Molecular Recognition by Protonated O-BISDIEN and Its Metal Complexes

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The protonated forms of the basic ligand 1,4,7,13,16,19-hexaaza-10,22-dioxacyclotetracosane or [24]ane-N6O2 (O-BISDIEN) recognize certain anions. The compounds studied are malonic acid, phosphoric acid, glycine, acetohydroxamic acid, and potassium phosphonous formate (KOOCPH(O)(OK)) in their various protonated and anionic forms. Detailed formation constants measuring this recognition are reported for all species found. [24]-ane-N6O2 also forms 1:1 and 1:2 ligand to divalent transition metal ion complexes, with a variety of protonated species and one dinuclear hydroxo bridged form. All of these cationic complexes of O-BISDIEN exhibit recognition toward the same substrates. The quantitative formation constants for the species formed are also reported. Finally, equilibria and kinetics are reported for the formation of dioxygen complexes of selected O-BISDIEN–dicobalt–substrate systems. All the H-bonded and metal ion coordinated species formed are discussed in the light of the principles of molecular recognition.

Introduction

Chloride and bromide ions were found to coordinate in aqueous solution to protonated polyamine cryptands as early as 1975.[1] By NMR and Cl^- ISE methods the stability of the H-bonded complex formed between an H_4L^{4+} and Cl^- was reported as >4.5 log units where L is an N_4 macrocyclic ligand. This complex showed remarkable selectivity over that formed by the larger Br^- ion.[2] Since then many simple ions were studied by NMR to determine their degree of recognition by various protonated polyamine cryptands.[3,4] Potentiometric methods were later introduced in order to make more accurate measurements and to help distinguish the more minor interactions with cryptands, in particular with O-BISTRIEN.[5-8]

O-BISDIEN (**1**) the ligand of this study, is an H_6L macrocyclic ligand possessing a pair of diethylenetriamine moieties connected by means of two five-atom diethyl ether bridges. It is capable of up to hexaprotonation and binuclear metal ion coordination. The binuclear centers have in turn been shown to react with various bridging molecules or ions.[9-13] In related work several tetraamine macrocycles were studied for complexation with ATP.[14,15] In O-BISDIEN, the simplest example of bridge formation between two metal centers is the OH^- ion[16] which forms bridging complexes with great facility. Other examples of bridging groups studied in this laboratory are imidazolate, oxalato, mesoxalato, glycinato, catecholate, and 3,5-disulfocatecholate, which form with various stabilities with the various protonated forms of O-BISDIEN alone or with protonated mononuclear metal complexes or with its dinuclear complexes.[9-13,17] Even without metal ion involvement this macrocyclic ligand is remarkably capable in the recognition of negative substrates and can even catalyze hydrolytic reactions and syntheses such as are illustrated in the work with ATP, AMP, and ADP and other negative anions with its tetra-, penta- and hexaprotonated forms.[18-23] Oxalate, malonate, sulfate, maleate, and fumarate had also been a subject of complex formation with cyclic, bicyclic, and acyclic polyamines but not with O-BISDIEN.[24] The X-ray crystal structure of O-BISDIEN hexahydrochloride shows that in the solid state one chloride seems to be more intimately associated unsymmetrically with two pairs of opposite N^+–H groups.[25,26] Any interferences concerning the folding of O-BISDIEN free base or of its complexes are largely irrelevant since the structure is that of a hexahydrochloride, whose chloride counterions and aquo molecules are apparently largely responsible for the observed bowl conformations found.

In the case when the metal ion is cobalt(II), an additional peroxide bridge forms under dioxygen, concomitantly converting cobalt(II) to formally cobalt(III) (**2**). In peroxo-bridged complexes of this type, if the other bridging ligand is a reductant, a redox reaction may occur, resulting in the net flow of electrons from the substrate to the peroxide resulting in oxidation of the substrate and reduction of the dioxygen to water. Such oxidation studies had been performed on oxalate, ketomalonate, and catechols, and others are in progress.[10-13,17]

The purpose of the present work is to demonstrate this recognition phenomenon by the introduction of various types of new bridges. While the emphasis is on recognition, for some systems this paper also treats dioxygen complex formation between O-BISDIEN, cobalt, and ternary ligand in the presence and absence of dioxygen. These ligands are glycine, acetohydroxamic

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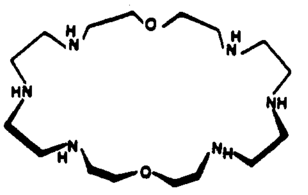
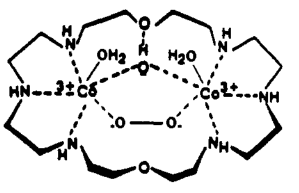
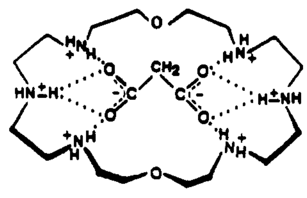


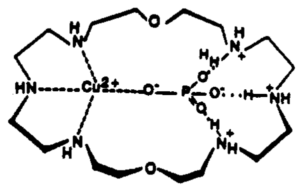
1 O-BISDIEN



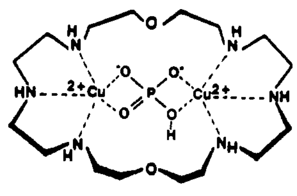
2 O-BISDIEN hydroxo-bridged dicobalt dioxygen complex



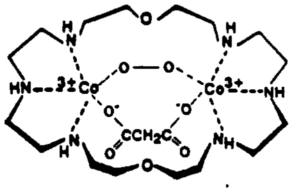
3 Possible H-bonding modes in the complex H_6BdMal^{4+}



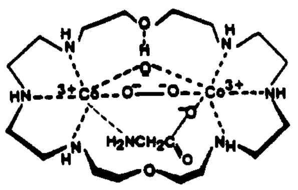
4 Possible coordinate bonding in $[Cu(HPO_4)H_3Bd]^{3+}$



5 Possible coordindate bonding in $[Cu_2(HPO_4)Bd]^{2+}$



6 Suggested coordinate bonding in $[Co_2O_2(Mal)Bd]^{2+}$



7 Suggested coordinate bonding in $[Co_2(OH)(Gly)O_2Bd]^{2+}$

acid, potassium phosphonous formate, and malonic acid, which were not subjects of previous equilibrium studies with O-BISDIEN.[27]

Experimental Section

Potentiometric Titrations. All pH calibrations with standard dilute strong acid at 0.100 M ionic strength were performed in order to measure hydrogen ion concentration directly; hence the symbol containing brackets p[H] is used throughout to emphasize its meaning: $-\log_{10}[H^+]$.

Reagents. O-BISDIEN was used as the colorless, semicrystalline hexahydrochloride obtained as a generous gift from Jean-Marie Lehn of Strasbourg, France. All other substances used were reagent grade chemicals. The titrant KOH solutions were prepared by standard volumetric techniques with Dilut-IT ampules from Baker. Argon was used to protect the experiments from CO_2 contamination, while the O_2 employed was first purged through a dilute KOH trap.

Potentiometry Particulars. Each titration utilized at least 10 points per neutralization of a proton or hydrolytic reaction (about 65 points for hexaprotonated O-BISDIEN) plus some extra points beyond neutralization. The p[H] range was in general from >2 to <11. The pK_w was 13.78, which was kept fixed during refinements. Most of the results are based on single titrations, reflecting the scarcity of O-BISDIEN. The program BEST[28] was used for calculation.

Estimated errors are temperature <0.02 °C, KOH delivery <1 ppt, KOH and HCl concentrations 1 ppt, p[H] reproducibility, <0.002 in buffer regions, absolute p[H] accuracy <0.001 at low pH and <0.01 at high p[H], millimoles of O-BISDIEN <3 ppt, millimoles of other ligands <2 ppt, and millimoles of Cu(II) and Co(II) <2 ppt. Reported errors in the constants were computed on the basis of the deviation in each constant necessary to double the standard deviation of the pH interval which the constant represents. This procedure tends to overestimate the errors and therefore is "safe".

Ligands Alone. A rather standardized procedure was followed for each prototropic substance.

Into a 100-mL jacketed-thermostated titration cell, equipped with p[H] and reference electrodes, fitted with inert gas (argon) inlet–outlet and a 10-mL precision piston buret, were placed 5.000 mL of 1.000 M KCl (to set the ionic strength at 0.100) and a weighed quantity corresponding to 0.1 mmol of ligand and 45.00 mL of distilled, degassed water. This makes 50.00 mL of an experimental solution containing 2.0 × 10^{-3} M ligand, which was then allowed to stand at least $^1/_2$ h at 25.0 °C. Pairs of p[H] vs milliliters of 0.1027 M KOH added were recorded at equally spaced intervals at every 0.100 mL of base until somewhat more base was added over that necessary to neutralize the titratable protons present on the ligand.

Acidification of amino acids and of salts of acids and back-titration was achieved with 0.0941 M HCl.

Metal–Ligand Systems. Solutions were prepared as above except appropriate aliquots of standardized metal chloride solutions were added to achieve integral ratios of metal ion to ligand of 1:1, 1:2, and 1:3. The potentiometric equilibrium data were obtained as above, but more time was allowed for equilibration.

Metal–Binary Ligand Systems. As described above, ~60 mg (0.1 mmol) of O-BISDIEN·6HCl was weighed directly and mixed with 0.1 and 0.2 mmol of the metal ion, 0.10 mmol of the bridging ligand, and 5.00 mL of 1.00 M KCl and diluted to 50.00 mL with redistilled, degassed water. Some regions of the data collected required up to 15 min between recordings.

Co(II) Systems under O_2. Oxygen was introduced to O-BISDIEN Co(II) systems and titrated with 0.500-mL increments spaced at least 6 h apart in order to reach an acceptable compromise between duration of the experiment and its accuracy.

Electronic Spectra. UV–vis spectra were measured generally from 600 to 300 nm with a PE Model 553 spectrophotometer equipped with

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(28) Motekaitis, R. J. *Determination and Use of Stability Constants*, 2nd ed.; VCH Publishers: New York, 1992.

a constant-temperature cell compartment with a 1.000-cm quartz cell and prebalanced with the pure reference electrolyte solution.

Kinetic measurements were followed in an apparatus consisting of a 1.000-cm quartz spectrophotometric flow cell connected through a peristaltic pump to a thermostated titration cell equipped with a Gilmont 2.000-mL precision buret for delivery of titrant, glass and reference electrodes, gas inlet for argon or oxygen and gas outlet tube and stirred by means of a magnetic stirring bar.

Results and Discussion

Recognition of Malonic Acid by Protonated O-BISDIEN. In preparation for the quantitative determination of the stability constants of malonate with the various protonated forms of O-BISDIEN, very precise protonation constants were obtained for each substance separately under the conditions of the experiment. (The values are precise in the sense that not only do they recalculate the titration curve nearly exactly but also they are experimentally self-consistent relative to all other experiments related to this work. As is shown in the footnote of Table II, their accuracy relative to work done earlier is generally within 0.03 log units or better. It is this internal precision which enables both the enumeration of molecular complex species present and computation of their recognition constants.) Hence for malonic acid, H_2Mal, its potentiometric curve was calculated back to a precision of 0.002 p[H] units using the two equilibria

$$\mathrm{Mal^{2-} + H^+ \rightleftharpoons HMal^-} \qquad \log K^{\mathrm{H}}_1 = 5.269$$

$$\mathrm{HMal^- + H^+ \rightleftharpoons H_2Mal} \qquad \log K^{\mathrm{H}}_2 = 2.625$$

Similarly, the six log protonation constants for O-BISDIEN, Bd, which were found under the present experimental conditions and reproduce the titration curve within 0.003 p[H] units are

$$\mathrm{Bd + H^+ \rightleftharpoons HBd^+} \qquad \log K^{\mathrm{H}}_1 = 9.620$$

$$\mathrm{HBd^+ + H^+ \rightleftharpoons H_2Bd^{2+}} \qquad \log K^{\mathrm{H}}_2 = 8.885$$

$$\mathrm{H_2Bd^{2+} + H^+ \rightleftharpoons H_3Bd^{3+}} \qquad \log K^{\mathrm{H}}_3 = 8.285$$

$$\mathrm{H_3Bd^{3+} + H^+ \rightleftharpoons H_4Bd^{4+}} \qquad \log K^{\mathrm{H}}_4 = 7.618$$

$$\mathrm{H_4Bd^{4+} + H^+ \rightleftharpoons H_5Bd^{5+}} \qquad \log K^{\mathrm{H}}_5 = 3.815$$

$$\mathrm{H_5Bd^{5+} + H^+ \rightleftharpoons H_6Bd^{6+}} \qquad \log K^{\mathrm{H}}_6 = 3.301$$

With the above values of individual protonation constants, the solution data on O-BISDIEN containing an equimolar quantity of malonic acid were resolved showing the presence of six equilibrium species:

$$\mathrm{H_6Bd^{6+} + HMal^- \rightleftharpoons H_7BdMal^{5+}} \qquad \log K^{\mathrm{R}}_7 = 2.2(1)$$

$$\mathrm{H_6Bd^{6+} + Mal^{2-} \rightleftharpoons H_6BdMal^{4+}} \qquad \log K^{\mathrm{R}}_6 = 4.2(1)$$

$$\mathrm{H_5Bd^{5+} + Mal^{2-} \rightleftharpoons H_5BdMal^{3+}} \qquad \log K^{\mathrm{R}}_5 = 3.70(6)$$

$$\mathrm{H_4Bd^{4+} + Mal^{2-} \rightleftharpoons H_4BdMal^{2+}} \qquad \log K^{\mathrm{R}}_4 = 2.38(6)$$

$$\mathrm{H_3Bd^{3+} + Mal^{2-} \rightleftharpoons H_3BdMal^{+}} \qquad \log K^{\mathrm{R}}_3 = 2.05(4)$$

$$\mathrm{H_2Bd^{2+} + Mal^{2-} \rightleftharpoons H_2BdMal} \qquad \log K^{\mathrm{R}}_2 = 1.81(8)$$

where K^{R}_i is the recognition constant of protonation degree i and the entries are listed in order of appearance from low to high p[H]. Possible H-bonding for the most stable of these species, $H_6(BD)Mal^{4+}$, is illustrated by formula 3.

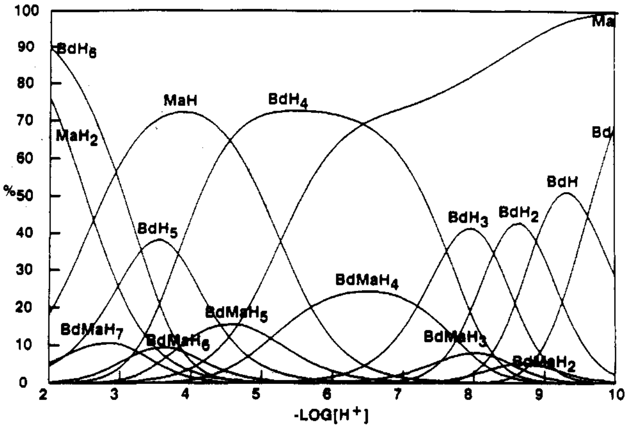

Figure 1. Species distribution diagram showing the species formed as a function of p[H] when a 1:1 molar ratio of 2.09×10^{-3} M O-BISDIEN (Bd) and malonic acid (H_2Ma) is equilibrated at 25.0 °C, $\mu = 0.100$ M KCl.

Table I. log of Host Formation Constants with Protonated Forms of O-BISDIEN

			log K^{R}_i						
ion	log K^{H}_1	log K^{H}_2	6	5	4	3	2	1	ref
malonate[a]	5.27	2.63	4.2	3.70	2.38	2.05	1.81		this work
ketomalonate	3.52	1.82	5.15	4.52	3.65	4.16	3.83	3.39	12
oxalate	3.38	1.0	4.68	3.59	2.06				10
catecholate	13.3	9.30	none						29
tironate[b]	12.5	7.62	none						29

[a] The errors associated with each constant are stated in the text next to the defining equation. [b] 1,2-Dihydroxybenzene-3,5-disulfonic acid.

As the degree of protonation on Bd increases, its affinity for Mal^{2-} increases, as measured by the magnitude of K^{R}_i. But there are other factors which determine the relative concentrations of these variously protonated ternary complexes. Figure 1 shows that just as p[H] determines the state of protonation of the Bd molecule it also determines the degree of protonation of the substrate. At p[H] values up to 2, Bd is in its hexaprotonated state and malonate is practically all H_2Mal. Obviously, there could be no interaction between the two major species. Gradually, as the p[H] is increased, H_2Mal dissociates, producing a significant concentration of $HMal^-$ which readily combines with the high concentration of H_6Bd^{6+} to form the initial ternary complex H_7BdMal^{5+}. At p[H] 3.6 $HMal^-$ as well as H_5Bd^{5+} reach their maximum concentration, favoring the formation of H_6BdMal^{4+}. Similarly, near p[H] 4.6 Mal^{2-} starts forming while H_5Bd^{5+} reaches its maximum concentration, favoring the formation of H_5BdMal^{3+}. Beyond p[H] 5.3 there are no more protonated forms of malonic acid and hence the relative concentrations of the recognition complexes at their respective maxima decrease with p[H]. While the greatest observed concentration favors the symmetrical H_4BdMal^{2+} configuration, intrinsically it is the H_6BdMal^{4+} complex which is the most stable, but it barely exceeds 9% formation because of strong proton competition. On the other hand, $HBdMal^-$ probably is too weak to measure at these concentrations. While it may appear quite remarkable how strong the recognition of Mal^{2-} can be, it should be borne in mind that there is not only a favorable topological relationship between these ions leading to strong, possibly linear hydrogen bonds but also a very favorable Coulombic factor.

Other dinegative ligands which have been studied by these authors are mesoxalic acid and oxalic acid, and their results are compared with this work in Table I. There is no question that

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(29) Kimura, E.; Sakonaka, A.; Yatsunami, T.; Kodama, M. *J. Am. Chem. Soc.* **1981**, *103*, 3041; **1982**, *104*, 3182.

Table II. Literature Comparisons for Malonate Binding Constants to the Protonated Forms of Various Cyclic Polyamines

macrocycle	log K^R_i								ref
	8	7	6	5	4	3	2	1	
[24]ane-N6O2 (O-BISDIEN)			4.2	3.70	2.38	2.05	1.81		this work
[24]ane-N6			3.30	2.60	2.45				24, 30
[27]ane-N6O3			3.8						31
[32]ane-N6			2.75	2.05	1.35				30, 32
[38]ane-N6			3.25						32
[38]ane-N6			3.80	2.65	2.20				30
[15]ane-N5						weak			33
[16]ane-N5						1.82			33
[17]ane-N5						1.40			33
[18]ane-N6						1.52			33
[32]ane-N8	3.9								31
O-BISTREN			3.10	2.00					4

ketomalonate is still the strongest recognized substrate of all the entries in the Table I. Since the keto group is highly hydrated, this unusual interaction is probably helped by additional hydrogen-bonding to the ether bridging oxygens of O-BISDIEN. In contrast, the malonate methylene is considerably hydrophobic and is probably not as well accommodated in this solvated environment. Oxalate is shorter and considerably more acidic, but O-BISDIEN is also very flexible. The catechols possess extremely weak, monodentate aromatic hydroxy groups and are therefore not capable of forming a complex at low p[H], where they are neutral. At high p[H] they are at least partly dissociated, but the macrocycle is devoid of protons under these conditions and does not H-bond to the catecholate.

The case for recognition can be strengthened when some comparisons are made with the meager existing work in the literature. While the work herein reported deals with O-BISDIEN, the only comparisons possible are those of a common ligand with existing cyclic polyamines.

Focusing in on the N6 (or greater) systems capable of at least hexaprotonation, it becomes apparent that the largest malonate constant listed in Table II is 4.2 found for O-BISDIEN in this work. When the same ring size is considered while all nitrogens are connected with trimethylene groups, H_6L^{6+} and the H_5L^{5+} corresponding forms of O-BISDIEN show about 1.0 log unit of enhancement over that shown for [24]ane-N6. But even the H_4L^{4+} form of O-BISDIEN might in fact show this specificity if the authors of [24]ane-N6 had not chosen to combine together the species H_4L^{4+}, H_3L^{3+}, H_2L^{2+} and possibly H_1L^{+} as H_4L^{4+}, thus inadvertently increasing the value of H_4L^{4+} of [24]ane-N6 to 2.45, a trifle higher than 2.38 for O-BISDIEN. Malonate is also found to exhibit increased attraction for hexa protonated [27]ane-N6O3, but the stability constant of 3.8 is lower than 4.2 shown for O-BISDIEN. There are conflicting data for [38]ane-N6 reported by two authors shown in Table II of 3.25 vs 2.75, but in either case these values and all others are lower than those associated with O-BISDIEN. It may be added that the remaining N5 and N7 ligands are not capable of full protonation while only the octapositive ion of [32]ane-18 is reported, and therefore these cases are not readily comparable with this work.

Other Protonated O-BISDIEN Guests. As part of the survey of a diverse family of potential guests, glycine, acetohydroxamic acid, phosphonous formic acid, and phosphoric acid were studied. It was found that both glycine and acetohydroxamic acid do not interact significantly with the protonated forms of O-BISDIEN. Their log protonation constants were redetermined and found to be 9.58 and 2.36 for glycine and 9.28 for the acetohydroxamic acid. The lack of strong recognition is due to these high protonation constants and the magnitude of the protonation constants for O-BISDIEN. Thus by the time the p[H] is raised to 9.6 or 9.3, respectively, to get half of the guest molecules deprotonated, the O-BISDIEN distribution consists of the unreactive forms: half Bd free base, one-fourth HBd^{+}, and one-fourth H_2Bd^{2+}, and hence becomes very uninviting to the mononegative ligands. However for the acetohydroxamic acid anion (Acx^-), the following three species were identified: H_7BdAcx^{6+}, H_6BdAcx^{5+}, H_5BdAcx^{4+} with corresponding log overall constants (β values) of formation of 54.05, 50.25, and 45.82 respectively:

$$7H^+ + Bd + Acx^- \rightleftharpoons H_7BdAcx^{6+} \qquad \log \beta = 54.05$$

$$6H^+ + Bd + Acx^- \rightleftharpoons H_6BdAcx^{5+} \qquad \log \beta = 50.25$$

$$5H^+ + Bd + Acx^- \rightleftharpoons H_5BdAcx^{4+} \qquad \log \beta = 45.82$$

Expressed as stepwise recognition constants, these equations become

$$H_6Bd^{6+} + HAcx \rightleftharpoons H_7BdAcx^{6+} \qquad \log K^R{}_7 = 3.25$$

$$H_6Bd^{6+} + Acx^- \rightleftharpoons H_6BdAcx^{5+} \qquad \log K^R{}_6 = 8.73$$

$$H_5Bd^{5+} + Acx^- \rightleftharpoons H_5BdAcx^{4+} \qquad \log K^R{}_5 = 7.60$$

While significantly larger recognition constants were found, the high protonation constant of acetohydroxamic acid precluded a large degree of formation of H_6BdAcx^{5+} and H_5BdAcx^{4+}. The relatively high magnitudes of the formation constants representing association are surprising and, in the absence of an X-ray structure determination, can be taken as an indication of a better geometric and H-bond fit for the acetohydroxamate anion.

Phosphonous formic acid proved to be too unstable in acid solution to study its interactions with O-BISDIEN although its log protonation constants were determined via a fast back-titration from its dipotassium salt to be 3.19 and 1.7. However at low and even intermediate p[H] values the solutions drift because of autodecomposition so that the required precise measurements for interactions with the protonated forms of the macrocycle were deemed not possible, although it is certain by analogy that such interactions should take place.

Phosphate is a smaller anion, and judging from its log protonation constants (11.74, 6.75, and 1.72), only $H_2PO_4^-$ and HPO_4^{2-} are important between p[H] 2 and 10. However six H-bonded bridging species were formed with O-BISDIEN depending on the solution p[H] and the magnitudes of the protonation constants, as summarized in the following equations:

$$H_6Bd^{6+} + H_2PO_4^- \rightleftharpoons H_8BdPO_4^{5+} \qquad \log K^R{}_8 = 2.66(5)$$

$$H_6Bd^{6+} + HPO_4^{2-} \rightleftharpoons H_7BdPO_4^{4+} \qquad \log K^R{}_7 = 6.97(3)$$

$$H_5Bd^{5+} + HPO_4^{2-} \rightleftharpoons H_6BdPO_4^{3+} \qquad \log K^R{}_6 = 5.2(1)$$

$$H_4Bd^{4+} + HPO_4^{2-} \rightleftharpoons H_5BdPO_4^{2+} \qquad \log K^R{}_5 = 2.6(1)$$

$$H_3Bd^{3+} + HPO_4^{2-} \rightleftharpoons H_4BdPO_4^{+} \qquad \log K^R{}_4 = 1.85(7)$$

$$H_2Bd^{2+} + HPO_4^{2-} \rightleftharpoons H_3BdPO_4^{0} \qquad \log K^R{}_3 = 1.49(7)$$

It is clear that the two most favored recognition equilibria involve the interaction of the hexa- and pentaprotonated O-BISDIEN molecules with the dinegative biphosphate anion. Not only is stability achieved through Coulombic attraction but also the phosphate molecule possesses at least three sites for hydrogen-bond formation. Also the remaining site has a proton which is capable of forming a fourth hydrogen bond. The remaining four

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(30) Hosseini, M. W.; Lehn, J. M. *Helv. Chim. Acta* **1986**, *69*, 587.

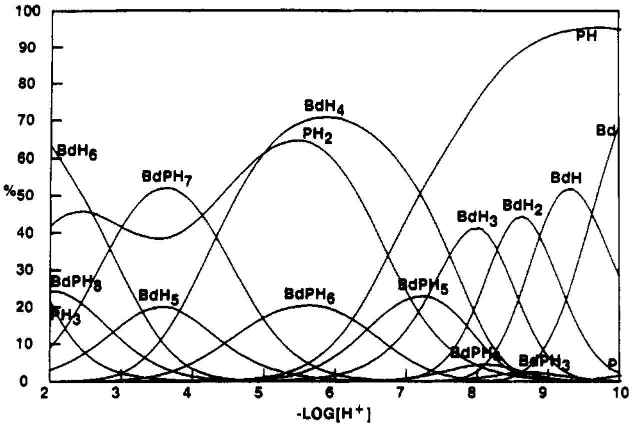

Figure 2. Species distribution diagram showing the species formed as a function of p[H] when 2.02×10^{-3} M O-BISDIEN (Bd) and 1.96×10^{-3} M phosphate (H_3P) are equilibrated at 25.0 °C, $\mu = 0.100$ M KCl.

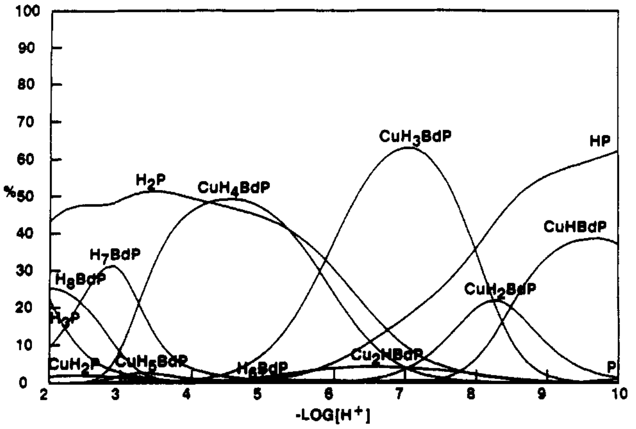

Figure 3. Species distribution diagram showing the species formed as a function of p[H] when 2.08×10^{-3} M O-BISDIEN (Bd), 2.12×10^{-3} M phosphate (H_3P), and 2.08×10^{-3} M copper(II) are equilibrated at 25.0 °C, $\mu = 0.100$ M KCl. Only phosphate-containing species are shown.

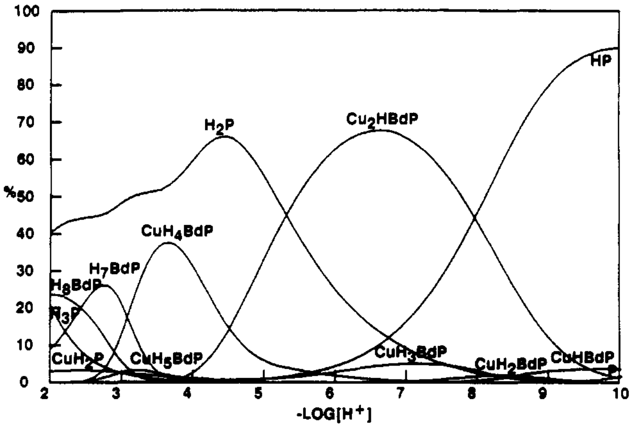

Figure 4. Species distribution diagram showing the species formed as a function of p[H] when 2.02×10^{-3} M O-BISDIEN (Bd), 1.96×10^{-3} M phosphate (H_3P), and 3.90×10^{-3} M copper(II) are equilibrated at 25.0 °C, $\mu = 0.100$ M KCl. Only phosphate-containing species are shown.

interactions are weaker for differing reasons. $H_8BdPO_4^{5+}$ forms in a weaker fashion because of the mononegative $H_2PO_4^-$ ion. The ion $H_5BdPO_4^{2+}$ is more reluctant to form for geometric reasons. $H_4BdPO_4^+$ and $H_3BdPO_4^0$ are weak because there are fewer hydrogens for hydrogen-bonding.

Figure 2 is interesting in that it shows the phosphate–O-BISDIEN species formed as a function of p[H]. The relative concentration of the 7-, 6-, and 5-protonated complexes at first appears out of order relative to the decreasing magnitude of the corresponding recognition constants. One would expect $H_5BdPO_4^{2+}$ to have a much lower concentration. However note that above p[H] 6.75, the value corresponding to the protonation constant of HPO_4^{2-}, that the actual concentration of HPO_4^{2-} changes from the negligible to finite-and-large values. Thus, even though the log $K^R_5 = 2.64$ is small, the concentration conditions are very favorable for its (i.e. $H_5BdPO_4^{2+}$) formation. Note that the small extents of formation of $H_4BdPO_4^+$ and H_3BdPO_4 are controlled not only by their small equilibrium constants but also by the relative concentration of any individual overlapping protonated form of O-BISDIEN present.

As far as HPO_4^{2-} is concerned, its binding has not been previously measured with O-BISDIEN nor with other hexaprotonated macrocyclic ligands. Thus comparison of its binding strength to hexaprotonated moieties cannot be made. However Kimura did measure its interaction with the triprotonated form of [18]ane-N6 macrocycle and found the log value to be 1.16. Our value is considerably larger at 1.85. Although HPO_4^{2-} is not really analogous to AMP^{2-} (however the Coulombic charge is the same), the binding of the latter had been studied with several hexaprotonated N6 macrocycles. With hexaprotonated [24]ane-N6 and [27]ane-N6O3 the AMP^{2-} ion exhibits log stability constants of 3.40[19,31] and 4.7,[31] respectively. With O-BISDIEN, the values[18,19] for AMP^{2-} are 6.95 for H_6L^{6+}, 5.00 for H_5L^{5+}, and 2.85 for H_4L^{4+}. These values are amazingly similar to those measured in this work for biphosphate: 6.97, 5.2, and 2.6, respectively.

Guests of Metal Complexes of O-BISDIEN. Copper–O-BISDIEN–Phosphate. Divalent metal ions, and in particular Cu(II), had already been shown to form both 1:1 and 1:2 ligand to metal complexes with O-BISDIEN:[9] $CuBd^{2+}$, $CuH_{-1}Bd^+$, $CuHBd^{3+}$, CuH_2Bd^{4+}, CuH_3Bd^{5+}, Cu_2Bd^{4+}, $Cu_2H_{-1}Bd^{3+}$ and $Cu_2H_{-2}Bd^{2+}$. Mononuclear complex formation is favored when 1:1 ligand to metal ion solutions are prepared and dinuclear complexes are favored in 1:2 ligand to metal overall stoichiometry. Thus for both 1:1 and 1:2 ligand to metal ratios, the p[H] profiles obtained in the presence of phosphate show that the following interactions are significant:

$$CuH_3Bd^{5+} + H_2PO_4^- \rightleftharpoons CuH_5BdPO_4^{4+} \quad \log K^R_{15} = 2.0(4)$$

$$CuH_3Bd^{5+} + HPO_4^{2-} \rightleftharpoons CuH_4BdPO_4^{3+} \quad \log K^R_{14} = 6.45(6)$$

$$CuH_2Bd^{4+} + HPO_4^{2-} \rightleftharpoons CuH_3BdPO_4^{2+} \quad \log K^R_{13} = 4.11(5)$$

$$CuHBd^{3+} + HPO_4^{2-} \rightleftharpoons CuH_2BdPO_4^{+} \quad \log K^R_{12} = 3.3(2)$$

$$CuBd^{2+} + HPO_4^{2-} \rightleftharpoons CuHBdPO_4^{0} \quad \log K^R_{11} = 2.8(2)$$

$$Cu_2Bd^{4+} + HPO_4^{2-} \rightleftharpoons Cu_2HBdPO_4^{2+} \quad \log K^R_{21} = 4.5(2)$$

Only six of the eight O-BISDIEN copper(II) complexes possess recognition characteristics for phosphate. $CuH_{-1}Bd^+$ and $Cu_2H_{-2}Bd^{2+}$ are self-explanatory in their lack of reactivity. The inertness of $Cu_2H_{-1}Bd^{3+}$ is logical when one recalls that the Cu_2Bd^{4+} ion has very high affinity for the OH^- ion, much higher than phosphate can compete with.

$$Cu_2Bd^{4+} + OH^- \rightleftharpoons Cu_2(OH)Bd^{3+} \quad \log K^{OH} = 7.27$$

The species possessing the highest recognition constant for HPO_4^{2-} is CuH_3Bd^{5+} (4), while the lowest is $CuBd^{2+}$, with

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(31) Dietrich, B.; Hosseini, M. W.; Lehn, J. M.; Sessions, R. B. *J. Am. Chem. Soc.* **1981**, *103*, 1281.

(32) Hosseini, M. R.; Lehn, J. M. *J. Am. Chem. Soc.* **1982**, *104*, 3525.

(33) Szpoganicz, B.; Motekaitis, R. J.; Martell, A. E. *Inorg. Chem.* **1990**, *29*, 1467.

Table III. Summary of Measured Formation Constants of H(I)[a] and Co(II)[b] with Ligands, μ = 0.100 M KCl, t = 25.0 °C

quotient	malonic acid	glycine	acetohydroxamic acid	phosphonous formate	O-BISDIEN[c]
$[HL]/[H][L]$	5.27	9.58	9.28	3.19	9.62
$[H_2L]/[H][HL]$	2.62	2.36		1.7	8.89
$[H_3L]/[H][H_2L]$					8.2
$[H_4L]/[H][H_3L]$					7.62
$[H_5L]/[H][H_4L]$					3.82
$[H_6L]/[H][H_5L]$					3.30
$[ML]/[M][L]$	2.92	4.67	4.99		9.81
$[ML_2]/[L][ML]$	1.68	3.81	3.92		
$[ML_3]/[L][ML_2]$	0.7	2.36	2.66		
$[MLOH][H]/[ML]$		10.09			
$[M_2L(OH)][H]/[M]^2[L]$					4.50
$[MHL]/[H][ML]$					7.37
$[MH_2L]/[H][MHL]$					6.27

[a] Successive literature protonation constants: malonic acid[34] 5.28, 2.63; glycine[34] 9.58, 2.34; acetohydroxamic acid[34] 9.31; O-BISDIEN·6HCl[9] 9.65, 8.92, 8.30, 7.64, 3.81, 326. [b] Successive literature Co(II) ion formation constants: malonic acid[34] 2.93, 2.5; glycine[34] 4.67, 3.79, 2.4; acetohydroxamic acid[34] 5.1, 3.8; O-BISDIEN[9] 9.73. [c] Other literature log stability constants:[9] (MHL) 7.58; (MH_2L) 5.97.

decreasing values in between as the number of positive protonated nitrogens decreases. Once again, HPO_4^{2-} not only possesses high charge but also has structural properties (tetrahedral symmetry) naturally fitting into the space between the protonated diethylenetriamine moiety and the metal ion to which it can coordinate. Even when the nitrogens are not protonated, the HPO_4^{2-} ion can coordinate to the Cu^{2+} ion as well as it can hydrogen-bond to the neutral nitrogens. The reason $\log K^R{}_{11}$ is 2.8 and is less than that of the Cu^{2+} reaction with HPO_4^{2-} (3.3) may be related the energy required to unfold a part of O-BISDIEN during the transformation of $CuBd^{2+}$ into $CuHBdPO_4^0$ (**5**). Such unfolding is irrelevant in the case of the Cu^{2+} ion. The $\log K^R{}_{15}$ is only 2.0, but note that it is a dihydrogen phosphate which is crowding itself into CuH_3L^{5+} to give $CuH_5BdPO_4^{4+}$, a species possessing a diprotonated bridging group. Such structural speculations could be resolved with the help of an X-ray crystal structure determination if it were possible to isolate a single crystal of a $CuBd^{2+}$ salt and $CuHBdPO_4$.

Figures 3 and 4 show the various phosphate interactions discussed above for 1:1:1 and 1:1:2 O-BISDIEN to phosphate to copper(II), respectively. Only the phosphate-containing species are shown. In the mononuclear system, almost the entire p[H] range shows substantial concentrations of coordinated phosphate. In the dinuclear system, above p[H] ~9, the aforementioned dinuclear μ-hydroxo species eventually displaces all of the phosphate.

Cobalt–O–BISDIEN-Malonate. Although Co^{2+} is a weak complexer for carboxylic acids, its affinity for malonate was redetermined under the conditions of this work. Two stability constants were found, and their values are compared in Table III

$$Mal^{2-} + Co^{2+} \rightleftharpoons CoMal \qquad \log K_{ML} = 2.92$$

$$Mal^{2-} + CoMal \rightleftharpoons Co(Mal)_2^{2-} \qquad \log K_{ML} = 1.68$$

with the other ligands measured. Note that the numerical values are 2 orders of magnitude smaller for the cobalt(II) complex compared to the affinity of the proton. $\log K_{ML}$ for O-BISDIEN with Co^{2+} was found to be 9.81 (KCl), which is in good agreement with previous work (9.73) in KNO_3 as a supporting electrolyte. In a certain sense, all the constants discussed are somewhat dependent on the background electrolyte in that specific anion interactions from the background electrolyte were not factored out. In this work, an M_2L complex was not detected, although previous work (KNO_3) found a value of 2.7. In this work it was fortunately possible to reach a = 6.5 (a = moles of base added per mole of ligand present), so that a numerical constant was evaluated for the formation of $Co_2L(OH)^{3+}$ before cobalt hydroxide separated as was the case in the previous study.

$$2Co^{2+} + Bd \rightleftharpoons Co_2Bd(OH)^{3+} + H^+ \qquad \log \beta = 4.50$$

The two protonated complexes MHL^{3+} and MH_2L^{4+} were also found to form.

$$CoBd + H^+ \rightleftharpoons MHBd^{3+} \qquad \log K^H{}_{MHL} = 7.37$$

$$CoHBd^{3+} + H^+ \rightleftharpoons MH_2Bd^{4+} \qquad \log K^H{}_{MHL} = 6.27$$

The differences between these values and those in the literature are tentatively attributable to the different salts used as background electrolyte; however, it is possible that other factors were also involved.

Of the four Co(II)–O-BISDIEN complexes listed in Table III, three showed some degree of molecular recognition for malonate ions to produce five species: $CoHBdMal^+$, CoH_2BdMal^{2+}, CoH_3BdMal^{3+}, $Co_2H_{-1}BdMal^+$, and Co_2BdMal^{2+}. The equilibrium expressions are

$$CoHBd^{3+} + Mal^{2-} \rightleftharpoons CoHBdMal^+ \qquad \log K^R{}_{11} = 3.15(8)$$

$$CoH_2Bd^{4+} + Mal^{2-} \rightleftharpoons CoH_2BdMal^{2+} \qquad \log K^R{}_{12} = 3.39(6)$$

$$CoH_2Bd^{5+} + HMal^- \rightleftharpoons CoH_3BdMal^{3+} \qquad \log K^R{}_{13} = 4.7(1)$$

$$Co_2H_{-1}Bd^{3+} + Mal^{2-} \rightleftharpoons Co_2H_{-1}BdMal^+ \qquad \log K^R{}_2 = 3.1(2)$$

$$Co_2H_{-1}Bd^{3+} + Mal^{2-} \rightleftharpoons Co_2BdMal^{2+} + OH^- \qquad \log K^R{}_{20} = -2.2(1)$$

The equilibria symbolized by $\log K^R{}_{11}$ and $\log K^R{}_{12}$ are in stepwise order and thus increase slightly with the additional proton. The equilibrium symbolized by $\log K^R{}_{13}$ is written in terms of a reaction with monohydrogen malonate since CoH_3Bd^{5+} does not exist. Nevertheless the recognition constant $\log K^R{}_{13}$ is greater than $\log K^R{}_{12}$. The first binuclear (μ-hydroxo) complex forms a malonato-bridged species in contrast to the observations of the dicopper phosphate system discussed above. Note that all of the recognition constants in the above block of equations are greater in magnitude than the normal stability constant of Co^{2+} with Mal^{2-}. Formation of bridges over several centers is consistent with the observed magnitudes of the constants. The recognition constant $\log K^R{}_{20}$ = −2.2 is written as an OH^- displacement reaction, and it is considered remarkable that malonate is only 2 orders of magnitude disfavored over a hydroxo bridge, thus making it possible to observe this species before the p[H] gets too high. Figure 5 illustrates

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(34) Smith, R. M.; Martell, A. E. *Critical Stability Constants Database*, NIST project, 1992 (in preparation).

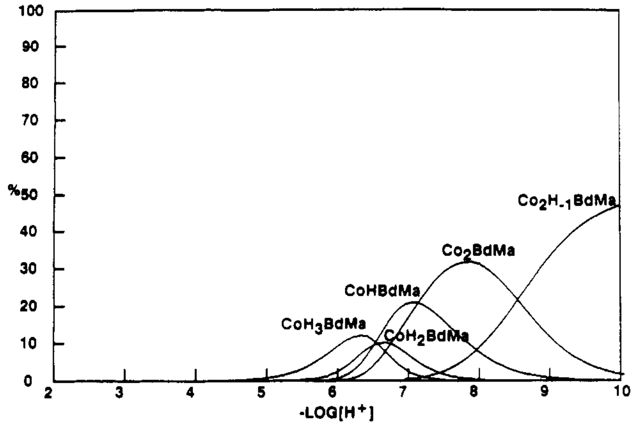

Figure 5. Species distribution diagram showing the species formed as a function of p[H] when 2.11×10^{-3} M O-BISDIEN (Bd), 2.11×10^{-3} M malonate (H_2Ma), and 4.20×10^{-3} M cobalt(II) are equilibrated at 25.0 °C, $\mu = 0.100$ M KCl. Only malonate-containing complex species are shown.

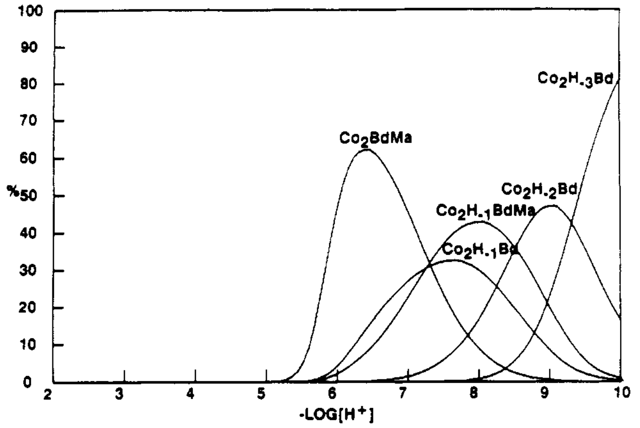

Figure 6. Species distribution diagram showing only the dioxygen-containing species formed as a function of p[H] when 2.13×10^{-3} M O-BISDIEN (Bd), 2.11×10^{-3} M malonate (H_2Ma), and 4.25×10^{-3} M cobalt(II) are equilibrated at 25.0 °C, $\mu = 0.100$ M KCl. There are 37 species considered in the background of this calculation. $P_{O_2} = 1.00$ atm.

the p[H] dependence of the various O-BISDIEN/Co(II) malonato adducts discussed in this section.

A different p[H] profile is obtained for the O-BISDIEN, cobalt(II) malonate system when it is carried out in the presence of dioxygen. From the differences, two equilibrium constants leading to the formation of $Co_2BdMal(O_2)^{2+}$ and $Co_2(OH)BdMal(O_2)^+$ were obtained to reproduce the new curve. The equilibration is very slow and hence takes several days to get the necessary points in the dioxygen region.

$$\log\,[Co_2BdMal(O_2)^+]/[Co^{2+}]^2[Bd][Mal^{2-}]P_{O_2} = 19.6(1)$$

$$\log\,[Co_2(OH^-)BdMal(O_2)^{2+}][H^+]/[Co^{2+}]^2[Bd][Mal^{2-}]P_{O_2} = 12.3(1)$$

In Figure 6, the dioxygen complexes are plainly obvious, especially the non-hydroxo-bridged $Co_2BdMal(O_2)^{2+}$ (**6**), where apparently the malonato bridge has displaced the hydroxo bridge and is the only major species near p[H] 6.

Cobalt–O-BISDIEN–Glycinate. Whereas the malonate stability constants of cobalt(II) are small, three stepwise reactions occur with glycinate and in addition a hydrolysis reaction was determined.

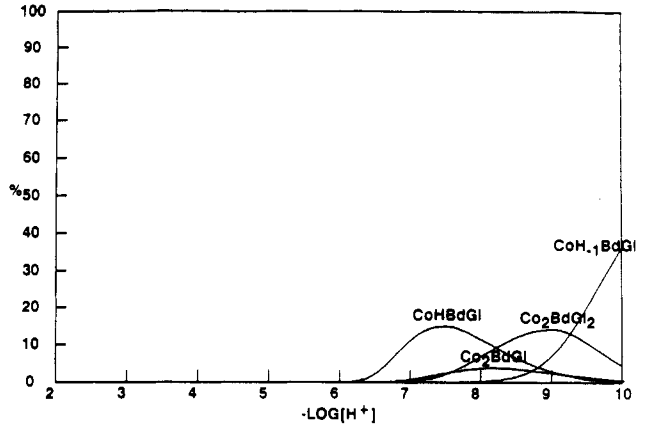

Figure 7. Species distribution diagram showing the species formed as a function of p[H] when 1.99×10^{-3} M 1:1:2 O-BISDIEN (Bd), 2.04×10^{-3} M glycine (Gl), and 4.03×10^{-3} M cobalt(II) are equilibrated at 25.0 °C, $\mu = 0.100$ M KCl. Only glycine-containing complex species are shown.

$$Gly^- + Co^{2+} \rightleftharpoons CoGly^+ \qquad \log K_{ML} = 4.67(1)$$

$$Gly^- + CoGly^+ \rightleftharpoons Co(Gly)_2 \qquad \log K_{ML_2} = 3.81(1)$$

$$Gly^- + Co(Gly)_2 \rightleftharpoons Co(Gly)_3^- \qquad \log K_{ML_3} = 2.36(1)$$

$$CoGly^+ \rightleftharpoons CoGly(OH) + H^+ \qquad \log K^{OH} = -10.09(1)$$

The magnitude of these constants is such that a millimolar 1:3 cobalt to glycine solution would completely coordinate cobalt by p[H] 9. This certainly could not be said of malonic acid.

When O-BISDIEN is studied under argon with cobalt(II) and glycine, four new molecular recognition equilibrium species are identified, of which three are major while the last one is minor. Co(OH)BdGly, $CoHBdGly^{2+}$, $Co_2Bd(Gly)_2^{2+}$, and Co_2BdGly^{3+}.

$$[Co(OH)BdGly][H^+]/[Co^{2+}][Bd][Gly^-] = 10^{4.33}$$

$$[CoHBdGly^{2+}]/[Co^{2+}][Bd][Gly^-][H^+] = 10^{21.94}$$

$$[Co_2Bd(Gly)_2^{2+}]/[Co^{2+}]^2[Bd][Gly^-]^2 = 10^{21.58}$$

$$[Co_2BdGly^{3+}]/[Co^{2+}]^2[Bd][Gly^-] = 10^{16.57}$$

The second quotient may be rewritten into a more intuitive form using the overall $CoHBd^{3+}$ formation constant.

$$CoHBd^{3+} + Gly^- \rightleftharpoons CoHBdGly^{2+} \qquad \log K^R_1 = 4.8$$

This recognition constant is slightly higher than the normal stability constant of the cobalt ion, therefore showing the participation of the protonated nitrogen in some sort of H-bonding. In comparing the last two quotients one can write an equation for the addition of a second glycinate to one that is already there.

$$Co_2BdGly^{3+} + Gly^- \rightleftharpoons Co_2Bd(Gly)_2^{2+} \qquad \log K^R_2 = 5.0$$

Previously,[29] in KNO_3 an overall log constant for the formation of Co_2Gly^{4+} was found to be 12.4. Such a species was not found present in the work in KCl electrolyte. Nevertheless, by subtraction of this formation equation from the last quotient above, the recognition constant for the dinuclear case can be approximated as

$$Co_2Bd^{4+} + Gly^- \rightleftharpoons Co_2BDGly^{3+} \qquad \log K^R_1 = 4.1$$

This constant is even higher than that of the first glycinate, and

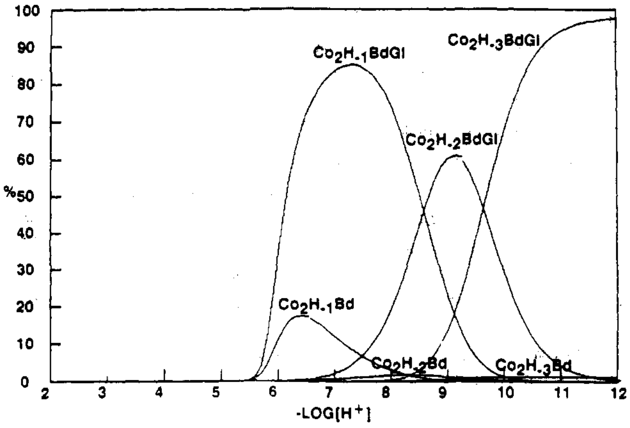

Figure 8. Species distribution diagram showing only the dioxygen-containing species formed as a function of p[H] when 1.92 × 10^{-3} M 1:1:2 O-BISDIEN (Bd), 1.92 × 10^{-3} M glycine (Gl), and 3.81 × 10^{-3} M cobalt(II) are equilibrated at 25.0 °C, $\mu = 0.100$ M KCl. There are 35 species considered in the background of this calculation. $P_{O_2} = 1.00$ atm.

Table IV. Rate Constants for the Formation of Dicobalt(II) Dioxygen Complexes at 45 °C, $\mu = 0.100$ M (KCl)

system	k_{obs}, s^{-1}	system	k_{obs}, s^{-1}
Bd–O_2	1.6×10^{-3}	Bd–Pf–O_2	1.3×10^{-3}
Bd–Gly–O_2	1.9×10^{-3}	Bd–Mal–O_2	9.5×10^{-4}
Bd–AcX–O_2	1.0×10^{-3}		

it would seem logical that this molecule involves the presence of two glycinato bridges between the cobalts.

Figure 7 shows the weak recognition that O-BISDIEN–cobalt complexes exhibit for the monoanionic glycinate ligand. Most of the remaining glycine concentration is distributed among the various cobalt complexes that are formed (see Table IV).

Under oxygen, there are three glycine-containing O-BISDIEN–cobalt–dioxygen complexes which actually swamp those formed from dicobalt–O-BISTREN alone. Their stoichiometries are $Co_2Bd(OH)Gly(O_2)^{2+}$ (7), $Co_2BdH_{-2}Gly(O_2)^{+}$, and $Co_2BdH_{-3}Gly(O_2)$. The first complex is the expected one; however, the last two probably involve replacements of coordinated neutral nitrogens by negative OH^-'s. Their overall stability constants are as follows.

$$\log\,[Co_2(OH^-)BdGly(O_2)^{2+}][H^+]/[Co^{2+}]^2[Bd][Gly^-]P_{O_2} = 16.1(1)$$

$$\log\,[Co_2(OH)_2BdGly(O_2)^{2+}][H^+]^2/[Co^{2+}]^2[Bd][Gly^-]P_{O_2} = 7.5(1)$$

$$\log\,[Co_2(OH)_3BdGly(O_2)^{2+}][H^+]^3/[Co^{2+}]^2[Bd][Gly^-]P_{O_2} = -2.1(1)$$

These can be directly compared when expressed as Gly^- reacting with O-BISDIEN dicobalt–dioxygen complexes.

$$Co_2Bd(OH)(O_2)^{3+} + Gly^- \rightleftharpoons Co_2Bd(OH)Gly(O_2)^{2+} \qquad \log K = 7.0$$

$$Co_2Bd(OH)_2(O_2)^{2+} + Gly^- \rightleftharpoons Co_2Bd(OH)_2Gly(O_2)^{+} \qquad \log K = 6.6$$

$$Co_2Bd(OH)_3(O_2)^{+} + Gly^- \rightleftharpoons Co_2Bd(OH)_3Gly(O_2) \qquad \log K = 6.3$$

The fact that the values decrease means that the glycinate is more weakly bound to the dinuclear cobalt macrocyclic complexes as the number of coordinated OH^- ions increases. Figure 8 illustrates the formation of the three dioxygen complexes starting at p[H] 5.75 and going higher.

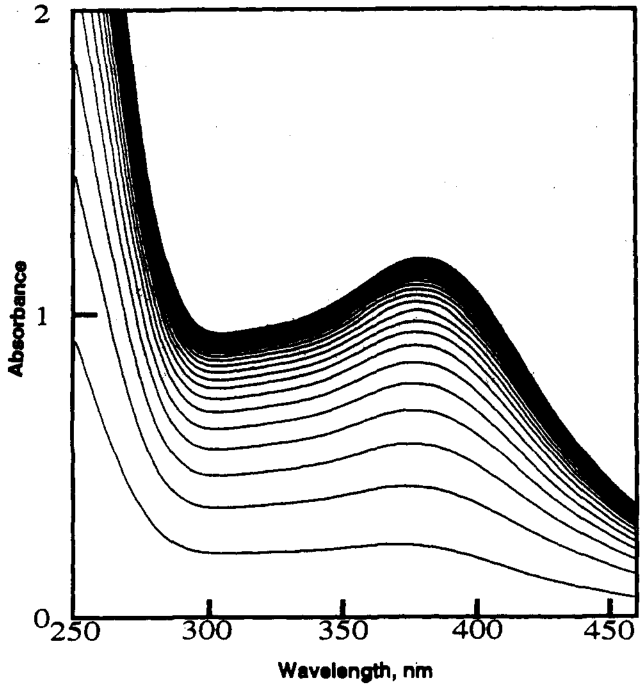

Figure 9. Electronic spectra scanned every 2 min showing the formation of the bis(cobalt) O-BISDIEN-μ-hydroxo-μ-glycinato-μ-dioxygen complex at 6 × 10^{-4} M concentration. Absorbance is plotted against wavelength using a 1.00-cm quartz cell, $\mu = 0.100$ M KCl at 45.0 °C. This is a typical formation curve before decomposition sets in.

Cobalt–O-BISDIEN–Acetohydroxamate. Acetohydroxamic acid possesses a basicity similar to that of glycine except it is monobasic and is not dipolar. That is why it is not surprising that its 1:1, 1:2, and 1:3 stability constants are found to be very similar to those of glycine.

$$Acx^- + Co^{2+} \rightleftharpoons CoAcx^+ \qquad \log K_{ML} = 4.99(1)$$

$$Acx^- + CoAcx^+ \rightleftharpoons Co(Acx)_2 \qquad \log K_{ML_2} = 3.92(1)$$

$$Acx^- + Co(Acx)_2 \rightleftharpoons Co(Acx)^-_3 \qquad \log K_{ML_3} = 2.66(1)$$

In the presence of O-BISDIEN, only two Co^{2+} mixed-ligand species were identified, $CoBdAcx^+$ and $Co_2Bd(Acx)_2{}^{2+}$, and their overall stability constants were found to be 14.66 and 22.82 log units, respectively. It is informative to re-express the formation of the mononuclear complex as a reaction with Acx^-.

$$CoBd^{2+} + Acx^- \rightleftharpoons CoBdAcx^+ \qquad \log K^R = 4.93$$

Note once again the more favorable recognition constant than the normal stability constant for the Co^{2+} ion alone. It should be recalled that there are protons on the macrocycle nitrogens, and hydrogen bonds are probably involved in the binding of hydroxamate within the macrocycle.

A p[H] profile was attempted under dioxygen, but computations could not be carried out since the p[H] never stabilized enough to determine even approximate constants.

Cobalt–O-BISDIEN–Dioxygen Complex Kinetics. The formation of the various dioxygen complexes is not an instantaneous process since considerable rearrangement of all functional groups must take place. The temperature was raised to 45 °C in order to make the rate measurements more readily measurable.

Table IV is a summary of the rate constants obtained where possible for typical formation reactions of encapsulated dioxygen complexes. In Table IV, the k_{obs} values computed for the formation from original spectrophotometric data are listed. A typical sample is shown in Figure 9 which depicts successive spectra obtained every 2 min when one O-BISDIEN, two Co(II), and one glycine (1 mM) are mixed and heated at 45 °C. From a plot of $\log_e (A_\infty - A_t)$ vs time the slope was set equal to k_{obs}.

In all instances k_{obs} was found to be within a range of 1–2 times the lowest rate constant. Since complexes of different structures were forming, it is not surprising that the rate for Bd–O_2 formation is neither the slowest nor the fastest of the rates shown in Table III. The kinetic experiments showed two things: (1) there are no short-lived oxygenated intermediates, and (2) the half-life for formation is on the order of minutes. The spectrophotometric–kinetic experiment was also complementary to the potentiometry, since all of the complexes formed in slightly different ways and the spectra were all somewhat different in detail.

When one of the bridging groups is a reducing agent, there is a possibility that it would be oxidized by the coordinated dioxygen with the electron transfer occurring through the cobalt(II/III) centers. Studies of such redox reactions with some of the bridging groups described above will be the subject of future investigations.

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