

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 $[\text{CoL}]^+$, $[\text{CoL}_2]$, $[\text{Co}(\text{HL})]^{2+}$, and $[\text{CoL}(\text{HL})]^+$ at 25 °C and $I = 0.1 \text{ mol dm}^{-3}$ NaCl. The stoichiometries and stabilities of the cobalt(II) complexes are compared with those for homologous amino-acids $\text{H}_3\text{N}^+\text{[CH}_2\text{]}_n\text{CH}(\text{NH}_2)\text{CO}_2^-$ ($n = 1-4$). Equilibrium data for the formation of the μ -dioxxygen adduct $[\text{L}_2\text{CoO}_2\text{-CoL}_2]$ in aqueous solution ($\log K_{\text{O}_2} = 7.77 \pm 0.04$) 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 $[\text{CoL}_n]^{(2-n)+}$, $[\text{Co}(\text{HL})_n]^{2+}$ ($n = 1$ or 2), and $[\text{CoL}(\text{HL})]^+$ were characterised, and for each ligand one of the species was oxygen-sensitive. Formation of the labile μ -dioxxygen 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 $[\text{CoL}]^+$, $[\text{CoL}_2]$, $[\text{Co}(\text{HL})]^{2+}$, and $[\text{CoL}(\text{HL})]^+$ 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 $[\text{CoL}_2]$ is oxygen-sensitive and gives a mono-bridged μ -dioxxygen adduct $[\text{L}_2\text{CoO}_2\text{CoL}_2]$ at $\text{pH} > 7$.

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 analysis² 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 $[\text{H}^+]$ 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 ($\text{HL}\cdot n\text{HCl}$), and (ii) $\text{HL}\cdot n\text{HCl}$ and cobalt(II) chloride, are deposited as Supplementary Publication No. SUP 21751 (4 pp.),[†] as are pH and $[\text{O}_2](\text{aq})$ 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, $I = 0.1 \text{ mol dm}^{-3}$. The stepwise protonation constants were computed from \bar{n}_{H} (obs.) \ddagger -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 $\bar{n}_{\text{H}} = 2.1-0.46$. *R* Factors⁴ of *ca.* 0.4–0.5% were achieved and there were no systematic trends in the residuals,⁵ $\bar{n}_{\text{H}}(\text{obs.}) - \bar{n}_{\text{H}}(\text{calc.})$.

For titrations of Na[OH] against solutions of $\text{HL}\cdot n\text{HCl}$ (*ca.* $3 \times 10^{-3} \text{ mol dm}^{-3}$), cobalt(II) chloride (*ca.* $1.2 \times 10^{-3} \text{ mol dm}^{-3}$), and NaCl ($I = 0.10 \text{ mol dm}^{-3}$) 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 $2\text{H}_2\text{L}^+ + \text{Co}^{2+} + 4\text{OH}^- \longrightarrow [\text{CoL}_2] + 2\text{H}_2\text{O}$, plus the uptake of 1 mol of hydroxide per mol of excess of ligand (*i.e.* the end-point for the reaction $\text{H}_2\text{L}^+ + \text{OH}^- \longrightarrow \text{HL} + \text{H}_2\text{O}$ 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 $c_{\text{H}}(\text{obs.}) - c_{\text{H}}(\text{calc.})$ values at low pH ($c_{\text{H}} = \text{total}$

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.

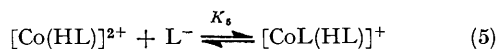
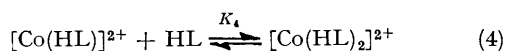
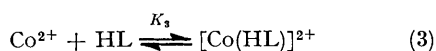
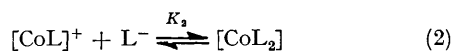
[†] For details see Notices to Authors, No. 7, *J.C.S. Dalton*, 1975, Index issue (items less than 10 pp. are supplied as full-size copies).

[‡] $\bar{n}_{\text{H}} =$ Average number of protons bound per ligand molecule.

¹ T. S. Kee and H. K. J. Powell, *J.C.S. Dalton*, 1975, 2023.

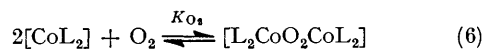
² G. Gran, *Analyst*, 1952, **77**, 661.

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



important (bidentate) co-ordinating agent [reactions (3)—(5)]. There was no evidence for the formation of $[\text{Co}(\text{HL})_2]^{2+}$; 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 \pm standard deviation from seven titrations) are given in the Table. Calculation of distribution curves

$[\text{CoL}_2]$. 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 $\log K_{\text{O}_2} = 7.77 \pm 0.04$. The K_{O_2} values were independent



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 $\text{dm}^3 \text{mol}^{-1} \text{cm}^{-1}$). Stadtherr *et al.*⁶ assigned such a two-band u.v. spectrum to a μ -dioxygen adduct (and a single-band spectrum, with λ_{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

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

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

^a Ref. 1; $I = 0.10 \text{ mol dm}^{-3} \text{ NaCl}$. ^b This work, $I = 0.10 \text{ mol dm}^{-3} \text{ NaCl}$; mean \pm 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; $I = 1.0 \text{ mol dm}^{-3} \text{ K}[\text{NO}_3]$.

established that under the conditions employed ($c_{\text{M}} : c_{\text{L}} \sim 1 : 2.5$) the concentration of $[\text{CoL}]^+$ is $>30\%$ of c_{M} at pH 6.95—8.5 and a maximum (62% of c_{M}) at pH 7.65. For $[\text{Co}(\text{HL})]^{2+}$ and $[\text{CoL}(\text{HL})]^+$ 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.

A titration of $\text{Na}[\text{OH}]$ 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 $[\text{CoL}_2]$. It was not possible to establish conclusively whether the minor species $[\text{CoL}(\text{HL})]^+$ (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 $[\text{CoL}_2]$ 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. $3.3 \times 10^{-3} \text{ mol dm}^{-3}$) and NaCl ($I = 0.10 \text{ mol dm}^{-3}$) at a given pH and with an initial $[\text{O}_2]$ ca. $2.6 \times 10^{-4} \text{ mol dm}^{-3}$. The constant K_{O_2} was calculated for reaction (6) $\{K_{\text{O}_2} = ([\text{O}_2]_0 - [\text{O}_2]_{\text{eq}})/[\text{O}_2]_{\text{eq}} -$

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

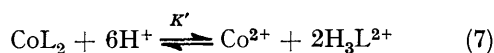
⁷ A. Albert, *Biochem. J.*, 1952, **50**, 690 (published values at 20 °C, and $I = 0.025 \text{ mol dm}^{-3}$, $\log K_1 = 10.44$, $\log K_2 = 8.24$; corrected to 25 °C assuming $\Delta H_1 = 54.8 \text{ kJ mol}^{-1}$ and $\Delta H_2 = 52.8 \text{ kJ mol}^{-1}$, $\log K_1 = 10.28$ and $\log K_2 = 8.08$).

25 °C and $I = 0.10 \text{ mol dm}^{-3} \text{ NaCl}$. These constants have been reported previously^{7,8} but for different ionic strengths or media and cannot be compared with our data¹ for homologous amino-acids at $I = 0.10 \text{ mol dm}^{-3} \text{ NaCl}$. 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, NH_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 $\text{H}_2\text{N}^+[\text{CH}_2]_n\text{CH}(\text{NH}_2)\text{CO}_2^-$ ($n = 1-4$) 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}

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; $I = 0.15 \text{ mol dm}^{-3} \text{ Na}[\text{ClO}_4]$.

Cobalt Complexes.—Albert⁷ reported stability constants for the formation of complexes $[\text{CoL}_2]$ ($\text{L}^- =$ tridentate diaminocarboxylate ligand), where for $\text{L}^- = 2,3$ -diaminopropanoate $\log K_1 K_2 = 11.8$ and for $\text{L}^- = 2,4$ -diaminobutanoate $\log K_1 K_2 = 12.8$. His results are in qualitative agreement with the present work (Table) which establishes that for both $[\text{CoL}]^+$ and $[\text{CoL}_2]$ 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 $\log K' = \log K_1 K_2 K_3 (\text{protonation}) - \log \beta_2(\text{CoL}_2)$. This reaction allows for ligand



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 $\text{L}^- = 2,4$ -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 $[\text{Co}(\text{HL})_x]^{2+}$ [HL is the bidentate ligand $\text{H}_3\text{N}^+[\text{CH}_2]_n\text{CH}(\text{NH}_2)\text{CO}_2^-$]. This arises from (i) the increased basicity of both the terminal amino-group ($\log K_1$) and the α -aminocarboxylate group ($\log K_2 K_3$), and (ii) the decreased stability of the co-ordinated $\text{H}_2\text{N}^+[\text{CH}_2]_n\text{CH}(\text{NH}_2)$ 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 $[\text{CoL}]^+$ or $[\text{CoL}_2]$. The stabilities of $[\text{Co}(\text{HL})]^{2+}$ ($\log K_3$) and $[\text{Co}(\text{HL})_2]^{2+}$ ($\log K_4$) reflect the base-weakening effect which the terminal NH_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, $[\text{L}_2\text{CoO}_2\text{CoL}_2]$ and $[\text{L}_2\text{Co}(\text{O}_2)(\text{OH})\text{CoL}_2]^-$, can be distinguished by their u.v. absorption spectra. The 2:1 adduct formed by bis-(1-2,4-diaminobutanoato)cobalt(II) has a two-band u.v. spectrum (λ_{max} 313 and 375 nm, ϵ ca. 10 000 and 7 500 $\text{dm}^3 \text{mol}^{-1} \text{cm}^{-1}$) at pH 9.2–10.3 indicative of a mono-bridged μ -dioxygen species. Assignment of this stoichiometry 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 $[\text{CoL}_2]$ 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 Munakata¹³ studied the formation of the 2,4-diaminobutanoate adduct $[\text{L}_2\text{CoO}_2\text{CoL}_2]$ at 30 °C. His value of $\log K_{\text{O}_2} = 6.8$ (pH 8.7) will be in error because of the assumption that formation of $[\text{CoL}_2]$ is complete in oxygen-free solution at this pH (actual degree of formation of $[\text{CoL}_2] > 70\%$ at 25 °C).

The values of $\log K_{\text{O}_2}$ 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 7.17¹ respectively, 25 °C) do not parallel the stabilities of the respective oxygen-sensitive cobalt(II) complexes, $[\text{CoL}_2]$ or $[\text{CoL}(\text{HL})]^+$. Such a correlation might be expected if $\log \beta([\text{CoL}_2]$ or $[\text{CoL}(\text{HL})]^+)$ 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 $\log \beta$ for the different ligands, the sum $\Sigma \log K_i$ (protonation) is a better estimate of the donor power of the ligand. McLendon and Martell¹⁴ recently reported a linear free-energy relation between $\log K_{\text{O}_2, \text{OH}}$ {for formation of $[\text{L}_2\text{Co}(\text{O}_2)(\text{OH})\text{CoL}_2]^-$ } and $\Sigma \log K_i$ (summed over all ligand donor groups co-ordinated to the metal) for a series of poly-

¹⁰ B. N. Palmer and H. K. J. Powell, *J.C.S. Dalton*, 1974, 2086.

¹¹ M. Gold and H. K. J. Powell, *J.C.S. Dalton*, 1976, 230.

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

¹³ M. Munakata, *Bull. Chem. Soc. Japan*, 1971, **44**, 1791.

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-diaminopropanoate¹ fit their correlation, while our data for the mono-bridged adducts with 2,3-diaminopropanoate,¹ 2,4-diaminobutanoate, 2,5-diaminopentanoate (adduct formed

¹⁵ G. H. Nancollas and H. K. J. Powell, *J. Amer. Chem. Soc.*, 1972, **94**, 2664.

by $[\text{CoL}(\text{HL})]^+$),¹ and histidine ($\log K_{\text{O}_2} = 6.63$,¹⁵ $\Sigma \log K_{\text{f}} = 32.1$ 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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¹⁶ R. Leberman and B. R. Rabin, *Trans. Faraday Soc.*, 1959, **55**, 1660.
