received support as a National Science Foundation Undergraduate Summer Research participant.

Registry No. $Mo(CN)_8^{4-}$, 17923-49-8; $Mo(CN)_8^{3-}$, 17845-99-7; MnO_4^-, 14333-13-2; Mn^{2+}, 16397-91-4.

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Interaction of Oxygen with the Cobalt(II)-Histidine Complex in Strongly Basic Solution

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Received June 4, 1973

Cobalt(II) ions can coordinate with two molecules of L-histidine to form an octahedral complex in which each ligand is terdentate both in solution[1] and in the solid state.[2] The complex reacts rapidly with oxygen in solution to form $Co_2(his)_4O_2$ (his = histidine), almost certainly a binuclear complex containing an -O-O- bridge.[3] The kinetics of the reversible interaction of O_2 with the cobalt(II) complex in aqueous solution have been investigated.[4] These are consistent with a two-step mechanism *via* the formation of a 1:1 Co-O_2 species, which is present, however, only in undetectable concentrations. The 2:1 oxygen adduct picks up more O_2 only very slowly to give a mixture of cobalt(III) mononuclear products.[5]

The addition of base to Co(L-his)$_2$ produces a blue solution as soon as the pH reaches around 11.5. This was apparently first noted by McDonald and Phillips,[1] who examined the pmr of the blue solution. They concluded that there had been ionization of the proton at the 3-nitrogen position of the imidazole rings with the concomitant formation of a tetrahedral 2:1 histidine-cobalt(II) complex, with the four nitrogens binding and detachment of the carboxylate groups. Subsequent examination of cobalt(II)-histidine solutions from pH ~10 to 1 *M* OH^- indicated that the spectra cannot be interpreted simply in terms of an equilibrium between one octahedral and one tetrahedral species.[6,7] However, one species with a violet color is fully developed in solutions 1 *M* in NaOH[6,7] and although it is not possible to establish the equivalents of protons lost per cobalt(II), the spectrum strongly suggests that it is a tetrahedral complex with four nitrogen donor atoms,[7] and we shall refer to it as such. The tetrahedral, like the octahedral form, picks up O_2 also and turns brown.[1,6,7,8] The stoichiometry of the oxygenation is Co:O_2 = 2:1, but the product has markedly different spectral characteristics from that obtained from the octahedral form.[8] It has only a single strong absorption maximum at 366 nm, whereas the oxygenated octahedral cobalt(II) complex (pH ~10) shows bands at 385 and 329 nm.[8] This difference is attributed to the formation of a double O_2,OH-bridged product from the tetrahedral and a single O_2-bridged product from the octahedral starting material.[7] In this note we report on the kinetics of O_2 uptake by the tetrahedral species in 1 *M* hydroxide solution, as well as brief examination of some other amino acid and peptide complexes.

Experimental Section

Materials. All chemicals were reagent grade. The L-histidine was supplied by Nutritional Biochemicals. Cobalt(II) solutions were standardized by titration with EDTA using murexide indicator.

Kinetic Experiments. The formation of the oxygenated histidine complex was followed spectrophotometrically using a Lucite stopped-flow apparatus. The optical density increases at 360-380 nm gave rate constants for the fast reaction which were identical with those obtained from the smaller optical density increase at ~475 nm. The slower second step in the reaction was followed by observing the subsequent slow decrease in optical density at 475 nm. The reactions were initiated in most cases by mixing a deoxygenated solution of cobalt(II), L-histidine, and either NaOH or KOH with a solution containing oxygen. Reactions were run both with 1 *M* OH^- in each syringe and with 2 *M* OH^- in the aqueous oxygen solution. At the low cobalt(II) concentrations necessary for observing the reaction using stopped-flow techniques a large excess of histidine was essential in order to prevent formation of cobalt-hydroxy species before the reaction with oxygen could be completed. Runs with low histidine: Co(II) ratios were achieved by allowing a low-pH solution of histidine and cobalt(II) to react with a solution containing oxygen and the desired concentration of OH^-. Solutions with NaOH and KOH as base gave identical results. Most kinetic runs were at a total $[OH^-]$ of 1.0 *M* but some runs at $[OH^-]$ up to 2.0 *M* indicated only a small rate dependence upon the OH^- concentration. No attempt was made to control ionic strength in these ≥ 1.0 *M* solutions. In the kinetic runs the concentration of Co(II) complexes was ≥ 10 times that of O_2 and pseudo-first-order rates were obtained. The kinetics of O_2 uptake by other cobalt(II) complexes were followed spectrally at appropriate wave lengths.

Results and Discussion

Our first experiments were carried out using a twofold ratio of histidine:Co^{2+} in 1 *M* OH^- concentration. It was usually difficult to maintain a homogeneous solution long enough to study the reaction with oxygen, when using the low cobalt(II) concentrations necessary to obtain reaction times within the stop-flow range. By mixing the cobalt(II)-histidine solution at low pH with O_2-2 *M* KOH or NaOH, the reaction, however, could be studied, the octahedral-tetrahedral conversion having been checked to be complete within mixing. In the ranges of [Co(II)] = 1-44 m*M*, [histidine] = 2-88 m*M*, and [KOH] = 1.0 *M* the oxygenation was strictly second order at 25°, $k = 1.8 \pm 0.2 \times 10^3\ M^{-1}\ \text{sec}^{-1}$ (Table I). Only one reaction step was observed although a subsequent slower reaction (see below) may have been masked by precipitation.

When we used histidine:Co^{2+} ratios >2:1, it was easier to maintain dilute solutions of reactants, but then we found the surprising result that there was a marked dependence of the second-order rate constant associated with a fast step on the concentration of free histidine (Figure 1). The full rate law is shown in (1), where *Co(his)$_2$ represents the tetrahedral

$$\text{rate} = k_{\text{obsd}}[O_2] = k_1[{}^*\text{Co(his)}_2][O_2] + k_2[{}^*\text{Co(his)}_2][\text{his}][O_2] \qquad (1)$$

species which is considered completely formed in 1 *M* $[OH^-]$. At 25° and $I = 1.0\ M$, $k_1 = 1.8 \times 10^3\ M^{-1}\ \text{sec}^{-1}$ and $k_2 = 2.2 \times 10^6\ M^{-2}\ \text{sec}^{-1}$ (see Table I). In the experiments where excess histidine was used, it was easy to see, even visually, an

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Table I. Kinetic Data for Uptake of O_2 by Co(II) Complexes in Solution at 25°

[Co(II)], mM	[Histidine],[a] mM	k_{obsd}, sec^{-1}	$10^3 k_{obsd} \cdot$ [Co(II)]$^{-1}$, M^{-1} sec^{-1}
0.22	4.0	1.9	8.6
0.22	8.4	4.1	19
0.22	17	7.7	35
0.44	7.9	8.2	19
0.44	12	14	32
0.44	17	15	38
0.88	0.0	1.7	1.9
0.88	0.84	3.2	3.6
0.88	7.0	18	20
0.88	11	19	21
0.88	16	33	38
1.76	0.88	16	9.1
1.76	5.3	45	25
1.76	14	88	50
44	0.0	76	1.7

[Co(II)], mM	[Glycylglycine],[b] mM	k_{obsd}, sec^{-1}	$10^3 k_{obsd} \cdot$ [Co(II)]$^{-1}$, M^{-1} sec^{-1}
0.28	19.5[c]	2.6	9.3
0.28	9.5[c]	2.3	8.2
0.28	19.5[c]	2.3	8.2
0.55	9.0[d]	3.6	7.1
0.55	9.0[d]	4.1	7.5
1.10	18.0[d]	10.5	9.5

[Co(II)], mM	[Glycylglycinamide],[e] mM	k_{obsd}, sec^{-1}	$10^4 k_{obsd} \cdot$ [Co(II)]$^{-1}$, M^{-1} sec^{-1}
0.11	5.0[f]	7.7	7.0
0.22	15[f]	20	9.0
0.44	16[f]	32	7.2

[a] [Free histidine] = [histidine]$_{total}$ − 2[Co(II)] all at 1 M KOH. [b] Free ligand concentration. [c] pH 11.6. [d] pH 12.3. [e] Total ligand concentration. [f] pH 12.

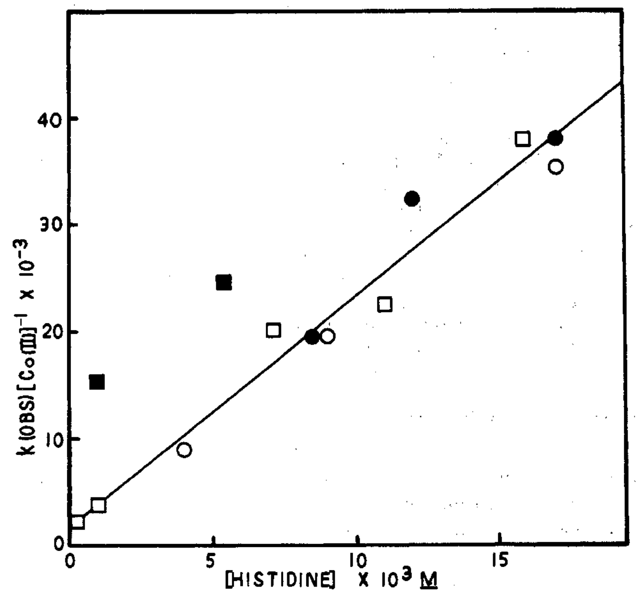

Figure 1. Plot of k_{obsd}[Co(II)]$^{-1}$ × 10^{-3} M^{-1} sec^{-1} *vs.* [histidine] × 10^3 M. [Histidine] is uncomplexed ligand calculated as [histidine]$_{total}$ − 2[Co(II)]: [Co(II)] = 0.22 × 10^{-3} M (○); [Co(II)] = 0.44 × 10^{-3} M (●); [Co(II)] = 0.88 × 10^{-3} M (□); [Co(II)] = 1.76 × 10^{-3} M (■).

initial deep brown intermediate, fairly quickly going to a lighter brown color. This intermediate plunged rapidly into a buffer at pH 9–10 gave a spectrum identical with that of the singly bridged oxygenated complex and so *could* be such a species which then slowly reacts in 1 M OH^- to give the doubly final product (obtained under all histidine:Co^{2+} conditions) in much the same way as is observed with the cobalt(II)-triethylenetetramine system.[9] Experiments showed that all the oxygen had been taken up in forming the intermediate. The conversion of the intermediate to the final product was first order with a rate constant ~0.03 sec^{-1} at 25° independent of initial cobalt(II) and histidine concentrations.

The different product from oxygenation of the tetrahedral species, compared with the octahedral, could arise from the reaction of the latter with 1 M OH^- ion. We can now be certain, however, that the tetrahedral species interacts directly with O_2. The value for k_1 compared with the corresponding value for the octahedral species (3.5 × 10^3 M^{-1} sec^{-1})[4] indicates that there would have to be over 50% octahedral species present to occount for the uptake characteristics and this is extremely improbable.[6,7] Further, the uptake rate would be very dependent on [OH^-] and little difference is observed in 1 M and 2 M KOH. Finally, the rate enhancement by free ligand is unique to the tetrahedral species, since we have checked that it does not occur with the octahedral complex.

The k_1 and k_2 paths correspond to transition complexes of the compositions $[Co(his)_2O_2]^{\ddagger}$ and $[Co(his)_3O_2]^{\ddagger}$, respectively. The first presumably refers to direct interaction of O_2 with the tetrahedral species to form a 1:1 adduct, of unknown stereochemistry, and resembles here the behavior of the octahedral complex, with a remarkably similar rate constant. We cannot explain with conviction the second path. There may be an equilibrium among the tetrahedral species, histidine, and an adduct (containing three coordinated histidines), which reacts with O_2 in a rate-determining step to form a product which rapidly transforms to the singly bridged intermediate.

We have examined briefly other cobalt(II) complexes with related ligands to see how their behavior compares with that of histidine. Histamine forms a deep blue (tetrahedral) complex with cobalt(II) in strong base.[7]

A 100-fold excess of ligand is necessary to avoid precipitation so that it is difficult to examine the effect of ligand on the rate of oxygen uptake. We measured a second-order rate constant of 1.5 × 10^4 M^{-1} sec^{-1} at 25° (I = 1.0 M KOH). Second-order rate constants for the reaction of cobalt(II) complexes of glycylglycine and glycylglycinamide with O_2 at pH ≥11.5 are 8.0 × 10^3 and 7.8 × 10^4 M^{-1} sec^{-1} at 25°. At these pH's the complexes are probably low-spin octahedral complexes which have lost peptide and amide protons.[10] The value for the glycylglycine complex is quite close to that indirectly determined by earlier workers at much lower pH (~1.0 × 10^3 M^{-1} sec^{-1}).[11] The rate constants are insensitive to free ligand concentration. The values for the rate constants are monotonously similar to those for many other octahedral cobalt(II) complexes examined.[3] In all the complexes examined the fast reactions are followed by slower reactions which may involve double-bridge formation or even breakdown to mononuclear cobalt(III) complexes since the latter is known in certain cases to occur quite rapidly.[10]

Acknowledgment. We are grateful to the National Science Foundation which supported this work (Grant GP 16580).

Registry No. Co(L-histidine)$_2$, 43176-10-9; histidine, 7006-35-1; glycylglycine, 556-50-3; glycylglycinamide, 20238-94-2.

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