# Coenzyme $B_{12}$ Model Studies: An Electrochemical Comparison of Cobaloxime and Co[$C_2$(DO)(DOH)$_{pn}$] Complexes to Coenzyme $B_{12}$

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**Abstract:** An electrochemical comparison of both alkyl and nonalkyl cobaloxime and Co[$C_2$(DO)(DOH)$_{pn}$] $B_{12}$ model complexes is made to five coenzyme $B_{12}$ complexes. The five $B_{12}$ complexes were chosen from Lexa and Savéant's recent electrochemical studies of $B_{12}$ as representative examples of Co(III)/Co(II), Co(II)/Co(I), and RCo(III)/RCo(II) redox couples that include a range of axial ligation. Cyclic voltammetry, coulometry, and some spectroelectrochemical studies are presented that focus mainly upon the RCo model complexes. The products and major mechanistic features of Co–C bond cleavage from the reduced RCo(II) intermediate are presented for the RCo[$C_2$(DO)(DOH)$_{pn}$] model. The results demonstrate that the Co[$C_2$(DO)(DOH)$_{pn}$] model is a closer electrochemical mimic of $B_{12}$ than is the cobaloxime model. The limitations of these models and the results of this study are discussed in the context of recent electrochemical studies of other models.

Model studies in search of chemical precedent for the 11 adenosylcobalamin-dependent rearrangement reactions continue to receive attention. In our studies of diol dehydratase[2a] and of thermolysis of cobalt–carbon bonds,[2b] the use of a $B_{12}$ model has proven necessary.[2c] The bis(dimethylglyoximato)cobalt or cobaloxime model[3] is widely accepted and employed as a coenzyme $B_{12}$ model. A body of qualitative results exists suggesting that, while there is qualitative agreement, there are *quantiative differences* in cobaloxime and cobalamin chemistry. For example, *Co*-formylmethyl-,[4a] *Co*-isopropyl-,[4b] and $\alpha$-phenethylcobaloximes[4c] are more stable than their cobalamin counterparts, an observation that is supported by recent quantitative studies by Halpern.[4c] Quantitative axial base binding constant data demonstrate that methyl(aquo)cobaloxime binds pyridine with[5a] a $K$ (association) = $10^{3.3}$ (20 °C, $H_2O$) while methyl(aquo)cobinamide binds pyridine with[5b] a $K$ (association) = $10^{1.0}$ (ambient temperature, $H_2O$). Moreover, a disturbing but neglected feature of the cobaloxime model is the formal −2 charge on its bis(dimethylglyoximato) tetradentate ligand. The corrin in coenzyme $B_{12}$ and, for example, the Co[$C_2$(DO)(DOH)$_{pn}$] $B_{12}$ model[6] shown in Figure 1 have equatorial ligands with formal −1 charges.

Previous electrochemical[7a-g] and other comparative studies[7h-j] demonstrate that cobaloxime and Co[$C_2$(DO)(DOH)$_{pn}$] (Figure 1) are the closest noncorrin or nonporphyrin[8] coenzyme $B_{12}$ models, although a quantitative comparison of these two models with $B_{12}$, heretofore, had not been made.[8c] A detailed electrochemical comparison seemed ideal since (1) it would yield exact thermodynamic redox potentials that might prove important to mechanistic studies, (2) it would yield valuable kinetic information on redox-coupled axial ligand changes, and (3) reduction of such RCo complexes results in cobalt–carbon bond cleavage. A major role of adenosylcobalamin is to provide a good source of adenosyl radicals, although the radical-forming step in the $B_{12}$-dependent rearrangement reactions remains poorly understood. Lexa and Savéant's recent, thorough electrochemical studies[9] on Co(III), Co(II), and RCo(III) cobalamins and cobinamides provide rigorous and quantitative electrochemical criteria that any good $B_{12}$ model should be able to reproduce. In particular, their work provides an operational electrochemical definition of a satisfactory $B_{12}$ mimic. The model should reproduce: (1) the Co(III)/Co(II), Co(II)/Co(I), and RCo(III)/RCo(II) $E_{1/2}$ values, (2) the redox-coupled axial ligand changes, and (3) the details of the cobalt–carbon bond cleavage upon reduction of alkylcobalamins and

(1) (a) University of Vermont; (b) University of Oregon.

(2) Finke, R. G.; McKenna, W. *J. Chem. Soc., Chem. Commun.* **1980**, 460; (b) Finke, R. G.; Smith, B. L., submitted for publication. (c) The continued interest in model studies stems from the complexity of the coenzyme $B_{12}$ mediated reactions as well as difficulties in establishing some parts of the mechanism through studies of the enzyme.[2d] In our mechanistic work,[2a,b] the requirements of relatively large amounts of pure, well-characterized materials and the need for $^1$H NMR and other spectroscopic "handles" were best satisfied by the use, at least initially, of a $B_{12}$ model. (d) See the discussion on p 90 of Babior, B. M.; Krouwer, J. S. *CRC Crit. Rev. Biochem.* **1979**, *6*, 35. See also p 257 of Abeles, R. H. "Biological Aspects of Inorganic Chemistry"; Wiley-Interscience: New York, 1976; p 245.

(3) Schrauzer, G. N. *Acc. Chem. Res.* **1968**, *1*, 97.

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(5) (a) Sakurai, T.; Fox, J. P.; Ingraham, L. L. *Inorg. Chem.* **1971**, *10*, 1105; (b) Pailes, W. H.; Hogenkamp, H. P. C. *Biochemistry* **1968**, *7*, 4160.

(6) (a) Costa, G.; Mestroni, G.; de Savorgnani, E. *Inorg. Chim. Acta* **1969**, *3*, 323. In this paper Costa notes that his model has the same formal charge on the planar ring as the corrin in $B_{12}$. (b) Costa, G.; Mestroni, G.; Tauzer, G. *J. Chem. Soc., Dalton Trans.* **1972**, 450.

(7) The electrochemistry of Costa's model[7a-c] and of the cobaloxime model[7d-f] has received previous attention and a review has appeared.[7g] (a) Costa, G.; Puxeddu, A.; Reisenhofer, E. *Experientia, Suppl.* **1971**, *18*, 235; (b) Costa, G.; Puxeddu, A.; Reisenhofer, E. *J. Chem. Soc., Dalton Trans.* **1972**, 1519; (c) Costa, G.; Puxeddu, A.; Reisenhofer, E. *J. Chem. Soc., Chem. Commun.* **1971**, 993, (d) Schrauzer, G. N.; Windgassen, R. J. *J. Am. Chem. Soc.* **1966**, *88*, 3738; (e) Costa, G.; Mestroni, G.; Puxeddu, A.; Reisenhofer, E. *J. Chem. Soc. A* **1970**, 2870; (f) Costa, G.; Puxeddu, A.; Tauzher, G. *Inorg. Nucl. Chem. Lett.* **1968**, *4*, 319; (g) A summary of early electrochemical results relevant to $B_{12}$ can be found on p 197 of Brown, D. G. *Prog. Inorg. Chem.* **1973**, *18*, 177; (h) Costa, G. *Pure Appl. Chem.* **1972**, *30*, 335; (i) Bigotto, A.; Costa, G.; Mestroni, G.; Pellizer, G.; Puxeddu, A.; Reisenhofer, E.; Stefane, L.; Tauzher, G. *Inorg. Chim. Acta Rev.* **1970**, *4*, 41; (j) Costa, G. *Coord. Chem. Rev.* **1972**, *8*, 63.

(8) Electrochemical data on Co(tetraphenylporphyrin)[8a] and a second[8b] porphyrin $B_{12}$ model has appeared. (a) Lexa, D.; Savéant, J. M.; Soufflet, J. P. *J. Electroanal. Chem.* **1979**, *100*, 159; (b) "Vitamin $B_{12}$, Proceedings on the 3rd European Symposium on Vitamin $B_{12}$ and Intrinsic Factor", Zagalah, B., Friedlich, W., Eds.; W. de Gruyter: Berlin, 1979; see pp 171 and 173 and references therein. (c) A preliminary account of this work has appeared: Finke, R. G.; Smith, B. L.; Droege, M. W.; Elliott, C. M.; Hershenhart, E. *J. Organomet. Chem.* **1980**, *202*, C25.

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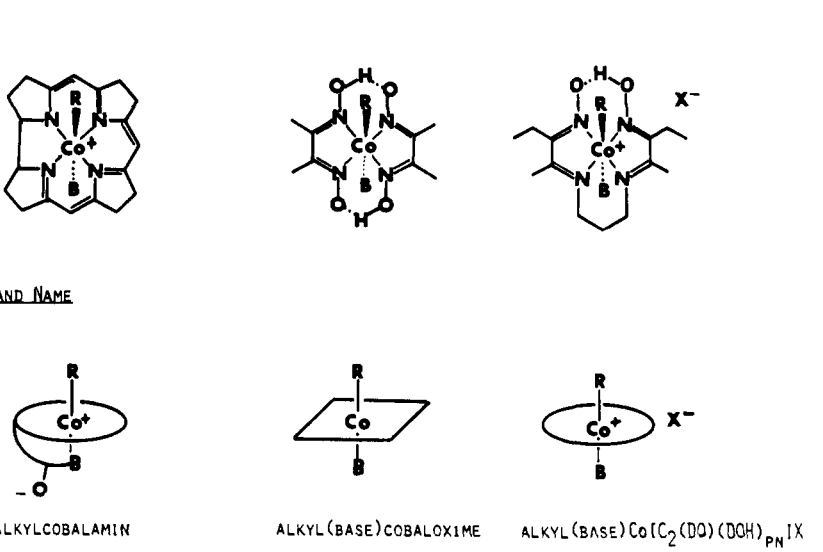



**Figure 1.** The corrin macrocycle in an alkylcobalamin (left), the cobaloxime (center), and the $Co[C_2(DO)(DOH)_{pn}]$ (right) models. Only the unsubstituted corrin ring and the axial ligands are shown for the alkylcobalamin.

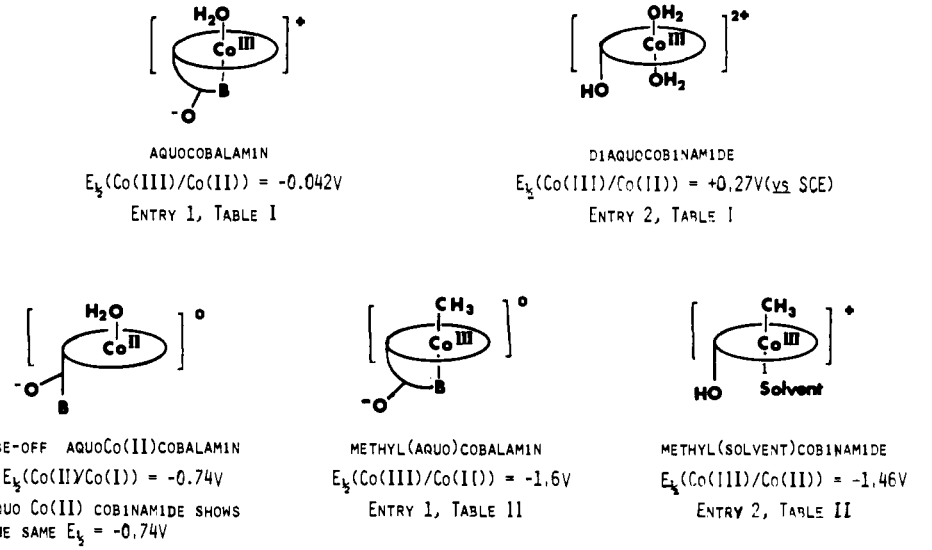



**Figure 2.** Key $B_{12}$ complexes and their $E_{1/2}$ values for comparison to the $B_{12}$ models.

-cobinamides. The key $B_{12}$ complexes that the two models will be compared to are shown in Figure 2. Additional comparisons to the extensive, pH-dependent electrochemistry of $B_{12}$ are possible,[9h] but the compounds in Figure 2 were chosen as a representative range of $B_{12}$ derivatives that include a variety of axial ligation in the key oxidation states.

The primary objectives of this study are as follows: (1) to prepare, isolate, and fully characterize the necessary model complexes with the correct axial ligation for comparison to the $B_{12}$ complexes in Figure 2; (2) to study by cyclic voltammetry, coulometry, and optically transparent thin-layer electrode (OTTLE) techniques the electrochemistry of the model complexes; and (3) to examine thoroughly the electrochemistry of the RCo complexes of the models in order to find conditions where chemical reversibility and thus reliable $E_{1/2}$ values are obtained.

In the alkylcobalamins and alkylcobinamides, Lexa and Sevêant have shown that conditions of low temperature and dimethylformamide/propanol solvent gave quasi-reversible to reversible cyclic voltammograms. In the present study, a dramatic and surprising dependence upon axial base concentration has been discovered for the $RCo[C_2(DO)(DOH)_{pn}]^+$ complexes.

## Experimental Section

**A. General.** The synthesis and the electrochemistry of all of the cobalt alkyls was carried out under red light to avoid the known photodecomposition of these materials.

i. **Chemicals.** Acetonitrile, *n*-propanol, methylene chloride (Aldrich, Gold label), and dimethylformamide (Burdick and Jackson) were used without further purification. Tetrahydrofuran (Aldrich, Gold label) was distilled under nitrogen from sodium and benzophenone. Tetra-*n*-butylammonium hexafluorophosphate was used as supporting electrolyte and was prepared by metathesis of $NH_4PF_6$ and $n$-$Bu_4NI$ in aqueous solution followed by two recrystallizations from ethanol. 1,5,6-Trimethylbenzimidazole was prepared by the literature procedure[10] (mp 143.5–144 °C; lit.[10] mp 142–143 °C). 1-Methylimidazole (Aldrich) was used without further purification.

ii. **Equipment.** All electrochemical measurements were performed on a PAR Model 173 potentiostat/galvanostat in conjunction with a PAR Model 175 universal programmer and Model 179 digital coulometer. For the scan-rate range 0.05–1 V/s, voltammograms were recorded on a HP Model 7045A X–Y recorder. For faster scan rates, a Tektronix Model RM 502A oscilloscope equipped with a type C-5A camera was used. Unless otherwise stated, all experimental potentials are reported vs. SCE. An internal colbalticinium standard[11] was employed for evaluation of the junction potential variation with temperature. The potential ($V$) vs. SCE for the cobalticinium Co(III)/Co(II) couple can be evaluated for the two solvent systems employed from the following experimentally determined relations:

(10) Simonov, A. M.; Pozharskii, A. E.; Marianovskii, V. M. *Ind. J. Chem.* **1967**, *5*, 81.
(11) Gubin, S. P.; Smirnova, S. A.; Denisovich, L. I. *J. Organomet. Chem.* **1971**, *30*, 257.

$$E^{0'}_{Cp_2Co^+} = -0.941 + (8.0 \times 10^{-4})T$$

for acetonitrile solutions and

$$E^{0'}_{Cp_2Co^+} = -0.900 + (5.3 \times 10^{-4})T$$

for DMF/propanol solutions where $T$ is in °C.

Optical measurements were performed with a Cary 14 spectrophotometer in either its normal configuration or with the sample compartment modified to accomodate the optically transparent thin-layer electrode cell.

Conductivity measurements were made with a Radiometer (Copenhagen) CDM 2e conductivity meter and a type CDC114 cell (cell constant = 1.69 $cm^{-1}$).

$^1H$ NMR were obtained on a XL-100 NMR spectrometer, and elemental analyses were obtained from the University of Oregon microanalytical laboratory.

iii. **Cyclic Voltammetry.** A three-electrode cell was used with a platinum bead working, platinum wire auxiliary, and a saturated calomel reference electrode unless otherwise stated. For low-temperature experiments, a thermostated cell was used with a refrigerated liquid circulator.

iv. **Coulometry.** Experiments were carried out in a three-compartment "H" cell with fine glass frit dividers. The working electrode was a platinum gauze, the auxiliary was a platinum wire, and the reference was a silver wire pseudoreference electrode. $O_2$ sensitivity of the electrogenerated products required that all experiments be performed in a Vacuum Atmospheres Corporation inert atmosphere box under $N_2$. Coulometric $n$ values were obtained either from direct measurement (PAR Model 179 digital coulometer) or by measuring the area under the current-time curve.

v. **Spectroelectrochemistry.** The optically transparent thin-layer electrode (OTTLE) was constructed as described previously.[12]

**B. Preparation of the Required Nonalkyl Cobalt Complexes.** (The numbering and abbreviated structures for complexes I through XII are given in Tables I and II.) The three step synthesis of IV, $ICo[C_2(DO)(DOH)_{pn}]I$, from readily available starting materials has been described.[13] Cobalt diiodide material used in this study gave a ±0.3% C, H, N analysis and showed the published $^1H$ NMR.

**$\{Co[C_2(DO)(DOH)_{pn}](1,5,6\text{-trimethylbenzimidazole})\}(PF_6)_2$ (V).** In a 250-mL Erlenmeyer flask 1.0 g (1.7 mmol) of $ICo[C_2(DO)(DOH)_{pn}]I_2$ and 276 mg (1.7 mmol) of 1,5,6-trimethylbenzimidazole were dissolved in 100 mL of $CH_2Cl_2$ with stirring, after which 0.946 g (2.2 equiv) of $AgPF_6$ was added. The solution was stirred for 0.5 h and then filtered to remove AgI. The solution was then rotary evaporated to about a 20-mL volume. About 1 mL of methanol was added and then the flask was placed in a −22 °C freezer for 12 h. The red crystals which developed were filtered, washed with methanol, and dried under vacuum at 25 °C for 12 h. Anal. ($C_{23}H_{35}N_6O_2Co\ P_2F_{12}$) C, H, N. $^1H$ NMR (acetone-$d_6$) $\delta$ ($Me_4Si$) 1.18 (t, 6 H, $J$ = 7 Hz), 2.32 (s, 3 H), 2.40 (s, 3 H), 2.88 (s, 6 H), 3.00–3.40 (m, 6 H), 3.80 (s, 3 H), 4.40–4.70 (m, 4 H), 7.32 (s, 1 H), 7.50 (s, 1 H), 7.68 (s, 1 H).

**$Cl[Co(DMG)_2](1,5,6\text{-trimethylbenzimidazole})$ (VI).** A procedure analogous to that used by Schrauzer[14] was used. In a 250-ml Erlenmeyer flask 1.0 g (4.2 mmol) of $CoCl_2 \cdot 6H_2O$ and 1.07 g (9.24 mmol) dimethylglyoxime were dissolved in 100 mL of hot methanol containing 0.168 g of NaOH (4.2 mmol). One equivalent (0.67 g) of 1,5,6-trimethylbenzimidazole was added, immediately producing a yellow–brown solution. The flask was cooled to room temperature and then bubbled with air for 15 min, which caused the precipitation of a yellow–brown microcrystalline solid. The flask remained undisturbed for 45 min, after which the solid was filtered and washed with 50 mL of $H_2O$ followed by washing with 50 mL of ethanol and then 50 mL of ether. Recrystallization was accomplished with $CHCl_3$, yield = 1.36 g (54%). Anal. ($C_{18}H_{26}N_6O_4CoCl \cdot CHCl_3$) C, H, N. $^1H$ NMR ($CDCl_3$) $\delta$ ($Me_4Si$) 2.36 (s, 18 H), 3.72 (s, 3 H), 7.00 (s, 1 H), 7.84 (s, 1 H), 8.00 (s, 1 H).

**$Co(II)(DMG)_2(1,5,6\text{-trimethylbenzimidazole})_2$.** The $Co(II)(DMG)_2(1,5,6\text{-trimethylbenzimidazole})_2$ was prepared analogous to the preparation of $Co(II)(DMG)_2(py)_2$ except 1,5,6-trimethylbenzimidazole was used in the place of pyridine.[15a,b] Anal. ($C_{28}H_{38}N_8O_4Co$) C, H, N. $^1H$ NMR ($CDCl_3$) $\delta$ ($Me_4Si$) 2.16 (s, 6 H), 2.36 (s, 18 H), 3.76 (s, 6 H), 7.32 (s, 2 H), 7.94 (s, 2 H), 7.04 (s, 2 H).

**C. Preparation of the Required Cobalt Alkyl Complexes.** A detailed procedure for the preparation of $RCo[C_2(DO)(DOH)_{pn}]X$ and related complexes has recently been published,[13] including the preparation of $\{MeCo[C_2(DO)(DOH)_{pn}]OH_2\}PF_6$ (IX), $\{n\text{-}BuCo[C_2(DO)(DOH)_{pn}]OH_2\}PF_6$ (X), and $\{n\text{-}BuCo[C_2(DO)(DOH)_{pn}](1,5,6\text{-trimethylbenzimidazole})\}PF_6$, which were used in the present study. Each of these complexes gave a satisfactory ±0.3% C, H, N analysis and exhibited the published 100-MHz $^1H$ NMR spectrum.

**Methyl(aquo)cobaloxime, $MeCo(DMG)_2OH_2$ (XI).** This alkylcobaloxime was prepared by the literature procedure.[14] Anal. ($C_9H_{19}N_4O_5Co$) C, H, N. $^1H$ NMR (acetone-$d_6$) $\delta$ ($Me_4Si$) 0.50 (s, 3 H), 2.14 (s, 12 H).

**$n$-BuCo(DMG)$_2$(1,5,6-trimethylbenzimidazole) (XII).** The following procedure, which is analogous to that of Schrauzer,[4b] was used. In a Schlenk cross[13] fitted with two solid addition side arms were plated 1.50 g (6.3 mmol) of $CoCl_2.6H_2O$ and 1.46 g (13.0 mmol) of dimethylglyoxime. In one side arm was placed 1 g (6.3 mmol) of 1,5,6-trimethylbenzimidazole and in the other 0.02 g (0.53 mmol) of $NaBH_4$. The Schlenk cross was evacuated and then filled with $N_2$. Methanol (250 mL; degassed by three freeze/pump/thaw cycles) was needlestocked into the reaction vessel, and the $CoCl_2 \cdot 6H_2O$ and dimethylglyoxime were dissolved with stirring to produce a red solution. The 1,5,6-trimethylbenzimidazole was added, causing the solution to become darker red. One gram of 50% NaOH (degassed) was then needlestocked into the solution, causing the solution to again darken. The solution was cooled in an ice bath and 2.4 g (3-fold excess) of $n$-butyl bromide was needlestocked into the reaction vessel, producing a brownish-red solution. The $NaBH_4$ was added along with 0.5 mL of 50% NaOH. The reagents were stirred for 15 min and then poured into 1 L of water, precipitating the yellow $n$-BuCo(DMG)$_2$(1,5,6-trimethylbenzimidazole). After 12 h the yellow product was filtered and washed with water. The solid was recrystallized from methanol/water, giving 350 mg (9.4%) of a mixture of orange needles and yellow fibrous solid. Anal. ($C_{22}H_{35}N_6O_4Co$) C, H, N. $^1H$ NMR ($CDCl_3$) $\delta$ ($Me_4Si$) 0.78 (t, 3 H), 1.0–1.9 (m, 6 H), 2.08 (s, 12 H), 2.36 (s, 6 H), 3.74 (s, 3 H), 7.06 (s, 1 H), 7.92 (s, 1 H), 7.96 (s, 1 H).

**$Me_2Co[C_2(DO)(DOH)_{pn}]$.** Of the various methods described[6b] for the preparation of $Me_2Co[C_2(DO)(DOH)_{pn}]$, only the following procedure was successful in our hands. Two grams (3.45 mmol) of $ICo[C_2(DO)(DOH)_{pn}]I$, IV, and 1.0 g (26.5 mmol) of $NaBH_4$ were placed in a double Schlenk apparatus[13] equipped with a solid-addition side arm for the $NaBH_4$. The apparatus was evacuated and refilled with $N_2$, and 100 mL of degassed 50% $H_2O$/EtOH was added via needlestock techniques. Methyl iodide (>1 mL; bubbled with $N_2$ to degas) was added followed by slow addition, over 5 min, of the $NaBH_4$. Vigorous gas evolution resulted and the $Me_2Co[C_2(DO)(DOH)_{pn}]$ precipitated almost immediately. The filtered product was washed (EtOH) and air dried to yield 400 mg (36%) of bright orange material. Recrystallization was accomplished from acetone/$H_2O$. $^1H$ NMR ($CDCl_3$) $\delta$ ($Me_4Si$) 0.06 (s, 6 H), 1.04 (t, 6 H, $J$ = 7 Hz), 2.0–2.4 (m, 2 H), 2.20 (s, 6 H), 2.70 (s, 4 H, $J$ = 7 Hz), 3.67 (t, 4 H, $J$ = 6 Hz), 19.54 (s, 1 H).

**D. Conductivity Studies To Determine the Extent of Axial Halide Dissociation.** The following molar conductivities (mho $cm^{-1}$ $M^{-1}$) were obtained for $4.5 \times 10^{-4}$ M $CH_3CN$ solutions at 25 °C: $ICo[C_2(DO)(DOH)_{pn}]I$, $8.6 \times 10^{-2}$ mho $cm^{-1}$ $M^{-1}$; $ClCo(DMG)_2$(1,5,6-trimethylbenzimidazole) initially gave no conductance above the background but on heating and stirring for ca. 2 h it showed a limiting molar conductance of $9.7 \times 10^{-2}$ mho $cm^{-1}$ $M^{-1}$; $ICo[C_2(DO)(DOH)_{pn}]$(1,5,6-trimethylbenzimidazole), $9.7 \times 10^{-2}$ mho $cm^{-1}$ $M^{-1}$; $n\text{-}Bu_4N^+PF_6^-$, $8.6 \times 10^{-2}$ mho $cm^{-1}$ $M^{-1}$.

## Results

The cobaloxime and $Co[C_2(DO)(DOH)_{pn}]$ complexes required to compare these models to each of the $B_{12}$ analogues listed in Figure 2 were prepared without complications and were identified by 100-MHz $^1H$ NMR and elemental analysis. These compounds and the results of cyclic voltammetry, coulometry, and spectroelectrochemical experiments are summarized in the figures and in Tables I and II. The results summarized in each figure are presented and discussed in order, and conductivity data obtained are presented as they are required to interpret the electrochemistry. A summary of Lexa and Savéant's electrochemical data on the

(12) (a) Murray, R. W.; Heineman, W. R.; O'Dom, G. W. *Anal. Chem.* **1967**, *39*, 1666. (b) Wightman, R. M. Ph.D. Thesis, University of North Carolina, Chapel Hill, NC, 1974.

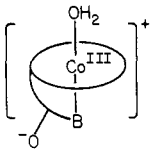
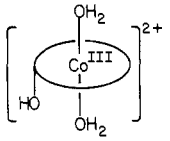
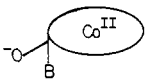
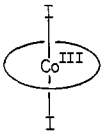
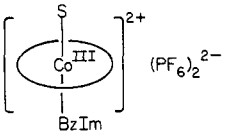
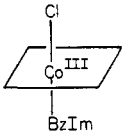
(13) Finke, R. G.; Smith, B. L.; McKenna, W. A.; Christian, P. A. *Inorg. Chem.* **1981**, *20*, 687.

(14) Schrauzer, G. N.; *Inorg. Synth.* **1968**, *11*, 62.

(15) (a) Schneider, P. W.; Phelan, P. F.; Halpern, J. *J. Am. Chem. Soc.* **1969**, *91*, 77; (b) Schrauzer, G. N.; Windgassen, R. J. *Chem. Ber.* **1966**, *99*, 602. (c) Larson, R. C.; Iwamoto, R. T., Adams, R. N. *Anal. Chim. Acta* **1961**, *25*, 371.

(16) Endicott, J. F.; Lilie, J.; Kuszaj, J. M.; Ramaswamy, B. S.; Schmonsees, W. G.; Simic, M. G.; Glick, M. D.; Rillema, D. P. *J. Am. Chem. Soc.* **1977**, *99*, 429.

Table I

| entry | compd | compd no. | figure no. | Co redox couple | solvent | temp, °C | $E_{1/2}$, V vs. SCE | $\Delta E_p$, mV | scan rate, V/s | $n$ | $i_a/i_c$ | comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 |  | I | | III/II | $H_2O$ | 22 | −0.042 | >450 | 0.100 | 1 | | ref 9a |
| 2 |  | II | | III/II | $H_2O$ | 22 | +0.27 | >200 | 0.200 | 1 | | ref 9a |
| 3 |  | III | | II/I | $H_2O$ | 22 | −0.74 | 59 | | (1) | 1 | ref 9d, reversible |
| 4 |  | IV | 3a | III/II<br>II/I | $CH_3CN$<br>$CH_3CN$ | RT[a]<br>RT | −0.10<br>−0.71 | 100<br>63 | 0.200<br>0.200 | 1<br>1 | 1<br>1 | |
| 5 |  | V | 3b | III/II<br>II/I | $CH_3CN$<br>$CH_3CN$ | RT<br>RT | −0.04<br>−0.71 | 94<br>63 | 50<br>0.200 | | 1 | irrev at slow scans |
| 6 |  | VI | 4 | III/II<br>II/I | $CH_3CN$<br>$CH_3CN$ | RT<br>RT | −0.4[b]<br>−1.12 | 230<br>80 | 0.200<br>0.200 | | 1<br>1 | excess *N*-MeIm added (×10³) |

[a] Room temperature. [b] −0.70 for the Co(III)/Co(II) couple of the bis imidazole complex.

$B_{12}$ complexes will be delayed until the Discussion section, although some comparisons of the $B_{12}$ and model electrochemistry will be made in this section. The results on the nonalkyl model complexes are presented first followed by the more extensive results on the alkylcobaloxime and alkyl $Co[C_2(DO)(DOH)_{pn}]$ complexes.

**Electrochemistry of the Nonalkyl Cobalt Complexes.** Conductivity data on $[(CH_3CN)Co[C_2(DO)(DOH)_{pn}]I]^+I^-$ (IV) demonstrates that it is, as formulated, a 1:1 electrolyte in $CH_3CN$. The cyclic voltammetry of IV between +0.5 and −1.0 in $CH_3CN$ at Pt is shown in Figure 3a. The results observed are consistent with the redox behavior generally found for cobalt complexes of square planar nitrogen macrocycles. The Co(II)/Co(I) couple, $E_{1/2}$ = −0.71 V vs. SCE, is reversible and relatively insensitive to moderate concentrations of axial ligands, while the Co(III)/Co(II) couple, $E_{1/2}$ = −0.10 V, shows chemical reversibility (ipa/ipc ≈ 1) but has a much slower rate of electron transfer than the Co(II)/Co(I) couple ($\Delta E_p$ = 107 mV at 0.2 V/s) and is quite dependent upon the exact axial ligation. Similarly, a slow electron transfer in the Co(III)/Co(II) couple of aquocobalamin was observed by Lexa and Savéant, behavior which they ascribed to the increase in axial bond lengths accompanying reduction to Co(II).[9a]

Figure 3b shows the voltammogram of [(solvent) $Co[C_2(DO)(DOH)_{pn}]BzIm^{2+}](PF_6)_2^{2-}$ (V) (BzIm = 1,5,6-trimethylbenzimidazole). The reversible Co(II)/Co(I) wave at $E_{1/2}$ = −0.71 V is readily assigned to the same Co(II)/Co(I) couple observed in Figure 3a for IV. In fact, all the nonalkyl $Co[C_2(DO)(DOH)_{pn}]$ complexes studied herein produce a nearly identical Co(II)/Co(I) wave. A slight dependence of this couple on solvent is observed; for example, in THF $E_{1/2}$ = −0.78, whereas in $CH_3CN$ $E_{1/2}$ = −0.71 V. The relative insensitivity of the Co(II)/Co(I) couple is consistent with weak axial interactions in these complexes (which are thought to be five coordinate in the Co(II) oxidation state[15a,16]) as well as with relative weak interactions of the Co(I) produced

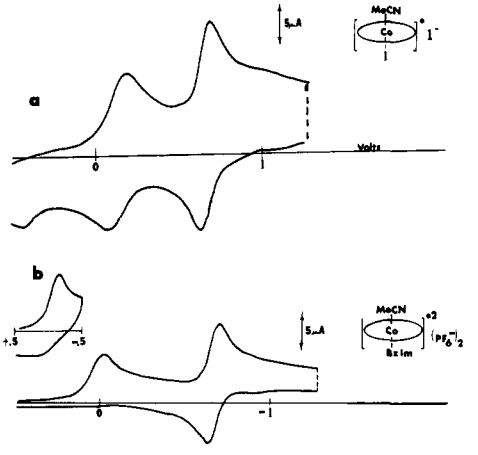



**Figure 3.** Cyclic voltammetry in acetonitrile, 0.1 M $TBAPF_6$ of (a) IV, $9.83 \times 10^{-4}$ M, at 200 mV/s, (b) V, $3.50 \times 10^{-4}$ M, at 200 mV/s; the insert shows V at 50 V/s.

with solvents like THF or $CH_3CN$. The Co(III)/Co(II) couple in V (Figure 3b) is shifted ca. 100 mV positive relative to the same couple in IV. This behavior is consistent with the unit increase in positive charge on going from IV to V. This Co(III) reduction wave is irreversible at moderate scan rates. Fast scan rates (50 V/s) begin to compete with axial base loss from the Co(II) product so that a partial reoxidation wave is observed, $E_{1/2}$ = −0.04 V, as shown in the insert of Figure 3b. Upon the addition of 1,5,6-trimethylbenzimidazole or *N*-methylimidazole (*N*-MeIm), the wave sharpens into a nearly reversible couple, $E_{1/2}$ = −0.2 V.

Conductivity measurements demonstrate that $ClCo(DMG)_2BzIm$, (VI) completely, albeit slowly, dissociates its axial chloride ion in $CH_3CN$. The cyclic voltammogram of the resulting

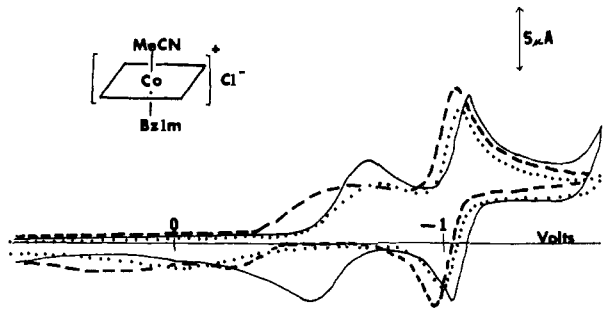



**Figure 4.** Cyclic voltammetry at 0.20 V/s in acetonitrile, 0.1 M $TBAPF_6$ of VI, $8.88 \times 10^{-4}$ M: (–) *N*-methylimidazole added ($\sim 10^3$ molar excess); (– – –) pure compound; (···) 15-fold molar excess of 1,5,6-trimethylbenzimidazole added.

cationic complex is shown in Figure 4. The reversible Co(II)/Co(I) wave occurs at $E_{1/2} = -1.12$ V, which is 0.4 V more difficult to reduce than the same Co(II)/Co(I) couple in $B_{12}$ or in the $Co[C_2(DO)(DOH)_{pn}]$ model. As shown in Figure 4, the Co(III)/Co(II) reduction wave is poorly defined and the reoxidation even more so. Upon the addition of stoichiometric excesses of 1,5,6-trimethylbenzimidazole or *N*-methylimidazole the wave sharpens into a chemically reversible but slow electron-transfer Co(III)/Co(II) redox couple, $E_{1/2} = -0.70$ V. We assign the $E_{1/2} = -0.70$ V couple to $[(N\text{-MeIm})Co(DMG)_2(N\text{-MeIm})]^{2+}$ and the more positive $E_{1/2} \approx -0.4$ V couple to $[(CH_3CN)Co(DMG)_2(BzIm)]^{2+}$. The above results are consistent with Schrauzer's observation[4b] that $ClCo(DMG)_2$(pyridine) and [(pyridine)$Co(DMG)_2$(pyridine)]$^+ClO_4^-$ in $CH_3CN$ show the same polarographic waves at −0.67 V (Co(III)/Co(II)) and at −1.44 V (Co(II)/Co(I)) vs. 0.01 M $Ag^+/Ag$ (or at −0.38 and −1.15 V vs. SCE, respectively, using the literature[15c] value of $E = +0.29$ V for 0.01 M $Ag^+/Ag$ in $CH_3CN$ vs. SCE).

**Electrochemistry of the Alkylcobalt Complexes.** The cyclic voltammograms of the alkylcobalt complexes are more complicated due to axial base and cobalt–carbon bond cleavage upon reduction. In recent studies[9e] of methylcobalamin (VII, entry 1, Table II), $E_{1/2} = -1.6$ V, and methylcobinamide (VIII, entry 2, Table II), $E_{1/2} = -1.47$ V, Savéant and Lexa avoided adsorption problems by using nonmercury electrodes in a DMF/propanol solvent system and suppressed Co–C bond cleavage in low-temperature, rapid-scan cyclic experiments. Previous electrochemical studies[7a-c] of $[RCo[C_2(DO)(DOH)_{pn}DMF]^+ClO_4^-$ complexes in DMF were under conditions that did not suppress Co–C cleavage and show a polarographic $E_{1/2}$ (R = Me) of −0.85 V vs. SCE with the reduction reaction $RCo(III) + e^- \rightarrow RCo(II) \rightarrow {}^1/_2R_2Co(III) + {}^1/_2Co(I)$. The incorrect axial ligation and especially the irreversible nature of these polarographic $E_{1/2}$ values preclude any meaningful comparison to the electrochemical results on $B_{12}$. In the present study these problems have been overcome. Reversible $E_{1/2}$ values have been measured that can be directly compared to $B_{12}$ and a dramatic dependence upon the axial base concentration has been discovered.

The voltammogram of $[CH_3Co[C_2(DO(DOH)_{pn}OH_2]^+PF_6^-$ (IX), in 1:1 DMF/propanol shows a deceptively simple, apparently quasireversible wave (Figure 5a). However, multiple scan experiments unambiguously identify the reoxidation wave in Figure 5a as due to the alkyl-free Co(I). Peak-height comparisons and coulometry indicate that no more than 50% of the complex ultimately ends up in the Co(I) form. On cooling the solution, a new meta-stable and unidentified product appears, $E_p = -0.30$ V (Figure 5b). It was anticipated that the addition of an axial base with a significant trans effect, such as *N*-MeIm, would further decrease the chemical reversibility. Instead, the addition of $>10^3$ molar excess of *N*-methylimidazole has the unexpected effect of making the system nearly reversible with $E_{1/2} = -1.20$ V, in which the $E_p = -0.30$ V and Co(I), $E_{1/2} = -0.71$, products are totally absent (Figure 5c). On warming this solution, considerable chemical reversibility is still observed, confirming that the major function of added *N*-methylimidazole is to *inhibit* the RCo decomposition mechanism. Similar experiments were initially tried

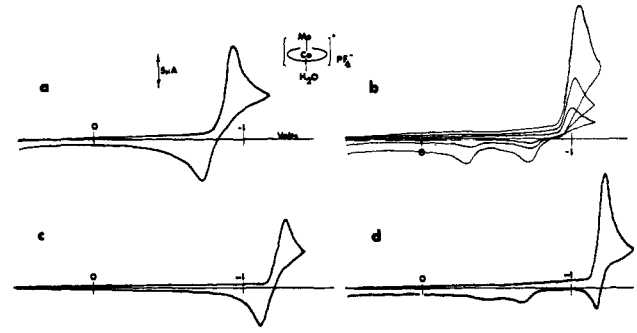



**Figure 5.** Cyclic voltammetry in 1:1 DMF/propanol, 0.1 M $TBAPF_6$ of IX: (a) room temperature, 200 mV/s; (b) −20 °C; 50, 200, 1000 mV/s; (c) −21 °C, 200 mV/s, *N*-methylimidazole (10% v/v added); (d) room temperature, 200 mV/s, *N*-methylimidazole (10% v/v added). All concentrations = $7.55 \times 10^{-4}$ M.

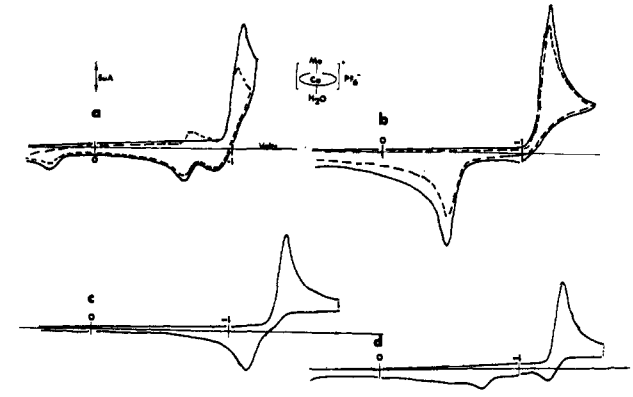


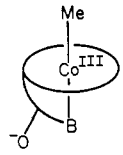
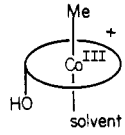
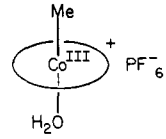
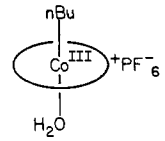
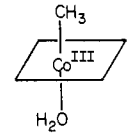
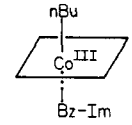

**Figure 6.** Cyclic voltammetry of IX in acetonitrile, 0.1 M $TBAPF_6$: (a) concentration = $7.35 \times 10^{-4}$ M, at room temperature, 500 mV/s; (–) initial scan, (--) steady state; (b) concentration = $7.35 \times 10^{-4}$ M, −25 °C at 500 mV/s, (–) initial scan, (--) steady state; (c) concentration = $7.75 \times 10^{-4}$ M, −26 °C, 200 mV/s with *N*-methylimidazole (10% v/v added); (d) concentration = $7.75 \times 10^{-4}$ M, room temperature, 200 mV/s with *N*-methylimidazole (20% v/v added).

using the base 1,5,6-trimethylbenzimidazole, but the large amounts of base required necessitated a switch to the commercially available, liquid *N*-methylimidazole.

A comparison of the cyclic voltammetry of IX in $CH_3CN$ (Figure 6) with that just presented in DMF/propanol (Figure 5) demonstrates that there is a considerable difference in the chemical behavior of the methyl complex IX in the two solvent systems. In particular, the methyl complex has a lower apparent stability in acetonitrile. In Figure 6a, a new, variable current reoxidation peak is observed, $E_p = +0.3$ V, about the same size as the $E_p = -0.66$ V, Co(I) peak. As is shown below, the +0.3 V wave is not due to the $Me_2Co(III)$ product but rather must be due to a different RCo(II)· decomposition product. Additional waves due to post reduction chemical products are observed ($E_{1/2} = -1.2$ V, $E_p$(anodic) = −0.9 V) if one scans more negative than the ca. −1.0 V shown in Figure 6a. If the solution is cooled (Figure 6b), yet another new species is observed, $E_p = -0.51$, which multiple scan experiments demonstrate is coupled to the RCo(III) reduction peak, probably by a reversible chemical step. The $E_p = -0.51$ wave can plausibly be assigned to the oxidation of a RCo(II)-($CH_3CN$) species. If *N*-methylimidazole is added (Figure 6c), a quasi-reversible $E_{1/2} = -1.30$ V couple due to $[MeCo[C_2(DO)(DOH)_{pn}]N\text{-MeIm}]^+$ is observed. If the solution is warmed (Figure 6d), less reversibility is observed than was observed under similar conditions in DMF/propanol (Figure 5d).

We have examined the cyclic voltammetry of authentic $Me_2Co[C_2(DO)(DOH)_{pn}]$ in 1:1 DMF/propanol at Hg and find essentially the electrochemistry that Costa reports[7a] of $E_p = -0.98$, −0.74, and +0.08 V (200 mV/s, −22 °C), although there is evidence of adsorption problems. In $CH_3CN$ at Pt and at 20 °C, the dimethyl complex shows a single, irreversible oxidation peak,

Table II

| entry | compd | compd no. | figure no. | redox couple | solvent | temp, °C | $E_{1/2}$ or ($E_p$), V vs. SCE | $\Delta E_p$, mV | scan rate, V/s | $n$ | $i_a/i_c$ | comment |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 |  | VII | | III/II | DMF/prop | −30 | −1.6 | 100 | 100.0 | (1) | | reversible, ref 9e |
| 2 |  | VII | | III/II | DMF/prop | −20 | −1.47 | 100 | 100.0 | (1) | | reversible, ref 9e |
| 3 |  | IX | 5a | III/II | DMF/prop | RT | (−0.94) | | 0.200 | | | |
| 4 | same as above | IX | 5b | III/II | DMF/prop | −21 | (−1.01) | | 0.200 | | | |
| 5 | same as above | IX | 5c | III/II | DMF/prop | −21 | −1.20 | 170 | 0.200 | | 1 | 1 mL of *N*-MeIm added to 10 mL of solution |
| 6 | same as above | IX | 5d | III/II | DMF/prop | RT | −1.16 | 62 | 0.200 | | 0.4 | 1 mL of *N*-MeIm added to 10 mL of solution |
| 7 | same as above | IX | 6a | III/II | $CH_3CN$ | RT | (−1.06) | | 0.500 | | | |
| 8 | same as above | IX | 6b | III/II | $CH_3CN$ | −25 | (−1.22) | | 0.500 | | | |
| 9 | same as above | IX | 6c | III/II | $CH_3CN$ | −26 | −1.30 | 268 | 0.200 | | 0.7 | 1 mL of *N*-MeIm added to 10 mL of solution |
| 10 | same as above | IX | 6d | III/II | $CH_3CN$ | RT | −1.26 | 103 | 0.200 | | 0.2 | 2 mL of *N*-MeIm added to 10 mL of solution |
| 11 |  | X | 7a | III/II | $CH_3CN$ | −25 | (−1.21) | | 1.000 | 1 | 1 | |
| 12 | same as above | X | 7b | III/II | $CH_3CN$ | −25 | −1.28 | 130 | 0.100 | | 1 | 1 mL of *N*-MeIm added to 10 mL of solution |
| 13 | same as above | X | 7c | III/II | $CH_3CN$ | RT | −1.24 | 72 | 0.100 | | 1 | 1 mL of *N*-MeIm added to 10 mL of solution |
| 14 |  | XI | 8a | III/− | $CH_3CN$ | −26 | (−2.2) | | 0.200 | | | |
| 15 | same as above | XI | 8b | III/− | $CH_3CN$ | −26 | (−2.3)[a] (−2.5) | | 0.200 | | | 1 mL of *N*-MeIm added to 10 mL of solution |
| 16 |  | XII | 9a | III/− | $CH_3CN$ | RT | (−1.9) | | 0.200 | >1[b] | | $n$ value variable[b] |
| 17 | same as above | XII | 9b | III/− | $CH_3CN$ | −25 | (−2.35) | | 0.200 | | | |
| 18 | same as above | XII | 9c | III/− | $CH_3CN$ | −25 | (−2.2)[a] (−2.5) | | 1.000 | | | 2 mL of *N*-MeIm added to 10 mL of solution |
| 19 | same as above | XII | 9d | III/− | $CH_3CN$ | RT | (−2.2)[a] (−2.4) | | 0.500 | | | 2 mL of *N*-MeIm added to 10 mL of solution |

[a] Two waves observed. [b] A catalytic cycle involving reductive Co–R cleavage, butyl group oxidative addition from the $Bu_4N^+$ electrolyte by the electrochemically generated Co(I), then back to reductive cleavage would show $n > 1$. Such a cycle has precedent.[8a]

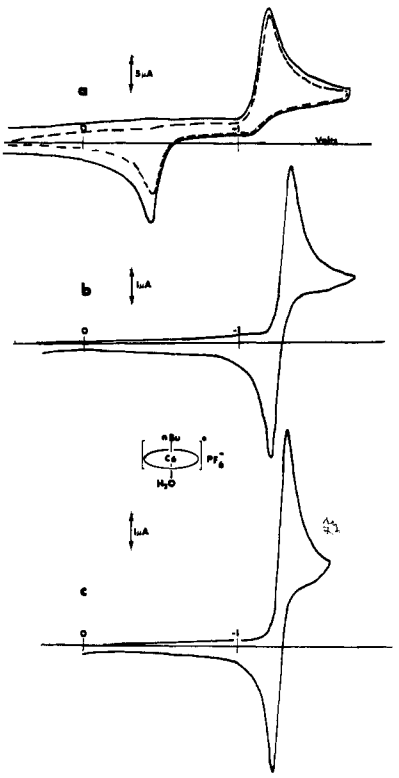


**Figure 7.** Cyclic voltammetry in acetonitrile, 0.1 M $TBAPF_6$ of X, concentration = $5.50 \times 10^{-4}$ M: (a) −25 °C, 1000 mV/s, (–) initial scan, (--) steady state; (b) −25 °C, 100 mV/s, *N*-methylimidazole (10% v/v added); (c) room temperature, 100 mV/s, *N*-methylimidazole (10% v/v added).

$E_p$ = +0.52 V (200 mV/s), which is quite different than the $E_p$ = +0.03 (Hg, $Bu_4NClO_4$, DMF) assigned by Costa[7a] to the dimethyl complex.

The $[n\text{-BuCo}[C_2(DO)(DOH)_{pn}]OH_2]^+PF_6^-$ complex X (Figure 7a–c) shows the expected qualitative similarities to the methyl complex (Figure 6a–d). (The room temperature cyclic of X is analogous to that shown in Figure 6a and has been omitted.) The most striking difference is the greatly increased apparent stability of the reduced *n*-butyl complex. With *N*-methylimidazole at low temperature, a highly reversible $E_{1/2}$ = −1.28 V couple is observed (Figure 7b). The interesting feature here is that this reversibility is maintained upon warming (Figure 7c). A comparison of the methyl complex (Figure 6d) to the butyl complex (Figure 7c) shows the enhanced apparent Co–C bond stability of the butyl derivative relative to the methyl complex. If irreversible homolysis, RCo(II) → R· + Co(I), were occurring, the opposite order of Me vs. Bu stabilities should obtain. On the other hand, the observed Me < Bu stability as well as the observed dependence upon axial base is consistent with a bimolecular decomposition mechanism, such as $RCo(II)\cdot + RCo(III)^+ \rightarrow R_2Co(III) + Co(II)^+$. The other possible, previously suggested[7a] mechanism, $RCo(III)^+ + 2e^- \rightarrow RCo(I)^-$ and then $RCo(I)^- + RCo(III)^+ \rightarrow Co(I) + R_2Co(III)$, is less consistent with the observed $\Delta E_p \geq 60$ mV and its implied $n$ = one electron.

Alkylcobaloxime complexes have received surprisingly little attention in previous electrochemical studies. They were characterized,[7d,f] for example, as giving two irreversible polarographic waves in acetonitrile at 25 °C. For $CH_3Co(DMG)_2OH_2$ and $CH_3Co(DMG)_2$(pyridine), the first one-electron wave is reported at −1.7 V and −1.75 V vs. $Ag^+/Ag$ (or ca. −1.4, −1.46 vs. SCE[15c]), respectively. The cobaloxime $CH_3Co(DMG)_2OH_2$ (XI) reduces at far more negative potentials in our hands, showing a totally irreversible reduction wave at $E_p$ = −2.2 V in $CH_3CN$ at low temperatures (Figure 8a). It is, in fact, reduced at such negative potentials that the potential limit of the preferred solvent mixture of DMF/propanol on platinum is reached before any reduction of XI occurs. An attempt to extend the useful potential range

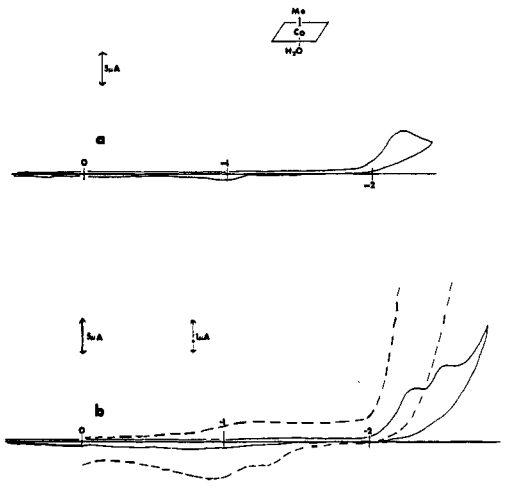


**Figure 8.** Cyclic voltammetry in acetonitrile, 0.1 M $TBAPF_6$ of XI, concentration = $1.06 \times 10^{-3}$ M: (a) −26 °C, 200 mV/s; (b) −26 °C, 200 mV/s, *N*-methylimidazole (10% v/v added); (---) 1-μA current scale.

in DMF/propanol by the use of a Hg electrode failed when XI showed significant adsorption problems similar to those reported by Savéant and Lexa for $B_{12}$ alkyls.[9e] The most striking difference between the electrochemistry of the alkylcobaloximes and that of alkylcobalamins, cobinamides, and $RCo[C_2(DO)(DOH)_{pn}]^+$ complexes is the *total chemical irreversibility* of the alkylcobaloximes under all conditions examined of added *N*-methylimidazole, low temperature, and scan rate. Complete irreversibility was observed even with 20% v/v of *N*-methylimidazole at −30 °C and 200 V/s. The addition of a large excess of *N*-methylimidazole to the −26 °C solution does produce changes (Figure 8b), but none of the waves observed can be readily identified as, for example, Co(I) cobaloxime.

The reduction of the *n*-butylcobaloxime, $n\text{-BuCo}(DMG)_2$(1,5,6-trimethylbenzimidazole) (XII), closely parallels the analogous methyl compound; it shows a completely irreversible reduction under all conditions of solvent, temperature, added base, and scan rate up to 200 V/s at −30 °C with 20% v/v of *N*-methylimidazole. The −25 °C reduction of XII has an $E_p$ at ca. −2.35 V which is 150 mV negative of the $E_p$ = −2.2 V of the methyl case XI (entry 14). It also shows a strong $E_p$ vs. scan rate dependence, which suggests a very rapid, irreversible, follow-up step.[17] On the reoxidation scan, an $E_p$ = −1.08 V peak probably due to Co(I) is observed as well as an unassigned peak at 0.0 V. The precise decomposition mechanism of the reduced $RCo(DMG)_2^-$ is complex as demonstrated by the low-temperature and added-base cyclic voltammograms (Figure 9b–d).

**Coulometry, OTTLE, Spectroscopic and Other Results.** Coulometry was performed on the nonalkyl and butyl compounds and, where available, the *n* values are presented in Tables I and II. In general, coulometric *n* values (bulk and thin layer) agreed with cyclic voltammetric n values within experimental error.

Reduction of $[n\text{-BuCo}[C_2(DO)(DOH)_{pn}]$(1,5,6-trimethylbenzimidazole)$]^+PF_6^-$ showed $n$ = 0.96 for the first reduction wave and $n$ = 0.7 upon reoxidation. The reduced solution showed an absorption $\lambda_{max}$ = 640 nm characteristic of Co(I) and a $\lambda_{max}$ = 425 due, presumably, to the formation of $[(n\text{-Bu})_2Co[C_2(DO)(DOH)_{pn}]$. The Co(I) $\lambda_{max}$ = 640 nm spectrum was also obtained in both an OTTLE experiment and by the exhaustive electrolysis of $ICo[C_2(DO)(DOH)_{pn}]I$. In the case of $[MeCo[C_2(DO)(DOH)_{pn}]OH_2]^+PF_6^-$ in $CH_3CN$ ($\lambda_{max}$ = 388, 425 nm), a bulk electrolysis reduction gave n ≃ 1 and $\lambda_{max}$ = 640 nm due to Co(I), and $\lambda_{max}$ = 405 nm identical with that of authentic $Me_2Co[C_2(CO)(DOH)_{pn}]$. A cyclic voltammogram of this reduced solution showed the anodic peak expected for Co(I)/Co(II) but surprisingly

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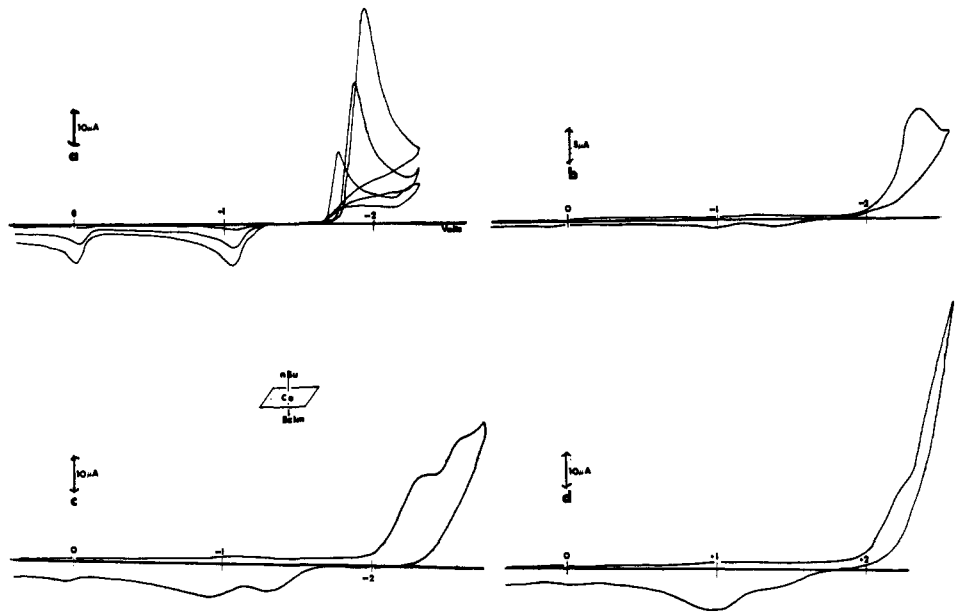

**Figure 9.** Cyclic voltammetry of XII in acetonitrile, 0.1 M $TBAPF_6$: (a) room temperature, 50, 200, 500 mV/s; (b) −25 °C, 200 mV/s; (c) −25 °C, 200 mV/s, *N*-methylimidazole (20% v/v added); (d) room temperature, 200 mV/s, *N*-methylimidazole (20% v/v added); [(a) concentration = $9.30 \times 10^{-4}$ M, (b–d) concentration = $6.30 \times 10^{-4}$ M].

did not show a significant $E_{pa} = +0.52$ V peak characteristic of authentic $Me_2Co[C_2(CO)(DOH)_{pn}]$. Moreover, none of the cyclic voltammograms of the methyl(aquo)complex, Figure 5 or 6, show the $E_{pa} = +0.52$ V expected for the $Me_2Co(III)$ product. In order to explain both the visible spectroscopy results where $Me_2Co(III)$ and Co(I) are observed as well as the cyclic voltammetry results where only Co(I) is detected, we surmise that electrochemically generated Co(II) (from the oxidation of Co(I)) and $Me_2Co(III)$ are reacting to give $MeCo(III)^+$ and MeCo(II). The overall, apparent mechanism and resultant oxidation stoichiometry, shown below, would leave little unreacted $Me_2Co(III)$ in the diffusion layer to be oxidized at +0.52 V and would show only the $E_{pa} = -0.70$ V, Co(I)/Co(II) oxidation wave. The rather unexpected

$$Co(I)^+ + e^- \qquad E_{pa} = -0.70 \text{ V}$$

$$Co(II)^+ + Me_2Co(III) \rightarrow MeCo(III)^+ + MeCo(II)$$

$$MeCo(II) \rightarrow MeCo(III)^+ + e^-$$

$$\text{Net: } Co(I) + Me_2Co(III) \rightarrow 2MeCo(III)^+ + 2e^-$$

prediction is one of significant chemical reversibility of the overall ECE process of $MeCo(III)^+$ reduction then reoxidation. In support of this prediction and thus the above scheme, reoxidation of a $CH_3CN$ solution of $Me_2Co(III)$ and Co(I) generated by bulk reduction of $[MeCo[C_2(CO)(DOH)_{pn}]OH_2]^+PF_6^-$ showed the expected $n = 1$ and both the cyclic voltammogram and the visible spectrum of the reoxidized solution were nearly identical with that observed for authentic $[MeCo[C_2(DO)(DOH)_{pn}]OH_2]^+PF_6^-$ in $CH_3CN$. (In several repeat cyclic voltammograms of the methyl(aquo)complex in $CH_3CN$, the $E_{pa} = +0.03$ V (Figure 6a) variable intensity wave was essentially absent.)

Bulk electrolysis of *n*-$BuCo(DMG)_2$(1,5,6-trimethylbenzimidazole) showed a current vs. time curve that reproducibly decayed to a nonzero value corresponding to $n > 1$, with larger ($n > 4$) values being obtained with longer electrolysis times. The reduced solution showed a $\lambda_{max} = 370$, 560, and 600 (shoulder) nm and a nearly featureless cyclic voltammogram after reoxidation, confirming the fact that alkylcobaloximes irreversibly decompose upon reduction.

## Discussion

The major objectives of this research were essentially twofold. The first objective was the preparation of model complexes with the correct axial ligation for comparison to the $B_{12}$ analogues in Figure 2 and the elucidation of the kinetic and thermodynamic aspects of their electrochemistry. The second objective was to focus on the reduction of the alkylcobalt model complexes and, where possible, to obtain reversible $E_{1/2}$ values and to elucidate the details of the decomposition of the reduced RCo(II) species.

The comparison of the cobaloxime and the $Co[C_2(DO)(DOH)_{pn}]$ electrochemical results to $B_{12}$ demonstrates that the $Co[C_2(DO)(DOH)_{pn}]$ complex is a closer electrochemical mimic of $B_{12}$ than is the more widely employed cobaloxime model. The Co(III)/Co(II) $E_{1/2}$ values for aquocobalamin of −0.042 V (entry 1, Table I) and the Co(II)/Co(I) value for base-off aquo Co(II) cobalamin −0.74 V (entry 3, Table I) as well as the wave shapes are closely reproduced by the $Co[C_2(DO)(DOH)_{pn}]$ model with $E_{1/2} = -0.04$ V for $[(CH_3CN)Co[C_2(DO)(DOH)_{pn}]BzIm]^{2+}$ (entry 5, Table I) and −0.71 V for the Co(II)/Co(I) couple (entries 4 and 5, Table I). The cobaloxime model with its formally −2 charged planar ligand shows $E_{1/2} = -0.40$ V and −1.12 V (entry 6, Table I), being 0.4 V too difficult to reduce on the average. The Co(III)/Co(II) $E_{1/2} = +0.27$ V of diaquocobinamide is close to the literature value of $E_{1/2} = +0.16$ reported by Costa[7a] for $[(DMF)Co[C_2(DO)(DOH)_{pn}](DMF)]^{2+}$, while polarographic $E_{1/2}$ values for $[(H_2O)Co(DMG)_2(H_2O)]^+$ are near 0.0 V although the waves for the diaquocobaloxime were irreversible and preceded by an absorption wave,[7f] and the potentials are probably not reliable. A compilation of Co(II)/Co(I) potentials of cobalt-containing macrocycles found, as this study has, that this couple is relatively insensitive to potential axial ligands or solvents.[7g] It was concluded,[7g] therefore, that the Co(II)/Co(I) potential measures primarily the electronic influence of the equatorial tetradentate ligand. To the extent that this is true, Costa's model ($E_{1/2} = -0.71$ V) has an equatorial ligand effect closer to that of $B_{12}$ ($E_{1/2} = -0.74$ V) than does the cobaloxime model ($E_{1/2} = -1.12$ V).

Neither the cobaloxime model nor the $Co[C_2(DO)(DOH)_{pn}]$ model can reproduce exactly the electrochemistry of alkyl $B_{12}$ complexes. Methylcobalamin (entry 1, Table II) and methyl(DMF)cobinamide (entry 2, Table II) have $E_{1/2}$ values of −1.6 and −1.47 V, respectively, at low temperatures where suppression of Co–C bond cleavage is achieved. This cleavage normally yields Co(I) and presumably R· and/or $R^-$.[8b] The complexes $(CH_3Co[C_2(DO)(DOH)_{pn}]N\text{-MeIm})^+PF_6^-$ and $(CH_3Co[C_2(DO)(DOH)_{pn}]solvent)^+PF_6^-$ (solvent = DMF or $CH_3CN$) show $E_{1/2} = -1.23 \pm 0.05$ V (entries 5, 6, 9, 10; Table II) and $E_p = -0.94$ to −1.22 V (entries 3, 4, 7, 8; Table II), respectively, being about 0.4 V too easy to reduce on the average. In both $B_{12}$ and the $Co[C_2(DO)(DOH)_{pn}]$ model, base-on species are in the range of 150 to 300 mV harder to reduce than the base-off species. The

cobaloximes $CH_3Co(DMG)_2$(N-MeIm) and $CH_3Co(DMG)_2$(solvent), where solvent = DMF or $CH_3CN$, show $E_p$ values of ca. −2.5 V (entry 15, Table II) and −2.2 V (entry 14, Table II), respectively, being about 0.7 V too difficult to reduce. Because of the fast, irreversible follow-up reactions, $E_p$ values cited are probably positive of the true $E_{1/2}$ values,[17] making the alkylcobaloxime $E_{1/2}$ values even more negative. The complete irreversibility of the alkylcobaloximes under all electrochemical conditions examined is a clear difference between $B_{12}$ and the cobaloxime model.

Only for the $RCo[C_2(DO)(DOH)_{pn}]^+$ complexes are any details known for the decomposition of the reduced RCo(II) intermediate. The exact products and stepwise mechanisms for both the reduced alkyl $B_{12}$ and alkylcobaloxime complexes remain obscure. The cyclic voltammetry, coulometry, OTTLE, axial base dependence, and relative apparent stabilities methyl < butyl in the reduced $RCo[C_2(DO)(DOH)_{pn}]^+$ complexes are all consistent with the postulated, reversible ECE process. The high, apparent stability in the presence of base and the greater stability of the butyl compound emphasize the importance of a five-coordinate alkyl species and the bimolecular nature, respectively, of the decomposition mechanism.

As noted in the introduction, other possible noncorrin $B_{12}$ models such as Co(salen), Co(saloph) or Co(bae) complexes are even more difficult to reduce than Co(DMG) complexes[7a,h-j] and generally show nonalkyl Co(III)/Co(II) couples in the range of −0.25 to −0.9 V vs. SCE.[7e] Interestingly, Lexa and Savéant have recently shown[8a] that cobalt tetraphenylporphyrin, Co(TPP), with its formally −2 tetradentate equatorial ligand, shows $E_{1/2}$(Co(II)/Co(I)) = −0.80 V and $E_{1/2}$(RCo(III)/RCo(II)) = −1.3 V. These values are close to the −0.74 and −1.47 (alkylcobinamide) $B_{12}$ values and emphasize the limitations of oxidation state formalisms in deciding which tetradentate ligand will best model $B_{12}$. On the basis of the R = butyl derivative, Lexa and Savéant conclude that the RCo(TPP) is an extremely poor model for dealing with the properties of the (presumably R = Me) alkyl $B_{12}$ intermediates. Our results suggest that in both the Co(TPP) and $B_{12}$ systems the examination of methyl and *n*-butyl as well as other alkyls could prove valuable. A synthetic, formally −1 charged, corrin-like $B_{12}$ model has appeared.[8b] It shows Co(III)/Co(II), Co(II)/Co(I), and RCo(III) (solvent) $E_{1/2}$ values at −0.19, −0.98, and −1.22 V vs. SCE (reported as −0.48, −1.27, −1.51 vs. 0.01 M $Ag^+/Ag$ in DMF), which are about 0.2 V negative of the $Co[C_2(DO)(DOH)_{pn}]$ values reported herein. The retention of configuration at carbon seen upon electrochemical reductive cleavage of the Co–C bond in these $B_{12}$ model complexes is also worth noting. A very recent paper by Murakami and co-workers has examined two corrin $B_{12}$ models by several physical techniques. Their closest electrochemical mimic, Co(1,19-dimethyl-AD-didehydrocorrin) or Co(BDHC) shows Co(III)/Co(II) $E_{1/2}$ = +0.47 V and Co(II)/Co(I) $E_{1/2}$ = −0.71 V (vs. SCE in $CH_3OH$; Co(II)/Co(I) = −0.55 V in DMF). This work also concludes that the formal charge of the equatorial tetradentate ligand strongly affects the Co(III)/Co(II) potentials, which vary from +0.97 V (SCE) for the formally −1, 1,19-dimethyl-AD-tetradehydrocorrin complex to −0.26 V for a formally −3 corrole ligand.

In summary, the $Co[C_2(DO)(DOH)_{pn}]$ coenzyme $B_{12}$ model pioneered by Costa is a considerably closer electrochemical mimic of $B_{12}$ than is the much more widely used cobaloxime model. The lack of an appended axial benzimidazole, the different apparent Co–R bond stabilities, the ca. 0.4 V too positive $E_{1/2}$ values of the cobalt alkyls, and the inability of any simple model to reproduce possible conformational[19] changes and steric effects in the more complicated coenzyme are, however, limitations of the Costa model which should be noted.[20]

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(20) (a) A referee has remarked, "that the cobaloximes as a rule form somewhat more stable organocobalt derivatives than the corrins is one of their great advantages and not a shortcoming. I also think there is nothing fundamentally wrong with having no appended axial base or less steric hinderance. These differences could also be declared as positive attributes of the models rather than limitations". We certainly would agree that, in many cases, the differences between a model and the primary bioinorganic system might be quite useful or might yield some of the most important insights into the primary system. We would even offer recent work[20b] as a case in point where the more stable Co–C bond in cobaloximes is a definite advantage. Furthermore, we do not wish to undermine in any way the enormous contributions of the cobaloxime model to $B_{12}$ and inorganic chemistry. Our point is that at the current, relatively sophisticated (yet still incomplete) level of knowledge about coenzyme $B_{12}$ and the $B_{12}$-dependent rearrangement reactions, additional model studies that will be required need to be interpreted with the differences in mind of that model as compared to the corrin analogue. Known cobaloxime differences include too strong a Co–C bond, a wrong overall charge and resultant different electrochemical and other properties, axial base binding constants that are too high, and different symmetry properties of the HOMO of the polyene skeleton in cobaloximes as compared to the $\pi_7$ of the corrin (which is involved in the so-called "strain orbital").[20c] There are also numerous studies suggesting cobaloximes have cis coordination sites and thus chemistry and mechanisms available to them that organocorrins presumably do not.[20d-f] Wood and Brown[20g] previously noted differences in $B_{12}$ and cobaloxime axial ligand exchange kinetics and concluded "the results of such differences between $B_{12}$ and cobaloximes leads one to question whether cobaloximes are appropriate model systems with which to study kinetic aspects related to the mechanism of catalysis of $B_{12}$". Hill has also cautioned that "the relationship of the chemistry of the simple cobalt complexes to the function of $B_{12}$-dependent enzymes should be made with caution".[20h] As the Costa model becomes better studied, important differences between it and coenzyme $B_{12}$ are surely to emerge as well. A concrete example of where the use of a close $B_{12}$ mimic is important concerns the question of participation of cobalt in the rearrangement step of the 11 $B_{12}$-dependent rearrangement reactions. Since the formation of a Co-substrate–carbon bond in, for example, diol dehydratase,[2a] or electron transfer $Co(II) + R\cdot \rightarrow Co(III)^+ + R^-$ in methylmalonyl Co-A mutase are reasonable and often discussed possibilities, models with different Co–C bond stabilities and greatly different Co(III)/Co(II) potentials than $B_{12}$, respectively, should probably be avoided. (b) Randaccio, L.; Bresciani-Pahor, N.; Toscano, P. J.; Marzilli, L. G. *J. Am. Chem. Soc.* **1980**, *102*, 7372; (c) Salem, L.; Eisenstein, O.; Anh, N. T.; Burgi, H. B.; Devaquet, A.; Segal, G.; Veillard, A. *Nouv. J. Chim.* **1979**, *1*, 335; (d) Tyrlik, S.; Kucharska, M. M.; Wolochowicz, I. *J. Mol. Catal.* **1979**, *6*, 393; (e) Atkins, M. P.; Golding, B. T.; Bury, A.; Johnson, M. D.; Sellers, P. J. *J. Am. Chem. Soc.* **1980**, *102*, 3630; (f) Atkins, M. P.; Golding, B. T.; Sellars, P. J. *J. Chem. Soc., Chem. Commun.* **1978**, 954; (g) Wood, J. M.; Brown, D. G. *Struct. Bonding (Berlin)* **1972**, *11*, 47; (h) Hill, H. A. O. *Chem. Br.* **1976**, *12*, 119.