Oxygen Carrier and Redox Properties of Some Cobalt Chelates, Including Vitamin B_{12r}

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Summary Equilibrium constants for the reversible dioxygen uptake by neutral cobalt(II) chelates with the same electronic structure show that the tendency to form dioxygen adducts increases with an increase in the ease of oxidation of cobalt(II) to cobalt(III), but on this basis vitamin B_{12r} has a smaller tendency to add dioxygen than is expected.

ELECTRON spin resonance results indicate that the reaction of $Co^{II}LB$ (L = tetradentate ligand; B = axial base), with molecular oxygen can be described as an electron transfer from cobalt to oxygen.[1] The principle role of the cobalt as the 'host', then, is believed to be that of a reducing agent, and the ability of cobalt to transfer the electron should be related to the ability of B and L to force electron density on to cobalt.[2] Previous workers have suggested that variations in oxygen uptake are indeed related to changes in electron density on cobalt,[3] but until now, it was not quantified by measurement of the redox potentials of the systems.

Preliminary results obtained in our laboratories indicate that an empirical correlation does exist between log $K(O_2)$ of the reversible equilibrium (1) and the redox potential of

$$\mathrm{CoL(py)} + \mathrm{O_2} \overset{K(\mathrm{O_2})}{\rightleftharpoons} \mathrm{CoL(py),O_2} \qquad (1)$$

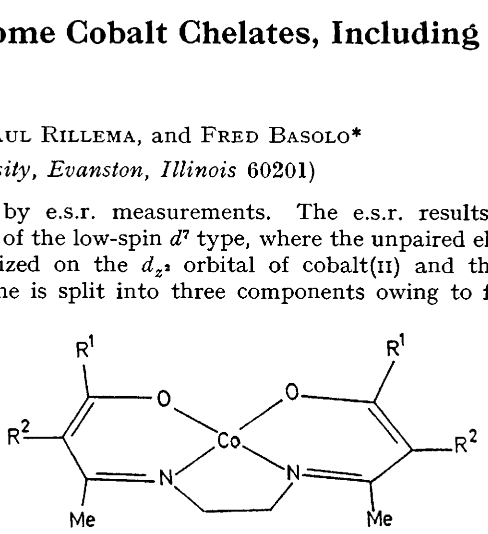
the reversible electrochemical reaction (2) for *neutral* cobalt chelates.

$$\mathrm{Co^{III}L(py)_2^+} \underset{-e}{\overset{+e}{\rightleftharpoons}} \mathrm{Co^{II}L(py)_2} \qquad (2)$$

For the oxygen uptake experiments, CoL(py) was prepared *in situ* by addition of the appropriate amount of pyridine as determined spectrophotometrically, and confirmed by e.s.r. measurements. The e.s.r. results show spectra of the low-spin d^7 type, where the unpaired electron is localized on the d_{z^2} orbital of cobalt(II) and the ^{59}Co hyperfine is split into three components owing to further interaction of the unpaired electron with one axial pyridine.[1] From the change in optical density at an appropriate wavelength accompanying addition of O_2 to a complex [equation (1)], the fraction Y of $CoL(py)O_2$ present was calculated. The equilibrium constant was determined from the Hill relation (3). In all cases, a value of $n = 1$ was

$$Y/(1 - Y) = \frac{\mathrm{CoL(py)}}{\mathrm{CoL(py)O_2}} = KP(\mathrm{O_2})^n \qquad (3)$$

obtained in agreement with the equilibrium expression and e.s.r. results which show the adducts to be one-to-one species.



(A)

R^1	R^2	Compound	Ref.
Me	H	Co(acacen)	3a
Me	Ph	Co(Phacacen)	3a
Me	Me	Co(Meacacen	3a
Ph	H	Co(benacen)	3a
Me	H		
S replaces O		Co(sacsacen) ..	3a, 7, 8

TABLE

Equilibrium constants for oxygen uptake by some cobalt(II) chelates, and halfwave potentials

Compound	Solvent	Temp. (t/°C)	log K (O_2)^a	$E_{1/2}$/V^b
(1) Co(acacen)(py)	Toluene	−31	−0·28	−0·59
(2) Co(Phacacen)(py)	”	−31	−0·89	−0·55
(3) Co(Meacacen)(py)	”	−31	−1·12	−0·54
(4) Co(benacen)(py)	”	−31	−1·36	−0·50
(5) Co(sacsacen)(py)	”	−31	−2·12	−0·33
(6) Co(*p*-MeOTPP)(py)	”	−31	−3·1	−0·23
Co(*p*-MeOTPP)(py)	DMF	−50	−1·20	−0·23
B_{12r}^{c}	”	−50	−1·56	−0·27^f
B_{12r}^{c}	MeOH	−50	−1·98	−0·27^f
(Co[[14]-tetene N_4](py)$^{2+d}$	”	−50	−3·69^e	−0·23

[a] Constants were determined using 1·2% pyridine by volume, except where indicated. Error limits for log $K(O_2)$ are ±0·02; standard state of 1 torr. [b] Measurements were made in neat pyridine solutions containing the compound and 0·1M-$EtNClO_4$. $E_{1/2} = \pm$ 0·01 V *vs.* S.C.E. Potential is for anodic wave, $Co^{II} \rightarrow Co^{III}$, at hanging drop mercury electrode, recorded as reduction potentials. [c] No added pyridine. [d] 10% pyridine. [e] Calculated from activation parameters, $\Delta H° = -$ 11 kcal/mol, $\Delta S° = -$ 66 cal K^{-1} mol^{-1}. [f] The potential for B_{12} was determined in a pyridine solution of B_{12a}.

The half-wave reduction potentials were determined in neat pyridine solution by cyclic voltammetry.[4] The electrode reaction probably corresponds to (2), owing to a similarity in potential whether starting with Co^{III}(acacen)-(py)$_2^+$ (ref. 5) or with Co^{II}(acacen)(py). For the reduction of other tetradentate ligand complexes of cobalt(III), the redox potential was a function of the ligand field strength of the two axial ligands.[6] It is reasonable, then, that as the ligand field strength of one axial ligand goes to zero (five-co-ordinate), the redox potential will still be a function of the ligand field strength of the remaining axial ligand. Consequently, the relative redox potentials of the six-co-ordinate species also provides a measure of the relative redox potentials of the corresponding five-co-ordinate systems.

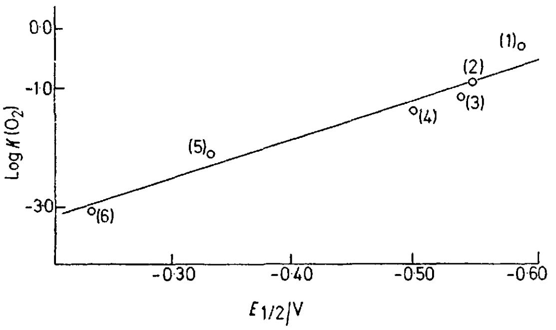
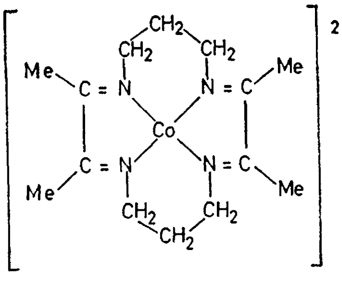


FIGURE. Dioxygen uptake *vs.* redox potential for several neutral CoL(py) complexes. The numbers refer to the compounds in the Table.

The symbols used to represent the neutral cobalt compounds and references to literature preparations are given below structure (A), and αβγδ-tetra-(*p*-methoxyphenyl)-porphinatocobalt(II) is given the symbol Co(*p*-MeOTPP).[9] Values of the equilibrium constants and redox potentials are given in the Table. The Figure shows the linear relation between $E_{1/2}$ and log $K(O_2)$. We have further found that this same approach can be used to predict the oxygen uptake ability of a given cobalt chelate as the axial ligand, B, is varied.[10]

We have found, however, that some systems such as vitamin B_{12r}, hereafter referred to as B_{12r}, and obtained by the reduction of B_{12a} with potassium formate,[11] are anomalous. On the basis of redox potentials (Table), the ease of oxygen uptake should be better for B_{12r} than for Co(*p*-MeOTPP)py. For oxygen uptake measurements in the same solvent, it is found that Co(*p*-MeOTPP)(py) is a better O_2 carrier than is B_{12r}. Two reasonable explanations for this discrepancy are possible: either steric effects of the acetamide groups hinder reversible oxygenation of B_{12r}, or the residual charge on the cobalt decreases the ability of B_{12r} to carry dioxygen reversibly. The *X*-ray structure of B_{12} shows that the negative phosphate group on the benzimidizole 'linkage arm' is *ca.* 9 Å from the cobalt,[12] certainly too far to neutralize completely the positive charge on the cobalt–corrin unit.

In an effort to test the importance of charge on the dioxygen uptake properties of these systems, a dipositively charged cobalt chelate of similar redox potential in neat pyridine ($E_{1/2}$ = − 0·23) to that of Co(*p*-MeOTPP) was examined. The cation[13] [Co([14]-tetene N_4]$^{2+}$ (B) forms a five-co-ordinate complex with pyridine which has e.s.r. properties similar to those of Co(*p*-MeOTPP)(py). Furthermore, four imine bonds constrain the macrocyclic ligand to planarity which means the dioxygen uptake is not subject to steric effects.



(B)

Reversible oxygenation experiments in methanol show that B_{12r} is 50 times better as an oxygen carrier than is the [Co([14]-tetene N_4)(py)]$^{2+}$ complex. These experiments indicate that residual charge has a direct influence on the ability of cobalt chelates to carry dioxygen reversibly.

Thus, B_{12r} falls between the neutral Co(*p*-MeOTPP)py and the dipositively charged $[Co([14]\text{-tetene } N_4)(py)]^{2+}$.

In conclusion, the redox parameter is an important method of assessing the oxygen uptake ability of similarly charged cobalt complexes. The results show that among species of similar redox potential but differing charge, ***neutral*** metal chelates function as the best oxygen carriers.

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[1] D. Diemente, B. H. Hoffman, and F. Basolo, *J. Amer. Chem. Soc.*, 1970, **92**, 61.

[2] P. A. Rock, *Inorg. Chem.*, 1968, **7**, 837.

[3] (a) A. L. Crumbliss and F. Basolo, *J. Amer. Chem. Soc.*, 1970, **92**, 55. (b) H. C. Stynes and J. A. Ibers, *ibid.*, 1972, **94**, 1559. (c) G. Tauzher, G. Amiconi, E. Antonini, M. Brunori, and G. Costa, *Nature*, 1973, **241**, 222. (d) F. A. Walker, *J. Amer. Chem. Soc.*, 1973, **95**, 1154.

[4] R. S. Nicholson and I. Shain, *Analyt. Chem.*, 1966, **36**, 706.

[5] G. Costa, G. Mestroni, A. Puxeddu, and E. Reisenhofer, *J. Chem. Soc.* (*A*), 1970, 2870.

[6] D. P. Rillema, J. F. Endicott, and E. Papaconstatinou, *Inorg. Chem.*, 1971, **10**, 1739.

[7] We thank Dr. J. L. Corbin of Kettering Scientific Research in Yellow Springs, Ohio, for a gift of sacsacen.

[8] R. M. C. Wei and S. C. Cummings, *Inorg. Nuclear Chem. Letters*, 1973, **9**, 43.

[9] F. A. Walker, *J. Amer. Chem. Soc.*, 1970, **92**, 4235.

[10] M. J. Carter, D. P. Rillema, and F. Basolo, unpublished observation.

[11] J. H. Bayston, N. K. King, F. D. Looney, and M. E. Winfield, *J. Amer. Chem. Soc.*, 1969, **91**, 2775.

[12] D. C. Hodgkins, J. Kamper, M. MacKay, J. Pickworth, K. N. Trueblood, and J. G. White, *Nature*, 1956, **64**, 178.

[13] (a) S. C. Jackels, K. Farmery, E. K. Barefield, and D. H. Busch, *Inorg. Chem.*, 1972, **11**, 2893; (b) D. P. Rillema and J. F. Endicott, *J. Amer. Chem. Soc.*, 1972, **11**, 8711.