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Preparation and Physical Properties of Alkylcobalt Complexes of the Coenzyme B_{12} Model Complex $RCo[C_2(DO)(DOH)_{pn}]X$

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A detailed and convenient three-step synthesis of $Co[C_2(DO)(DOH)_{pn}]I_2$ (IV) is described beginning with readily available starting materials. The 70–80% reduction of the diiodide IV to 1-g quantities of the crystalline Co(I) $Co[C_2(DO)(DOH)_{pn}](CO)$ (V) is presented as are the ^{13}CO-exchange reaction of V and its alkyl halide oxidative additions as a clean and efficient synthesis of $RCo[C_2(DO)(DOH)_{pn}]X$ complexes. Transformation of the alkyl halide adducts to $[RCo[C_2(DO)(DOH)_{pn}](base)]^+PF_6^-$ and BF_2-bridged derivatives is also described. Some of the key physical properties of the alkyl–cobalt complexes are also presented including their extent of axial halide dissociation, the pyridine binding constant of the methyl derivative, the photochemical cleavage of the alkyl–cobalt bond in the presence of $HMn(CO)_5$, and the properties of the oxime O···H···O bridge.

Introduction

A detailed picture of the mechanism of the 12 adenosylcobalamin dependent rearrangement reactions is slowly emerging from a large number of enzymic as well as chemical model studies.[1] Remaining mechanistic questions include (1) the kinetic and thermodynamic aspects of the initial cobalt–carbon bond thermolysis,[2] (2) the extent, if any, of cobalt participation in the rearrangement step, and (3) in the absence of Co participation, whether the rearrangement occurs via a R^+, $R\cdot$, or R^- species.[3]

Several years ago we initiated a program aimed at addressing these remaining mechanistic questions with initial emphasis on the chemical model approach. We were also interested in understanding more completely the interface[4a] between the biochemical-enzymic and chemical-model approaches to adenosylcobalamin chemistry as they did not seem to enjoy the synergism these approaches find in, for example, efforts to understand other metalloproteins such as hemoglobin[4b] or cytochrome P 450.[4c,d]

Recently, we have reported the results of our investigations of the remaining mechanistic questions in adenosylcobalamin-dependent chemistry. These studies, although still incomplete, have led to (1) the first preparation, characterization, and subsequent reactions of a protected form of the putative cobalt-bound diol dehydratase rearrangement intermediate,[5] (2) a kinetic and mechanistic investigation of the cobalt–carbon bond homolysis of $RCo[C_2(DO)(DOH)_{pn}]X$ complexes,[6] and (3) an electrochemical comparative study[7] of the closest two B_{12} models, Costa's $[RCo[C_2(DO)(DOH)_{pn}]B]^+X^-$, (Ia and Ib) model, and the more widely used but incorrectly charged RCo[bis(dimethylglyoximato)] or cobaloxime model II.

A cornerstone of our studies has been the high-yield preparation of the necessary $[RCo(C_2(DO)(DOH)_{pn}]X$ complexes, via RX oxidative addition, to the isolable cobalt(I) carbonyl complex $Co[C_2(DO)(DOH)_{pn}](CO)$ (eq 1). Herein we report

$$\underset{\text{V (blue)}}{Co^{I}CO} + RX \text{ (excess)} \xrightarrow[\substack{25\text{–}80\ ^\circ C\\ 65\text{–}90\%\\ \text{isolated}\\ \text{yields}}]{\text{benzene}} CO + \underset{\substack{\textbf{1–9, Table I}\\ \text{(orange)}}}{R[Co]X} \quad (1)$$

the full details of the $C_2(DOH)_{2_{pn}}$ ligand preparation, the preparation of $Co[C_2(DO)(DOH)_{pn}]I_2$, the 70–80% yield reduction of the cobalt diiodide to give 1.0-g amounts of crystalline, storable $Co^I[C_2(DO)(DOH)_{pn}](CO)$, the smooth RX oxidative additions to this Co^ICO complex in 65–90% isolated yields, and the physical properties of the resulting alkyl-[Co]halide adducts.

Experimental Section

(A) General Data. (i) Methods for Handling Air-Sensitive Compounds. Reactions involving air-sensitive materials like $Co[C_2(DO)(DOH)_{pn}](CO)$ were handled with use of standard Schlenk tube techniques[8] and an inert-atmosphere (N_2), double-length Vacuum Atmospheres drybox. The H_2O and O_2 levels were maintained at <1 ppm as monitored by a lighted 60-W light bulb with a hole in the glass that typically lasted for several weeks. House N_2 was further purified by passage through both the Linde 4-Å molecular sieves and a heated $20 \times 1^1/_2$ in. glass column of BASF R3-11 oxygen scavenger in the black (reduced) form. Air-free transfers were affected by Hamilton gas-tight syringes or needlestock (stainless-steel cannula) transfers. Light was excluded from all the cobalt alkyls at all times because of the known sensitivity of these materials to photochemical homolysis. Benzene was distilled under N_2 from CaH_2 while THF was distilled under N_2 from sodium benzophenone ketyl. Dry, degassed solvents were stored in the drybox after the <1 ppm O_2 box atmosphere was bubbled through them for 15 min. Elemental analyses were obtained from the University of Oregon microanalytical laboratory.

(ii) Equipment. IR spectra were recorded on a Beckman IR-10 or IR-5A. NMR spectra were obtained on a Varian XL-100 and UV–visible spectra on a Cary 15. Conductivity measurements were made with use of a Radiometer (Copenhagen) type CDM2e conductivity meter and type CDC114 cell (cell constant = 1.69 cm^{-1}). The cell constant was checked by the method of Fuoss[9] and found to be the 1.69-cm^{-1} value within experimental error.

(iii) Materials. Commercial carbon monoxide (AIRCO) and alkyl halides (Aldrich) were used as received. $BF_3{\cdot}OEt_2$ was distilled under N_2 from CaH_2. 1,5,6-Trimethylbenzimidazole was prepared by the literature method[10] (mp 143.5–144 °C; lit.[10] mp 142–143 °C). $HMn(CO)_5$ was prepared by Edgell's method.[11]

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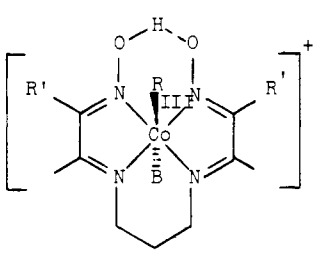
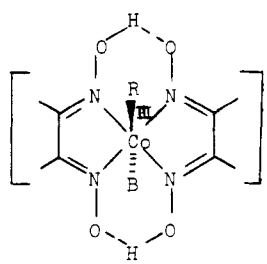


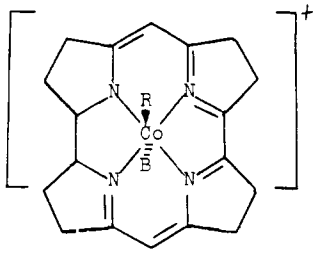
Ia (R=Et) $(RCo[C_2(DO)(DOH)_{pn}]B)^+X^-$

Ib (R=Me) $(RCo[(DO)(DOH)_{pn}]B)^+X^-$



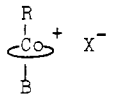
II

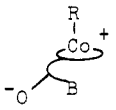
(alkyl(base)cobaloxime)



Coenzyme B_{12}

(unsubstituted corrin ring only is shown)





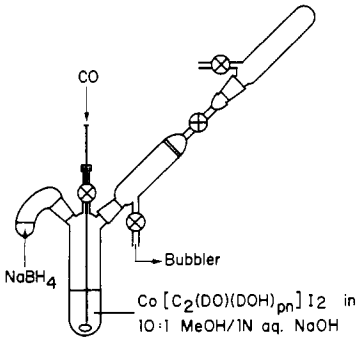
Ethyl (Bromomethyl)methylmalonate. This oxidative addition substrate was prepared with use of the literature procedure[12] for the malonic ester synthesis on a one-tenth (0.5 mmol) scale and dropwise addition of the $Na^+[CH_3C(CO_2Et)_2]^-$ in dry EtOH to freshly distilled CH_2Br_2 in dry EtOH. Fractional distillation and collection of the ca. 130–140 °C (at 17 mmHg) fraction yielded 75% pure (^1H NMR) product. Redistillation at 17 mmHg yielded 16.9 g (11%) of a fraction boiling at 135–142 °C that was ca. 87% of the desired material. ^1H NMR ($CDCl_3$): $\delta(Me_4Si)$ 1.3 (t, 6 H, J = 7 Hz), 1.5 (s, 3 H), 3.8 (s, 2 H), 4.2 (q, 4 H, J = 7 Hz).

(B) Macrocyclic Ligand Synthesis. (i) 3-Oximino-2-pentanone. This first step in the ligand synthesis was accomplished with use of the general method of α-oximino ketone synthesis due to Ferris.[13] In a hood, methyl nitrite was bubbled, at a rate sufficient to maintain a vigorous reflux, into a three-neck flask fitted with a condenser, a stopper, and a gas dispersion tube and containing a stirred mixture of 2-pentanone (102 g, 1.19 mol), 400 mL of diethyl ether, and 15 mL of concentrated HCl. The methyl nitrite was generated in a separate three-neck flask by dropping-funnel addition of a solution of H_2SO_4 (100 mL) and H_2O (95 mL) onto a stirred slurry of $NaNO_2$ (112 g, 1.62 mol), methanol (66 g, 2.08 mol) and H_2O (75 mL). After the addition of methyl nitrite was complete, the ether solution was neutralized with saturated $NaHCO_3$. The aqueous layer was extracted once with ether, and the combined ether portions were dried over $MgSO_4$. The product crystallized from cold Et_2O/hexane and then was recrystallized from hexane until 70 g (52%) of white crystals (mp 61–62 °C) were obtained. IR (CCl_4): 3560 (s), 3300 (br), 2950, 2920, 2850, 1685 (s, br) cm^{-1}. ^1H NMR ($CDCl_3$): $\delta(Me_4Si)$ 1.03 (t, 3 H), 2.4 (s, 3 H) on 2.6 (q, 2 H). Cruder mixtures (mp ca. 57–60 °C) of the syn and anti isomers have been carried on without complications.

(ii) Preparation of $C_2(DOH)_{2_{pn}}$(2,10-diethyl-3,9-dimethyl-1,4,8,11-tetraazaundeca-1,3,8,10-tetraene-1,11-diol) (III). The $C_2(DOH)_{2_{pn}}$ ligand, III, was formed by a Schiff's base condensation of the α-ketooxime and 1,3-diaminopropane analogous to Uhlig and Friedrich's procedure.[14] Thus 30 g (0.26 mol) of 3-oximino-2-pentanone, 9.6 g (0.13 mol) of 1,3-diaminopropane (Aldrich), and 200 mL of isopropyl ether from a new, unopened bottle were heated for at least 4 h under reflux until 4–6 mL of H_2O was collected in a Dean–Stark trap. The volume of ether was reduced to 100 mL with use of a rotary evaporator, and then the crystalline product was obtained after several days from the refrigerated solution (31 g, 90%). Recrystallization from isopropyl ether/hexane yielded 68% of pure ligand (mp 143–144 °C). Any unused isopropyl ether was immediately disposed of to prevent peroxide formation. ^1H NMR (acetone-d_6): $\delta(Me_4Si)$ 1.0 (t, 6 H, J = 7 Hz), 2.04 (s, 6 H), 2.74 (q, 4 H, J = 7 Hz), 3.60 (t, 4 H, J = 7 Hz).

(iii) Insertion of Cobalt into the Ligand. Synthesis of $Co^{III}[C_2(DO)(DOH)_{pn}]I_2$ (IV). A solution of 14.3 g (60 mmol) $CoCl_2 \cdot 6H_2O$ in 50 mL of H_2O and a solution of 80.0 g (0.480 mol) of KI in 75 mL of H_2O were added to a solution of 16.1 g (60 mmol) of the $C_2(DOH)_{2_{pn}}$ ligand in 150 mL of acetone. Compressed air was bubbled through the reaction solution at room temperature for 3–4 h. A green-brown solid was collected by frit and washed with ca. 6 L of H_2O until the washings were nearly colorless and then with 2 L of ethanol and 2 L diethyl ether followed by air-drying to yield 20.2 g (58%) of dark green microcrystals. The crude product was Soxhlet extracted with acetone and then recrystallized by reducing the volume of the solution and cooling to yield 18.6 g (53%) of lustrous green crystals. Anal. ($C_{13}H_{23}N_4O_2I_2Co$) C, H, N, I. λ_{max} (THF) = 460 nm. ^1H NMR ($CDCl_3$): $\delta(Me_4Si)$ 1.16 (t, 6 H, J = 7.5 Hz), 2.55 (s, 6 H), 2.65 (m, 2 H), 3.05 (q, 4 H, J = 7.5 Hz), 4.15 (br t, 4 H, J = 5 Hz), 19.42 (s, 1 H, O···H···O).

(C) Preparation of the Cobalt(I) Carbonyl $Co[C_2(DO)(DOH)_{pn}](CO)$ (V). In a hood, the double-neck Schlenk apparatus



was assembled, including an attached Schlenk filter and a solid ($NaBH_4$) addition side arm. The apparatus was evacuated and refilled with N_2 several times after 2.5 g (4.31 mmol) of $Co[C_2(DO)(DOH)_{pn}]I_2$ and a stir bar were placed in the bottom of the double-neck Schlenk and 0.65 g (2 equiv) of $NaBH_4$ was placed in the solid addition side arm. With use of needlestock techniques, 250 mL of a thoroughly degassed (3 cycles freeze/pump/thaw) solution of 10 vol % 1 N aqueous NaOH in MeOH was added. (Since the slowest step of this preparation is the degassing of the solvents, it is more efficient to prepare twice the necessary quantities of degassed solvents and then do the reaction twice in a row.) Carbon monoxide was bubbled through the cooled (0 °C), rapidly stirred solution, and the $NaBH_4$ was added to the solution in small portions with the help of an electric vibrator or gentle tapping. The deep blue color initially formed on $NaBH_4$ addition rapidly turned dark green as the reaction proceeded. Carbon monoxide bubbling was continued until no more CO is consumed ($^1/_2$–1 h). Most, *but not all*, of the methanol was then evaporated under vacuum with use of a *lukewarm* bath during which a red-purple microcrystalline solid precipitated from the aqueous basic solution. (The Schlenk apparatus was volumetrically marked at the beginning of a run so that the final volume would be slightly greater than the 10% × 250 mL of H_2O/NaOH = 25 mL of MeOH added. If all the MeOH is removed, byproducts are precipitated on the desired cobalt carbonyl, giving an inferior product.) The precipitate was

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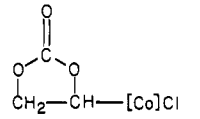
Table I. Alkyl–Cobalt(III) Complexes Prepared by Oxidative Addition to $Co^{I}[C_2(DO)(DOH)_{pn}](CO)$

entry	R[Co]X	isolated yields, %
1	CH_3[Co]I	85
2	*n*-Bu[Co]Br	69
3	$PhCH_2$[Co]Cl	90
4	$CH_3C(CO_2Et)_2CH_2$[Co]Br	73
5		80
6	[*n*-Bu[Co]Bz-Me]$^+PF_6^-$	67
7	[Me[Co]OH_2]$^+PF_6^-$	45
8	[*n*-Bu[Co]OH_2]$^+PF_6^-$	67
9	$(CH_3)_2CH$[Co]Br	8

collected in the Schlenk filter and washed with 250 mL of distilled and degassed (three freeze/pump/thaw cycles) water. The Schlenk filter containing the product was detached from the apparatus under a fast N_2 flow, a securely fastened cap was attached, and the apparatus was transfered into the inert-atmosphere drybox where a vacuum hose was attached for overnight drying at <0.1 mmHg. The product 1.0–1.2 g (70–80%) was removed from the frit the next day and stored in the box. The last traces of the product were often collected from the Schlenk filter with use of benzene and then used in an oxidative addition reaction. (We have found you cannot use 2× the materials in the same amounts of solvents without a much poorer yield (~20%) although scale up by 5–10× with use of a larger apparatus should be possible.) IR (THF): ν_{CO} = 1972 cm^{-1}; $\nu_{^{13}CO}$ = 1925 cm^{-1}. λ_{max}(THF) = 626 nm. The elemental analysis suggests a H_2O-solvated complex. Anal. Calcd for $C_{14}H_{23}N_4O_3Co{\cdot}0.2\ H_2O$: C, 46.98; H, 6.59; N, 15.65. Found: C, 45.38; H, 6.55; N, 15.25. Repeat anal. Found: C, 45.93; H, 6.46; N, 15.05. Karl Fischer analysis for water (Galbraith Laboratories): calcd, 1.0% H_2O; found, 0.8% H_2O. ^1H NMR (benzene-d_6): $\delta(Me_4Si)$ 1.29 (t, 6 H, J = 7 Hz), 1.48 (s, 6 H), 1.8 (m, 1 H), 2.3–3.5 (m, 9 H total), 19.7 (s, 1 H).

(D) General $RCo[C_2(DO)(DOH)_{pn}]X$ Preparation via RX Oxidative Addition to $Co[C_2(DO)(DOH)_{pn}](CO)$. RX oxidative addition products **1–5** (Table I) were prepared by the following general procedure. In the drybox, 200 mg (0.56 mmol) of $Co[C_2(DO)(DOH)_{pn}](CO)$ was placed with a stir bar and 30 mL of distilled (CaH_2) degassed benzene in a 30-mL round-bottom flask to yield a deep blue solution. An excess (5–10 equiv) of alkyl halide was added, and the solution was stirred after being wrapped with aluminum foil to protect it from light. If necessary the solution was also heated until the blue Co(I) color was replaced by the red-orange cobalt(III)–alkyl color. The product was removed from the box, and all subsequent manipulations were done either with light excluded or in subdued light. If an orange cobalt–alkyl precipitate was observed, it was filtered and washed with benzene. Additional product was usually obtained by chromatography on a 1000-μm preparative SiO_2 plate eluting with THF and collecting the orange middle band that usually follows a leading green dihalide, $Co[C_2(DO)(DOH)_{pn}]X_2$, band and proceeds a dark band remaining at the origin. Recrystallization can often be accomplished by using Et_2O/THF at −22 °C. If no product precipitates directly out of the benzene reaction mixture, the benzene is removed and the residue taken up in Et_2O/THF for crystallization. Judging by the yields obtained, benzene is often a prefered oxidative addition solvent relative to THF.

(i) MeI Adduct. A 10-fold excess of methyl iodide to V was stirred at −25 °C for 3 h during which the color changed to orange. During rotary evaporation of the benzene, the orange product precipitated. It was collected and washed with cold benzene and dried (yield 85%). Anal. ($C_{14}H_{26}N_4O_2CoI$) C, H, N. ^1H NMR ($CDCl_3$): $\delta(Me_4Si)$ 0.69 (s, 3 H), 1.10 (t, 6 H, J = 7 Hz), 2.28 (s, 6 H), 2.74 (m, 6 H), 3.5–4.3 (m, 4 H).

(ii) *n*-BuBr Adduct. A 10-fold excess of *n*-BuBr to V was stirred at 80 °C under N_2 for 36 h. The resulting orange solution was evaporated to dryness under reduced pressure and the residue taken up in Et_2O/THF. Cooling at −20 °C for 18 h yielded 54% of an analytically pure, dark orange semicrystalline solid. Subsequent preparations of this material gave 63% and 69% yields. Anal. ($C_{17}H_{32}N_4O_2CoBr$) C, H, N. ^1H NMR (acetone-d_6): $\delta(Me_4Si)$ 0.74 (t, 2 H, J = 7 Hz), 1.06 (t, 9 H, J = 7 Hz), 1.0–1.4 (m, 4 H), 2.36 (s, 6 H), 2.7 (m, 6 H), 3.8 (m, 4 H).

(iii) $PhCH_2X$ Adduct. Excess benzyl chloride was stirred with V at 25 °C for 3 h. The red-orange precipitate was filtered, washed with cold benzene, and dried (vacuum, 25 °C) overnight (yield 90%). The benzyl iodide adduct is best prepared by NaI/acetone exchange of the axial chloride for iodide on the benzyl chloride compound. Direct addition of freshly recrystallized $PhCH_2I$ failed to give good yields of the oxidative addition product due, presumably, to the ready decomposition of the $PhCH_2I$. Anal. ($C_{20}H_{30}N_4O_2CoCl$) C, H, N adduct. ^1H NMR ($CDCl_3$): $\delta(Me_4Si)$ 1.10 (t, 6 H, J = 7 Hz), 2.16 (s, 6 H), 2.54 (s, 2 H), 2.5–3.0 (m, 6 H), 3.15–4.05 (m, 4 H), 6.60–7.2 (AA'BB'C, 5 H). (Both the analysis and NMR data are for the $PhCH_2Cl$ adduct.)

(iv) Ethyl (Bromoethyl)methylmalonate Adduct (Entry 4, Table I). A 2.3-fold excess of the alkyl bromide was refluxed overnight in benzene with 220 mg (0.62 mmol) of the $Co[C_2(DO)(DOH)_{pn}](CO)$ complex with use of aluminum foil for protection from light. The next day TLC (SiO_2, acetone) showed only a single orange spot (R_f = 0.57). The benzene was removed, and a small amount of Et_2O was added followed by enough THF to dissolve the solid. Cooling at −22 °C overnight followed by a 4/1 Et_2O/THF wash and drying yield 207 mg (56%) of orange crystals. A second crop of larger red crystals was obtained in the same way (65 mg) for a total yield of 73%. Anal. ($C_{22}H_{38}N_4O_6CoBr$) C, H, N. IR (KBr): 1720 cm^{-1}. ^1H NMR ($CDCl_3$): $\delta(Me_4Si)$ 1.13 (t, 6 H, J = 7 Hz), 1.20 (t, 6 H, J = 7.5 Hz), 1.24 (s, 3 H), 1.63 (s, 2 H), 2.32 (s, 6 H), 2.8 (q on m, 6 H), 3.6 (br t, 2 H, J (apparent) = 13 Hz), 4.02 (q, 4 H, J = 7 Hz) on 4.0 (b t, 2 H)).

(v) 4-Chloro-2-dioxolanone (or Chloroethylene Carbonate) Adduct. The preparation and full characterization of this adduct has been described in detail elsewhere,[5b] including the results of a single-crystal X-ray diffraction structural analysis.

(vi) $[RCo[C_2(DO)(DOH)_{pn}]Bz\text{-}Me]^+PF_6^-$. The R = *n*-butyl and other alkylcobalt 1,5,6-trimethylbenzimidazole derivatives can be prepared as follows. In a 25-mL Erlenmeyer flask, 1 equiv of alkyl[cobalt]halide adduct (generally ca. 200-mg scale) and 1.1 equiv of 1,5,6-trimethylbenzimidazole were dissolved in hot methanol (10 mL) followed by the addition of 1 equiv of $Ag^+PF_6^-$. The resulting AgX precipitate was removed by a medium frit after gentle warming for 5 min on a steam bath. The solution was returned to the steam bath and concentrated to about 2 mL. It was then capped with a septum stopper and cooled to −22 °C overnight to yield a yellow to brown, generally noncrystalline solid which was washed with cold methanol and vacuum-dried at 25 °C for at least 5 h. The yield was 67% in the case of $[n\text{-}BuCo[C_2(DO)(DOH)_{pn}]Bz\text{-}Me]^+PF_6^-$. Anal ($C_{27}H_{44}N_4O_2CoPF_6$) C, H, N. ^1H NMR (acetone-d_6): $\delta(Me_4Si)$ 0.74 (t, 2 H, J = 7 Hz), 1.08 (t, 6 H, J = 8 Hz), 1.5–1.8 (m, 7 H), 2.34 (s, 3 H), 2.36 (s, 3 H), 2.52 (s, 6 H), 2.64–2.94 (m, 6 H), 3.82 (s, 3 H), 3.74–4.24 (m, 4 H), 8.06 (s, 1 H), 7.34 (s, 1 H), 7.58 (s, 1 H).

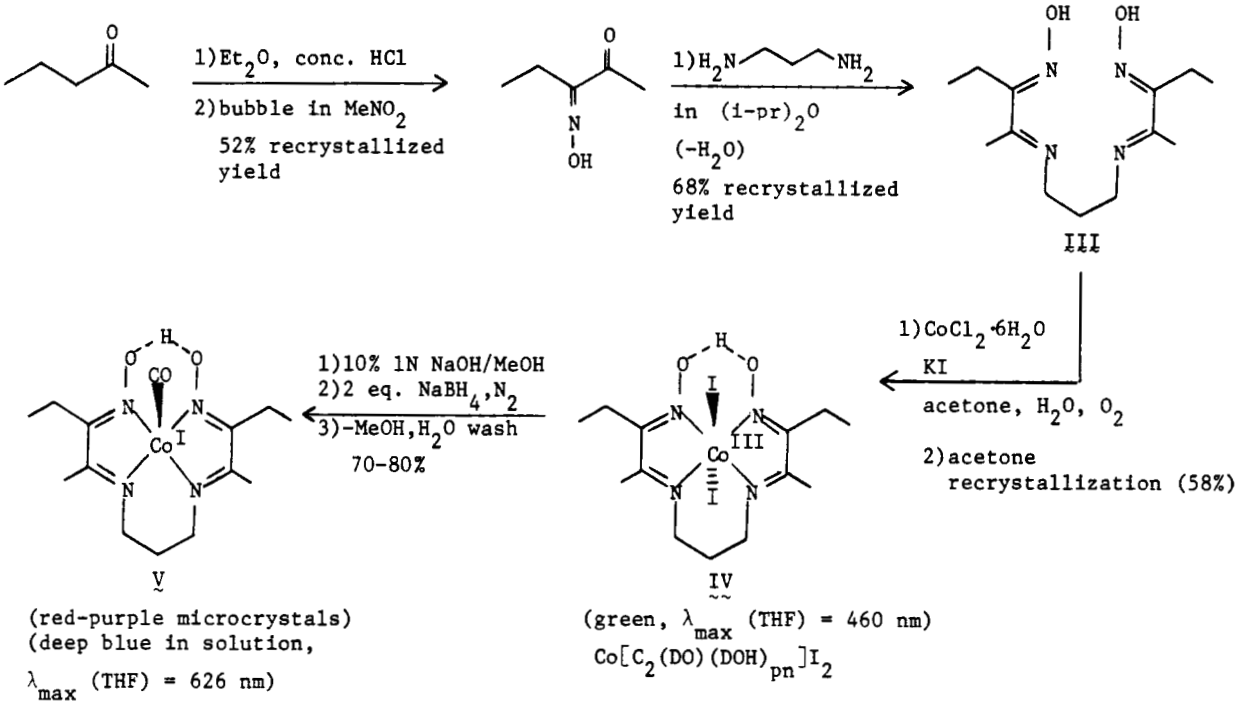
(vii) and (viii) $[RCo[C_2(DO)(DOH)_{pn}]OH_2]^+PF_6^-$. The R = methyl and *n*-butyl derivatives were prepared analogous to the 1,5,6-trimethylbenzamidazole derivatives in part vi except that the 1,5,6-trimethylbenzimidazole was omitted. Generally 2–3 drops of water must be added to the methanol solutions in order to induce crystallization of the alkylcobalt salt. The $[n\text{-}BuCo[C_2(DO)(DOH)_{pn}]OH_2]^+PF_6^-$ was prepared as 67% of 2–3 mm long deep red needles in this fashion while $[MeCo[C_2(DO)(DOH)_{pn}]OH_2]^+PF_6^-$ was prepared as 45% of deep red microcrystals. H_2O is required by the analytical data and was confirmed in the case of the *n*-butyl complex by a Karl Fischer titration (Galbraith Laboratories): calcd, 3.3% H_2O; found, 2.5% H_2O.

For the *n*-butyl complex: Anal ($C_{17}H_{34}N_4O_3CoPF_6$) C, H, N. ^1H NMR (acetone-d_6): $\delta(Me_4Si)$ 0.74 (t, 2 H), 1.10 (t, 6 H, J = 7 Hz), 1.5–1.9 (m, 7 H), 2.46 (s, 6 H), 2.70–3.0 (m, 10 H on solvent residuals), 3.8–4.0 (m, 4 H).

For the methyl complex: Anal ($C_{14}H_{28}N_4O_3CoPF_6$) C, H, N. ^1H NMR (acetone-d_6): $\delta(Me_4Si)$ 0.74 (s, 3 H), 1.10 (t, 6 H, J = 7 Hz), 2.22 (quin, 2 H, J = 8 Hz), 2.48 (s, 6 H), 2.78 (q, 4 H, J = 8 Hz), 3.90 (apparent d, 4 H).

(ix) Isopropyl Halide Adducts. In benzene with use of freshly distilled (P_2O_5) isopropyl bromide and with careful attention to the exclusion of light, a small yield of the isopropyl bromide adduct was prepared and identified by ^1H NMR. Thus in the drybox 6 equiv of isopropyl bromide (bp 59 °C) and 200 mg of $Co[C_2(DO)$-

Scheme I. Ligand Synthesis and the Preparation of $CoI[C_2(DO)(DOH)_{pn}](CO)$



$(DOH)_{pn}](CO)$ in 15 mL of benzene were stirred at <59 °C for at least 24 h. An analytical TLC (SiO_2, THF) of the red-orange solution in the drybox showed green cobalt dibromide (R_f = 0.63), orange product (R_f = 0.38), and a slow moving red material (R_f = 0.06) which is probably $Co^{II}[C_2(DO)(DOH)_{pn}]Br$. Column chromatography in the box (SiO_2, THF) with light exclusion yielded ca. 20 mg (8%) of slightly impure (by TLC) orange isopropyl bromide adduct. ^1H NMR (benzene-d_6) showed the distinct doublet δ 0.35 (6 H, J = 7 Hz) characteristic of the isopropyl group in addition to the usual ligand peaks δ 1.1 (t, 6 H, J = 7 Hz), 1.6 (s, 6 H), 1.9 (m, 2 H), ca. 2.7 (m, 5 H), and 3.6 (m, 4 H, J = 7 Hz). THF was also tried as a reaction solvent, and, affter 18 h, the blue solution turned green rather than orange. TLC in the drybox showed no orange alkyl but only green cobalt dibromide and a little red Co(II). Isolation (72% of crude) followed by acetone/EtOH recrystallization yielded 53% of $Co[C_2(DO)(DOH)_{pn}]Br_2$. In a similar experiment, the attempted oxidative addition of isopropyl iodide yielded, after SiO_2/CH_2Cl_2 chromatography and recrystallization, 30% of the diiodide, $Co[C_2(DO)(DOH)_{pn}]I_2$.

(x) BF_2-Bridged Derivatives. The proton bridging the two oxime oxygens can be replaced by a BF_2 bridge as follows (illustrated for the *n*-BuBr adduct). The *n*-BuBr adduct was prepared as in part ii on a 200-mg scale of cobalt carbonyl. Dry THF (20 mL) was added to the orange benzene solution of $n\text{-}BuCo[C_2(DO)(DOH)_{pn}]Br$ followed by 1 equiv of freshly distilled $BF_3 \cdot OEt_2$ and stirring overnight. After removal of the solvents, -22 °C recrystallization from THF/Et_2O gave 140 mg (49%) of analytically pure orange $OB(F_2)O$-bridged product. An infrared spectrum shows that several bands present in the starting O···H···O-bridged material (IR (KBr): 1490 (probably $\nu_{O\text{-}H\text{-}O}$), 1220–1300 (several bands), 845, 865 cm^{-1}) are absent in the BF_2-bridged product and are replaced by new bands (IR (KBr): 1120, 1080, 1010 ($\nu_{B\text{-}F}$), 920 and 950 (probably ν_{BO}). (In the nonalkyl dichloride $Co[C_2(DO)(DOH)_{pn}]Cl_2$, a $\nu_{O\text{-}H\text{-}O}$ = 1680 cm^{-1} is observed and is completely absent in the BF_2-bridged dichloride.) Anal. ($C_{17}H_{31}N_4O_2CoBrF_2B$) C, H, N, F.

(E) n-BuCo[C_2(DO)(DOH)$_{pn}$]Br Photochemical Cleavage in the Presence of $HMn(CO)_5$. In the drybox 3.3 mg of $n\text{-}BuCo[C_2(DO)(DOH)_{pn}]Br$ was dissolved in 25 mL of *o*-dichlorobenzene with strict exclusion of light. Three milliliters were then placed in a cuvette which was septum capped and removed from the box. After 200 equiv of freshly prepared $HMn(CO)_5$ was added via syringe, the absorbance vs. time at λ = 475 nm and at λ = 626 nm (due to[6] $[Co^IC_2(DO)(DOH)_{pn}]$) was recorded during a repetitive sequence of 10 min in the dark and then 10 min exposed to diffuse fluorescent room light. The absorbance readings at 475 nm were then corrected for the shoulder due to the product. This correction was made with use of the ϵ (475 nm) of the product and a knowledge of the reaction stoichiometry.[6] The results were then graphed (Figure 1).

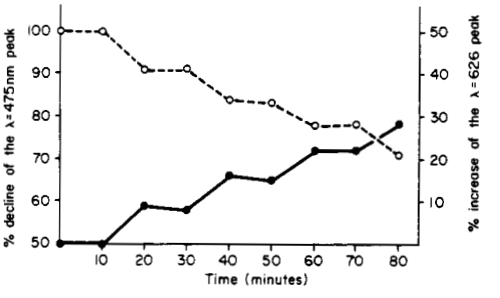


Figure 1. Diffuse room light photolysis of $n\text{-}BuCo[C_2(DO)(DOH)_{pn}]Br$ in the presence of $HMn(CO)_5$ (in *o*-dichlorobenzene at ambient temperature).

(F) ^{13}CO Exchange with $Co[C_2(DO)(DOH)_{pn}](^{12}CO)$. Labeled 90% ^{13}CO was bubbled through a THF solution of $Co[C_2(DO)(DOH)_{pn}](^{12}CO)$ ($\nu_{^{12}CO}$ = 1972 cm^{-1}), and the IR spectrum was recorded ($\nu_{^{13}CO}$ = 1925 cm^{-1}). On bubbling ordinary ^{12}CO back through the solution, the original $\nu_{^{12}CO}$ = 1972 cm^{-1} carbonyl band was regenerated.

(G) Axial Base Binding Constant for $[CH_3Co[C_2(DO)(DOH)_{pn}]OH_2]^+PF_6^-$ and Pyridine. An analytically pure sample of $[CH_3Co[C_2(DO)(DOH)_{pn}]OH_2]^+PF_6^-$ was used to prepare a 3.0×10^{-4} M 50% aqueous methanol solution. With using an aliquot of this solution and diluted aliquots, it was determined that Beer's Law was obeyed.

To a separate aliquot was added pyridine freshly distilled from BaO, and the disappearance of the aquo complex (λ = 460 nm, $\epsilon = 2.65 \times 10^3$ M^{-1} cm^{-1}; λ = 400 nm, $\epsilon = 1.8 \times 10^3$ M^{-1} cm^{-1}) and appearance of the pyridine adduct (λ = 430 nm, $\epsilon = 2.4 \times 10^3$ M^{-1} cm^{-1}; λ = 405 nm, $\epsilon = 2.4 \times 10^3$ M^{-1} cm^{-1}) were monitored at nine pyridine concentrations in the range of 1.9×10^{-3}–6.8×10^{-1} M. A clean isobestic point was observed at 445 nm. The data was analyzed, and error bars were assigned both by Drago's method[15] and by the usual log [pyridine] vs. log ([pyridine adduct]/[aquo adduct]) plot.[16] Both

(15) Drago, R. S. "Physical Methods in Chemistry"; W. B. Saunders: Philadelphia, 1977; p 90.
(16) Hayward, G. C.; Hill, H. A. O.; Pratt, J. M.; Vanston, N. J.; Williams, R. *J. Chem. Soc.* **1965**, 6485 (Method 3A).

methods gave the same result, $K_{assoc} = 105 \pm 20$ (or $10^{2.0 \pm 0.1}$) M^{-1} (pyridine, 22 °C, 50% aqueous methanol).

Results and Discussion

(I) Synthesis of $Co[C_2(DO)(DOH)_{pn}]I_2$ (IV). A convenient, three-step synthesis of 20 g of IV in 21% overall yield was achieved with use of standard synthetic organic reactions (Scheme I). It is worth noting that our synthesis places ethyl groups at the 2 and 10 positions of the macrocycle (R′ = Et (Ia)) which gives it increased solubility in organic solvents over the R′ = Me (Ib) derivative pioneered by Costa.[17,18] This increased solubility has already proven crucial to our studies.[5] The chloro–ethylenecarbonate adduct (Table I, entry 5) has, for example, a maximum solubility of ca. 11 mg/mL of CH_3OH (0.024 M).

(II) Reductive Synthesis of $Co[C_2(DO)(DOH)_{pn}](CO)$ (V). The reductive preparation of the R′ = Me (Ib) analogue of V was reported previously by Costa[17b,c] although no yield was reported. Furthermore, we have scaled up his preparation by (4–8)-fold and have modified and optimized this reduction. Our best procedure involves the 70–80% yield, 1.0-g scale preparation of V (Scheme I) using 2 equiv of $NaBH_4$ in 10% v/v 1 N NaOH/MeOH under N_2. The Co^ICO compound is less O_2 sensitive and less reactive than the noncarbonyl Co(I) complex in solution and can be stored without decomposition in the solid state under N_2. It should be noted that the 5-coordinate PPh_3 and *N*-methylimidazole–cobalt(I) adducts have also been isolated.[17b]

The exact mechanism of the reduction has not been elucidated although the fact that no color change is observed until the $NaBH_4$ is added to the $Co[C_2(DO)(DOH)_{pn}]I_2$, aq. NaOH/MeOH, plus CO solution rules out a kinetically important contribution of the previously suggested pathway,[17b] $Co(III)^{2+} + CO + OH^- \rightarrow [Co^{III}C(O)OH]^+$ and $[Co^{III}C(O)OH]^+ + OH^- \rightarrow Co(I) + CO_2 + H_2O$. Furthermore, we find that, if 2.7×10^{-4} mmol of red $Co^{II}[C_2(DO)(DOH)_{pn}]Cl$ (λ_{max}(MeOH) = 520 nm) is dissolved in 25 mL of 0.75 M NaOH in MeOH, the base induces the well-known $2Co(II) \rightleftharpoons Co(I) + Co(III)$ disproportionation to ca. 20% blue $Co^I[C_2(DO)(DOH)_{pn}]$ (λ_{max}(MeOH) = 620 nm), ca. 58% Co(II), and, by difference, 22% of Co(III) $Co[C_2(DO)(DOH)_{pn}]Cl_2$. These results suggest the following as a precedent, three-step, reduction mechanism: $NaBH_4$ reduction to Co(II) (and/or Co(I)), base-induced Co(II) to Co(I) disproportionation, and then CO capture of the coordinatively unsaturated Co(I) species.

The lability of the carbon monoxide in V was demonstrated by the rapid exchange on bubbling ^{13}CO to a THF solution of V to yield $Co[C_2(DO)(DOH)_{pn}](^{13}CO)$ and then the regeneration of the ^{12}CO (1972 cm^{-1}) IR band upon subsequent bubbling with unlabeled ^{12}CO.

(III) $RCo[C_2(DO)(DOH)_{pn}]^+X^-$ Complexes. (i) Preparation via RX Oxidative Addition to V. Primary alkyl halide oxidative additions to a blue benzene solution of V under N_2 proceed smoothly with CO liberation according to the stoichiometry (eq 1) reported previously by Costa.[17b] His focus, however, was on the overall preparation of R_2Co^{III} compounds, and he did not report the derivatives we have prepared (Table I). Furthermore, neither the yields, the scope, nor ^1H NMR data for the products of this useful reaction have previously been reported.

Scheme II. Three Routes for the Preparation of $RCo[C_2(DO)(DOH)_{pn}]X$ Complexes

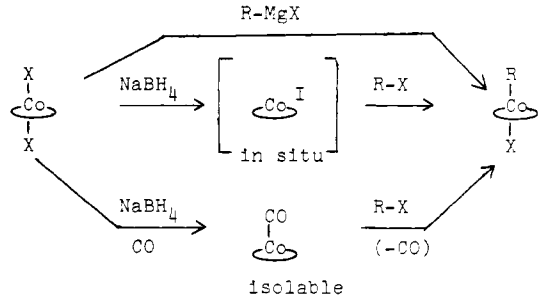


Table II. Conductivity Data

entry	compound	concn, M	molar conductivity,[a] Ω^{-1} cm^{-1} M^{-1}
	In Methanol		
1	$[Ph_3P{=}N{=}PPh_3]^+Cl^-$	5.5×10^{-3}	0.56×10^{-2}
2	$Et_3NH^+Cl^-$	5.5×10^{-3}	0.85×10^{-2}
3	$Co[C_2(DO)(DOH)_{pn}]I_2$	1.0×10^{-3}	0.85×10^{-2}
4	4-(1,3-dioxolan-2-one)-$Co[C_2(DO)(DOH)_{pn}]Cl$	5.5×10^{-3}	0.62×10^{-2}
	In *o*-Dichlorobenzene		
5	$Bu_4N^+PF_6^-$	4.5×10^{-4}	1.3×10^{-2}
6	(*n*-BuCo$[C_2(DO)(DOH)_{pn}]$-Bz-Me)$^+PF_6^-$	4.5×10^{-4}	1.4×10^{-2}
7	$PhCH_2Co[C_2(DO)(DOH)_{pn}]Cl$	4.5×10^{-4}	none
8	$PhCH_2Co[C_2(DO)(DOH)_{pn}]I$	4.5×10^{-4}	none

[a] At 25 °C.

The range of analytically pure alkyl halide adducts possible and their yields is indicated by the data in Table I. Benzene is preferred to THF for these reactions and the yields are generally nearly quantitative since recrystallized yields were >65–80%. The liberation of 1 equiv of CO was previously confirmed by[17c] GLC. Side products include some $Co^{II}[C_2(DO)(DOH)_{pn}]X$ (oxidized to Co(III) in air) and green $Co^{III}[C_2(DO)(DOH)_{pn}]X_2$ which are readily separated from the orange cobalt alkyls by crystallization or SiO_2 chromatography, if necessary. The main advantages of the oxidative addition to V (Scheme II) over the other known[17] routes derive from the ability to prepare and store 1.0-g amounts of the less O_2-sensitive cobalt carbonyl V for use at later dates and the no work-up, high-yield synthesis of the R[Co]X adducts. The main limitations derive from the decreased reactivity due to back-bonding requirements of the carbon monoxide and the inability to use secondary substrates such as isopropyl bromide or iodide. It is not clear at this point whether the predominence of $Co[C_2(DO)(DOH)_{pn}]X_2$ products using the secondary halides is due to the oxidative addition mechanism or the thermolysis of the alkyl[Co]X products at the temperatures required for oxidative addition. Preliminary mechanistic work[19] shows, however, that CH_3I oxidative addition exhibits typical second-order kinetics while $(CH_3)_2CHI$ shows a more complex kinetic behavior. It is also worth noting that at least some R[Co]X adduct has been obtained by the oxidative addition route for $HOCH_2CH_2Br$ (36%; impure by analysis and ^1H NMR even after chromatography) and $BrCH_2CH(OEt)_2$ (pure after SiO_2/THF chromatography) but that repeated attempts[5b] under a variety of conditions failed to yield any formylmethyl[Co]Cl adduct using $ClCH_2CHO$.

A range of axially ligated or BF_2-bridged derivatives can also be prepared, as outlined in Scheme III and documented in the Experimental Section.

(17) (a) Costa, G.; Mestroni, G.; de Savorgnani, E. *Inorg. Chim. Acta* **1969**, *3*, 323. (b) Costa, G.; Mestroni, G.; Tauzher, G. *J. Chem. Soc. Dalton Trans.* **1972**, 450. (c) Costa, G.; Mestroni, G.; Pellizer, G.; Tauzher, G.; Licari, T. *Inorg. Nucl. Chem. Lett.* **1969**, *5*, 515.

(18) Costa has also reviewed his work on cobalt chelates: (a) Bigotto, A.; Costa, G.; Mestroni, G.; Pellizer, G.; Puxeddu, A.; Reisenhofer, E.; Stefani, L.; Tauzher, G. *Inorg. Chim. Acta Rev.* **1970**, *4*, 41. (b) Costa, G. *Pure Appl. Chem.* **1972**, *30*, 335. (c) Costa, G. *Coord. Chem. Rev.* **1972**, *8*, 63.

(19) Finke, R. G.; Schiraldi, D. A., experiments in progress.

Scheme III. Some Transformations of the Oxidative Addition Product

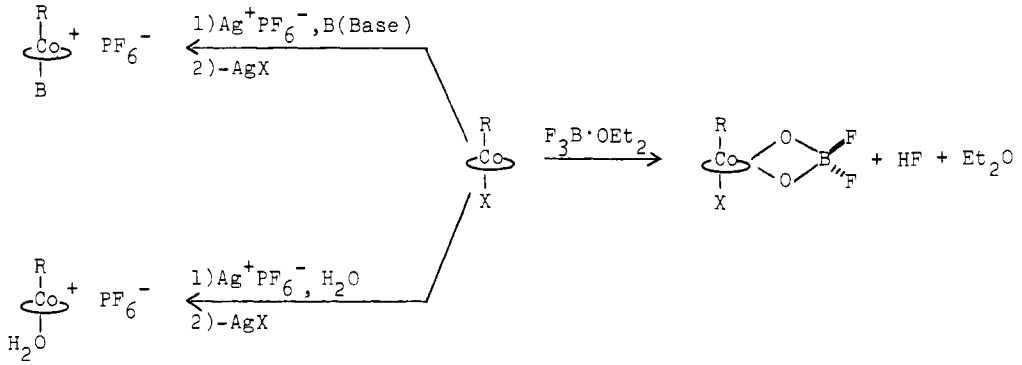


Table III. Comparison of Axial Base Binding Constants, K_{assoc}, for R[Co]OH_2 + Base ⇌ R[Co]Base + H_2O

entry	compd	base (solvent)	temp, °C	K_{assoc}, M^{-1}	ref
1	$(CH_3Co[C_2(DO)(DOH)_{pn}]OH_2)^+PF_6^-$	pyridine (50% aqueous methanol	22	$10^{2.0\pm0.1}$	this work
2	methylaquocobinamide	pyridine (H_2O)	ambient	$10^{1.04}$	21
3	methylaquocobaloxime	pyridine (H_2O)	20	$10^{3.3}$	22
			45	$10^{3.0}$	22
	methyl(H_2O or OH^-)cobaloxime	pyridine (H_2O with 1 N KOH)	50	$10^{1.8\pm0.4}$	23

(ii) Physical Properties of $RCo[C_2(DO)(DOH)_{pn}]X$ Complexes. There is a considerable body of knowledge[20] on the physical properties of such alkylcobalt complexes, and we will focus, therefore, on only those properties requiring additional attention.

(a) Axial Halide, X^-, Dissociation in Solution. Primarily because the data was required in our model diol dehydratase[5] and alkyl cobalt thermolysis[6] studies, we have determined the extent of axial halide dissociation of several key compounds in CH_3OH and *o*-dichlorobenzene. The data (Table II) includes 1:1 electrolytes like $Bu_4N^+PF_6^-$, $(Ph_3P)_2N^+Cl^-$, or $Et_3NH^+Cl^-$ as reference points. In CH_3OH, entries **1–4**, the significant thermodynamic trans influence of the alkyl group in the 2-dioxolanone-4-cobalt complex (entry 4) results in >70% if not 100% dissociation of the axial chloride. (The different sizes and hence mobilities of the Bu_4N^+ reference and RCo^+ preclude a more exact percentage in the absence of the normal conductivity vs. concentration data and its analysis by, for example, the Fuoss equation.) In the less polar *o*-dichlorobenzene there is, as one might expect, no detectable Cl^- or I^- dissociation in the benzyl halide adducts. One can replace Cl^- with I^- using NaI in acetone however. This behavior is consistent with previous studies[20d] showing that such RCo^{III} macrocyclic complexes are relatively soft, class b metal acids and thus prefer F < Cl < Br < I and O < S < N < P ligands.

(b) Axial Base Binding Constants. The pyridine binding constant of $(MeCo[C_2(DO)(DOH)_{pn}]OH_2)^+PF_6^-$ has been measured and compared to its cobinamide and cobaloxime counterparts since such data were previously not available.[20e] The results (Table III) show that both models, but especially the cobaloxime model, bind pyridine more tightly than does methylaquocobinamide. A solution of 50% methanol/water rather than just water as a solvent was required to solubilize the $(MeCo[C_2(DO)(DOH)_{pn}]OH_2)^+$.

(c) Kinetic and Thermodynamic Aspects of Thermal Homolysis and (d) Electrochemical Properties. These aspects of alkyl$Co[C_2(DO)(DOH)_{pn}]X$ complexes have been examined in detail in separate publications.[6,7]

(e) Photochemical Liability. The facile photochemical homolysis of alkyl–cobalt bonds in macrocyclic complexes is well-known.[20a-c,24] We required, however, a more exact idea of just how light sensitive our alkylcobalt complexes were to avoid this reaction in our thermal homolysis studies.[6] To determine the sensitivity to room light, we took advantage of the radical trapping reagent $HMn(CO)_5$ and the *thermolysis* stoichiometry we have established in other work,[6] $R[Co]X + 2HMn(CO)_5 \rightarrow RH + Co(I) + HX + Mn_2(CO)_{10}$. Thus a 2.8×10^{-4} M *n*-$BuCo[C_2(DO)(DOH)_{pn}]Br$ in *o*-dichlorobenzene solution was prepared, and 200 equiv of freshly prepared $HMn(CO)_5$ was added all with the strict exclusion of light. As outlined in the Experimental Section, several cycles of darkness, exposure to the diffuse room light, and then a return to the darkness of the Cary 15 for measurement of the alkylcobalt absorbance, at λ_{max} = 475 nm, and appearance of the $Co^I[C_2(DO)(DOH)_{pn}]$ product, at λ_{max} = 626 nm, were performed. The results (Figure 1) show that each 10 min of diffuse room light causes about an 8% decrease in the alkylcobalt complex. The results also suggest that the known[6] thermolysis stoichiometry of one R(Co)X → one Co(I) is maintained in this photolysis experiment.

(f) Properties of the O···H···O Bridge. The O···H···O bridge in I (ν_{O-H-O} = 1680 cm^{-1}; ^1H NMR ($CDCl_2$) $\delta(Me_4Si)$ ca. 19 for $Co[C_2(DO)(DOH)_{pn}]Cl_2$) can be chemically noninnocent but may be replaced by a $O-BF_2-O$ bridge if desired. This O···H···O bridge is probably quite similar to the same type of bridge found in cobaloximes where a 50-s^{-1} (25 °C) exchange rate and δ ($CDCl_3$; Me_4Si) ca. 18 for the hydrogen-bonded bridge has been found.[25] In the related $Rh^I[(DO)(DOH)_{pn}]$ complex, oxidative additions at rhodium are complicated by reaction of protonic and Lewis acids at the O···H···O bridge.[26]

(20) (a) Dodd, D.; Johnson, M. D. *Organomet. Chem. Rev.* **1973**, *52*, 1. (b) Pratt, J. M.; Craig, P. J. *Adv. Organomet. Chem.* **1973**, *11*, 331. (c) Brown, D. G. *Prog. Inorg. Chem.* **1973**, *18*, 177. (d) Reference 20a, p 45. (e) Reference 20a, Table 12.
(21) Pailes, W. H.; Hogenkamp, H. P. C. *Biochemistry* **1968**, *7*, 4160.
(22) Sakurai, T.; Fox, J. P.; Ingraham, L. L. *Inorg. Chem.* **1971**, *10*, 1105.
(23) Brown, K. L. *J. Am. Chem. Soc.* **1979**, **101**, 6600.
(24) Endicott, J. F.; Netzel, T. L. *J. Am. Chem. Soc.* **1979**, *101*, 4000.
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(26) Collman, J. P.; Murphy, D. W.; Dolcetti, G. *J. Am. Chem. Soc.* **1973**, *95*, 2687.

Summary

The stepwise, efficient synthesis of the coenzyme B_{12} model complexes $RCo[C_2(DO)(DOH)_{pn}]X$ and their derivatives has been described. Included were detailed syntheses from readily available starting materials for the $C_2(DOH)_2pn$ ligand, for the diiodide $Co[C_2(DO)(DOH)_{pn}]I_2$, for the crystalline cobalt (I) carbonyl complex $Co[C_2(DO)(DOH)_{pn}](CO)$, and for the high-yield, oxidative addition of primary alkyl halides to this Co^ICO complex. Several of the physical properties necessary to optimally utilize these alkylcobalt complexes were also presented.

Acknowledgment. Financial support in the early stages of this work was provided by a PRF grant and a Faculty Research Award from the Office of Scientific and Scholarly Research at the University of Oregon. The support of NIH Grant AM-26214 is also gratefully acknowledged. We also wish to thank Professor J. P. Collman (NSF Grant CHE 78-09443) for his support during the initial synthesis of the cobalt(I) carbonyl complex.

Registry No. III, 75961-81-8; IV, 75962-04-8; V, 75504-41-5; $CH_3[Co]I$, 75962-05-9; *n*-Bu[Co]Br, 75962-06-0; $PhCH_2[Co]Cl$, 75962-07-1; $CH_3C(CO_2Et)_2CH_2[Co]Br$, 75962-08-2; $OC(O)OCH_2CH[CO]Cl$, 75504-42-6; $[n\text{-Bu[Co]Bz-Me}]^+PF_6^-$, 75962-10-6; $[Me[Co]OH_2]^+PF_6^-$, 75962-12-8; $[n\text{-Bu[Co]OH}_2]^+PF_6^-$, 75962-14-0; $(CH_3)_2CH[Co]Br$, 75962-15-1; $Co^{II}[C_2(DO)(DOH)_{pn}]Br$, 75962-16-2; $Co[C_2(DO)(DOH)_{pn}]Br_2$, 75962-17-3; $n\text{-BuCo}[C_2(DO)(DOB(F_2))_{pn}]Br$, 75975-14-3; $[CH_3[Co]py]^+$, 75962-18-4; ethyl (bromomethyl)methylmalonate, 75511-41-0; 3-oximino-2-pentanone, 609-29-0; methyl nitrite, 75-52-5; 2-pentanone, 107-87-9; 1,3-diaminopropane, 109-76-2; MeI, 74-88-4; *n*-BuBr, 109-65-9; $PhCH_2Cl$, 100-44-7; $(CH_3)_2CHBr$, 75-26-3; $BF_3{\cdot}OEt_2$, 109-63-7; $[Ph_3P{=}N{=}PPh_3]^+Cl^-$, 21050-13-5; $Et_3NH^+Cl^-$, 554-68-7; $Bu_4N^+PF_6^-$, 3109-63-5; $Co[C_2(DO)(DOH)_{pn}]Cl_2$, 75962-19-5; $Co^I[C_2(DO)(DOH)_{pn}]$, 75962-20-8; $Co^{II}[C_2(DO)(DOH)_{pn}]Cl$, 75504-43-7; $Co[C_2(DO)(DOH)_{pn}](^{13}CO)$, 75962-21-9.

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Electrochemical and Spectral Speciation of Iron Tetrakis(*N*-methyl-4-pyridyl)porphyrin in Aqueous Media

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The $Fe^{III}Fe^{II}TMPyP$ compound was studied as a function of pH with use of optically coupled electrochemical techniques. In acidic solution $Fe^{III}TMPyP$ undergoes a one-electron reduction with an $E_{0.85}$ of ±0.18 (±0.01) V and a k_s of 5.8 (±0.9) × 10^{-3} cm s^{-1} at a highly polished, glassy carbon electrode. Experiments indicate that four ferric species (three monomeric and one dimeric) and two ferrous species (both monomeric) are sufficient to explain the electrochemical results between pH 1 and 13. Proton equilibria exist between the three ferriporphyrin monomers with pK_a values of ca. 4.7 and 6.5. A proton equilibrium also exists between the ferroporphyrin species with a pK_a value ca. 7. A monomer–dimer equilibrium exists between the ferric species in alkaline solutions with a dimerization constant of 2 × 10^3 M^{-1}.

The metal macrocyclic compounds, notably the iron and cobalt phthalocyanines and porphyrins, have been of interest to chemists for many years as models for a variety of biological processes.[1] Among these have been their relevance to the mechanism of oxygen transport and storage and of charge transfer including the rapid transformation of molecular oxygen to water in the mammalian respiratory system. It has been this latter recognition that prompted electrochemists to utilize water-insoluble metal phthalocyanines, metal porphyrins, and hemins adsorbed on electrode surfaces as catalysts for oxygen reduction.[2] Indeed, the catalysis is quite marked in terms of the decrease in the oxygen overpotential, particularly at graphitic electrodes in acidic media. In addition to the problems of reproducibility and of stability for long-termed activity, the elucidation of the heterogeneous mechanism for oxygen involving the adsorbed compounds has been difficult.

Recently, a water-soluble iron porphyrin, (tetrakis(*N*-methyl-4-pyridyl)porphyrin)iron(III) pentakis(bisulfate) (Fe^{III}- or $Fe^{II}TMPyP^{5+\text{ or }4+}$, omitting the counterion) has been reported to be an effective catalyst for the reduction of oxygen.[3] This particular porphyrin exhibited one of the most positive reduction potentials of several metal-centered, water-soluble porphyrins studied (for example, zinc, copper, ruthenium, and manganese). Besides being water soluble, it was electroactive over a wide range of pH (<1–14), with the reduced form reacting rapidly with oxygen. In addition, it was readily synthesized and purified according to the procedures of Hambright and Fleischer[4] and Pasternack et al.[5]

The reaction sequence for the $Fe^{III}TMPyP$-catalyzed oxygen reaction was described as a simple EC regeneration mechanism[3]

$$Fe^{III}TMPyP^{5+} + e^- \rightleftharpoons Fe^{II}TMPyP^{4+} \quad (1)$$

$$Fe^{II}TMPyP^{4+} + {}^1/_2O_2 + H^+ \xrightarrow{k_f} Fe^{III}TMPyP^{5+} + {}^1/_2H_2O_2 \quad (2)$$

where reaction 2, between the reduced form of the iron porphyrin and oxygen, was assumed to take place in the homogeneous solution phase. The electrode potential for the O_2 reduction was governed by the redox potential of reaction 1. Evidence to date has suggested that hydrogen peroxide is the primary product, which is the stoichiometry reflected by reaction 2.

Rotating ring-disk electrode (RRDE)[6] experiments have indicated that the rate of $Fe^{II}TMPyP^{4+}$ removal by O_2 was very fast, on the order of (4–5) × 10^7 M^{-1} s^{-1} (pH 9). With

(1) For example, see R. D. Jones, D. A. Summerville, and F. Basolo, *Chem. Rev.*, **79**, 139 (1979); *Acc. Chem. Res.*, **10**, 265 (1977).
(2) For discussion see E. Yeager *NBS Spec. Publ. (U.S.)*, **No. 455**, 203–219 (1976).
(3) T. Kuwana, M. Fujihira, K. Sunakawa, and T. Osa, *J. Electroanal. Chem. Interfacial Electrochem.*, **88**, 299 (1978).
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(5) (a) R. F. Pasternack, H. Lee, P. Malek, and C. Spencer, *J. Inorg. Nucl. Chem.*, **39**, 1865 (1977); (b) R. F. Pasternack and E. G. Spiro, *J. Am. Chem. Soc.*, **100**, 968 (1978).
(6) A. Bettelheim and T. Kuwana, *Anal. Chem.*, **51**, 2257 (1979).

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