Metal Chelates of Sulphur-containing Polyamine Macrocycles and Oxygenation of the Corresponding Cobalt(II) Complexes †

Mutsuo Kodama
Department of Chemistry, College of General Education, Hirosaki University, Bunkyo, Hirosaki 036, Japan
Tohru Koike, Noriko Hoshiga, Ryosuke Machida, and Eiichi Kimura *
Department of Medicinal Chemistry, Hiroshima University School of Medicine, Kasumi, Hiroshima 734, Japan

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The protonation and complex formation of macrocyclic polyamines containing a sulphur donor atom, 1-thia-4,7,10-triazacyclododecane (L^4) and 1-thia-4,7,11,14-tetra-azacyclohexadecane (L^5), have been investigated with the metal ions Co^{II}, Ni^{II}, Cu^{II}, Hg^{II}, and Fe^{II}. The equilibrium and kinetic constants for formation of the dioxygen adducts of the cobalt(II) chelates in aqueous solutions are also reported, and compared with previous data for the analogous macrocycles containing nitrogen, oxygen, and pyridine instead of sulphur. The values of log K_{ML} for the macrocyclic polyamines follow the trend $N > S > O$. Oxygenation of the cobalt(II) complexes of L^4 and L^5 yields μ-peroxo-adducts as with the nitrogen and oxygen analogues, and the O_2-affinity order is $N \geqslant S > O$.

The interaction of dioxygen with metal complexes has attracted considerable attention for its intrinsic interest and as a model for biological phenomena.[1–3] Most of the previous work in aqueous solutions has employed acyclic aliphatic polyamines,[4] amino acids or peptides [5] as typical ligands and almost exclusively Co^{II} as the metal ion.

Recently it was found that structural modifications of saturated macrocyclic polyamine ligands confer a variety of interesting and useful properties upon the enclosed metal ions and their reactions with O_2.[6–16] For homologous cobalt(II) macrocyclic tetra-amine complexes the cavity size is the sole factor that determines the structure and stability of the O_2 adducts; the smaller (with respect to the size of Co^{II}) 12- (L^1) and 13-membered macrocycles yield μ-peroxo-μ-hydroxo-species, that of the larger ring being more stable, while a 14-membered homologue gives a monobridged μ-peroxo-adduct.[8] The O_2 adduct of a larger 15-membered tetra-amine complex immediately decomposes.[8] A pyridyl donor in a 16-membered penta-amine macrocycle L^8 stabilizes an otherwise very unstable 2 : 1 $Fe-O_2$ adduct in aqueous solutions, which may be the first model of hemerythrin, a biological O_2 carrier.[10] Two imide anions in a 16-membered penta-amine macrocycle can provide high-spin Ni^{II} with reversible O_2 binding as well as O_2-activating abilities.[11] Finally, certain macrocyclic polyamine complexes of Cu^{II} and Ni^{II} can exhibit strong interactions with the superoxide anion O_2^-.[12,13]

The present study deals with new macrocyclic polyamine ligands that are modifications of the prototype tetra-amine (L^1) [8] and penta-amine (L^2) ligands [9] where one of the ring NH groups is replaced by the softer donor sulphur: 1-thia-4,7,10-triazacyclododecane (L^4) [17] and 1-thia-4,7,11,14-tetra-azacyclohexadecane (L^5). The stabilities of the metal chelates formed by these ligands with Co^{II}, Fe^{II}, Ni^{II}, Cu^{II}, and Hg^{II} were first investigated to determine the effects of the replacement of a nitrogen by a sulphur atom.[18] Then, the equilibrium and rate constants for the reaction of the cobalt(II) complexes with molecular oxygen were determined. The stabilities of the complexes of the homologue L^3,[10] containing the harder donor atom oxygen were also studied for comparison. Very recently,[4] the co-ordinating tendencies of the acyclic ligands L^6 and L^7 towards Co^{II} and the oxygenation of the corresponding complexes were reported.

Experimental

Syntheses.—The preparation of ligand L^4 has briefly been communicated.[17] We describe it in more detail. A mixture of dimethyl thiodiglycolate (5.4 g, 30 mmol) and 1,5-diamino-3-azapentane (3.1 g, 30 mmol) in absolute methanol (600 cm^3) was refluxed for 3 d. Concentration of the solution to *ca.* 50 cm^3 precipitated 1.1 g of 1-thia-4,7,10-triazacyclododecane-3,11-dione, m.p. 212 °C (decomp.), M^+ 217, which was reduced with a large excess of diborane in refluxing tetrahydrofuran (thf) (150 cm^3) for 3 h. After treatment with 6 mol dm^{-3} HCl and then NaOH, L^4 was extracted into EtOH and twice recrystallized from CH_3CN; yield 0.37 g, m.p. 208 °C (Found: C, 50.9; H, 10.1; N, 22.5%; M^+ 189. Calc. for $C_8H_{19}N_3S$: C, 50.8; H, 10.1; N, 22.2%; M^+ 189). Silica gel t.l.c.: R_f 0.61 in $CHCl_3$–MeOH–28% aqueous NH_3 (5 : 2 : 0.5). ^1H N.m.r. ($CDCl_3$): δ 3.0—2.4 (m, 19 H).

1-*Thia*-4,7,11,14-*tetra-azacyclohexadecane*, L^5. A mixture of dimethyl thiodiglycolate (3.0 g, 17 mmol) and 1,9-diamino-3,7-diazanonane (2.2 g, 14 mmol) in absolute MeOH (600 cm^3) was refluxed for 9 d. Evaporation of the solvent left a solid product, 1-thia-4,7,11,14-tetra-azacyclohexadecane-3,15-dione, which was recrystallized from n-butanol; yield 0.8 g, m.p. 137—138 °C, M^+ 274. After reduction of the cyclic diamide (0.6 g) with a large excess of diborane, L^5 was purified as its tetrahydrochloride salt (0.6 g), m.p. 245—246 °C (Found: C, 33.8; H, 6.7; N, 14.5. $C_{11}H_{26}N_4S\cdot4HCl$ requires C, 34.0; H, 6.8; N, 14.4%). Silica gel t.l.c.: R_f 0.52 in $CHCl_3$–MeOH–28% aqueous NH_3 (1 : 2 : 0.5): *m/z* 246 (M^+ as free base). ^1H N.m.r. (taken as free base in $CDCl_3$): δ 3.0—2.6 (m, 10 H), 2.6 (s, 4 H), and 1.9—1.6 (m, 2 H).

Reagents and Apparatus.—Metal ion stock solutions were prepared and standardized as described before.[18] The polarographic apparatus was as used previously.[18–23] For the potentiometric titrations we used a Kyoto Electronics AT-117A model automatic pH meter (equipped with glass and silver–silver chloride electrodes) calibrated with standard HCl and NaOH (both 10^{-3} mol dm^{-3} at $I = 0.2$ mol dm^{-3} with $NaClO_4$) to read $-\log [H^+]$ rather than activity. For O_2 uptake a Yellow Springs oxygen monitor (model 53) was employed.

Potentiometric Measurements.—The ligand hydrochloride salts (50 cm^3 solutions) were titrated potentiometrically with

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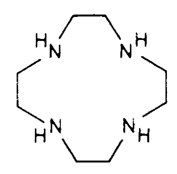
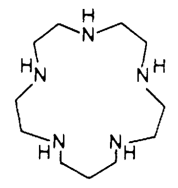
† *Non-S.I. unit employed*: B.M. ≈ 9.27×10^{-24} A m^2.



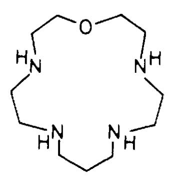
L^{1}

1,4,7,10-Tetraazacyclododecane



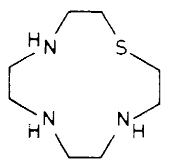
L^{2}

1,4,7,11,14-Pentaazacyclohexadecane



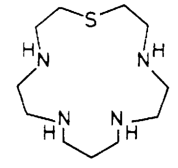
L^{3}

1-Oxa-4,7,11,14-tetraazacyclohexadecane



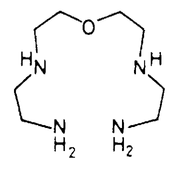
L^{4}

1-Thia-4,7,10-triazacyclododecane



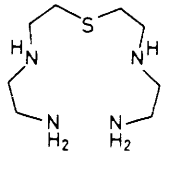
L^{5}

1-Thia-4,7,11,14-tetraazacyclohexadecane



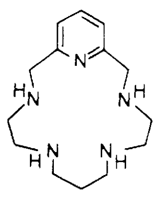
L^{6}

1,11-Diamino-6-oxa-3,9-diazaundecane



L^{7}

1,11-Diamino-6-thia-3,9-diazaundecane



L^{8}

3,6,10,13,19-Penta-azabicyclo-[13.3.1]nonadeca-1(19),15,17-triene

Table 1. Typical initial-rate data for the reaction of Co^{II} with L^{4} and L^{5} under an argon atmosphere at 25 °C and I = 0.2 mol dm^{-3}

Ligand	$10^3[Co^{2+}]_0$	$10^3[L]_0$	$10^3[MeCO_2^-]_0$	pH	$k_{obs.}$ *
		mol dm^{-3}			dm^3 mol^{-1} s^{-1}
L^{4}	1.2	1.0	200	4.78	$4.9_7 \times 10^{-2}$
	1.2	1.0	200	5.19	$8.2_9 \times 10^{-2}$
	1.2	1.0	200	5.55	$1.5_4 \times 10^{-1}$
	1.2	1.0	50	5.55	$6.2_5 \times 10^{-2}$
	1.2	3.0	200	5.55	$1.5_0 \times 10^{-1}$
	5.0	1.0	200	5.55	$1.5^9 \times 10^{-1}$
L^{5}	1.2	1.0	200	4.68	2.2_7
	1.2	1.0	200	4.96	2.8_6
	1.2	1.0	200	5.30	4.3_4
	1.2	1.0	50	5.30	1.7_8
	1.2	3.0	200	5.30	4.3_8
	5.0	1.0	200	5.30	4.3_0

* Observed (from initial slope) rate constant.

standard NaOH solution (CO_2-free) in the presence of equimolar Fe^{II} (10^{-3} mol dm^{-3}), Co^{II} (1.5×10^{-3} mol dm^{-3}), and Ni^{II} (10^{-3} mol dm^{-3}) in an argon atmosphere, as described before.[8,9] The corresponding aerobic titration curves for Co^{II} yielded the oxygenation constants. The molar concentration of O_2 in air-saturated aqueous solution is 2.7 (2.3) × 10^{-4} mol dm^{-3} at 25 (35) °C.[24] All of the solutions were adjusted to 0.2 mol dm^{-3} ionic strength by addition of $NaClO_4$.

Oxygen-uptake Measurements.—To an air-saturated unbuffered solution was added $[CoL]^{2+}$ complex and the accompanying change in O_2 concentration was measured at 35 °C. For calibration we used a triethylenetetra-amine (trien) complex of Co^{II} that is known to form a 2 : 1 $[CoL]^{2+}$–O_2 complex.[1] The experiments were repeated three times.

Kinetic Measurements.—$[CoL]^{2+}$ *Complex formation.* The rates of reaction of Co^{2+} with L in acetate buffers (0.2 mol dm^{-3}, $4.6 < pH < 5.7$) in an argon atmosphere were measured with anodic polarographic apparatus[25] by monitoring the decreasing anodic wave height of the uncomplexed L. The observed rate constants were determined by the initial-slope method (to 20% completion of the overall reactions). Typical rate data are shown in Table 1.

O_2 *Uptake by* $[CoL]^{2+}$. Deoxygenated solutions of $[CoL]^{2+}$, prepared *in situ* by mixing Co^{2+} with L (5% excess) in tris-(hydroxymethyl)methylamine, $NH_2C(CH_2OH)_3$ (for L^{4}), or acetate buffers (for L^{5}) (complete complexation in *ca.* 1 h), were mixed with a known concentration of O_2 in the same buffers. The kinetics of the $[CoL]^{2+}$–O_2 formation were measured with a stopped-flow apparatus by monitoring the increasing absorbance at 370 nm. The initial-slope method (to 20% completion of the overall reactions) was employed to determine the rate constants. Typical rate data are shown in Table 2.

Magnetic Susceptibility.—Solution magnetic susceptibilities ($\mu_{eff.}$) were measured using the Evans method[26] on a Hitachi R-40 n.m.r. (90 MHz) spectrometer. The complex solution

Table 2. Typical initial-rate data for the reaction of $[CoL]^{2+}$ with O_2 at 25 °C and $I = 0.2$ mol dm^{-3}

Ligand	$10^3[CoL^{2+}]_0$	$10^3[O_2]$	10^3[Buffer]	$10^{-2}k$ [a]
	mol dm^{-3}			dm^3 mol^{-1} s^{-1}
L^4 [b]	2.0	0.135	100	3.9_1
	2.0	0.067_5	100	4.0
	2.0	0.033_8	100	3.8
	4.0	0.135	100	4.0_1
	2.0	0.135	200	3.8_2
L^5 [c]	0.5	0.135	200	180
	2.0	0.135	200	170
	0.5	0.067_5	200	180
	0.5	0.033_8	200	210
	0.5	0.135	200	200

[a] Observed (from initial slope) rate constants. [b] $NH_2C(CH_2OH)_3$ buffer, pH 7.50. [c] Acetate buffer, pH 5.70.

Table 3. Comparison of protonation constants for quadri- and quinque-dentate ligands

Ligand	log K_1	log K_2	log K_3	log K_4	log K_5
L^1 [a]	10.7	9.7	1.7	0.9	
L^2 [b]	10.64	9.49	7.28	1.7	1.5
L^3 [c]	9.35	7.90	4.90	*ca.* 3	
L^4 [d]	9.53	8.15	3.09		
	(9.23	7.95	2.9)		
L^5 [d]	9.33	8.85	4.49	3.2	
	(9.03	8.65	4.28	3.0)	
L^6 [e]	9.81	9.24	6.89	5.98	
L^7 [e]	9.78	9.10	6.51	5.64	
Acyclic N_5 [f]	10.36	9.65	8.50	4.70	2.40

[a] From ref. 19. At 25 °C and $I = 0.20$ mol dm^{-3}. [b] From ref. 22. At 25 °C and $I = 0.20$ mol dm^{-3}. [c] From ref. 9. At 35 °C and $I = 0.20$ mol dm^{-3}. [d] This study at 25 °C (35 °C) and $I = 0.20$ mol dm^{-3}. Confidence limits are ±0.005. [e] From ref. 4. At 25 °C. [f] 1,11-Diamino-3,6,9-triazaundecane. From D. B. Moss, C. Lin, and D. B. Rorobacher, *J. Am Chem. Soc.*, 1973, **95**, 5179. At 25 °C and $I = 0.1$ mol dm^{-3}.

(2×10^{-2} mol dm^{-3} in borate buffers) with 2% Bu^{t}OH was loaded into a standard 5-mm n.m.r. tube, into the centre of which was placed a 1.7-mm capillary and Teflon insert loaded with 2% Bu^{t}OH in borate buffer.

Results

Ligand Protonation Constants.—Mixed protonation constants [equation (1)] were determined from the hydrogen-ion concentrations (= pH) of aqueous solutions of each ligand

$$H^+ + H_{n-1}L^{(n-1)+} \overset{K_n}{\rightleftharpoons} H_nL^{n+},\quad K_n = [H_nL^{n+}]/[H^+][H_{n-1}L^{(n-1)+}] \qquad (1)$$

after each increment of base added. The determined values of log K_n for L^4 and L^5 are summarized in Table 3, along with those for the related ligands previously reported.

Metal Chelate Formation Constants.—A typical set of potentiometric titration curves for the ligand and metal (Ni, Co, Fe)-ligand equilibria is shown in Figure 1. The metal-ligand equilibria were best described by equation (2) in the buffer pH regions ($4 < pH < 5$). The hydrolysis of Co^{2+}

$$M + L \overset{K_{ML}}{\rightleftharpoons} ML,\ K_{ML} = [ML]/[M][L] \qquad (2)$$

(aq) or formation of $[CoL(OH)]^+$ can be neglected in the light of the reported value of K_{OH} $\{= [Co(OH)^+]/[Co^{2+}][OH^-]\}$ (log $K_{OH} = 5.1$ at 35 °C)[27] and the pH ranges used: pH > 4.75 for L^4 and pH > 5.0 for L^5. The K_{ML} values can be calculated from the mass-balance equations involving the total metal, total ligand, and total hydrogen-ion concentrations; equations for the triamine[18] (= L^4) and tetra-amine ligands[9] (= L^5) were derived previously. Apparently, the protonated chelate species $[M(HL)]^{3+}$ were not formed in sufficient concentration to be detected with our calculation method.

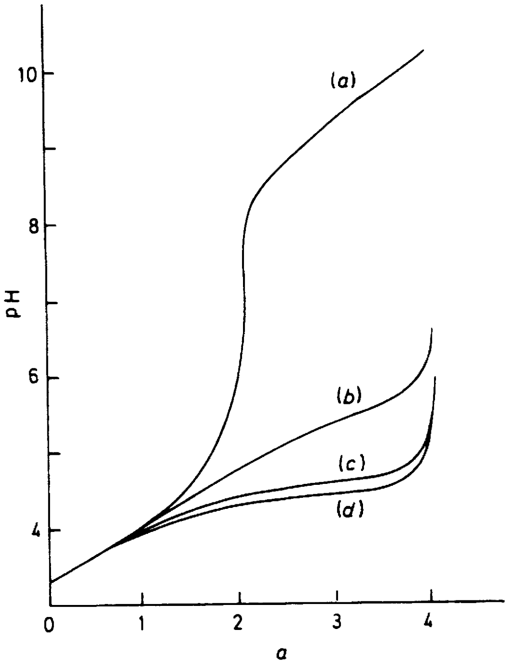


Figure 1. Anaerobic potentiometric titration curves of $L^5 \cdot 4HClO$ (1×10^{-3} mol dm^{-3}), alone (*a*) and in the presence of Fe^{II} (*b*), Ni^{II} (*c*) ($c_L = c_M = 1 \times 10^{-3}$ mol dm^{-3}), and Co^{II} (*d*) ($c_L = c_M = 1.5 \times 10^{-3}$ mol dm^{-3}) at $I = 0.2$ mol dm^{-3} and 25 °C; *a* is the number of moles of base added per mol of ligand

The chelation of Cu^{II} is so strong that virtually 100% of the macrocyclic ligands become complexed upon mere mixing of the ligand hydrochloride salts and Cu^{II}. Hence, for determination of the corresponding complexation constants the polarographic method described previously[19-22] was employed. The formation constants for Hg^{II} were determined by the anodic polarographic technique used previously for L^1[23] and L^2.[18]

All of the stability constants for Cu^{II}, Ni^{II}, Co^{II}, Fe^{II}, and Hg^{II} are summarized in Table 4. Relevant literature values are also given for comparison.

Oxygen Complex Formation Constants.—The cobalt(II)-sulphur-containing macrocycles are readily oxygenated. The L^4 complex is dark green which is unusual for μ-peroxo-adducts of cobalt(II)-polyamine complexes[1] (the μ-hydroxo-μ-peroxo-adduct with L^1 is brown),[10] while the L^5 complex is brown as is the L^2 complex that was identified as a μ-peroxo-adduct. Strong u.v.-visible absorption peaks indicative of O_2 adducts[1] occur at 375 nm (ε 6 800 dm^3 mol^{-1} cm^{-1}) for L^4 and 340 nm (shoulder, ε 7 700 dm^3 mol^{-1} cm^{-1}) for L^5. The stoicheiometry of $[CoL^4]^{2+}$–O_2 was determined to be 0.47 : 1 at 35 °C and pH 8—9 (initial $[CoL^{2+}] = 1.0 \times 10^{-4}$ mol dm^{-3}). For the L^5 complex, using an identical method,

Table 4. Complex formation constants (log K_{ML} with confidence limits) of quadri- and quinque-dentate ligands with various metal ions

Ligand	Cu^{2+}	Co^{2+}	Ni^{2+}	Fe^{2+}	Hg^{2+}
L^1 [a]	24.80	13.79	13.76	ppt.	25.50
L^2 [b]	27.10	15.85	18.10	ppt.	27.38
L^3 [c,d]	15.62 ± 0.03	11.42	12.30 ± 0.03	ppt.	<17
L^4 [c]	17.98 ± 0.05	11.11 ± 0.03	9.45 ± 0.03	7.82 ± 0.03	24.32 ± 0.05
L^5 [c]	24.14 ± 0.05	13.39 ± 0.03	12.66 ± 0.03	10.29 ± 0.03	25.15 ± 0.05
L^6 [e]	18.0	9.5	12.5	—	—
L^7 [e]	19.7	11.5	15.5	—	—
Acyclic N_5 [b]	22.8	13.7	17.4	ppt.	24.8

[a] Refs. 8, 19, and 23. [b] Refs. 9, 10, 18, and 22. [c] This study at 25 °C (for Cu^{2+} and Hg^{2+}) or 35 °C (Co^{2+}, Ni^{2+}, and Fe^{2+}) and $I = 0.20$ mol dm^{-3}. [d] Ref. 9. [e] Ref. 4.

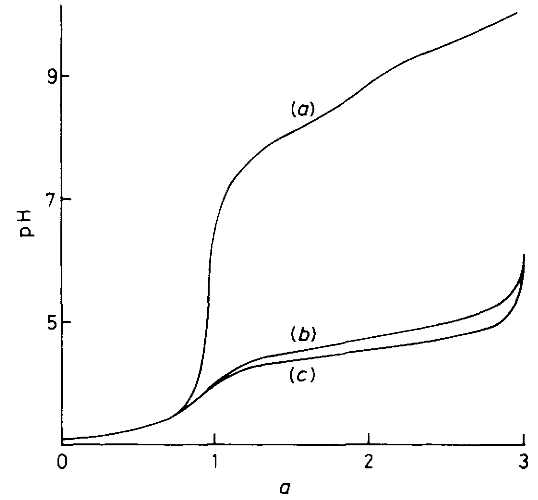


Figure 2. Potentiometric titration curves for $L^4 \cdot 3HClO_4$ alone (*a*) and in the presence of equimolar Co^{II} (1.5×10^{-3} mol dm^{-3}) under argon (*b*) and air (*c*) at $I = 0.2$ mol dm^{-3} and 25 °C

Table 5. Equilibrium constants for the oxygenation of cobalt(II complexes of quadri- and quinque-dentate ligands at 35 °C and $I = 0.20$ mol dm^{-3} (unless noted otherwise)

Ligand	log $K_{O_2,OH}'$ [a]	log K_{O_2}' [b]
L· [c]	0.8	
trien [c]	6.9	
L^2 [d]		7.9
L^3		4.6 ± 0.1
L^4		5.7 ± 0.1
L^5		7.3 ± 0.1
Acyclic N_5 [e]		15.8
L^6 [e]		2.2
L^7 [e]		8.4
L^8 [f]		9.6

[a] $K_{O_2,OH}' = [(CoL)_2(O_2)(OH)^{3+}][H^+]/[CoL^{2+}]^2[O_2]$; units of dm^3 mol^{-1}. [b] $K_{O_2}' = [(CoL)_2(O_2)^{4+}]/[CoL^{2+}]^2[O_2]$; units of dm^6 mol^{-}. [c] Ref. 8. [d] Ref. 9. [e] Ref. 4. [f] Ref. 10.

Table 6. Rate constants (with confidence limits) in dm^3 mol^{-1} s^{-1} for the formation of oxygen adducts at 25 °C and $I = 0.20$ mol dm^{-3}

Ligand	$10^{-2}k_H$ [a]	k_{2H} [a]	k [b]
L^1 [c]	2.5	2.5×10^{-2}	7.1×10^2
L^2 [d]		2.4×10^2	2.2×10^5
L^4	0.66 ± 0.07	$(3.8 \pm 0.4) \times 10^{-2}$	$(3.9 \pm 0.4) \times 10^2$
L^5	30 ± 10	4.7 ± 0.5	$(1.8 \pm 0.4) \times 10^4$

[a] See equation (6) in the text. [b] Second-order rate constant for the reaction between $[CoL]^{2+}$ and O_2. [c] Ref. 8. [d] Ref. 9.

the ratio was 0.48 : 1 at 35 °C and pH 7.90 (initial $[CoL^{2+}] = 1.0 \times 10^{-4}$ mol dm^{-3}). These data suggest formation of μ-peroxo-adducts.

Typical potentiometric equilibrium curves for L^4 with Co^{2+} under both argon and air atmospheres are shown in Figure 2. In air, the formation constants of the 2 : 1 $[CoL]^{2+}$–O_2 complexes could be determined from equation (3). For the triamine

$$K_{O_2} = \frac{[LCo\text{–}O_2\text{–}CoL^{4+}]}{[Co^{2+}]^2[L]^2[O_2]} \qquad (3)$$

L^4, the K_{O_2} value can be calculated from equation (4) derived in the same manner as described previously for tetra-amines.[8,9]

$$K_{O_2} = \frac{[3(\alpha_H)_L - \beta_H]^3[\alpha(\alpha_H)_L - \beta_H c_L]}{2(3c_L - \alpha)^4(\alpha_H)_L{}^2[O_2]} \qquad (4)$$

The titration data (in the region $1 < a < 2.5$) are fitted by equation (4); a plot of the numerator *vs.* the denominator of the right-hand side of equation (4) was linear passing through the origin and the slope gave K_{O_2}.

For the 2 : 1 $[CoL]^{2+}$–O_2 adduct with L^5, equation (5)

$$K_{O_2} = \frac{[4(\alpha_H)_L - \beta_H]^3[\alpha(\alpha_H)_L - \beta_H c_L]}{2(4c_L - \alpha)^4(\alpha_H)_L{}^2[O_2]} \qquad (5)$$

derived from (3) gave the best fit with the pH titration data. The definitions of the terms in this equation and its derivation were described in our previous papers.[8,9] The oxygenation constants obtained are listed in Table 5, along with those for relevant polyamines.

Kinetics of O_2 Adduct Formation.—Reaction of Co^{II} *with* L *in deoxygenated acetate buffers.* By exactly the same procedure applied to L^1 and L^2, the reactive species were shown to be $[Co(O_2CMe)]^+$ and monoprotonated HL^+ and diprotonated H_2L^{2+} for both L^4 and L^5 systems. The common rate law is as in equation (6).[8]

$$\text{rate} = k_H[Co(O_2CMe)^+][HL^+] + k_{2H}[Co(O_2CMe)^+][H_2L^{2+}] \qquad (6)$$

Reaction of preformed $[CoL]^{2+}$ *with* O_2. The rates for L^4 and L^5 were first order in $[CoL^{2+}]$ and first order in $[O_2]$. The overall second-order rate constants were independent of pH and of the buffer concentrations used. All the rate constants are listed in Table 6, along with other relevant values.

Discussion

Complexation Constants.—Table 3 compares the protonation constants of a set of quadri- and quinque-dentate polyamine ligands. The basicities of the macrocycles are significantly affected by the inclusion of the heteroatoms. The lower basicities of the first two (see log K_1 and log K_2 for L^4) or three nitrogens (log K_1 to log K_3 for L^3 and L^5) with respect to the corresponding values for L^1 or L^2 are attributed to the higher electronegativities of the S and O atoms. On the other hand, the relative basicities of the third (L^4) or fourth nitrogens (L^3 and L^5) are reversed. The anchimeric assistance available at the higher proton affinities of neighbouring nitrogens (a nitrogen is not easily protonated if a neighbouring atom is protonated) might explain the lower electron densities available for the corresponding nitrogens of L^4 or L^5.

The overall lower electron densities on the macrocyclic ligands should result in weaker metal–ligand interactions and hence lower K_{ML} values (Table 4). The values for the complexes of Cu^{II}, Co^{II}, Ni^{II}, and Fe^{II} with the 16-membered quinquedentate series L^2, L^3, and L^5 and the 12-membered quadridentate series L^1 and L^4 disclose the stability trend $N > S > O$. The softer S donor will bind more strongly with these transition-metal ions than the harder O donor, despite the similar ligand basicities for S and O (see Table 3). The same trend was seen in the acyclic homologues.[4] A general strong affinity of S for Hg^{2+} is illustrated by the outstandingly large stabilities of the L^4 and L^5 complexes. Another significant demonstration of the effect of the S donors is the appreciable stabilization of the otherwise very air-sensitive iron(II)–tetra-amine complexes in aqueous solution, which made possible the present pH-metric titrations.

It is interesting to compare the relative complexation tendencies of the macrocyclic and acyclic polyamines. Thus, log K_{ML} values for Cu^{II} and Co^{II} with L^5 are higher than the corresponding constants with L^7. Similarly, Co^{II} and Ni^{II} form more stable complexes with L^3 than with the acyclic counterpart L^6. This is a manifestation of the ' macrocyclic effects ' pertaining to all nitrogen polyamines.[19,22] The reason why the complex $[NiL^5]^{2+}$ (log $K_{ML} = 12.66$) is less stable than the acyclic $[NiL^7]^{2+}$ (log $K_{ML} = 15.5$)[4] is not understood.

Dioxygen Complexes.—Like other high-spin cobalt(II) complexes of quinquedentate polyamines, the pink high-spin cobalt(II) complex of L^5 ($\mu_{eff.} = 4.8$ B.M. at pH 7) rapidly interacts with O_2 to form a brown monobridged 2 : 1 µ-peroxo-species, as shown by the measurement of O_2 uptake, pH-metric titration, u.v.–visible absorption, and magnetic measurements ($\mu_{eff.} \approx 0$ B.M.). Its oxygenation constant K_{O_2}' $\{= [LCo\text{-}O_2\text{-}CoL^{4+}]/[CoL^{2+}]^2[O_2] = K_{O_2}/(K_{CoL})^2$ [see equation (37) of ref. 8]$\}$ is nearly comparable with that for $[CoL^2]^{2+}$, but much bigger than that for $[CoL^3]^{2+}$ (see Table 5).

For pink $[CoL^4]^{2+}$ (high spin, $\mu_{eff.} = 4.8$ B.M.), the O_2-uptake measurements, diamagnetism, and lack of e.s.r. signals all indicate a 2 : 1 µ-peroxo-adduct, analogous to the L^1 case.[9] However, unlike $[CoL^1]^{2+}$ which yields a dibridged µ-peroxo-µ-hydroxo-species, the L^4 complex remains as a µ-peroxo-bridged adduct in the comparable pH region, as shown by the pH-metric titration results (the end-point occurs at $a = 4.5$ for L^1 and 3 for L^4). This difference may be rationalized by considering the monobridged complex of L^4 to possess less Co^{3+} and peroxo-characters, in compliance with the soft S donor. The greenish colour of the $[CoL^4]^{2+}$–O_2 adduct may reflect some µ-superoxo-character (*i.e.* less electron density on the co-ordinated O_2). The reduction potentials $E_{\frac{1}{2}}$ for Co in the O_2 adduct are −0.28 V *vs.* s.c.e. with L^4 and −0.40 V with L^1, in agreement with the cobalt oxidation state being somewhat lower in the first case.

Further evidence in support of the $[CoL^4]^{2+}$–O_2 adduct formation comes from a decomposition experiment: after acidification of a solution of the $[CoL^4]^{2+}$–O_2 complex (0.14 mmol dm^{-3}, initial pH 10.15) to pH 1.5 with a few drops of concentrated $HClO_4$ under a nitrogen atmosphere, it slowly (over 1 h) decomposes (as shown by the absorption decrease at 375 nm) to a colourless solution containing Co^{2+}, L^4 (as protonated species), and free O_2. The liberation of O_2 (a two-step wave at −0.15 V *vs.* s.c.e.) was verified polarographically. Moreover, upon raising the solution pH to 10.5 in air, the green $[CoL^4]^{2+}$–O_2 solution was again obtained, the recovery being more than 95% based on the increased absorbance at 375 nm.

Kinetics of Formation of $[CoL]^{2+}$ *and Their* O_2 *Adducts.*—As with other complexes of nitrogen homologues[8] and L^2,[9] the times required for equilibration of pH-metric titrations were the same under anaerobic and aerobic conditions for the present macrocycles (25—30 min with L^4 and *ca.* 10 min with L^5 for each addition of 0.1 mol dm^{-3} NaOH titrant). This suggests slow formation of $[CoL]^{2+}$, followed by fast uptake of O_2.

Analysis of the second-order kinetics for the formation of $[CoL^4]^{2+}$ in acetate buffers under anaerobic conditions suggests a reaction scheme previously found for complexation of L^1 with Co^{2+},[8] Cu^{2+}, Zn^{2+}, Cd^{2+}, and Pb^{2+},[25] the reactive forms of the macrocycles being HL^+ and H_2L^{2+} and of the metal ion, $[M(O_2CMe)]^+$. The magnitudes of the second-order rate constants k_{2H} for the major reaction pathways (hence the overall complexation rates, too) are nearly the same for L^1 and L^4.

The kinetics of formation of $[CoL^5]^{2+}$ in acetate buffers are similar. The rate constant for the diprotonated ligand species, the major reactant in acetate buffer, is larger than the corresponding term for L^4, which accounts for the shorter equilibration time for $[CoL^5]^{2+}$. However, in comparison with $[CoL^2]^{2+}$,[8] this k_{2H} value is much smaller due to the lower ligand basicity.

The rates of O_2 uptake by preformed $[CoL]^{2+}$ chelates in $NH_2C(CH_2OH)_3$ (for L^4) or in acetate buffer (for L^5) exhibit a first-order dependence in $[CoL^{2+}]$ and also in $[O_2]$ for both macrocycles, with rate laws identical to those for L^1 [8] and L^2.[9] The difference in the structures of the O_2 adducts (µ-peroxo-µ-hydroxo with L^1 and µ-peroxo with L^4) does not affect the rate-controlling steps for L^1 and L^4. Comparison of the rates for $[CoL]^{2+}$ formation and O_2 uptake under the same conditions, *e.g.* $[Co^{2+}] = [L] = [CoL^{2+}] = [O_2] = 10^{-4}$ mol dm^{-3} and pH 5 (which actually occur during the potentiometric titrations), indicates that the reaction of $[CoL]^{2+}$ with O_2 is *ca.* 10^4 times faster than the formation of $[CoL]^{2+}$, with both L^4 and L^5. This is compatible with the earlier conclusion that the rate of $[CoL]^{2+}$ formation determines the rate of O_2 uptake in aerobic potentiometric titrations.

The second-order rate constant k for O_2 uptake with $[CoL^5]^{2+}$ is *ca.* 10^2 times larger than that with $[CoL^4]^{2+}$. This is a result of the extra axial co-ordination (either by N or S) that would enhance the dissociation of co-ordinated water (at the *trans* position) upon addition of O_2. A parallel rate difference was seen for L^2 and L^1, see Table 6. The kinetic effect of replacing a nitrogen atom by a less basic sulphur on the O_2 uptake is seen in the *ca.* ten-fold decrease in rate constant k for L^5 *vs.* L^2.

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