Cobalt(II)–2,4-Diaminobutanoate Complexes: Stability and Oxygenation in Aqueous Solution

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Equilibrium constants are reported for the protonation of L-2,4-diaminobutanoic acid (HL) and for the formation of the complexes $[CoL]^+$, $[CoL]_2]$, $[Co(HL)]^{2+}$, and $[CoL(HL)]^+$ at 25 °C and I = 0.1 mol dm^{-3} NaCl. The stoicheiometries and stabilities of the cobalt(II) complexes are compared with those for homologous amino-acids $\overset{+}{H_3N}\cdot[CH_2]_n\cdot CH(NH_2)CO_2^-$ (n = 1—4). Equilibrium data for the formation of the μ-dioxygen adduct $[L_2CoO_2CoL_2]$ in aqueous solution ($\log K_{O_2} = 7.77 \pm 0.04$) have been obtained by use of a polarographic oxygen analyser.

An earlier paper reported a thermodynamic study of the complexing between cobalt(II) and the amino-acids (HL) DL-2,3-diaminopropanoic acid and L-2,5-diaminopentanoic acid (ornithine).[1] Species of the type $[CoL_n]^{(2-n)+}$, $[Co(HL)_n]^{2+}$ (n = 1 or 2), and $[CoL(HL)]^+$ were characterised, and for each ligand one of the species was oxygen-sensitive. Formation of the labile μ-dioxygen adducts, and their decomposition with acid or ethylenediaminetetra-acetate (edta), was studied by use of a polarographic oxygen analyser. This work reports a similar study for the ligand L-2,4-diaminobutanoic acid (HL). The complexes $[CoL]^+$, $[CoL_2]$, $[Co(HL)]^{2+}$, and $[CoL(HL)]^+$ were characterised from potentiometric titrations. The first two complexes are more stable than their 2,3-diaminopropanoic acid analogues; this stability is discussed in terms of chelate ring size and ligand basicity. The complex $[CoL_2]$ is oxygen-sensitive and gives a mono-bridged μ-dioxygen adduct $[L_2CoO_2CoL_2]$ at pH > 7.

EXPERIMENTAL

Materials.—L-2,4-Diaminobutanoic acid dihydrochloride (Sigma) was used without further purification. The molarity of standard solutions of the ligand was determined by Gran's analysis [2] on data from titrations of the ligand hydrochloride with Na[OH]. These titrations established that the crystalline reagent contained *ca.* 1.5 mol of HCl per mol of amino acid. Methods for the preparation of stock cobalt(II) chloride solution and for potentiometric measurement of $[H^+]$ have been described.[1,3]

For potentiometric measurements on the co-ordination between Co^{II} and the ligand a polarographic oxygen electrode was included in the titration cell to establish that the cobalt(II)–ligand–acid solution was free from dissolved oxygen before titrating with standard alkali. The nitrogen-flushing and titration sequence for these experiments, and the methods and equipment involved in oxygen-uptake experiments, have been described.[1]

RESULTS AND CALCULATIONS

Representative pH data for titrations of Na[OH] against solutions of (*i*) L-2,4-diaminobutanoic acid hydrochloride (HL·*n*HCl), and (*ii*) HL·*n*HCl and cobalt(II) chloride, are deposited as Supplementary Publication No. SUP 21751 (4 pp.),† as are pH and $[O_2]$(aq) data for the titration of cobalt(II) chloride against oxygenated solutions of the ligand (pH 9.2—10.3). All the data are for 25 °C and NaCl solution, I = 0.1 mol dm^{-3}. The stepwise protonation constants were computed from $\bar{n}_H$ (obs.) ‡–pH data by use of the least-squares procedure described previously.[3] The protonation constants were determined for six titrations from *ca.* 19 data points in the range $\bar{n}_H$ = 2.1—0.46. R Factors [4] of *ca.* 0.4—0.5% were achieved and there were no systematic trends in the residuals,[5] $\bar{n}_H$(obs.) − $\bar{n}_H$(calc.).

For titrations of Na[OH] against solutions of HL·*n*HCl (*ca.* 3×10^{-3} mol dm^{-3}), cobalt(II) chloride (*ca.* 1.2×10^{-3} mol dm^{-3}), and NaCl (I = 0.10 mol dm^{-3}) the pH against titre curves showed a marked end-point at pH 4.5—6.2, corresponding to the removal of the carboxyl proton, then a buffer region at pH 6.5—8.5, and a marked inflexion (end-point) at pH 9.2—9.8. The second end-point corresponded to the completion of the reaction $2H_2L^+ + Co^{2+} + 4OH^- \longrightarrow [CoL_2] + 2H_2O$, plus the uptake of 1 mol of hydroxide per mol of excess of ligand (*i.e.* the end-point for the reaction $H_2L^+ + OH^- \longrightarrow HL + H_2O$ coincides with the observed end-point). The equilibrium reactions (1)—(5) were considered in interpreting data from the buffer region. (These equilibria were known to be important for one or both of the homologous ligands 2,3-diaminopropanoic acid and 2,5-diaminopentanoic acid.)

Interpretation in terms of only the two equilibrium reactions (1) and (2) gave a poor least-squares fit with the greatest c_H(obs.) − c_H(calc.) values at low pH (c_H = total

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† For details see Notices to Authors, No. 7, *J.C.S. Dalton*, 1975, Index issue (items less than 10 pp. are supplied as full-size copies).

‡ $\bar{n}_H$ = Average number of protons bound per ligand molecule.

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[2] G. Gran, *Analyst*, 1952, **77**, 661.

[3] G. R. Hedwig and H. K. J. Powell, *Analyt. Chem.*, 1971, **43**, 1206.

[4] A. Vacca, A. Sabatini, and M. A. Gristina, *Co-ordination Chem. Rev.*, 1972, **8**, 45.

[5] A. Braibanti, F. Dallavalle, E. Laporati, and G. Mori, *J.C.S. Dalton*, 1973, 323.

ionisable acid). This suggested that the species HL (a zwitterion protonated on the terminal amino-group) is an

$$\mathrm{Co^{2+} + L^- \overset{K_1}{\rightleftharpoons} [CoL]^+} \qquad (1)$$

$$\mathrm{[CoL]^+ + L^- \overset{K_2}{\rightleftharpoons} [CoL_2]} \qquad (2)$$

$$\mathrm{Co^{2+} + HL \overset{K_3}{\rightleftharpoons} [Co(HL)]^{2+}} \qquad (3)$$

$$\mathrm{[Co(HL)]^{2+} + HL \overset{K_4}{\rightleftharpoons} [Co(HL)_2]^{2+}} \qquad (4)$$

$$\mathrm{[Co(HL)]^{2+} + L^- \overset{K_5}{\rightleftharpoons} [CoL(HL)]^+} \qquad (5)$$

important (bidentate) co-ordinating agent [reactions (3)—(5)]. There was no evidence for the formation of $[\mathrm{Co(HL)_2}]^{2+}$; attempts to include this species in the refinement gave a negative parameter (K_4). The best least-squares fit was obtained by considering reactions (1)—(3) and (5). An R factor of 0.28—0.77% was achieved for 25—33 data points (pH 6.1—8.6) from each of seven titrations. Log K values (mean ± standard deviation from seven titrations) are given in the Table. Calculation of distribution curves established that under the conditions employed ($c_{\mathrm{M}} : c_{\mathrm{L}} \sim 1 : 2.5$) the concentration of $[\mathrm{CoL}]^+$ is $>30\%$ of c_{M} at pH 6.95—8.5 and a maximum (62% of c_{M}) at pH 7.65. For $[\mathrm{Co(HL)}]^{2+}$ and $[\mathrm{CoL(HL)}]^+$ the corresponding data are $>5\%$ for pH 6.0—7.8, max. (17.8%) at pH 7.01, and $>10\%$ for pH 6.8—8.57, max. (15.6%) at pH 8.01, respectively.

Equilibrium constants for the formation of cobalt(II) amino-acid complexes at 25 °C

	Amino-acid			
Equilibrium	DL-2,3-Diaminopropanoic acid [a]	L-2,4-Diaminobutanoic acid [b]	L-2,5-Diaminopentanoic acid [a]	2,6-Diaminohexanoic acid [c]
$\mathrm{Co^{2+} + L^- \overset{K_1}{\rightleftharpoons} [CoL]^+}$	6.55 ± 0.01	7.07 ± 0.04		
$\mathrm{[CoL]^+ + L^- \overset{K_2}{\rightleftharpoons} [CoL_2]}$	5.18 ± 0.01	5.39 ± 0.15		
$\mathrm{Co^{2+} + HL \overset{K_3}{\rightleftharpoons} [Co(HL)]^{2+}}$	2.91 ± 0.02	3.46 ± 0.03	3.48 ± 0.06	3.62
$\mathrm{[Co(HL)]^{2+} + HL \overset{K_4}{\rightleftharpoons} [Co(HL)_2]^{2+}}$			2.96 ± 0.06	3.06
$\mathrm{[Co(HL)]^{2+} + L^- \overset{K_5}{\rightleftharpoons} [CoL(HL)]^+}$		6.40 ± 0.10	3.42 ± 0.10	

[a] Ref. 1; $I = 0.10$ mol dm^{-3} NaCl. [b] This work, $I = 0.10$ mol dm^{-3} NaCl; mean ± standard deviation from seven titrations. [c] C. S. Sokol, H. Laussegger, L. J. Zompa, and C. H. Brubaker, *J. Inorg. Nuclear Chem.*, 1971, **33**, 3581; $I = 1.0$ mol dm^{-3} K[NO$_3$].

A titration of Na[OH] against an oxygenated solution of cobalt(II) chloride and 2,4-diaminobutanoic acid established that oxygen uptake commences at pH *ca.* 6.9 which (from distribution curves) corresponds with the initial formation of $[\mathrm{CoL_2}]$. It was not possible to establish conclusively whether the minor species $[\mathrm{CoL(HL)}]^+$ (present at pH 6.0—7.8) is oxygen-sensitive (as it is for HL = ornithine).[1] Oxygen uptake was studied quantitatively in the range pH 9.2—10.3; in this range $[\mathrm{CoL_2}]$ is the only monomeric cobalt(II) species in oxygen-free solution. Titrations involved the incremental addition of cobalt(II) chloride (0.299 mol dm^{-3}) to a solution of ligand (*ca.* 3.3×10^{-3} mol dm^{-3}) and NaCl ($I = 0.10$ mol dm^{-3}) at a given pH and with an initial $[\mathrm{O_2}]$ *ca.* 2.6×10^{-4} mol dm^{-3}. The constant $K_{\mathrm{O_2}}$ was calculated for reaction (6) $\{K_{\mathrm{O_2}} = ([\mathrm{O_2}]_0 - [\mathrm{O_2}]_{\mathrm{eq}})/[\mathrm{O_2}]_{\mathrm{eq}}\cdot[\mathrm{CoL_2}]^2\}$. Titrations were completed in 20 min and the reversibility of reaction (6) was established from 100% release of co-ordinated O$_2$ (5 min) on addition of excess of edta at pH 5.8. The average from four titrations was $\log K_{\mathrm{O_2}} = 7.77 \pm 0.04$. The $K_{\mathrm{O_2}}$ values were independent

$$\mathrm{2[CoL_2] + O_2 \overset{K_{O_2}}{\rightleftharpoons} [L_2CoO_2CoL_2]} \qquad (6)$$

of pH, suggesting that a dibridged μ-dioxygen-μ-hydroxo-species is not formed. The u.v. absorption spectra for freshly prepared solutions of the adduct established absorption maxima at 313 nm (ε *ca.* 10 000 per mol of adduct) and *ca.* 375 nm (sh, ε *ca.* 7 500 dm^3 mol^{-1} cm^{-1}). Stadtherr *et al.*[6] assigned such a two-band u.v. spectrum to a μ-dioxygen adduct (and a single-band spectrum, with $\lambda_{\max.}$ *ca.* 360 nm, to a dibridged μ-dioxygen-μ-hydroxo-adduct).

DISCUSSION

Protonation.—Protonation constants determined for L-2,4-diaminobutanoic acid were $\log K_1 = 10.36 \pm 0.04$, $\log K_2 = 8.227 \pm 0.010$, and $\log K_3 = 2.04 \pm 0.02$ at 25 °C and $I = 0.10$ mol dm^{-3} NaCl. These constants have been reported previously[7,8] but for different ionic strengths or media and cannot be compared with our data[1] for homologous amino-acids at $I = 0.10$ mol dm^{-3} NaCl. The equilibrium constant for protonation of the more basic terminal amino-group ($\log K_1$) increases in going from 2,3-diaminopropanoic acid (9.407) to 2,6-diaminohexanoic acid (10.54) with K_1 for the latter being similar to that for a primary alkylamine.[1] This is consistent with the decreasing inductive effect of the α-amino-carboxylate group as the length of the methylene chain between it and the terminal amino-group increases. The greater inductive effect of the terminal ammonium group, $\overset{+}{\mathrm{N}}\mathrm{H_3}$, as compared with an α-amino-carboxylate group, gives rise to an analogous but more pronounced trend in $\log K_2$ values, *i.e.* for the series $\mathrm{H_2N{\cdot}[CH_2]_{\mathit{n}}{\cdot}CH(NH_2)CO_2^-}$ (n = 1—4) values of $\log K_2$ for successive members differ by 1.52, 0.48, and 0.36, whereas values of $\log K_1$ differ by 0.95, 0.15, and 0.03 respectively.[1,9]

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[6] L. G. Stadtherr, R. Prados, and R. B. Martin, *Inorg. Chem.*, 1973, **12**, 1814.

[7] A. Albert, *Biochem. J.*, 1952, **50**, 690 (published values at 20 °C, and $I = 0.025$ mol dm^{-3}, $\log K_1 = 10.44$, $\log K_2 = 8.24$; corrected to 25 °C assuming $\Delta H_1 = 54.8$ kJ mol^{-1} and $\Delta H_2 = 52.8$ kJ mol^{-1}, $\log K_1 = 10.28$ and $\log K_2 = 8.08$).

[8] W. Schaeg and F. Schneider, *Z. physiol. Chem.*, 1961, **326**, 40.

[9] L. G. Sillen and A. E. Martell, 'Stability Constants of Metal–Ion Complexes,' *Special Publ.*, No. 25, The Chemical Society, London, 1971; $I = 0.15$ mol dm^{-3} Na[ClO$_4$].

Cobalt Complexes.—Albert[7] reported stability constants for the formation of complexes $[CoL_2]$ ($L^- =$ tridentate diaminocarboxylate ligand), where for $L^- =$ 2,3-diaminopropanoate log $K_1K_2 = 11.8$ and for $L^- =$ 2,4-diaminobutanoate log $K_1K_2 = 12.8$. His results are in qualitative agreement with the present work (Table) which establishes that for both $[CoL]^+$ and $[CoL_2]$ the 2,3-diaminopropanoate complexes (two five-membered chelate rings in the ligand) have lower stability constants than the 2,4-diaminobutanoate complexes (linked five- and six-membered chelate rings). The greater stability of the latter complexes may be examined in terms of (*i*) the contribution made by ligand basicity, and (*ii*) the relative stability of linked five-membered chelate rings as compared with linked five- and six-membered rings in co-ordination. The 2,3-diaminopropanoate ion is significantly less basic ($\Sigma\log K_i = 17.44$) than is the 2,4-diaminobutanoate (20.62) and this will be reflected in the stability of the ligand-to-metal donor interaction. The contribution from stability associated with ring size may be assessed from log K' for the conversion of the metal complex into a solvated metal ion plus protonated ligand, *e.g.* equation (7) where log $K' = \log K_1K_2K_3$(protonation) $- \log \beta_2(CoL_2)$. This reaction allows for ligand

$$CoL_2 + 6H^+ \overset{K'}{\rightleftharpoons} Co^{2+} + 2H_3L^{2+} \qquad (7)$$

basicity by considering the affinity of both metal and protons for the ligand; for a series of ligands the magnitude of K' can be taken as a measure of the relative stabilities of different co-ordinated chelate-ring systems.[10] The values for $L^- =$ 2,4-diaminobutanoate and 2,3-diaminopropanoate are 8.16 and 5.71 respectively, indicating that the complex with linked five-membered chelate rings has the more stable ring systems. It follows that the greater stability of 2,4-diaminobutanoate complexes is due to ligand basicity rather than to favourable ring size. This result is in accord with our observations[10,11] on copper(II) complexes with homologous polyamines.

The relative stability associated with co-ordinated six- and seven-membered chelate rings can be estimated by comparing log K_5 values for 2,4-diaminobutanoic acid (6.40) and 2,5-diaminopentanoic acid complexes (3.42); the lower stability for the latter complex arises despite the slightly greater basicity for this ligand.

The longer-chain diaminocarboxylates ($n = 3$ or 4) show a preference for formation of complexes $[Co(HL)_x]^{2+}$ [HL is the bidentate ligand $H_3\overset{+}{N}\cdot[CH_2]_n\cdot CH(NH_2)CO_2^-$]. This arises from (*i*) the increased basicity of both the terminal amino-group (log K_1) and the α-aminocarboxylate group (log K_2K_3), and (*ii*) the decreased stability of the co-ordinated $H_2N\cdot[CH_2]_n\cdot CH(NH_2)$ ring system as the value of n increases.[11] 2,6-Diaminohexanoic acid does not give a cobalt(II) complex in which L^- is a ligand, and 2,5-diaminopentanoic acid does not give $[CoL]^+$ or $[CoL_2]$. The stabilities of $[Co(HL)]^{2+}$ (log K_3) and $[Co(HL)_2]^{2+}$ (log K_4) reflect the base-weakening effect which the terminal $\overset{+}{N}H_3$ group has on the co-ordinating power of the α-aminocarboxylate function, and increase from 2,3-diaminopropanoic acid to 2,6-diaminohexanoic acid.

Oxygen Adducts.—Proton-balance studies and spectrophotometric studies on the 2 : 1 oxygen adducts formed by bis(2,3-diaminopropanoato)cobalt(II) and related amino-acid complexes[1,6] have established that the mono- and di-bridged adducts, $[L_2CoO_2CoL_2]$ and $[L_2Co(O_2)(OH)CoL_2]^-$, can be distinguished by their u.v. absorption spectra. The 2 : 1 adduct formed by bis(L-2,4-diaminobutanoato)cobalt(II) has a two-band u.v. spectrum ($\lambda_{max.}$ 313 and 375 nm, ε *ca.* 10 000 and 7 500 $dm^3\ mol^{-1}\ cm^{-1}$) at pH 9.2—10.3 indicative of a mono-bridged μ-dioxygen species. Assignment of this stoicheiometry is supported by the fact that the K_{O_2} values calculated for reaction (6) were independent of pH. Stadtherr *et al.*[6] made a similar deduction from spectrophotometric work over the range pH 9.5—12.5.

It is of interest that whereas the DL-2,3-diaminopropanoate complex $[CoL_2]$ oxygenates to form a μ-dioxygen-μ-hydroxo-species at high pH (>10.0) the L-2,4-diaminobutanoate does not. This may arise from the higher basicity (and donor strength) of the carboxylate group in the latter ligand (log $K_3 = 1.33$ and 2.04, respectively), for it is likely that co-ordination of hydroxide at high pH involves dissociation of a ligand carboxylate group from the metal ion, as is suggested for co-ordination of the dioxygen molecule.[12] Munakata[13] studied the formation of the 2,4-diaminobutanoate adduct $[L_2CoO_2CoL_2]$ at 30 °C. His value of log $K_{O_2} =$ 6.8 (pH 8.7) will be in error because of the assumption that formation of $[CoL_2]$ is complete in oxygen-free solution at this pH (actual degree of formation of $[CoL_2] \not> 70\%$ at 25 °C).

The values of log K_{O_2} for adducts involving the homologous ligands DL-2,3-diaminopropanoic acid, L-2,4-diaminobutanoic acid, and L-2,5-diaminopentanoic acid (8.90,[1] 7.77, and 7.17[1] respectively, 25 °C) do not parallel the stabilities of the respective oxygen-sensitive cobalt(II) complexes, $[CoL_2]$ or $[CoL(HL)]^+$. Such a correlation might be expected if log β($[CoL_2]$ or $[CoL(HL)]^+$) could be taken as a measure of the donor power of the ligand, and if this in turn relates to the ability of the cobalt ion to donate electron density to the oxygen molecule.[12] However, because of the contribution which chelate-ring stability (ring strain) makes to log β for the different ligands, the sum $\Sigma\log K_i$(protonation) is a better estimate of the donor power of the ligand. McLendon and Martell[14] recently reported a linear free-energy relation between log $K_{O_2,OH}$ {for formation of $[L_2Co(O_2)(OH)CoL_2]^-$} and $\Sigma\log K_i$ (summed over all ligand donor groups co-ordinated to the metal) for a series of poly-

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[12] R. G. Wilkins *Adv. Chem. Ser.*, No. 100, Amer. Chem. Soc., Washington, D.C., 1971.

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[14] G. McLendon and A. E. Martell, *J.C.S. Chem. Comm.*, 1975, 223.

amine-*N*-carboxylic acid ligands. Data for the formation of the dibridged adduct with 2,3-diaminopropanoate [1] fit their correlation, while our data for the monobridged adducts with 2,3-diaminopropanoate,[1] 2,4-diaminobutanoate, 2,5-diaminopentanoate (adduct formed by $[CoL(HL)]^+$),[1] and histidine ($\log K_{O_2} = 6.63$,[15] $\Sigma\log K_i = 32.1$ [16]) and their data for 1,10-phenanthroline (6.3, ~13) and 2,2′-bipyridyl (5.4, ~12) establish an analogous linear relation.

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