å^3, corresponding to a decrease in stability of about 0·4 logarithmic unit.   This is

considerably less than the observed values of 1·0 for copper and 1·3 for nickel (Table 1), and very much less than the values 2·7 for magnesium, 3·5 for calcium, 3·4 for strontium, and 3·5 for barium observed when the chelating diamine forms part of a more complex structure (Table 2). The predicted change in chelation energy on passing from a six- to a seven-membered ring is about 0·3 logarithmic unit, but the values found experimentally are again larger.

Actual values for the chelate effect cannot be calculated for amino-acids for lack of suitable reference data for monodentate ligands. However, on replacement of β-alanine by α-alanine the gain in chelation energy in logarithmic units per molecule chelated is 0·9 in the case of cobalt, 1·3 with nickel, 1·4 for copper, and 1·0 for zinc (Table 3). On Schwarzenbach's theory the magnitude of this effect could scarcely exceed 0·5 unit. Values for log β_2 corresponding to the attachment of two acetate ions would be needed to calculate the chelate effect for metal–dicarboxylate ion complexes, but hitherto data have been lacking. However, by using the value log $\beta_2 = 2·65$ for the cupric–diacetate complex (Fronaeus, *Acta, Scand. Chem.*, 1951, **5**, 859), the magnitude of the chelate effect is given by Chel $= \log K_1$ (oxalate) $- \log \beta_2$ (acetate) $= 3·47$. Similarly, using the value log $\beta_2 = 1·26$ for the nickel–diacetate ion complex we obtain Chel $= 4·0$. For both metals the effect is large and quite outside the range predictable by Schwarzenbach's theory.

Implicit in Schwarzenbach's theory is the simplifying assumption that there is no substantial heat change when two molecules of a monodentate ligand are replaced by a ring-system terminating in groups of the same type. Explicitly for such reactions as

$$M^{n+}, \text{aq.} + 2NH_3 \longrightarrow M(NH_3)_2{}^{n+}, \text{aq.} + 2H_2O \quad . \quad . \quad . \quad (1)$$

$$M^{n+}, \text{aq.} + \text{en} \longrightarrow M\,\text{en}^{n+}, \text{aq.} + 2H_2O \quad . \quad . \quad . \quad . \quad (2)$$
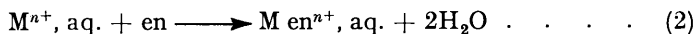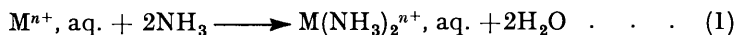
leading to the ligand exchange equation

$$M(NH_3)_2{}^{n+}, \text{aq.} + \text{en} \longrightarrow M\,\text{en}^{n+}, \text{aq.} + 2NH_3 \quad . \quad . \quad . \quad (3)$$
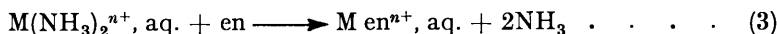
it is necessary to postulate that $\Delta H_1 \cong \Delta H_2$, so that $\Delta H_3 \cong 0$ or at least $\Delta H_3 \ll T\Delta S_3$, so that the value of the chelate effect (Chel $= \log K_3 = \log K_2/K_1$) is effectively determined by entropy considerations. From such an assumption there inevitably follows the conclusion that the magnitude of the chelate effect, and the magnitude of the stability decreases consequent upon ring enlargement, should be independent of the metal atoms involved— " Der Chelateffekt ist in der Tat unabhängig, oder weitgehend unabhängig von der Haftfestigkeit der einzelnen Ligandgruppe."

Experimental data do not support this generalisation. Among the more stable chelates of the transition metals the magnitude of the chelate effect can often be closely related to their individual stabilities. Thus for Co^{++}, Ni^{++}, and Cu^{++} we find linear relations

$$\text{Chel (1)} = \log K_1(\text{en})/K_1K_2(NH_3) = 0·20 \log K_1K_2(NH_3) + 1·40$$
$$\text{Chel (2)} = \log K\,(\text{en})/K_3K_4(NH_3) = 0·32 \log K_3K_4(NH_3) + 2·43$$

For these three metals Chel (1) is materially less than Chel (2). For cobalt and nickel we have Chel (3) $= \log K_3(\text{en})/K_5K_6(NH_3) = 3·54$ and 3·50, respectively, which represent still further increases of stability. While it is striking that the changes in the magnitude of the chelate effect increase for cobalt, nickel, and copper in the order in which these elements appear in the Irving–Williams series (*J.*, 1953, 3192), values of Chel (1) and Chel (2) for metals outside this series show no such linear relation to the stability of the reference ammonia complexes (Fig. 4). On the other hand, values of log $K_1(\alpha\text{-alanine})/K_1(\beta\text{-alanine})$ follow the Irving–Williams order (p. 3499). Such variations can scarcely be coincidental, and the fact that they are not predictable, even qualitatively, by Schwarzenbach's theory suggests that the latter is oversimplified. In a further paper (Irving and Dickens, in preparation) thermochemical measurements will be presented which will prove that in many cases where transition metals form complexes with formally uncharged diamines, the heat of reaction (i) differs from the heat change when two molecules of ammonia are co-ordinated, (ii) depends on the chain length of the ligand, (iii) varies with the nature of

the metal atom, and (iv) may contribute as substantially to the free-energy change as do various entropy terms.

In complexes involving neutral ligands there is no change during reaction in the formal charge on the ionised species. But in complexes formed by amino-acids or dicarboxylate ions, large entropy changes of some 25—100 cal./degree will be superimposed upon those due to other factors because the ordered arrangement of solvent around the ions is reduced on production of an uncharged (or lower charged) chelate complex. Thus for magnesium malonate $\Delta H_{298} = +3\cdot1$ kcal., while $T\Delta S = +7\cdot0$ kcal. (Evans and Monk, *Trans. Faraday Soc.*, 1952, **48**, 934), and for zinc malonate $\Delta H_{298} = +3\cdot06$ kcal. and $T\Delta S = +8\cdot17$ kcal. (James, *J.*, 1951, 153). Here the entropy increase is sufficient to overcome the endothermicity of the reaction. Still greater entropy changes would occur in the formation of complexes between the anion of ethylenediaminetetra-acetic acid carrying four negative charges and, *e.g.*, rare-earth cations. Increase in the chain-length of the ligand may well produce only minor alterations in a large total entropy effect, so that ring-enlargement

Fig. 4.   *The relation between the magnitude of the chelate effect and the stability of the reference ammonia complexes.*
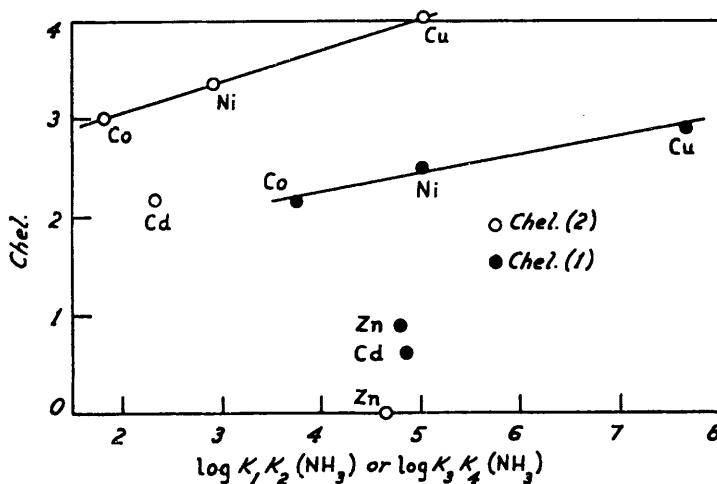
might effect relatively small changes in the ' chelate effect ' such as appear for the replacement reactions oxalate/malonate, malonate/glutarate, etc., of Table 5. If the stability of Enta complexes of the alkaline-earth and transition metals is due predominantly to entropy increases on chelation, it should be possible to correlate these with the standard entropies of the ions concerned. If the entropy changes on replacing Enta by its homologue $(HO_2C\cdot CH_2)_2N\cdot CH_2\cdot CH_2\cdot CH_2\cdot N(CH_2\cdot CO_2H)_2$ are negligible, the decreases in stability given in Table 2 must originate from differences in the heats of reaction which should depend upon specific properties such as the sum of the first and the second ionisation potential (Irving and Williams, *loc. cit.*). Thermochemical studies of both of these problems, which should contribute to a critical evaluation of Schwarzenbach's theory, are now in progress in these laboratories.

EXPERIMENTAL

Materials.—A commercial specimen of 1 : 3-diaminopropane (Messrs. Light & Co.) was refluxed over freshly fused and finely powdered barium oxide and fractionated, the fraction of b. p. 135—136°/760 mm. being collected in a weight-burette fitted with a " Sofnolite " guard tube. The purity, determined by titration of known amounts against standard hydrochloric acid, was never less than 98·5%. Glycine (a pure laboratory specimen), recrystallized several times from water, had m. p. 233° (decomp.). β-Alanine was prepared according to *Org. Synth.*, Coll. Vol. II, p. 19. After recrystallization it had m. p. 197° (decomp.). Both amino-acids were examined chromatographically and shown to be homogeneous.

" AnalaR " salts were used throughout and the apparatus and procedure for determining stability constants were substantially as previously described (Irving and Griffiths, *J.*, 1954, 213).

Acid Dissociation Constants of 1 : 3-*Diaminopropane.*—60 ml. of 0·1682M-hydrochloric acid, 25 ml. of 0·0666M-barium chloride, 11 ml. of 0·1M-potassium chloride, and 4 ml. of 1·605M-diamine solution in 0·1M-potassium chloride were transferred to the titration apparatus kept in a thermostat at 25° ± 0·05°, and the pH measured after successive additions of a 1·605M-solution of 1 : 3-diaminopropane in 0·1M-potassium chloride. The solution was stirred with a fine stream of nitrogen freed from carbon dioxide and equilibrated with water vapour. Steady potentials were obtained within 30 sec. The method of calculation was that described by Irving and Griffiths (*loc. cit.*).

Total vol. of diamine, ml.	pH	$\bar{n}_B$	pK (calc.)	Total vol. of diamine, ml.	pH	$\bar{n}_B$	pK (calc.)
4·00	8·83	1·571	8·97	12·2	10·70	0·553	10·72
4·16	8·93	1·511	8·97	12·36	10·72	0·5087	10·70
4·24	8·98	1·483	8·97	12·44	10·73	0·5055	10·71
4·32	9·025	1·455	8·97	12·52	10·74	0·5021	10·72
4·40	9·07	1·429	8·98	12·60	10·745	0·4999	10·72
4·48	9·11	1·404	8·975	12·68	10·75	0·4961	10·72
4·56	9·16	1·379	8·985	12·76	10·755	0·4927	10·72
4·64	9·20	1·355	8·99	12·84	10·76	0·4897	10·72
4·80	9·265	1·310	8·975	13·00	10·765	0·4838	10·72
				13·20	10·78	0·4764	10·72

Average value of $pK_{BH_2}{}^{++}$ 8·97(5)

Average value of $pK_{BH}{}^+$ 10·72

Formation Curve for Copper and 1 : 3-*Diaminopropane.*—A mixture of 60·00 ml. of 0·1682M-hydrochloric acid, 25 ml. of 0·0499M-copper sulphate, 3·00 ml. of 1·605M-diaminopropane, and 12 ml. of 0·1M-potassium chloride was transferred to the titration vessel, and the pH measured after successive additions of a 1·605M-solution of the diamine in 0·1M-potassium chloride. Values of $\bar{n}$ and pB were calculated as previously described (Irving and Griffiths, *loc. cit.*). The results are plotted in Fig. 1.

Dissociation Constants of Amino-acids.—A mixture of 50 ml. of 0·1100M-hydrochloric acid and 50 ml. of 0·05M-glycine in 0·05M-sodium chloride was titrated with carbonate-free 1·085M-sodium hydroxide in the titration apparatus in a thermostat at 20° ± 0·05°. The pH was measured as soon as the potentials became steady. Similar measurements were carried out with β-alanine. The two sets of dissociation constants reported in Table 3 were obtained by an obvious extension of the methods reported for the aliphatic diamines (*loc. cit.*). In a series of measurements in which the ionic strength was varied by the addition of sodium chloride it was confirmed that such changes had very little effect on the magnitude of $pK_{ZH_2}{}^\pm$ but considerably influenced that of $pK_{ZH}{}^\pm$. Values obtained in the present work lay on a smooth curve when plotted against μ or √μ with data in the literature (for references, see Irving and Williams, *J.*, 1953, 3192), and in calculating stability constants of metal complexes (see below) the value appropriate to the ionic strength used was obtained by interpolation.

Stability Constants of Metal Complexes of Glycine and β-*Alanine.*—These were calculated from data obtained at 20° by titration, with carbonate-free 1·100N-sodium hydroxide, of 50 ml. of a mixture of 0·025M-metal sulphate, 0·05M-glycine, and 0·055M-hydrochloric acid. With β-alanine the concentration of metal had to be reduced to M/120 to avoid premature precipitation. Typical results for the titration of nickel and β-alanine were as follows :

Ml. of 1·153N-NaOH	pH	$\bar{n}$	pB	Ml. of 1·153N-NaOH	pH	n	pB	Ml. of 1·153N-NaOH	pH	n	pB
2·20	4·58	0·0	7·35	2·60	7·15	0·647	4·49	2·94	8·42	1·520	3·29
2·40	5·90	0·112	5·99	2·72	7·62	0·984	4·04	2·96	8·49	1·566	3·23
2·50	6·69	0·363	4·92	2·74	7·71	1·017	3·96	2·98	8·57	1·600	3·16
2·52	6·80	0·418	4·81	2·86	8·13	1·333	3·57	3·00	8·63	1·656	3·10
2·54	6·90	0·474	4·72	2·88	8·20	1·381	3·50	3·04	8·78	1·730	2·97
2·56	6·98	0·529	4·64	2·90	8·27	1·424	3·43	3·08	8·90	1·801	2·85
2·58	7·06	0·585	4·56	2·92	8·35	1·474	3·37				

During the titration the ionic strength fell from 0·088 to 0·078 and the value $pK_{ZH}{}^+ = 10·26$ was used in the calculation of stability constants. With zinc the titration could only be carried up to $\bar{n} = 0·2$, so the value of log k_1 is very approximate.

Polarographic Measurements of Stability Constants.—Preliminary studies were carried out with a Tinsley recording polarograph but a manual instrument was used for the definitive measurements. The polarographic cell was kept in a thermostat at $25° \pm 0.1°$, and a normal calomel electrode was used with a saturated potassium chloride agar-agar bridge of low resistance. Plots of E versus $\log i/(i_{max.} - i)$ were drawn for every solution studied, the intercept giving $E_{\frac{1}{2}}$, the half-wave potential, and the slope the value of $0.059/p$; measurements were rejected if this measured slope differed significantly from the theoretical value of 0.0295 for a bivalent ion. Solutions were made up by weight from " AnalaR " reagents, and 1 : 3-diaminopropane was freshly distilled over barium oxide immediately before use.

Typical results are shown below for a copper solution of strength 10^{-4}M where the ionic strength was kept at 0.1 by addition of potassium nitrate. The capillary characteristics were $m^{\frac{2}{3}}t^{\frac{1}{6}} = 0.1432$ mg./sec., and 0.01% gelatin was present as a maximum suppressor. Three independent determinations of $E_{\frac{1}{2}}$ for 10^{-4}M-copper sulphate in 0.1M-potassium nitrate gave 0.0205, 0.0195, and 0.0199 v.

Concn. of 1 : 3-diaminopropane, [L], mole/l.	0	0.0194	0.0486	0.0973	0.1944	0.4860
Half-wave potential, $E_{\frac{1}{2}}$, v	0.2000	−0.3710	−0.3933	−0.4115	−0.4290	−0.4535

Plotted according to the equation

$$\Delta E_{\frac{1}{2}} = E_{\frac{1}{2}}\ (\text{complex}) - E_{\frac{1}{2}}\ (\text{simple}) = \frac{0.059}{p} \log K_n - \frac{0.059n}{p} \log [L]$$

these results give a line of slope 0.0585, so, since $p = 2$ for Cu^{++}, n must be 2 and the complex present is $Cu(dmp)_2^{++}$. The intercept has the value 0.4915, whence $\log \beta_2 = 16.67$ in satisfactory agreement with the potentiometric measurements.

Measurements with 1.075×10^{-3}M-cadmium ions under the same conditions gave the following results :

Concn. of 1 : 3-diaminopropane, mole/l.	0	0.0608	0.1215	0.1823	0.2673	0.3645	0.6075	1.215
− $E_{\frac{1}{2}}$, v	0.5820	0.7363	0.7530	0.7613	0.7640	0.7810	0.8005	0.8260

When the half-wave potential is plotted against the decadic logarithm of the concentration of diamine a segmented curve results. At high concentrations the slope is $0.086 = 0.059n/2$ for the Cd^{++} ion, whence $n = 3$ and the predominant species must be the tris-complex $Cd(dmp)_3^{++}$. With lower concentrations of ligand the slope is 0.057, whence $n = 2$, showing that the bis-complex $Cd(dmp)_2^{++}$ is now the principal species. From the intercepts the values $\log_{10} \beta_2 = 7.42$ and $\log_{10} \beta_3 = 8.03$ are obtained for the respective over-all stability constants.

In order to determine the stability constants of β-alanine–copper complexes polarographically, values of $E_{\frac{1}{2}}$ were measured in a series of buffer solutions (prepared from 0.1M-sodium hydroxide and 0.1M-potassium dihydrogen phosphate) each of which was 4.168×10^{-4}M with respect to cupric ion and 0.025M with respect to β-alanine. The ionic strength was adjusted to 0.1 in each case by addition of potassium nitrate, preliminary estimates of stability constants and measurements of pH enabling the correct amount to be arrived at by successive approximations. Typical results follow :

pH	8.05	8.82	9.26	9.72	10.23
− $\Delta E_{\frac{1}{2}}$, v	0.1515	0.1920	0.2150	0.2350	0.2550
$[\beta\text{-Alanine ion}]/[Cu^{2+}]$	0.4	1.7	4.5	11	25
$\log K_2$ (calc.)	12.96	12.81	12.69	12.58	12.61

The concentration of free amino-acid was calculated from the pH by using Henderson's equation and assuming the value $pK_{ZH+} = 10.36$ for the dissociation constant of the β-alanine zwitterion (May and Felsing, *J. Amer. Chem. Soc.*, 1951, **73**, 406). Values of $\log \beta_2$ calculated by the equation given previously are not constant because the ligand : metal ratio was too low in the less alkaline solutions. Omitting the results for pH 8.05 and 8.82, we obtain an average $\log \beta_2 = 12.65$, in satisfactory agreement with the potentiometric measurements.