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Synthesis and Characterization of New Dioxygen Carriers: A Reexamination of the "Fly-Over" Ligand System

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The synthesis, characterization and dioxygen binding ability of cobalt(II) complexes with 2,2′-(hexamethylenedioxy)bis[8-(salicylideneamino)naphthalene] and 2,2′-(*p*-xylylenedioxy)bis[8-(salicylideneamino)naphthalene] have been investigated. Although it was previously reported that the cobalt(II) complex of the tetramethylene-bridged fly-over ligand failed to bind O_2, the hexamethylene- and *p*-xylylene-bridged derivatives reported herein bind dioxygen reversibly. The dioxygen affinity of the hexamethylene complex is 0.007 (1) Torr^{-1} at −39.1 °C and 0.096 (1) Torr^{-1} at −55.3 °C. The affinity of the *p*-xylylene complex, at −56.2 °C [0.012 (1) Torr^{-1}], is significantly lower.

Introduction

In many biological systems capable of reversible dioxygen binding, the active metal site is separated from the surrounding environment by sheltering groups that form a hydrophobic pocket.[1-4] This feature has been incorporated into many inorganic model systems, including the "capped" porphyrins and the cyclidene family of complexes.[5-11] Several years ago, Martin and co-workers designed the "fly-over" ligand, a superstructured Schiff-base system (Figure 1), as a model for biological oxygen carriers.[12] Metal complexes of this ligand feature a square-planar coordination geometry with a trans N_2O_2 donor set. The rigid naphthyl risers are linked by a polymethylene diether bridge of variable length and are also attached to the chelating nitrogen atoms. This provides a nicely defined cavity on one side of the coordination plane. Advantages to the fly-over ligand system include readily synthesized Schiff-base complexes and an easily varied bridging group R.

Martin's group prepared the cobalt(II) complex having a tetramethylene linking group but observed no dioxygen binding to the metal center. A crystal structure of the analogous nickel complex suggests that the two naphthyl hydrogen atoms that project into the cavity sterically hinder the entry of the dioxygen.[13] The results of detailed studies on cobalt(II) complexes of lacunar cyclidene complexes have guided our reinvestigation of the fly-over systems.[14] The tetramethylene bridge produces a small rigid cavity, greatly limiting dioxygen affinity, while the longer hexamethylene bridge is flexible, having a conformation that provides a spacious cavity and a much higher dioxygen affinity. In cyclidene complexes, xylylene bridging groups produce dioxygen affinities similar to those of the tetramethylene bridge. However, if Martin's explanation of the behavior of the tetramethylene-bridged fly-over ligand is correct, a *p*-xylylene bridge might force the naphthyl groups apart and better accommodate an O_2 molecule. Using ESR spectroscopy, we have found that the cobalt(II) complexes containing a hexamethylene or a *p*-xylylene bridging group do indeed bind dioxygen reversibly and the dioxygen affinities can be determined by dioxygen titrations at low (≤−40 °C) temperatures.

Experimental Section

Materials. All solvents were reagent grade and were used as purchased without further purification, with the exception of those solvents used in the inert-atmosphere box. The latter were dried by the following recommended procedures, distilled under dry nitrogen, and thoroughly degassed prior to use.[15] The reagents used for ligand preparation were purchased from the Aldrich Chemical Co. and were used without further purification.

Physical Measurements. ^1H NMR spectra were recorded on a Bruker AM-250 FT spectrometer operating at 250.133 MHz at 304 K in $CDCl_3$. Spectra were referenced to the trace amounts of $CHCl_3$ impurity present in solution. The infrared spectra were determined on KBr pellets of the samples on a Perkin-Elmer 283B spectrophotometer in the range 4000–400 cm^{-1}. ESR spectra were obtained by using a Varian E-Line Century Series ESR spectrometer in the X-band region at 9.15 GHz on samples prepared as frozen toluene glasses in quartz ESR tubes. *N*-Methylimidazole was used as an added axial base. The **g** tensors and *A* values were determined relative to a DPPH external standard. Electron impact (EI) and fast atom bombardment (FAB) mass spectra were determined on a VG 70-250S and a Kratos MS-30 mass spectrometer, respectively. Visible and ultraviolet spectra were obtained on a Varian 2300 recording spectrophotometer interfaced to an IBM PC computer for data acquisition.

The air-sensitive samples were prepared in 10-mm quartz cells in the inert-atmosphere box (Vacuum Atmospheres), and the spectra were measured immediately upon removal. The samples were dissolved in toluene containing a 100-fold excess of *N*-methylimidazole. Exposure of the solutions to dioxygen was accomplished through use of Tylan Model FC-260 flow meters, which provided a control mechanism for varying the partial pressures of oxygen in the nitrogen/oxygen gas mixture used for bubbling through the cell. This gas mixture was presaturated with toluene. A Neslab constant-temperature circulation system was used to control the temperature of the cell by pumping cooled solvent (ethanol or methanol) through a Varian variable-temperature double-jacketed cell holder within the nitrogen-flushed cell compartment. The cell temperature was monitored by a calibrated copper–constantan thermocouple, which was attached to the cell holder.

Syntheses. 2,2′-(Hexamethylenedioxy)bis[8-(salicylideneamino)-naphthalene]. This ligand (hexamethylene) was prepared as reported in the literature.[12] EI mass spectrum: molecular ion peak at 608 amu.

2,2′-(*p*-Xylylenedioxy)bis[8-(salicylideneamino)naphthalene]. Preparation of the *p*-xylylene ligand generally followed the same procedures employed above, with the α,α′-dibromo-*p*-xylene replacing the 1,6-dibromohexane as the bridging linkage. The ligand was collected from a silica gel column, 40–200 mesh, using dichloromethane followed by ethyl acetate as eluants. The bright yellow band was evaporated to dryness and recrystallized from a mixture of dichloromethane and hexane. FAB mass spectrum: molecular ion peak at 629 amu. ^1H NMR in $CDCl_3$: 5.17 (singlet, 4 H), 6.91–7.81 (complex multiplets, 25 H), 8.69 (singlet,

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(1) Antonini, E.; Brunori, M. *Hemoglobin and Myoglobin and Their Reaction with Ligands*; Elsevier: New York, 1971; p 93.
(2) Shikama, K. *Coord. Chem. Rev.* **1988**, *83*, 73–91.
(3) Mlodnicka, T. *J. Mol. Catal.* **1986**, *36*, 205–242.
(4) Malmstrom, B. G. *Annu. Rev. Biochem.* **1982**, *13*, 21–59.
(5) Almog, J.; Baldwin, J. E.; Dyer, R. L.; Peters, M. *J. Am. Chem. Soc.* **1975**, *97*, 227.
(6) Niederhoffer, E. C.; Timmons, J. H.; Martell, A. E. *Chem. Rev.* **1984**, *84*, 137.
(7) Smith, T. D.; Philbrow, J. R. *Coord. Chem. Rev.* **1981**, *39*, 295–384.
(8) Almog, J.; Baldwin, J. E.; Huff, J. *J. Am. Chem. Soc.* **1975**, *97*, 227.
(9) Jones, R. D.; Summerville, D. A.; Basolo, F. *Chem. Rev.* **1979**, *79*, 139.
(10) Busch, D. H. *Proceedings of Symposium on Dioxygen Carriers and Dioxygen Activation*; Texas A&M University: College Station, TX, March 1987.
(11) Busch, D. H. *La Transfusione del Sangue* **1988**, *33*, 57–69.
(12) Hendrickson, A. R.; Hope, J. M.; Martin, R. L. *J. Chem. Soc., Dalton Trans.* **1979**, 1497.
(13) Baker, A. T.; Martin, R. L.; Taylor, D. *J. Chem. Soc., Dalton Trans.* **1979**, 1503.
(14) Alcock, N. W.; Lin, W.-K.; Cairns, C.; Pike, G. A.; Busch, D. H. *J. Am. Chem. Soc.* **1989**, *111*, 6630–6643.
(15) Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. *Purification of Laboratory Chemicals*; Pergamon Press: New York, 1980.

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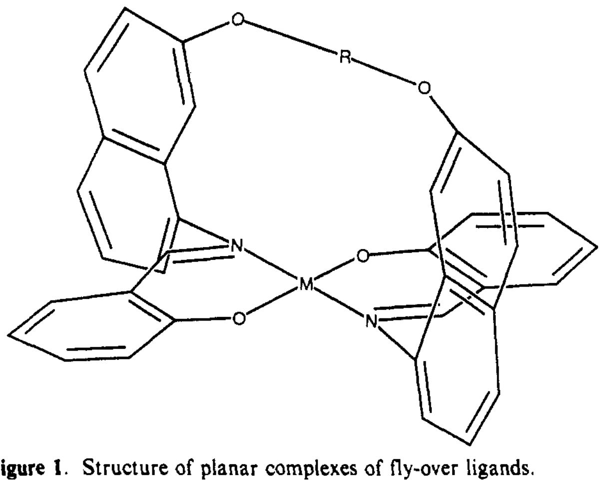

Figure 1. Structure of planar complexes of fly-over ligands.

2 H), and 13.32 ppm (singlet, 2 H). The singlets at 5.17, 8.69, and 13.32 ppm are assigned to the methylene, the vinyl, and the hydroxyl protons, respectively.

The Hexamethylene Cobalt(II) Complex. In the inert-atmosphere glovebox, the ligand, 2,2'-(hexamethylenedioxy)bis[8-(salicylideneamino)naphthalene] (0.20 g, 0.33 mmol), cobalt(II) acetate tetrahydrate (0.083 g, 0.33 mmol), and a trace amount of pyridine were gently heated at reflux for 1 h in ethanol (50 mL). the reaction mixture was stirred at ambient temperature overnight, and an orange precipitate was collected by filtration.

The *p*-Xylylene Cobalt(II) Complex. Because the procedure for the above hexamethylene complex produced primarily polymeric species, this complex was prepared by the slow addition of reactants under high-dilution conditions. Solutions of 2,2'-(*p*-xylylenedioxy)bis[8-(salicylideneamino)naphthalene] (0.184 g, 0.29 mmol, in 150 mL of an ethanol/dichloromethane mixture) and cobalt(II) acetate tetrahydrate (0.073 g, 0.29 mmol, in 150 mL of ethanol) were added via syringe pump at a rate of 6 mL/h into a three-neck round-bottom flask containing a reservoir of 200 mL of ethanol. The reaction mixture was vigorously stirred throughout the addition of the reagents and was then stirred overnight after the addition was complete. An orange precipitate was collected by filtration. The reaction was performed in a nitrogen-rich atmosphere, and the filtration was performed in air. At ambient temperature, no evidence for dioxygen binding was apparent.

Results and Discussion

The cobalt(II) complexes of the ligands having hexamethylene and *p*-xylylene bridging linkages were synthesized by the addition of stoichiometric amounts of cobalt(II) acetate tetrahydrate and the respective free ligands in a large excess of ethanol. In the preparation of the hexamethylene complex, the ligand, the cobalt salt, and a small amount of pyridine (for enhanced solubility of the ligand) were heated in ethanol in a one-pot reaction. The more dilute conditions in this system relative to the initial work by Martin and co-workers[12] favored the formation of a monomeric complex. The molecular ion peak observed at 665 amu corresponds to the monomeric species; this was the major peak in the EI mass spectrum.

In the *p*-xylylene case, however, similar reaction conditions resulted in the formation of an insoluble orange solid, suggesting that polymeric species had been produced. No parent molecular ion peak was observed in the mass spectrum for this product. Slow addition of the reagents, by syringe pump, into a reservoir of ethanol resulted in the formation of a relatively well-behaved microcrystalline orange product. This species is somewhat soluble in common organic solvents, particularly in the presence of a nitrogenous base such as pyridine. The FAB mass spectrum of this complex featured the molecular ion peak at 686 amu and additional expected fragmentation peaks.

Dioxygen Binding Studies. In the first reported synthesis of a cobalt(II) complex of the fly-over family of ligands (the tetramethylene-linked species), Martin and associates[12,13] reported that they were unable to observe any evidence for dioxygen binding. No details were given on the methods or conditions used in their tests for dioxygen binding. In light of the anticipated low dioxygen affinity for this class of complexes, we chose, as the axial base, a ligand known for its ability to enhance O_2 affinity, *N*-methylimidazole. Dioxygen binding studies were performed on 10^{-4} M cobalt(II) complex solutions in toluene with a 100-fold excess of the axial base.

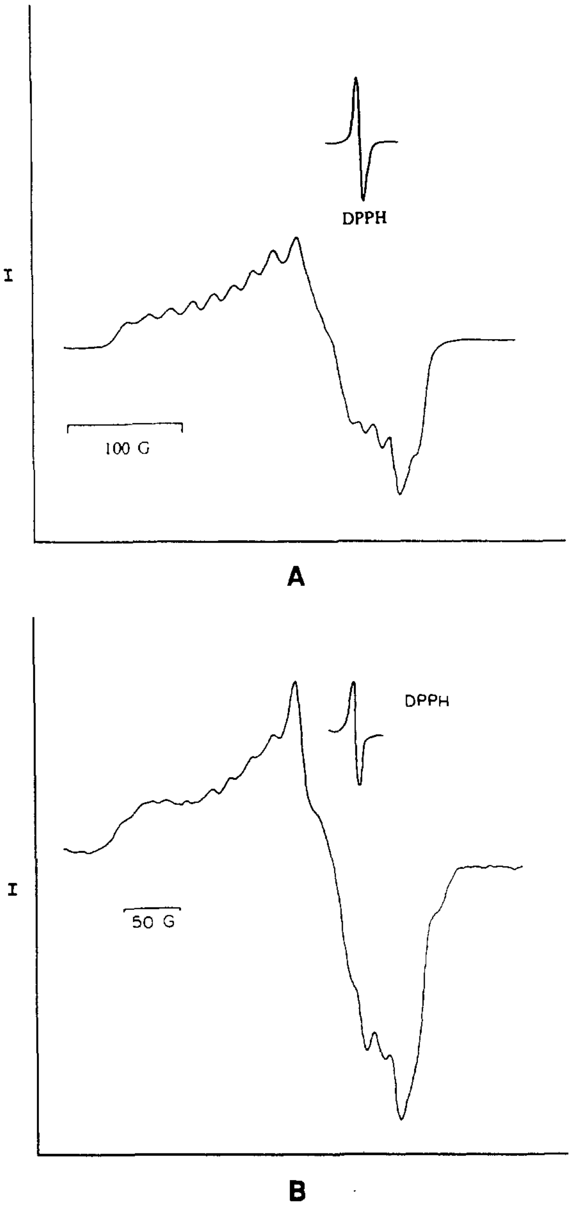

Figure 2. ESR spectra of the dioxygen adducts of the cobalt(II) complexes of fly-over ligands (X-band, toluene glass at 77 K): (A) bridging group hexamethylene; (B) bridging group *p*-xylylene.

The cobalt(II)-containing solutions described above were ESR silent at 77 K prior to exposure to dioxygen, suggesting that the metal is in the high-spin d^7 electronic configuration. This behavior has been observed for other N_2O_2 Schiff-base species.[16] Pure oxygen was bubbled through the solutions at room temperature, and the solutions were then rapidly cooled to 77 K. The ESR spectra (Figure 2) for the hexamethylene- and *p*-xylylene-linked compounds exhibit spectral features characteristic of 1:1 cobalt:dioxygen adducts, showing the typical eight-line hyperfine splittings that result from coupling of the unpaired electron with the cobalt nucleus ($I = {}^7/_2$). The values of $A_{\parallel}$, $g_{\parallel}$, and $g_{\perp}$ are 18.6 G, 20.90, and 1.987 and 18.2 G, 2.091, and 1.985 for the hexamethylene and the *p*-xylylene derivatives, respectively. Thus, these complexes do bind oxygen at sufficiently low temperatures (77 K).

In order to quantitatively determine the dioxygen affinities of these complexes, the solutions were equilibrated successively with

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(16) Glogowski, M. W. Ph.D. Dissertation, The Ohio State University, 1988.

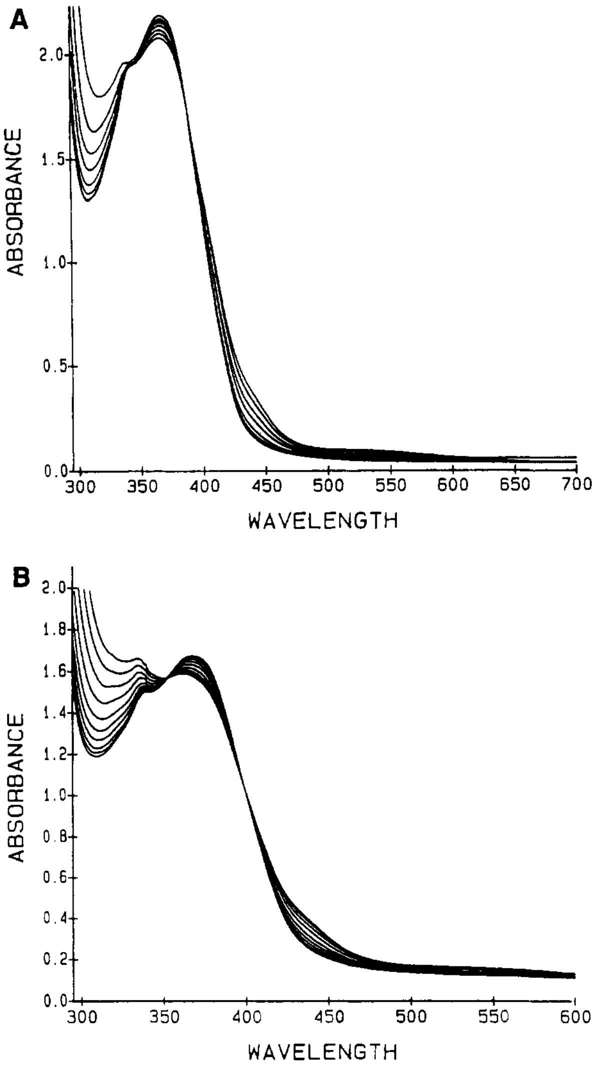

Figure 3. (A) Dioxygen titration of the hexamethylene-bridged complex (*N*-methylimidazole/toluene, −39.1 °C. (B) Dioxygen titration of the *p*-xylylene-bridged complex (*N*-methylimidazole/toluene, −56.2 °C).

increasing partial pressures of dioxygen, and the accompanying changes in spectral features were monitored by UV–vis spectroscopy. The dioxygen affinity, K_{O_2}, can be calculated by a nonlinear least-squares fit of the equation

$$A = \frac{A_0 + \{[\mathrm{CoLBO_2}] - [\mathrm{CoLB}]\}K_{O_2}[\mathrm{CoLB}]_0(P_{O_2})}{1 + K_{O_2}(P_{O_2})}$$

where CoLB and $\mathrm{CoLBO_2}$ represent the five-coordinate precursor cobalt(II) complex and its dioxygen adduct, respectively (L = ligand, B = axial base). A and A_0 are the observed absorbances at a given partial pressure of oxygen, P_{O_2}, and at $P_{O_2} = 0$, respectively.[17]

The dioxygen titrations of the hexamethylene derivative were performed at −39.1 and −55.3 °C. The spectral changes occurring at −39.1 °C are presented in Figure 3A where K_{O_2} at this temperature was determined to be 0.007 (1) $\mathrm{Torr^{-1}}$. At −55.3 °C, K_{O_2} is 0.096 (1) $\mathrm{Torr^{-1}}$. For the *p*-xylylene derivative, K_{O_2} was determined at −56.2 °C to be 0.012 (1) $\mathrm{Torr^{-1}}$. This titration is shown in Figure 3B. Figure 4 illustrates the essentially complete reversibility of dioxygen binding for this system. Trace A is the initial spectrum before exposure to dioxygen, trace B corresponds to the spectrum obtained on exposure to 100% dioxygen, and trace C is the spectrum obtained after purging with nitrogen for 20 min. As shown, scans A and C are nearly coincident. The system containing the hexamethylene derivative exhibits similar behavior.

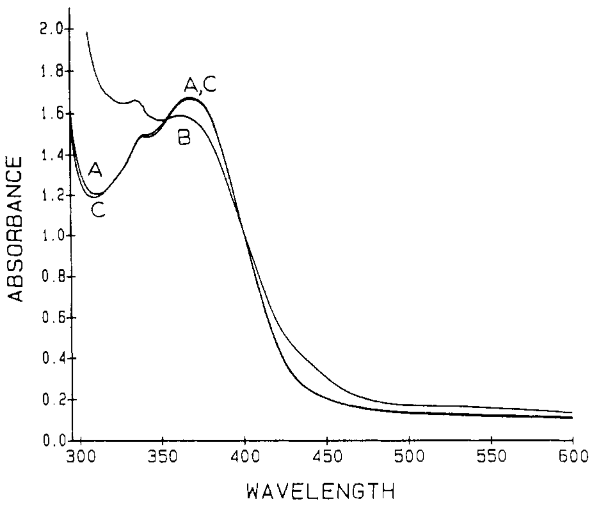

Figure 4. Demonstration of reversibility of the oxygenation of the *p*-xylylene-bridged complex (toluene/*N*-methylimidazole, −56.2 °C): (A) initial spectrum, N_2 atmosphere; (B) spectrum after equilibration with 1 atm of O_2; (C) spectrum after purging with N_2 for 20 min.

Clearly complexes of these *fly-over* Schiff-base ligands can bind dioxygen reversibly at low temperatures, albeit rather weakly, and no dioxygen binding ability is expected at room temperature. For the systems studied, the dioxygen affinity of the hexamethylene derivative is nearly an order of magnitude higher than that for the *p*-xylylene complex. Possibly this planar bridging group creates too shallow a cavity to easily accommodate the dioxygen, while the more flexible hexamethylene linkage can rise above the naphthyl risers, increasing the cavity height.

Studies on related *lacunized* cobalt(II) Schiff-base dioxygen carriers derived from bis(acetylacetone) ethylenediimine (acacen)[10,18] gave strongly contrasting results. Certain of those derivatives display strong dioxygen affinities at room temperature. However, it was also observed in those systems that the *p*-xylylene-bridged derivative suffered a substantial reduction of affinity when compared to the polymethylene-bridged derivatives. It is also true that the much studied *lacunar* cobalt(II) cyclidene complexes[19] exhibit much greater dioxygen affinities than those reported here. Since the unsubstituted cobalt(II) complexes of salen and acacen are not so different in behavior, some related *fly-over* Schiff-base derivatives of cobalt(II) might display greater affinities for dioxygen. However, this is not likely to be accomplished with the naphthyl riser used by Martin and in the present work, and this is in agreement with the original conclusions by the earlier workers. In view of the disappointingly low dioxygen affinities of the fly-over derivatives that have been studied, there is no reason to study the tetramethylene-bridged species further. Although it probably binds O_2 at very low temperatures, its dioxygen affinity would certainly be no higher than those reported here.

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(17) Thomas, R.; Fendrick, C. M.; Lin, W. K.; Glogowski, M. W.; Chavan, M. Y.; Alcock, N. W.; Busch, D. H. *Inorg. Chem.* **1988**, *27*, 2534–2540.

(18) Delgado, R.; Glogowski, M. W.; Busch, D. H. *J. Am. Chem. Soc.* **1987**, *109*, 6855–6857.

(19) Reference 10 and references therein.