Dynamics of dioxygen binding to vacant cobalt(II) sites in lacunar cyclidene complexes: barrier-free oxygenation

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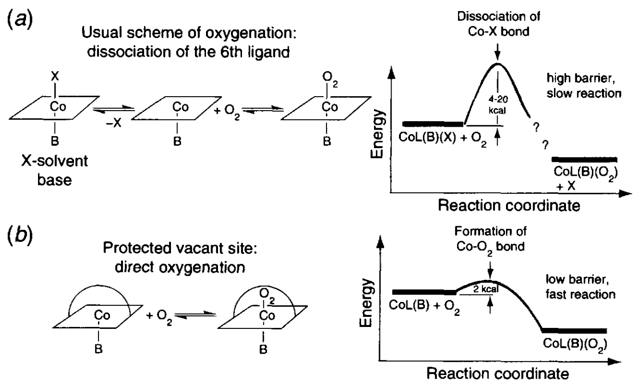
The kinetics of O_2 binding to a demonstrably vacant coordination site on a cobalt(II) ion are determined, revealing a radical-like character for the reaction, with a very low activation barrier (*ca.* 1–2 kcal mol^{-1}) and large entropically controlled rate constants, whose values approach those for myoglobin and haemoglobin (up to 10^8 dm^3 mol^{-1} s^{-1}).

Co^{II} complexes constitute the most popular and successful class of synthetic O_2 carriers.[1] In addition to the fundamental importance of understanding the dynamics of oxygen binding to Co^{II} complexes, rapid binding and/or dissociation rates are critical to many applications of O_2 carriers. In the limited number of kinetic studies reported,[2–8] the oxygenation rates of Co^{II} complexes were found to be slow compared to those for O_2 binding to natural dioxygen carriers. Second-order rate constants are in the range 10^7–10^8 dm^3 mol^{-1} s^{-1} for natural compounds,[9] and, with a few exceptions,[6,8] 2–3 orders of magnitude smaller for synthetic Co complexes[2]. Bond formation between the doublet state of low-spin d^7 Co^{II} ion and the triplet O_2 molecule is expected to be much faster than has been observed. The probable source of this behaviour is shown in Scheme 1(*a*). The dissociation of a Co– solvent or Co–ligand bond may be involved in the rate-determining step in 1 : 1 Co–O_2 adduct formation.[2]† This is strongly supported by recently determined activation volumes for reaction (1).[8] Consequently, the reported kinetic parameters do not correspond directly to the process of forming the Co–O_2 bond. Instead, they characterize the rather trivial process of axial ligand dissociation from Co^{II}. Additional complications arise because of the rapid formation of dinuclear complexes by Co–O_2 adducts [eqn. (2)].[2c,5,6a]

$$CoL + O_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} CoL(O_2) \qquad (1)$$

$$CoL(O_2) + CoL \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} CoL(O_2)CoL \qquad (2)$$

From the preceding discussion, we conclude that a vacant or unusually labile coordination site on Co^{II} is necessary to follow the dynamics of Co–O_2 bond formation [eqn. (1)]. In the systems reported here, the ligand environment of lacunar cyclidenes provides such vacant Co^{II} sites and has helped us elucidate the kinetic and mechanistic aspects of this process. The lacunar structures of the ligands prevents the coordination of solvent or axial base [pyridine (py) or *N*-methylimidazole (mim)], but not O_2 molecules, in the sixth position.[10,11] Co^{II} cyclidene complexes with C_4 and C_5 bridges are five-coordinate in the presence of py and mim, invariably with the axial base bound externally and opposite the O_2 binding site. Moreover, the 1 : 1 O_2 adducts of these lacunar Co^{II} cyclidene complexes do not tend to form μ-peroxo dimers,[10] leading us to expect simple O_2 binding and dissociation kinetics. Further, autoxidative ligand destruction is very slow on the timescale for O_2 binding (< 10^7 ×).[12]



Scheme 1

Kinetics were followed with a cryogenic stopped-flow instrument over the temperature range −75 to 0 °C.‡. The low temperatures used offer three advantages: (*i*) the reactions may be slower, facilitating more precise rate determinations; (*ii*) the equilibrium of eqn. (1) is shifted toward oxygen adduct formation, providing greater absorbance changes upon reaction; and (*iii*) competing autoxidation reactions are retarded. The observed absorbance changes over 320–480 nm (Fig. 1) agree with data obtained under equilibrium conditions.[10b,c] The observed rate constants (excess O_2) are independent of Co concentration and increase linearly with increasing O_2 concentration, supporting the simple reversible model [eqn. (1)]. The binding and dissociation rate constants k_1 and k_{-1} were found from eqn. (3).[13]

$$k_{obs} = k_1[O_2] + k_{-1} \qquad (3)$$

Equilibrium constants, K_{eq}, calculated from the rate constants are in a good agreement with those obtained earlier by spectrophotometric O_2 titrations.[10] Arrhenius plots were used to determine activation parameters for both the forward and reverse reactions (1).[13] The kinetic parameters are summarized in Table 1.

If solvent dissociation were a kinetically significant factor in a process for O_2 binding,† k_1 would be sensitive to the nature of the solvent. When a strong axial base (mim) is coordinated to Co^{II}, the kinetic parameters for the forward reaction are essentially independent of solvent. Therefore, dissociation of a solvent ligand is not important in the present case, in contrast to systems described elsewhere.[2,8] The negative values of the activation entropy support this conclusion, indicating a decrease in degrees of freedom at the transition state. This result is most consistent with bond forming.

The kinetic data reported here characterize the distinctive process of binding a free O_2 molecule to a vacant site at Co^{II}

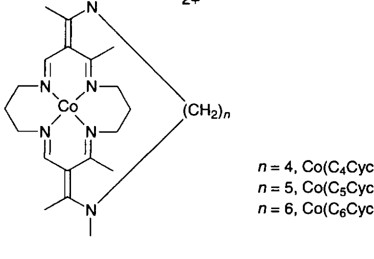


Table 1 Kinetic parameters for O_2 binding at 25 °C

		Binding			Dissociation		
Compound	Solvent (base)	k_1/dm^3 mol^{-1} s^{-1}	$\Delta H_1^\ddagger$/ kcal mol^{-1}	$\Delta S_1^\ddagger$/cal K^{-1} mol^{-1}	k_{-1}/s^{-1}	$\Delta H_1^\ddagger$/ kcal mol^{-1}	$\Delta S_{-1}^\ddagger$/cal K^{-1} mol^{-1}
Co(C_5Cyc)	Me_2CO (mim)	2.0×10^6	0.7	−28	1.1×10^4	18.4	22
Co(C_5Cyc)	MeCN (mim)	3.7×10^6	0.6	−27	9.2×10^3	17.8	19
Co(C_5Cyc)	MeOH (mim)	2.4×10^6	2.0	−23	1.6×10^4	18.6	23
Co(C_5Cyc)	Me_2CO (py)	2.3×10^6	2.6	−21	1.0×10^5	15	15
Co(C_4Cyc)	Me_2CO (mim)	5.4×10^4	2.2	−31	3.6×10^5	15.6	19
Co(C_6Cyc)[a]	Me_2CO (mim)	1×10^8	4	−10			
CoMb (SW)[b]	H_2O	4.8×10^7	9.2	7.6	4×10^3	17.8	17.7
FeMb (horse)[c]	H_2O	1.4×10^7	5.5	−7.2	1.0×10^1	19	9.4

[a] Preliminary data. [b] Ref. 9. [c] E. Antonini and M. Brunori, *Hemoglobin and myoglobin in their reactions with ligands*, North-Holland, Amsterdam, 1971.

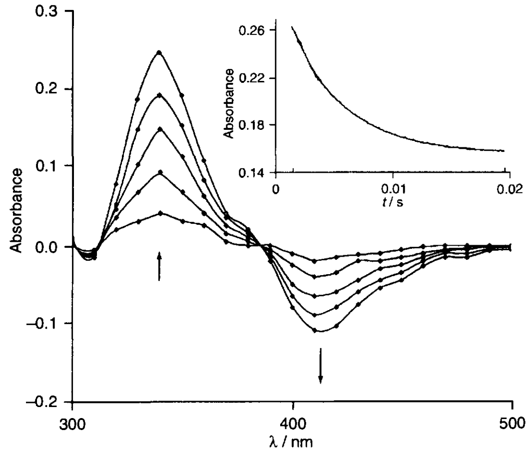


Fig. 1 Spectral changes [*vs.* spectrum of Co(C_5Cyc)] during the reaction of Co(C_5Cyc) with O_2 in MeCN–mim (1.5 mol dm^{-3}) at −40 °C. Spectra were registered 0.001, 0.002, 0.004, 0.007 and 0.018 s after mixing the reagents. C_{CoL} = 2.5×10^{-5}, C_{O_2} = 1.25×10^{-4} mol dm^{-3}. Inset: kinetic trace at 420 nm, superimposed with one-exponential decay curve fit.

[Scheme 1(*b*)]. The most striking feature of this reaction is its very low activation enthalpy (1–2 kcal mol^{-1}; cal = 4.184 J), the first such example corresponding to Co–O_2 bond formation. This result indicates that no significant energy expenditure is necessary to achieve the transition state. The interaction between Co^{II} and O_2 as they combine within the 'dry cavity' of the cyclidene ligand is apparently similar to a radical combination process. Earlier studies have pointed out the parallel behaviour of the reactions of macrocyclic Co^{II} complexes with O_2 and with alkyl radicals.[6a] Activation enthalpies for oxygenation of synthetic Co^{II} complexes have previously been found in the range 4–20 kcal mol^{-1}.[3,4] In all of those cases, it was concluded that the dissociation of a sixth ligand occurs prior to, or simultaneously with, Co–O_2 bond formation.

Despite the very small activation enthalpy for the oxygenation of Co^{II} cyclidenes in the presence of axial base, the rate constants k_1 show a strong dependence on bridge length ($10^3 \times$), bracketing the value of k_1 for Co myoglobin (Table 1). This entropic effect is attributed to the spatial constraints associated with entrance of O_2 into the cavity. The same structural feature which protects the vacant Co^{II} site from coordination by solvent or a large nitrogen base also partially restricts the availability of this vacant site for O_2. However, the difference in size between O_2 and solvent/base molecules allows one to optimize cavity size for rapid O_2 binding. In case of Co^{II} cyclidenes, the C_6 bridge provides such an optimum. The rate of oxygenation of [Co(C_6Cyc)(mim)]$^{2+}$ is slightly greater than that for Co(Mb) (Table 1), and almost 2 orders of magnitude greater than that for Co(C_5Cyc). The variation in the oxygen affinities of Co^{II} cyclidenes with bridge length is primarily determined by the differences in their rates of O_2 binding.

The kinetic parameters for the dissociation of the Co(C_5Cyc) O_2 adduct are also virtually solvent independent, but sensitive to the nature of the axial base. The significant decrease in k_{-1} when py is replaced with mim (an enthalpic effect) explains why complexes with mim have O_2 affinities 10–20 times greater than those with py.[10] The large values of the activation enthalpies and the positive values of activation entropy correspond to breaking of the Co–O_2 bond at the transition state. The apparent insensitivity of the dissociation rate to bridge length suggests that cavity size does not affect Co–O_2 bond strength.

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Footnotes

† The oxygen dependence associated with the kinetics of the solvent dissociation/oxygen binding process [Scheme 1(*a*)] can be rationalized with either a pre-equilibrium or steady-state model.

‡ Hi-Tech Scientific (England) SF-41 CryoStopped-Flow instrument equipped with a stainless-steel mixing chamber.

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