25 mL of THF. The solution was warmed to room temperature slowly and then heated at 55–60 °C for 1 h in the dark. When R = *n*-Pr, Ph, dark orange solutions resulted, while a brown solution resulted when R = Me_3Si. The reaction mixtures were then cooled to room temperature, and the solvent was removed under vacuum. The residues were extracted with pentane and the extracts then filtered. The pentane was removed under vacuum, and the crude product was purified by vacuum distillation in the case of $(RC{\equiv}C)_2Te$ (R = *n*-Pr, Me_3Si). In the case of $(PhC{\equiv}C)_2Te$, the products were extracted with a 5:1 pentane/toluene solution. After removal of the solvents under vacuum, 90% (based on $TeCl_4$) of the crude products were isolated. The byproduct $PhC{\equiv}CC{\equiv}CPh$ was sublimed out of the crude mixture (30% yield) under dynamic vacuum at 100 °C. However, even after multiple sublimations and extractions we were unable to remove all of the $PhC{\equiv}CC{\equiv}CPh$ to obtain an analytically pure sample of $(PhC{\equiv}C)_2Te$. The problem of separating and purifying $(PhC{\equiv}C)_2Te$ from this mixture has been previously reported.[11]

$(MeC{\equiv}C)_2Te$. The light yellow product was purified by recrystallization from pentane (mp = 50–52 °C) and can be fractionally distilled at 110 °C at 15 Torr (42% yield based on $TeCl_4$). Anal. Calcd for C_6H_6Te: C, 35.03; H, 2.94; Te, 62.03. Found: C, 35.00; H, 2.95; Te, 61.84. FTIR (diffuse reflectance/KBr): 3178 (m), 3166 (m), 3025 (sh), 2952 (ms), 2909 (s), 2839 (ms), 2721 (w), 2380 (w), 2171 (vs), 2164 (vs), 2034 (m), 1432 (s), 1364 (ms), 1263 (w), 1021 (ms), 997 (vs), 689 (m), 510 (w) cm^{-1}.

$(EtC{\equiv}C)_2Te$. The light yellow liquid was collected by vacuum distillation at 125 °C at 15 Torr (or 45–46 °C at 0.075 Torr) in 56% yield based on $TeCl_4$. Anal. Calcd for $C_8H_{10}Te$: C, 41.10; H, 4.31; Te, 54.58. Found: C, 41.04; H, 4.60; Te, 54.57. FTIR (neat/KBr plates): 2976 (vs), 2937 (s), 2913 (ms), 2878 (ms), 2838 (w), 2160 (ms), 1454 (m), 1429 (m), 1375 (w), 1312 (vs), 1069 (ms), 1029 (w), 886 (w), 779 (w), 526 (m) cm^{-1}.

$(n\text{-}PrC{\equiv}C)_2Te$. The pale yellow liquid was distilled at 67–68 °C at 0.075 Torr (69% yield based on $TeCl_4$). Anal. Calcd for $C_{10}H_{14}Te$: C, 45.87; H, 5.39; Te, 48.74. Found: C, 47.62; H, 5.55; Te, 47.24. FTIR (neat/KBr plates): 2962 (vs), 2933 (vs), 2901 (ms), 2871 (s), 2832 (w), 2161 (m), 1712 (w), 1462 (ms), 1425 (w), 1380 (w), 1338 (m), 1325 (w), 1274 (w), 1258 (sh), 1224 (w), 1092 (w), 1076 (w), 1057 (w), 1000 (w), 964 (m), 877 (w), 843 (w), 775 (w), 737 (w), 542 (w) cm^{-1}.

$(t\text{-}BuC{\equiv}C)_2Te$. The light yellow-green product was purified by recrystallization from pentane (mp = 62–64 °C) and can be fractionally distilled at 130 °C at 15 Torr (62% yield based on $TeCl_4$). Anal. Calcd for $C_{12}H_{18}Te$: C, 49.72; H, 6.26; Te, 44.02. Found: C, 49.88; H, 6.21; Te, 43.91. FTIR (diffuse reflectance/KBr): 3992 (w), 3892 (w), 3333 (w), 3249 (w), 3196 (w), 3080 (sh), 3035 (sh), 2969 (vs), 2928 (vs), 2906 (s), 2866 (s), 2814 (sh), 2802 (sh), 2389 (w), 2288 (w), 2167 (m), 2133 (ms), 1472 (ms), 1453 (s), 1390 (m), 1362 (s), 1248 (s), 1204 (ms), 1030 (m), 930 (m), 911 (m), 744 (ms), 530 (m), 482 (m), 469 (m) cm^{-1}.

$(Me_3SiC{\equiv}C)_2Te$. The light yellow liquid was collected by vacuum distillation at 135 °C at 15 Torr (60% yield based on $TeCl_4$). Anal. Calcd for $C_{10}H_{18}Si_2Te$: C, 37.30; H, 5.63; Si, 17.44; Te, 39.62. Found: C, 37.46; H, 5.65; Si, 17.42; Te, 39.39. FTIR (neat/KBr plates): 2960 (m), 2899 (w), 2859 (w), 2079 (m), 1409 (w), 1385 (w), 1250 (s), 1090 (w), 844 (vs), 760 (ms), 712 (s), 647 (w) cm^{-1}.

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Synthesis, Characterization, and Acid-Induced Decomposition of the α- and β-Diastereomers of (2-Hydroxyethyl)- and (2-Alkoxyethyl)cobalamins and Cobinamides

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A series of (alkoxyethyl)cobalt corrinoids ($ROCH_2CH_2CoC$, R = H, C_6H_5, $(CH_3)_2CH$, CH_3, CH_3CH_2, CF_3CH_2) has been prepared including the α- and β-diastereomers of the (alkoxyethyl)cobalamins ($ROCH_2CH_2Cbl$'s) and the α- and β-diastereomers of the (alkoxyethyl)cobinamides ($ROCH_2CH_2Cbi$'s). In addition, the deuterated analogue of (β-hydroxyethyl)cobalamin ([1,2-$^2H_4$]-β-$HOCH_2CH_2Cbl$) and the ^{13}C-enriched analogues of all four of the hydroxyethyl complexes (α- and β-[1,2-$^{13}C_2$]-$HOCH_2CH_2Cbl$'s and α- and β-[1,2-$^{13}C_2$]-$HOCH_2CH_2Cbi$'s) have been prepared. These compounds have been characterized by UV–visible spectroscopy, GC/MS identification of the organic products of their solid-state anaerobic pyrolysis, FAB MS, and ^1H, ^2H, ^{13}C, ^{19}F, and ^{13}C-edited ^1H NMR spectroscopy. All of the compounds are acid labile, decomposing with strictly first-order kinetics (at a given pH) at pH's of 0–4.4 in aqueous media and in aqueous sulfuric acid. The products of this decomposition for the β-$ROCH_2CH_2Cbl$'s were determined to be aquocobalamin (by UV–visible spectroscopy and HPLC retention), ethylene, and the alcohol, ROH (by GC/MS). Second-order rate constants have been determined for the base-on and base-off species of the β-$ROCH_2CH_2Cbl$'s as well as for the α-$ROCH_2CH_2Cbl$'s and the α- and β-$ROCH_2CH_2Cbi$'s. The reactivity is significantly dependent on the nature of R and varies by about 40-fold across each series of (alkoxyethyl)cobalt corrinoids. In addition, the base-on species of the β-$ROCH_2CH_2Cbl$'s are found to be 43- to almost 100-fold more reactive than the base-off species. Unlike the analogous cobaloximes in which the acid-induced decomposition is known to proceed via a σ-bonded ethylcobaloxime carbonium ion intermediate, no evidence of any kind could be found for the presence of an intermediate in the acid-induced decomposition of the (alkoxyethyl)cobalt corrinoids. The simplest mechanism which accounts for the data is thus a concerted elimination of the alcohol and the dealkylated cobalt corrinoid from the β-oxygen-protonated species, $RO(H)CH_2CH_2CoC^+$.

Introduction

There remains much interest in the mechanisms of reactions in which carbon–cobalt bonds of organocobalt complexes are cleaved. One such prototypical reaction is the thermal- and acid-induced decomposition of organocobalt species containing a β-oxygen substituent in the organic ligand. Examples of this reactivity include the acid-induced and the heterolytic component of the ther-

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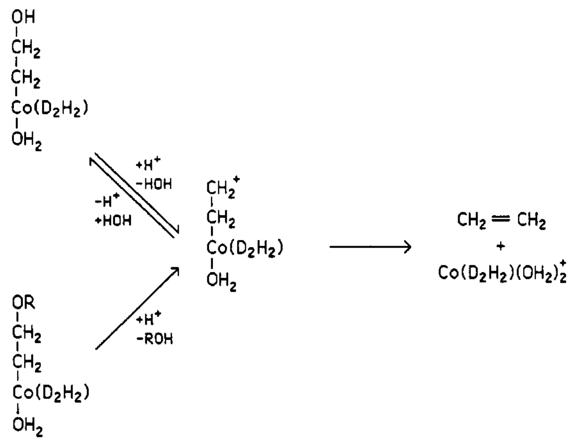
Scheme I



mally induced decomposition of (5′-deoxyadenosyl)cobalt corrinoids (AdoCba's),[1-5] the acid-induced decomposition of (2-hydroxyalkyl)- and (2-alkoxyalkyl)cobaloximes[6-13] and of (5′-deoxyadenosyl)cobaloxime,[14] the acid-induced decomposition and related alcoholysis of (2-acetoxyethyl)cobaloximes,[15-18] the acid-induced decomposition of (formylmethyl)cobaloxime and (formylmethyl)cobalamin and their acetals,[17-25] and the acid-induced decomposition of (2-aryl-2-ketoethyl)cobaloximes and cobalamins.[26,27]

The acid-induced decomposition of (2-hydroxyethyl)- and (2-alkoxyethyl)cobaloximes is of interest as its mechanism has been studied in detail.[11,12] This apparent elimination reaction has been shown to occur via a two-step mechanism (Scheme I) with the second step rate-limiting at all acidities.[12] The intermediate, which accumulates in strongly acidic media due to the reduced activity of water at such acidities,[28-30] has been shown by ^{13}C NMR spectroscopy to be a lyate ion-paired σ-bonded ethylcobaloxime carbonium ion, as shown in Scheme I. During acid-induced decomposition at mild acidities, where the intermediate does not accumulate, (2-alkoxyethyl)cobaloximes have been shown to be converted to (2-hydroxyethyl)cobaloximes via this intermediate, as indicated in Scheme I.[11,12]

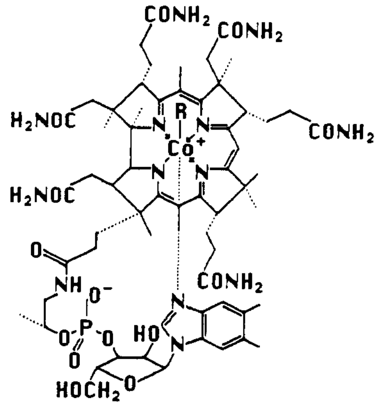


Figure 1. Structure of the cobalamin system. The structure shown is a base-on β-alkylcobalamin (β-RCbl), in which a 5,6-dimethylbenzimidazole nucleotide occupies the α-axial (i.e., "lower") position and the organic ligand occupies the β-axial (i.e., "upper") ligand position. In an α-alkylcobalamin (α-RCbl), the nucleotide is uncoordinated, the organic ligand occupies the α-axial ligand position, and the β-axial ligand position is (presumably) occupied by water. Cobinamides (Cbi's) are derivatives in which the phosphodiester linkage has been hydrolyzed and the nucleotide removed. The diastereomeric α- and β-RCbi's have bonding arrangements analogous to that of the α- and β-RCbl's.

Organocobalt corrinoids and simple organocobalt model complexes often display similar chemistry. However, in the rare instances where detailed mechanistic comparisons can be made, mechanistic differences can be found. For instance, the mechanism of the reaction of cob(II)alamin with alkyl halides[31] has been shown to be identical to that for cobalt(II) model complexes[32-37] for alkyl chlorides and alkyl bromides, but alkyl iodides react with cob(II)alamin and cobalt(II) model chelates by dissimilar mechanisms.[31] In order to provide additional opportunities for such comparisons, we have undertaken the preparation and characterization of a series of (2-hydroxyethyl)- and (2-alkoxyethyl)cobalt corrinoids to permit a study of their acid-induced decomposition.

Recently, this laboratory has reported that the reductive alkylation of cobinamides with alkyl halides results in formation of mixtures of diastereomeric β-alkyl- and α-alkylcobinamides[38,39] (β- and α-RCbi's;[1] Figure 1) in widely

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(1) Abbreviations: β-RCbl, β-alkylcobalamin; α-RCbl, α-alkylcobalamin; β-RCbi, B-alkylcobinamide; α-RCbi, α-alkylcobinamide; (CN)$_2$Cbl, dicyanocobalamin; (CN)$_2$Cbi, dicyanocobinamide; Ado, 5′-deoxyadenosyl-; RCo(D$_2$H$_2$)OH$_2$, alkylaquocobaloxime = alkylaquobis(dimethylglyoximato)cobalt(III). The structure of the cobalamin chelate and the stereochemistry of the various diastereomeric alkylcobamides are described in Figure 1.

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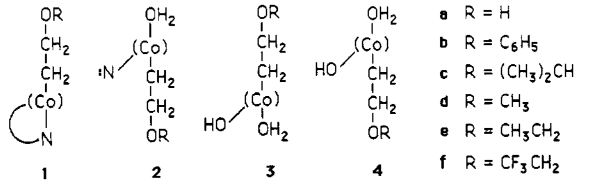
varying proportions depending on the nature of the alkyl group. Similarly, reductive alkylation of aquocobalamin (H_2OCbl) with alkyl halides in acidic media produces mixtures of the diastereomeric β- and α-alkylcobalamins (β- and α-RCbi's;[1] Figure 1). We now report the synthesis, characterization, and acid-induced decomposition of a series of β- (1) and α- (2) (2-hydroxyethyl)- and (2-alkoxyethyl)cobalamins and β- (3) and α- (4) (2-hydroxyethyl)- and (2-alkoxyethyl)cobinamides with alkoxy groups C_6H_5O, $(CH_3)_2CHO$, CH_3, CH_3CH_2, and CF_3CH_2. The $[1,2\text{-}^2H_4]$-β-$HOCH_2CH_2Cbl$ derivative of **1a** as well as the $[1,2\text{-}^{13}C_2]$ derivatives of **1a**, **2a**, **3a**, and **4a** have also been prepared. With the exception of our recent report of the 4 ethoxyethyl (**1a**–**4a**) compounds,[39] only 3 of these 29 compounds (β-$HOCH_2CH_2Cbl$,[14,40–44] β-$HOCH_2CH_2Cbi$,[14,44] and β-$CH_3OCH_2CH_2Cbl$[41]) have been reported previously.



Experimental Section

Materials. Aquocobalamin acetate was from Roussell, and Factor B[45] was prepared by a modification[46] of the method of Renz.[47] 2-Bromoethanol, 2-methoxyethyl bromide, 2-ethoxyethyl bromide, and 2-phenoxyethyl bromide (Aldrich) were redistilled before use. 2-(2,2,2-Trifluoroethoxy)ethanol was prepared by reaction of 2,2,2-trifluoroethanol (Aldrich) with potassium hydroxide, sodium iodide, and 2-bromoethanol, as described previously.[48] The product was converted to the bromide by a modification of the method of Ames and Bowman[49] (bp 45–46 °C/25 Torr, yield 68%). 2-Isopropoxyethanol (Aldrich) was brominated by the same procedure (bp 49–51 °C/40 Torr, yield 74%). $[1,2\text{-}^2H_4]$-2-Bromoethanol (99 atom % ^2H) and $[1,2\text{-}^{13}C_2]$-2-bromoethanol (99 atom % ^{13}C) were from Cambridge Isotope Laboratories.

In a typical synthesis of RCbi diastereomers, a solution of Factor B[45] (11.3 mg, 10.3 μmol) in 7 mL of 10% acetic acid was purged with argon for 1.5 h. Zinc wool (337 mg, 5.15 mmol), freshened briefly in 2.0 N HCl, was added and the reduction allowed to proceed for 30 min. The appropriate alkyl bromide (24-fold molar excess) was introduced through an argon-purged syringe, and the alkylation was allowed to proceed for 4 min (2 min for the $HOCH_2CH_2Cbi$'s). After filtration through a Büchner funnel, the reaction mixture was neutralized and excess alkylating agent removed by methylene chloride extraction. The reaction mixture was then desalted by chromatography on Amberlite XAD-2[46] resin, and the diastereomers were separated by semipreparative HPLC. Total, worked-up RCbi yields varied from 64% to 78% with a α-diastereomer comprising 38–56% of the total. Diastereomeric RCbl's were synthesized similarly, except that $H_2OCbl{\cdot}Ac$ replaced Factor B and 2% phosphoric acid replaced 10% acetic acid in order to increase the proportion of α-diastereomer.[50] The diastereomeric RCbl's were conveniently separated by flash chromatography on Amberlite XAD-2 resin using an increasing gradient of acetonitrile in water. Total yields of RCbl's varied from 57% to 88%, with the α-diastereomer comprising 13–36% of the total.

Methods. All manipulations with photosensitive alkylcobalt corrinoids were carried out in the dark with the aid of flashlights. UV–visible spectra were recorded on a Cary 219 spectrophotometer. RCba's were quantitated by conversion to their dicyano derivatives ($\epsilon_{368} = 3.04 \times 10^4\ M^{-1}\ cm^{-1}$)[51,52] by aerobic photolysis in excess cyanide. Values for the apparent pK_a for the base-on/base-off reaction[53] of the β-RCbl's were determined by spectrophotometric titration at 25.0 ± 0.1 °C, ionic strength 1.0 M (KCl), as described previously.[46]

Anaerobic pyrolysis of the solid β-RCbl's was performed in ReactiVials (Pierce) closed with Teflon Mininert valves (Pierce) at 225 °C, as described previously,[46] and the products were identified by GC/MS on a Finnigan 4500 GC/MS instrument equipped with a 6 m by 2 mm ID Carbopak B/1% SP1000 column. The organic products of the acid-induced decomposition of the β-RCbl's were determined using the same GC/MS system. Reaction mixtures (0.5 mL) containing β-RCbl in 1.0 M HCl were incubated at 25.0 ± 0.1 °C in ReactiVials closed with Mininert valves for 6 half-times, and the gas phase was sampled with a gastight syringe. Alcohol products were identified by GC/MS after neutralization of the reaction mixtures. FAB-MS was performed on a Kratos MS80RFA mass spectrometer with an Ion Tech FAB 11NF FAB source using 5–6 kV argon bombardment and a *m*-nitrobenzyl alcohol matrix[54,55] (10 μg/μL).

Analytical HPLC was performed with a 4.6 × 75 mm Beckman C_{18} or 4.6 × 250 mm C_8 Ultrasphere column using a 25 mM aqueous ammonium phosphate buffer, pH 3.0, and acetonitrile,[56] a 2.0 mL/min flow rate, and the gradient previously described.[39] Semipreparative HPLC was similarly performed on a 10 × 250 mm Beckman C_8 Ultrasphere column with a flow rate of 6.0 mL/min and the same solvents. The gradient was adjusted to maximize the desired separation.

Rate constants for the acid-induced decomposition of the (alkoxyethyl)cobalt corrinoids were determined spectrophotometrically on a Cary 219 spectrophotometer, the sample compartment of which was thermostated at 25.0 ± 0.1 °C with a circulating water bath. The increase in absorbance at 350 nm was monitored for all compounds. Samples (3.0 mL in quartz cuvettes) contained 3.1×10^{-5} M RCba and varying concentrations of HCl or 0.1 M buffer (acetate or chloroacetate) plus KCl (ionic strength 1.0 M) or varying concentrations of sulfuric acid in water, as appropriate. The increase in absorbance at 350 nm was monitored to completion (at least 6 half-times), or for reactions which were not complete after 48 h, the end-point absorbance was determined after photolysis with a tungsten lamp. First-order rate constants were determined from the slopes of plots of ln ($A_\infty - A_t$) vs time, where A_∞ is the end-point absorbance and A_t is the absorbance at time *t*, by the method of least squares. For the trifluoroethoxy complexes above pH 1.5, where the half-time for acid-induced decomposition exceeded 30 h, the first-order rate constants were determined by the method of initial rates.[57] The linear increase in absorbance at 350 nm during the first 2% of the reaction was monitored in solutions of 7.5×10^{-5} M complex. The first-order rate constants were calculated from the slopes of plots of absorbance vs time, and the end-point absorbance[57] was determined by photolysis. Rate constants determined in this manner at pH 1.50 were in excellent agreement with those determined at the same pH by following the reaction for 3 half-times and determining the end point by photolysis.

The pH of reaction mixtures was determined after each kinetic run using a Radiometer PHM84 pH meter and a Radiometer type

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C combined electrode. Acidities of sulfuric acid/water reaction mixtures were determined by titration of duplicate aliquots (100–500 μL) with standard KOH to a pH 7.0 end point. All such duplicate titrations values agreed to within 1%. Acidity function values were obtained from literature data, using the Cox and Yates generalized acidity function,[58] interpolating between literature data points when necessary.

Partial acid-induced decomposition experiments were performed as follows. Each of the six β-$ROCH_2CH_2Cbl$'s (ca. 1.5×10^{-4} M) was decomposed in 1.0 M HCl (1.0 mL volume) at 25.0 ± 0.1 °C for 1 half-time. A 1.0-mL volume of 2.0 M aqueous K_2HPO_4 was added to stop the reaction, and the reaction mixture was desalted by chromatography on Amberlite XAD-2 resin. The samples were concentrated and analyzed by HPLC.

^1H, ^{19}F, and ^{13}C NMR spectra were obtained on a GE QE 300 superconducting NMR spectrometer using a 5-mm broad-band probe. Samples contained 3–14 mM RCba in D_2O, and chemical shifts were determined relative to external trimethylsilyl propionate (for ^1H and ^{13}C spectra) of fluorobenzene (for ^{19}F spectra). ^2H and ^{13}C NMR spectra of labeled compounds were obtained on a Bruker AMX 300 superconducting NMR spectrometer using a 10-mm broad-band probe with and without broad-band ^1H decoupling. For ^2H NMR spectroscopy, the sample was in water and chemical shifts were determined relative to external deuteriochloroform (set to 7.24 ppm). ^{13}C spectral edited ^1H NMR spectra[59] were also obtained on a Bruker AMX 300 spectrometer using a 5-mm inverse detection probe and garptemp composite pulse ^{13}C decoupling.

Results and Discussion

Characterization of the (Alkoxyethyl)cobalt Corrinoids: UV–Visible Spectroscopy. All of the alkylcobalt corrinoids synthesized displayed typical UV–visible spectra. Upon aerobic photolysis, the α- and β-$ROCH_2CH_2Cbl$'s were readily converted to H_2OCbl and the α- and β-$ROCH_2CH_2Cbi$'s were readily converted to $(H_2O)_2Cbi$ as determined by their characteristic spectra and by HPLC retention times. Furthermore, the six β-$ROCH_2CH_2Cbl$'s underwent typical spectral changes upon acidification (pH 0.5) characteristic of the base-on to base-off transition due to uncoordination and protonation of the axial nucleotide in acid.[46,53] The most major of these spectral changes is a substantial blue shift of the longest wavelength (or α) band so that the red base-on cobalamins yield yellow base-off species. For the current compounds this blue shift varied from 64 to 68 nm. In addition, each of the six sets of four compounds with the same organic ligand displayed the relationships among their UV–visible spectra previously demonstrated for the organic ligands CH_3, CF_3CH_2, $NCCH_2$, CF_3, CF_2H, and $CH_3CH_2OCH_2CH_2$ (i.e., **1e**–**4e**).[38,39] Thus, the spectrum of the base-off form of each β-$ROCH_2CH_2Cbl$ is identical to that of the analogous β-$ROCH_2CH_2Cbi$, except in the UV region (i.e., $\lambda < 300$ nm) due to the UV absorption of the nucleotide in the former compounds. Similarly, the spectrum of each α-$ROCH_2CH_2Cbl$ is identical to the analogous α-$ROCH_2CH_2Cbi$ above 300 nm. In addition, the α-$ROCH_2CH_2Cbl$'s fail to undergo any visible spectral changes when acidified, displaying only the relatively small UV shifts attributable to protonation of the uncoordinated benzimidazole nucleotide.[46] These observations are consistent with the formulation of these compounds as structure **2**, in which coordination of the axial nucleotide is blocked at all pH's due to the presence of the α-organic ligand.

The spectral difference between each pair of α- and β-$ROCH_2CH_2Cbi$'s is also characteristic of the structural relationship as shown previously for other pairs of α- and β-RCbi's.[38,39] Thus, the only band showing a significant difference in energy between the pairs of diastereomeric α- and β-$ROCH_2CH_2Cbi$'s is the longest wavelength (or α) band, which is red shifted by 20–22 nm in each α-$ROCH_2CH_2Cbi$ relative to its β-diastereomer. For the pairs of alkylcobinamides with other organic ligands previously reported, this red shift varied from 8 to 40 nm. Thus, a red shift of the longest wavelength visible band appears to be diagnostic of the α-diastereomers. However, as would be expected from the similarity of the series of organic ligands, within each analogous series of compounds presently reported (ie., **1a**–**f**, **2a**–**f**, etc.) the UV–visible spectra are extremely similar, with transition energies varying by only a few nanometers across each series and molar absorptivities varying by no more than 10%.

Mass Spectrometry. (Alkoxyethyl)cobalt corrinoids were also characterized by FAB MS using a *m*-nitrobenzyl alcohol matrix.[54,55] As previously reported for β-CF_3CH_2Cbl,[38] the positive ion parent mass of zwitterionic β-RCbl's contains a proton from the matrix and thus occurs at MH^+. This is true for the β-$ROCH_2CH_2Cbl$'s (**1a**–**f**), as reported in Table I. However, the parent ion of α-RCbl's in positive ion mass spectra is pentacoordinate, as previously observed for α-CF_3CH_2Cbl,[38] and thus occurs at $MH^+ - H_2O$. Consequently, α- and β-RCbl's have identical positive ion parent masses as shown in Table I for the series of α- and β-$ROCH_2CH_2Cbl$'s (**1a**–**f**, **2a**–**f**). The positive ion parent of the cationic RCbi's, on the other hand, does not contain a proton from the matrix, as previously observed for α- and β-CF_3CH_2Cbi[38] and for β-AdoCbi.[5] However, these parent ions are also pentacoordinate in positive ion mass spectra and thus occur at $M^+ - H_2O$.[5,38] This phenomenon is seen for all of the diastereomeric $ROCH_2CH_2Cbi$'s, and each pair of diastereomers has an identical FAB mass spectrum (Table I).

The α- and β-$ROCH_2CH_2Cbl$'s (**1a**–**f**, **2a**–**f**) were further characterized by GC/MS determination of the products derived from the organic ligand upon anaerobic pyrolysis of the complexes in the solid state at 225 °C, as such analysis has been shown to be diagnostic of the nature of the organic ligand.[38,46,60] For the $HOCH_2CH_2Cbl$'s (**1a**, **2a**), the only product identified was acetaldehyde. However, the $CH_3CH_2OCH_2CH_2Cbl$'s (**1e**, **2e**) gave four products: diethyl ether, ethyl vinyl ether, ethanol, and ethylene. An analogous set of four products was obtained from the $(CH_3)_2CHOCH_2CH_2Cbl$'s (**1c**, **2c**). In addition to the analgous four products for R = CF_3CH_2, pyrolysis of the $CF_3CH_2OCH_2CH_2Cbl$'s (**1f**, **2f**) also yielded an uncharacterized isomer of difluoroethylene. For both the $CH_3OCH_2CH_2Cbl$'s (**1d**, **2d**) and the $C_6H_5OCH_2CH_2Cbl$'s (**1b**, **2b**) one of the four anticipated products was missing: methanol was not observed in the former case and no phenyl ethyl ether was detected in the latter case.

NMR Spectroscopy. Because the ^1H NMR spectra of cobalt corrinoids contain many overlapping resonances,[61–68]

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Table I. NMR and FAB MS Characteristics of the (Alkoxyethyl)cobamides[a]

R	Cba	$\delta(^{13}C)$			m/e(calc)[b]
		C_α	C_β	R	
H	β-Cbl[c]	26.41[d]	65.06[e]		1375.0 (1375.4)[f]
	α-Cbl[g]	17.89[h]	64.09[i]		1375.2 (1375.4)[j]
	β-Cbi[k]	20.10[l]	64.00[m]		1034.4 (1035.2)[n]
	α-Cbi[o]	17.59[p]	64.21[q]		1035.0 (1035.2)[r]
C_6H_5	β-Cbl[s]	22.61	72.85	118.37 (m), 124.46 (p), 132.40 (o), 159.76	1450.2 (1451.5)
	α-Cbl[t]	13.25	70.95	117.05 (m), 124.08 (p), 132.40 (o), 159.73	1452.5 (1451.5)
	β-Cbi[u]	17.27	71.68	117.49 (m), 124.18 (p), 132.41 (o), 159.67	1110.9 (1111.3)
	α-Cbi[v]	13.19	71.60	117.82 (m), 124.31 (p), 132.29 (o), 159.53	1111.3 (1111.3)
$(CH_3)_2CH$	β-Cbl[w]	x	71.03	23.60, 23.79, 74.55	1417.2 (1417.5)
	α-Cbl[y]	14.21	70.10	23.83, 23.89, 74.65	1417.0 (1417.5)
	β-Cbi[z]	15.78	69.42	23.50, 23.63, 74.68	1077.8 (1077.3)
	α-Cbi[aa]	13.92	70.13	23.75, 23.83, 74.68	1077.2 (1077.3)
CH_3	β-Cbl[bb]	21.95	76.04	59.41	1388.4 (1389.5)
	α-Cbl[cc]	14.08	74.96	59.35	1389.5 (1389.5)
	β-Cbi[dd]	15.50	74.64	59.48	1048.9 (1049.2)
	α-Cbi[ee]	13.27	75.01	59.36	1049.1 (1049.2)
CH_3CH_2	β-Cbl[ff]	22.32	73.71	16.64, 68.26	1403.0 (1403.5)
	α-Cbl[gg]	13.87	72.64	16.80, 68.19	1404.3 (1403.5)
	β-Cbi[hh]	15.80	72.20	16.61, 68.26	1062.7 (1063.3)
	α-Cbi[ii]	13.39	72.68	16.69, 68.20	1063.0 (1063.3)
CF_3CH_2	β-Cbl[jj]	22.86	76.45	69.00,[kk] 126.40[ll]	1456.2 (1457.5)
	α-Cbl[mm]	12.38	75.31	69.13,[nn] 126.47[oo]	1456.9 (1457.5)
	β-Cbi[pp]	14.84	74.92	69.11,[qq] 126.10[rr]	1117.1 (1117.2)
	α-Cbi[ss]	12.04	75.34	69.00,[tt] 126.41[uu]	1117.5 (1117.2)

[a] ^{13}C and ^1H chemical shifts reported downfield from trimethylsilyl propionate. ^{19}F chemical shifts reported downfield from C_6H_5F. [b] Parent ion masses calculated as MH^+ for β-$ROCH_2CH_2Cbl$'s, $MH^+ - H_2O$ for α-$ROCH_2CH_2Cbl$'s, and $M^+ - H_2O$ for α- and β-$ROCH_2CH_2Cbi$'s; see text. [c] ^2H and ^{13}C-edited ^1H NMR: 0.56, 1.31 (^2H $\Delta\nu_{1/2} = 20$ Hz), 1.94, and 2.50 ppm (^2H $\Delta\nu_{1/2} = 15$ Hz). [d] $\Delta\nu_{1/2} = 15$ Hz, $^1J_{CC} = 35.1$ Hz, $^1J_{HC} = 143.6$ Hz. [e] $\Delta\nu_{1/2} = 4.6$ Hz, $^1J_{CC} = 35.6$ Hz, $^1J_{HC} = 139.1$ Hz. [f] $m/e = 1379.0$ (calc m/e 1379.5) for [1,2-$^2H_4$]-β-$HOCH_2CH_2Cbl$ and 1378.9 (calc m/e 1377.5) for [1,2-$^{13}C_2$]-β-$HOCH_2CH_2Cbl$. [g] ^{13}C-edited ^1H NMR: 0.23, 1.27, 1.55, 2.07 ppm. [h] $\Delta\nu_{1/2} = 6.7$ Hz, $^1J_{CC} = 37.6$ Hz, $^1J_{HC} = 141.1$ Hz. [i] $\Delta\nu_{1/2} = 3.2$ Hz, $^1J_{CC} = 37.3$ Hz, $^1J_{HC} = 143.9$ Hz. [j] $m/e = 1376.4$ (calc m/e 1377.4) for [1,2-$^{13}C_2$]-α-$HOCH_2CH_2Cbl$. [k] ^{13}C-edited ^1H NMR: 0.0, 1.10, 1.27, 1.37 ppm. [l] $\Delta\nu_{1/2} = 5.4$ Hz, $^1J_{CC} = 36.8$ Hz, $^1J_{HC} = 143.2$ Hz. [m] $\Delta\nu_{1/2} = 3.0$ Hz, $^1J_{CC} = 36.7$ Hz, $^1J_{HC} = 145.2$ Hz. [n] $m/e = 1036.6$ (calc m/e 1037.2) for [1,2-$^{13}C_2$]-β-$HOCH_2CH_2Cbi$. [o] ^{13}C-edited ^1H NMR: 0.21, 1.33, 1.62, 2.20 ppm. [p] $\Delta\nu_{1/2} = 8.1$ Hz, $^1J_{CC} = 36.5$ Hz, $^1J_{HC} = 142.1$ Hz. [q] $\Delta\nu_{1/2} = 4.1$ Hz, $^1J_{CC} = 36.9$ Hz, $^1J_{HC} = 143.9$ Hz. [r] $m/e = 1037.2$ (calc m/e 1037.2) for [1,2-$^{13}C_2$]-α-$HOCH_2CH_2Cbi$. [s] ^1H NMR: C_6H_5O, 6.55, 6.91, 7.19 ppm; α-CH_2 (upfield member), 0.41 ppm. [t] ^1H NMR: C_6H_5O, 6.36, 6.90, 7.15 ppm; α-CH_2 (upfield member), 0.39 ppm. [u] ^1H NMR: C_6H_5O, 6.48, 6.88, 7.17 ppm; α-CH_2 (upfield member), 0.21 ppm. [v] ^1H NMR: C_6H_5O, 6.45, 6.88, 7.15 ppm; α-CH_2 (upfield member), 0.42 ppm. [w] ^1H NMR: $(CH_3)_2C$, 0.83 (d, $J = 6.1$ Hz), 0.87 (d, $J = 6.1$ Hz); α-CH_2 (upfield member), 0.53 ppm. [x] Not observed. [y] ^1H NMR: $(CH_3)_2C$, 0.77 (d, $J = 6.3$ Hz), 0.79 (d, $J = 6.0$ Hz); α-CH_2 (upfield member), 0.35 ppm. [z] ^1H NMR: $(CH_3)_2C$, 0.78 (d, $J = 4.8$ Hz), 0.80 (d, $J = 4.5$ Hz); α-CH_2 (upfield member), −0.03 ppm. [aa] ^1H NMR: $(CH_3)_2C$, 0.74 (d, $J = 6.1$ Hz), 0.78 (d, $J = 6.2$ Hz); α-CH_2 (upfield member), 0.26 ppm. [bb] ^1H NMR: CH_3O, 2.98 ppm; α-CH_2 (upfield member), 0.55 ppm. [cc] ^1H NMR: CH_3O, 2.82 ppm; α-CH_2 (upfield member), 0.38 ppm. [dd] ^1H NMR: CH_3O, 2.86 ppm; α-CH_2 (upfield member), 0.19 ppm. [ee] ^1H NMR: CH_3O, 2.88 ppm; α-CH_2 (upfield member), 0.24 ppm. [ff] ^1H NMR: CH_3, 0.89 ppm (t, $J = 7.0$ Hz); α-CH_2 (upfield member), 0.55 ppm. [gg] ^1H NMR: CH_3, 0.82 ppm (t, $J = 6.9$ Hz); CH_2O, 3.04 ppm (q, $J = 6.6$ Hz); α-CH_2 (upfield member), 0.31 ppm. [hh] ^1H NMR: CH_3, 0.82 ppm (t, $J = 7.1$ Hz); α-CH_2 (upfield member), 0.00 ppm. [ii] ^1H NMR: CH_3, 0.83 ppm (t, $J = 7.1$ Hz); CH_2O, 3.08 ppm (q, $J = 7.0$ Hz); α-CH_2 (upfield member) 0.25 ppm. [jj] ^{19}F NMR: CF_3, 39.49 ppm (t, $^3J_{HF} = 9.1$ Hz). ^1H NMR: α-CH_2 (upfield member), 0.59 ppm. [kk] q, $^2J_{FC} = 33.0$ Hz. [ll] q, $^1J_{FC} = 279.0$ Hz. [mm] ^{19}F NMR: CF_3, 39.59 ppm (s, $\Delta\nu_{1/2} = 44$ Hz). ^1H NMR: α-CH_2 (upfield member), 0.35 ppm. [nn] q, $^2J_{FC} = 33.0$ Hz. [oo] q, $^1J_{FC} = 278.3$ Hz. [pp] ^{19}F NMR: CF_3, 39.29 ppm (t, $^3J_{HF} = 9.0$ Hz). ^1H NMR: α-CH_2 (upfield member), 0.00 ppm. [qq] q, $^2J_{FC} = 35.3$ Hz. [rr] q, $^1J_{FC} = 276.0$ Hz. [ss] ^{19}F NMR: CF_3, 39.40 ppm (t, $^3J_{HF} = 9.1$ Hz). ^1H NMR: α-CH_2 (upfield member), 0.19 ppm. [tt] q, $^2J_{FC} = 33.0$ Hz. [uu] q, $^1J_{FC} = 278.3$ Hz.

it is difficult to characterize the organic ligands of the current series of compounds by ^1H NMR spectroscopy. However, the availability of deuterated 2-bromoethanol allowed the observation of the ^2H NMR spectrum of [1,2-$^2H_4$]-β-$HOCH_2CH_2Cbl$. The spectrum (Figure 2A) consists of four broad lines at 0.56, 1.31, 1.94, and 2.50 ppm.

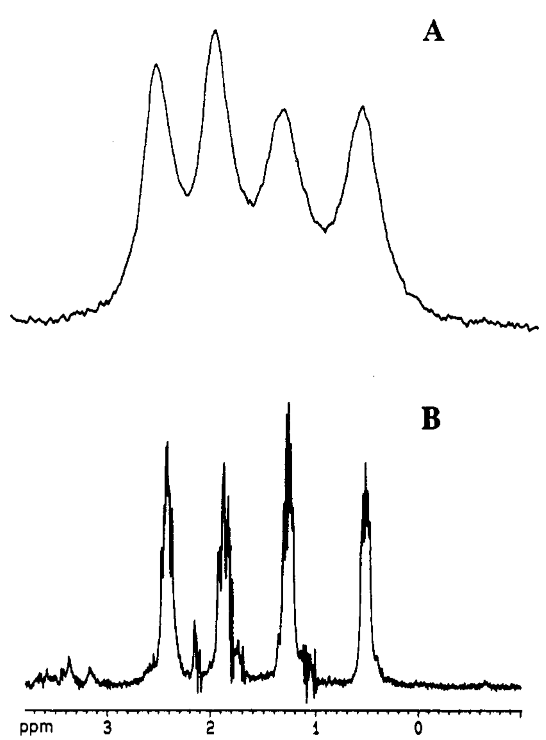

Figure 2. (A) ^2H NMR spectrum of β-[1,2-$^2H_4$]-$HOCH_2CH_2Cbl$, 2.2 mM in water (7500 transients). (B) ^{13}C-edited ^1H NMR spectrum of β-[1,2-$^{13}C_2$]-$HOCH_2CH_2Cbl$, 15 mM in D_2O.

The broader ($\Delta\nu_{1/2} = 20$ Hz), more upfield pair of lines may be assigned to the diastereotopic α-deuterons of the $HOC^2H_2C^2H_2$ ligand on the basis of chemical shift and the expectation that the α-deuterons should be broadened by quadrupolar relaxation by the cobalt nucleus ($I = {}^7/_2$) more than the β-deuterons.[69–73] The remaining pair of signals ($\Delta\nu_{1/2} = 15$ Hz) must then be assigned to the β-deuterons. Although these deuterons are not diastereotopic, they are clearly inequivalent, suggesting that the diastereotopic α-deuterons induce magnetic inequivalence in the β-deuterons, a phenomenon for which there is ample precedent in the ^1H NMR spectra of cobalt corrinoids.[63–68] As expected[74] due to the small magnetogyric ratio of the ^2H nucleus and the broadness of the resonances, the anticipated couplings among the α- and β-deuterons are not resolved. However, preparation of [1,2-$^{13}C_2$]-β-$HOCH_2CH_2Cbl$ by reductive alkylation of H_2OCbl with [1,2-$^{13}C_2$]-2-bromoethanol permitted direct observation of the α- and β-methylene protons via ^{13}C spectral edited ^1H NMR spectroscopy,[59] which allows selective observation of the protons attached to ^{13}C nuclei (Figure 2B). In this high-resolution spectrum, most of the anticipated couplings (i.e., doublets of doublets of doublets) have been resolved for all four proton resonances. Similar observations (not shown) of the α- and β-protons of the other three [1,2-$^{13}C_2$]-(hydroxyethyl)cobalt corrinoids were also made (Table I). Comparison of the ^1H spectra of β-$HOCH_2CH_2Cbl$ to that of the deuterated and ^{13}C-enriched derivatives allowed observation of the α-methylene proton resonances in the natural-abundance spectrum, but the

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β-methylene resonances are in the more crowded, downfield region and could not be observed. However, the upfield member of the diastereotopic α-methylene proton resonances occurs alone in the high-field region of the ^{1}H spectrum of all of the ROCH$_2$CH$_2$Cba's and could be readily identified (Table I). This multiplet occurred between 0.41 and 0.59 ppm for the six β-ROCHCH$_2$CH$_2$Cbl's (**1a–f**), between 0.30 and 0.39 ppm for the α-ROCH$_2$CH$_2$Cbl's (**2a–f**), between −0.03 and 0.21 ppm for the β-ROCH$_2$CH$_2$Cbi's (**3a–f**), and between 0.19 and 0.42 ppm for the α-ROCH$_2$CH$_2$Cbi's (**4a–f**).

Comparison of the ^{1}H spectra of each (hydroxyethyl)cobalt corrinoid with the analogous (alkoxyethyl)cobalt corrinoid permitted assignment of some of the ^{1}H resonances of the alkoxy groups. Within each series of compounds with the same organic ligand, the alkoxy ^{1}H resonances, when assignable, were much less sensitive to structure than the α-methylene resonances. For instance, the ethoxy methyl resonance was cleanly resolved in all four CH$_3$CH$_2$OCH$_2$CH$_2$Cba's and appeared as a triplet at 0.89 ppm (J = 7.1 Hz), 0.82 ppm (J = 6.9 Hz), 0.82 ppm (J = 7.1 Hz), and 0.83 ppm (J = 7.1 Hz) in the β-Cbl, α-Cbl, β-Cbi, and α-Cbi derivatives, respectively. The ethoxy methylene resonance could only be resolved in the spectra of the α-Cbl and α-Cbi and appeared as a quartet near 3.06 ppm (J = 7.0 Hz). In the isopropoxyethyl complexes (**1c–4c**), the isopropoxy methyl resonances appeared as a pair of doublets between 0.74 and 0.87 ppm (Table I) with coupling constants of about 6 Hz indicating that these methyl groups are inequivalent in these complexes. The isopropoxy methine resonance could not be assigned in any compound. Other assignable alkoxy proton resonances are given in Table I. In the ^{19}F NMR spectra of the (trifluoroethoxy)ethyl complexes (**1f–4f**) a fluorine triplet ($J \sim 9$ Hz) was evident near 39.5 ppm (downfield from C$_6$H$_5$F) in each compound except for α-CF$_3$CH$_2$OCH$_2$CH$_2$Cbl (**2f**) in which the fluorine resonance was a broad ($\Delta\nu_{1/2}$ = 44 Hz) singlet at 39.6 ppm, possibly reflecting interaction of the alkoxy group with the pendent benzimidazole nucleotide.

The ^{13}C-enriched (hydroxyethyl)cobalt corrinoids were also used to locate the ^{13}C resonances of the organic ligand. For [1,2-^{13}C$_2$]-β-HOCH$_2$CH$_2$Cbl, the ^{1}H-decoupled ^{13}C spectrum (Figure 3A) consisted of two doublets with a carbon–carbon coupling constant of about 35 Hz. In the ^{1}H-coupled spectrum (Figure 3B) each resonance was a triplet of doublets with proton–carbon coupling constants of about 140 Hz. Again, the more upfield, broader ($\Delta\nu_{1/2}$ = 15 Hz) signal is assignable to the α-carbon, and the narrower ($\Delta\nu_{1/2}$ = 5 Hz), downfield signal, to the β-carbon. The latter resonance (at 65.22 ppm) was readily located in the natural-abundance ^{13}C spectrum of unlabeled β-HOCH$_2$CH$_2$Cbl, and the anticipated quintet (unenhanced by the nuclear Overhauser effect) was unobservable in the ^{13}C spectrum of [1,2-^{2}H$_4$]-β-HOCH$_2$CH$_2$Cbl. However, the α-carbon resonances of organocobalt complexes are notoriously difficult to observe in natural-abundance ^{13}C spectra[70,75] due to their broadness. This problem was circumvented by observing natural-abundance ^{13}C spectra using a 90° observe pulse and shortening the repetition time to 500 ms, permitting the accumulation of ca. 100 000 transients in an overnight run. Although this method reduced the intensity of the signals of the unprotonated carbons, the broad α-carbon resonance of β-HOCH$_2$CH$_2$Cbl was readily located at 26.50 ppm. Again, the anticipated, unenhanced quintet was unobservable in the spectrum of [1,2-^{2}H$_4$]-β-HOCH$_2$CH$_2$Cbl. The results of similar observations of the other three (hydroxyethyl)cobalt corrinoids and their ^{13}C-enriched analogues are given in Table I. As previously observed for [^{13}C]-cyanocobalt corrinoids,[72] and for [^{13}C]-(methyl-, [1-^{13}C$_1$]-(ethyl-, and [1-^{13}C$_1$]-(carboxymethyl)cobalt corrinoids,[73] the ^{13}C linewidth of the α-carbon of β-HOCH$_2$CH$_2$Cbi is substantially smaller (5.4 Hz) than that of β-HOCH$_2$CH$_2$Cbl (15.0 Hz). As the broadening of the α-^{13}C resonances of alkylcobalt complexes is generally attributed to quadrupolar relaxation by the cobalt nucleus,[69–73] this implies that the α-carbon is more strongly coupled to the cobalt nucleus in the base-on β-Cbl's (i.e. trans to 5,6-dimethylbenzimidazole) than in the β-Cbi's (i.e., trans to water).

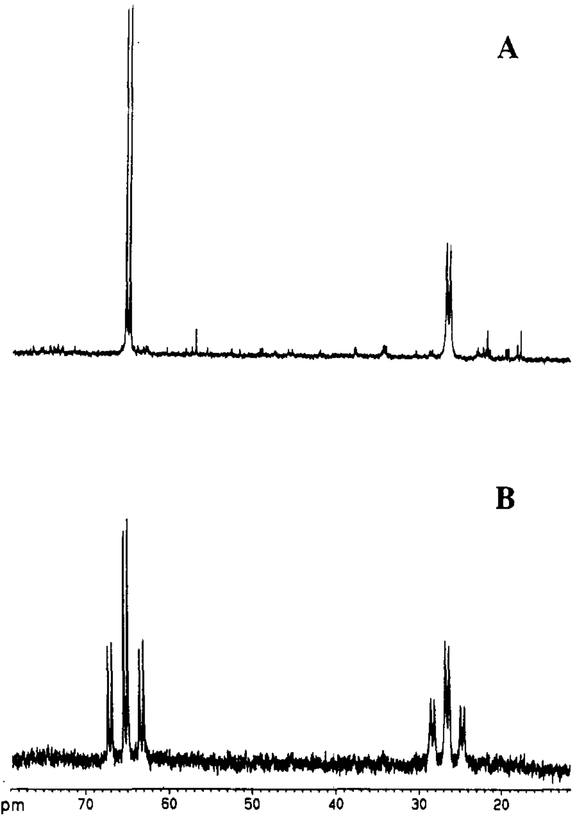

Figure 3. (A) ^{1}H-decoupled ^{13}C NMR spectrum of β-[1,2-^{13}C$_2$]-HOCH$_2$CH$_2$Cbl, 15 mM in D$_2$O (2048 transients). (B) ^{1}H-coupled ^{13}C NMR spectrum of the sample described in (A) (4096 transients).

By comparison of the natural-abundance ^{13}C spectrum of β-HOCH$_2$CH$_2$Cbl to the completely assigned spectra of β-AdoCbl[63] and of (β-adeninylpropyl)Cbl[67] the ^{13}C spectrum of β-HOCH$_2$CH$_2$Cbl could be nearly completely, if tentatively, assigned. While a number of ambiguities occur in the crowded regions (i.e., the methylene and carbonyl regions), such assignments of the corrin ring resonances are quite secure. In addition, these tentative assignments were in every case in agreement with the proton multiplicity of each carbon as revealed by ^{13}C distortionless enhancement by polarization transfer (DEPT)[76] spectra observed with $\pi/2$ and $3\pi/4$ proton read pulses. In a similar fashion, the natural-abundance spectra of β-HOCH$_2$CH$_2$Cbi (**3a**) could be tentatively assigned by comparison with those of base-off β-AdoCbl[64] and β-AdoCbi,[65] and those of α-HOCH$_2$CH$_2$Cbl (**2a**) and α-HOCH$_2$CH$_2$Cbi (**4a**) could be tentatively assigned by comparison with the recently assigned ^{13}C spectra of

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(75) Bied-Charreton, C.; Septe, B.; Gaudemer, A. *Org. Magn. Reson.* **1975**, *7*, 116.

(76) Page, D. T.; Doddrell, D. M.; Bendell, M. R. *J. Chem. Phys.* **1982**, *77*, 2745.

$(CN)_2Cbl$ and $(CN)_2Cbi$.[68] Armed with these assignments, the natural-abundance ^{13}C spectra of all of the other (alkoxyethyl)cobalt corrinoids could be tentatively assigned, and the C_a, C_β, and alkoxy ^{13}C resonances could be definitely assigned (Table I).

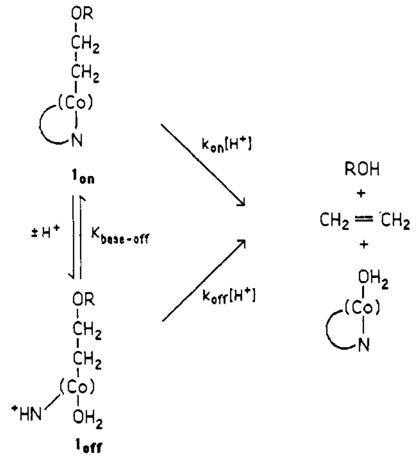
The C_α resonance was positively identified (for every compound except β-$(CH_3)_2CHOCH_2CH_2Cbl$ (**1c**), where it is presumably obscured by another resonance) as a broad, upfield resonance occurring between 21.9 and 22.9 for the β-$ROCH_2CH_2Cbl$'s (**1b** and **1d–f**), between 12.0 and 14.2 ppm for the α-$ROCH_2CH_2Cbl$'s (**2b–f**) and α-$ROCH_2CH_2Cbi$'s (**4b–f**), and between 14.8 and 17.8 ppm for the β-$ROCH_2CH_2Cbi$'s (**3b–f**). For each organic ligand, comparison of the C_a chemical shift of the β-$ROCH_2CH_2Cbl$ with that of the β-$ROCH_2CH_2Cbi$ shows the effect of substitution of the axial nucleotide ligand by water to be an upfield shift of the resonance by 5.3–8.0 ppm. This effect falls well within the range previously observed for other such pairs of Cbl's and Cbi's (2.6 ppm for β-CH_2CH_2Cbl and Cbi, 7.8 for β-CH_3Cbl and Cbi, 10.0 for β-$^-OOCCH_2Cbl$ and Cbi, and 12.4 for β-$HOOCCH_2Cbl$ and Cbi).[73] The β-carbon resonances were observed between 69.4 and 76.5 ppm and were much more sensitive to the nature of the alkoxy group than the α-carbon resonances. For a given organic ligand, however, the β-carbon resonances were much less sensitive to structure, the chemical shifts always falling within a 2.0 ppm range for any series of four compounds. As expected, the effect of substitution of the axial benzimidazole nucleotide by water on the chemical shift of the β-carbons is much smaller (1.2–1.6 ppm) than the effect on the α-carbon chemical shift.

Comparison of the ^{13}C resonances of both the α- and β-carbons between the α-$ROCH_2CH_2Cbl$'s and α-$ROCH_2CH_2Cbi$'s shows them to be very similar, as previously observed for α-CH_3Cbl and α-CH_3Cbi.[39] Comparison of the β-$ROCH_2CH_2Cbi$'s (**3a–f**) and the α-$ROCH_2CH_2Cbi$'s (**4a–f**) shows that, for a given organic ligand, the α-carbon resonance is 1.9–4.1 ppm upfield in the α-diastereomer relative to the β-diastereomer. This is surprising since the diastereomeric CH_3Cbi's showed the opposite effect, the ^{13}C resonance of the methyl carbon of the α-diastereomer being 1.5 ppm downfield from that of the β-diastereomer.[39,77]

The alkoxide ^{13}C resonances could always be assigned by comparison of the spectrum of a given (alkoxyethyl)cobalt corrinoid with that of the analogous (hydroxyethyl)cobalt corrinoid. Thus, two extra resonances (23.60 and 23.79 ppm) in the methyl region of the spectrum of β-$(CH_3)_2CHOCH_2CH_2Cbl$ could be assigned to the isopropoxy methyls, confirming their inequivalence as detected by ^1H NMR spectroscopy. The isopropoxy methine resonance was readily identified as an extra peak at 74.55 ppm. All of the alkoxy ^{13}C resonances could be similarly assigned, and these assignments are listed in Table I. For the ((trifluoroethoxy)ethyl))cobalt corrinoids (**1f–4f**) both the CF_3 resonance ($^1J_{FC} \sim 278$ Hz) and the trifluoroethoxy methylene resonance ($^2J_{FC} \sim 33$ Hz) were quartets due to fluorine–carbon coupling.

Within each analogous set of compounds, the ^{13}C spectra are extremely similar for the β-$ROCH_2CH_2Cbl$'s (**1a–f**), the β-$ROCH_2CH_2Cbi$'s (**3a–f**), and the α-$ROCH_2CH_2Cbi$'s (**4a–f**). For most of the corrin ring, methyl, and methylene carbons each resonance falls within a narrow window (<0.1 ppm) across the series of six compounds, and this relationship holds for the ribose and 5,6-dimethylbenzimidazole resonances in **1a–f** as well. However, the α-$ROCH_2CH_2Cbl$ (**2a–f**) series is less regular with occasional differences as large as 0.5 ppm across the series. In addition, the 5,6-dimethylbenzimidazole resonances in this series show significant differences from those of the free nucleotide, suggesting that the uncoordinated, pendent nucleotide interacts with the remainder of the structure as is the case with $(CN)_2Cbl$.[68,73,79] The details of these differences and their significance will be reported elsewhere.

Scheme II



Acid-Induced Decomposition of the (Alkoxyethyl)cobalt Corrinoids: (β-Alkoxyethyl)cobalt Corrinoids. In addition to the anticipated spectral changes due to the base-on to base-off transition, acidification of the β-$ROCH_2CH_2Cbl$'s (**1a–f**) also caused much slower, irreversible spectral changes which were isosbestic and strictly first order at a given pH. For instance, for β-$CH_3CH_2OCH_2CH_2Cbl$ (**1e**) at pH 0.56 (i.e., the base-off form) these spectral changes were isosbestic at 487, 370, 336, and 255 nm. The final spectrum was identical to that of H_2OCbl.[80] First-order rate constants, k_{obs}, for these decomposition reactions were obtained from the slopes of semilogarithmic plots of the increase in absorbance at 350 nm, and these plots were linear over 4 half-times. These observation are in contrast to those previously obtained with the analogous cobaloximes.[11,12] For these complexes, only $HOCH_2CH_2Co(D_2H_2)OH_2$ decomposed with strictly first-order kinetics. The $ROCH_2CH_2Co(D_2H_2)OH_2$'s (R = CH_3CH_2 and C_6H_5) showed a distinct lag attributed to the approach to a steady state due to accumulation of $HOCH_2CH_2Co(D_2H_2)OH_2$ via an ethylcobaloxime carbonium ion intermediate (Scheme I).

The cobamide product of the acid-induced decomposition of the β-$ROCH_2CH_2Cbl$'s was in all cases H_2OCbl as determined from its UV–visible spectrum and its HPLC retention time. The organic products were determined to be ethylene and the leaving group alcohol, ROH, by GC/MS measurements. In the case of $[1,2\text{-}^2H_4]$-β-$HOCH_2CH_2Cbl$, $^2H_4$-ethylene ($m/e = 32$) was the product while $[1,2\text{-}^{13}C_2]$-β-$HOCH_2CH_2Cbl$ produced $^{13}C_2$-ethylene ($m/e = 30$).

The pH dependence of k_{obs} is shown in Figure 4 for representative β-$ROCH_2CH_2Cbl$'s. These pH–rate profiles are characterized by two limbs of first-order dependence

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(77) In the ^{19}F NMR spectra of the diastereomeric CF_3CH_2Cbi's and CF_3Cbi's, the α-diastereomer also has the more downfield resonance, but in the CF_3HCbi's, the ^{19}F resonances are upfield in the α-diastereomer.

(78) Brown, K. L.; Hakimi, J. M. *J. Am. Chem. Soc.* **1986**, *108*, 496.

(79) Brown, K. L. *J. Am. Chem. Soc.* **1987**, *109*, 2277.

(80) Brown, K. L.; Marques, H. M.; Jacobsen, D. W. *J. Biol. Chem.* **1988**, *263*, 1872.

Table II. Rate and Equilibrium Constants for the Acid-Induced Decomposition of the (β-Alkoxyethyl)cobalamins and Cobinamides[a]

R	H	C_6H_5	$(CH_3)_2CH$	CH_3	CH_3CH_2	CF_3CH_2
			β-Cbl			
$pK_{base\text{-}off}$[b]	3.43 ± 0.01	3.53 ± 0.01	3.23 ± 0.01	3.25 ± 0.01	3.23 ± 0.01	3.17 ± 0.01
10^2k_{on},[c] $M^{-1}\ s^{-1}$	20.9 ± 0.1[d]	7.42 ± 0.1	3.70 ± 0.02	3.08 ± 0.03	2.33 ± 0.05	0.515 ± 0.005
10^4k_{off},[c] $M^{-1}\ s^{-1}$	28.5 ± 0.5[d]	7.50 ± 0.17	7.87 ± 0.08	6.08 ± 0.10	5.40 ± 0.03	0.917 ± 0.005
k_{on}/k_{off}	73.3	98.9	47.0	50.7	43.1	56.2
			β-Cbi			
10^4k_2,[e] $M^{-1}\ s^{-1}$	44.3 ± 0.6[d]	11.6 ± 0.2	9.77 ± 0.21	8.37 ± 0.22	7.59 ± 0.16	1.23 ± 0.08
$k_2^{\beta\text{-Cbi}}/k_{off}^{\beta\text{-Cbl}}$	1.55	1.55	1.24	1.38	1.41	1.34

[a] 25.0 ± 0.1 °C, ionic strength 1.0 M (KCl). [b] Equation 2. [c] Scheme II, determined from the slopes and intercepts of plots of eq 3. [d] Dunne[44] reported $k_{on} = 10.8\ M^{-1}\ s^{-1}$, $k_{off} = 48.3\ M^{-1}\ s^{-1}$, and $k_2 = 46.7\ M^{-1}\ s^{-1}$ at 32 °C and varying, but low, ionic strength. [e] Equation 6.

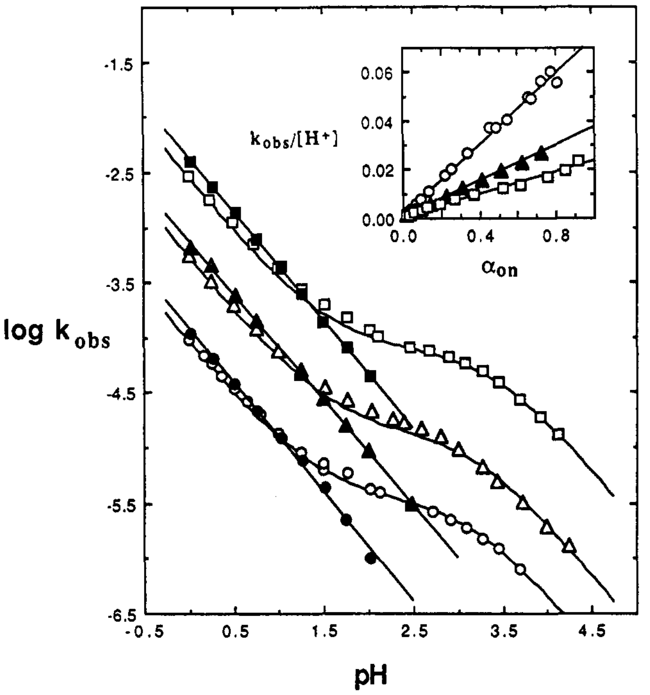

Figure 4. Dependence of the first-order rate constants, k_{obs}, on pH for the acid-induced decomposition of representative β-$ROCH_2CH_2Cbl$'s (open symbols) and β-$ROCH_2CH_2Cbi$'s (solid symbols), 25.0 ± 0.1 °C, ionic strength 1.0 M (KCl): (□, ■) R = H (**1a** and **3a**); (△, ▲) R = CH_3CH_2 (**1e** and **3e**); (○, ●) R = CF_3CH_2 (**1f** and **3f**). The solid lines were calculated from eq 1 (for the β-$ROCH_2CH_2Cbl$'s) or eq 7 (for the β-$ROCH_2CH_2Cbi$'s) and the rate and equilibrium constants in Table II. Inset: Representative plots of $k_{obs}/[H^+]$ vs α_{on} (eq 3) for the β-$ROCH_2CH_2Cbl$'s. Key: (○) R = C_6H_5 (**1b**); (▲) R = $(CH_3)_2CH$ (**1c**); (□) R = CH_3CH_2 (**1e**). Many points at low values of α_{on} are omitted for clarity. The solid lines are calculated from eq 3 using the rate and equilibrium constants in Table II.

on $[H^+]$ connected by a region of less than first-order behavior, as previously observed by Dunne[44] for β-$HOCH_2CH_2Cbl$. The simplest scheme which accounts for this behavior is shown in Scheme II, in which the base-on (1_{on}) and base-off (1_{off}) species undergo acid-induced decomposition with second-order rate constants k_{on} and k_{off}. Application of the law of mass action leads to the rate law of eq 1, where $K_{base\text{-}off}$ is defined in eq 2. The values of

$$k_{obs} = (K_{base\text{-}off}k_{on}[H^+] + k_{off}[H^+]^2)/(K_{base\text{-}off} + [H^+]) \tag{1}$$

$$K_{base\text{-}off} = [1_{on}][H^+]/[1_{off}] \tag{2}$$

$pK_{base\text{-}off}$ could be independently determined spectrophotometrically,[46] since the acid-induced decomposition of the β-$ROCH_2CH_2Cbl$'s was sufficiently slow to permit observation of the acid end points (at pH 1.0) before significant decomposition had occurred.[81] These values of $pK_{base\text{-}off}$ are collected in Table II and can be seen to vary over a narrow range (0.26 units across the series **1a–f**). Using these values, the second-order rate constants k_{on} and k_{off} (Scheme II) were determined from the slopes and intercepts of plots of eq 3, derived by rearranging eq 1, where

$$k_{obs}/[H^+] = (k_{on} + k_{off})\alpha_{on} + k_{off} \tag{3}$$

α_{on}, the fraction of β-$ROCH_2CH_2Cbl$ as the base-on species, is defined in eqs 4 and 5. Representative plots of eq 3 are shown in the inset to Figure 4. The second-order rate constants thus obtained are collected in Table II.

$$\alpha_{on} = [1_{on}]/([1_{on}] + [1_{off}]) \tag{4}$$

$$\alpha_{on} = K_{base\text{-}off}/(K_{base\text{-}off} + [H^+]) \tag{5}$$

These results show that the base-on species of the β-$ROCH_2CH_2Cbl$'s is 43- to almost 100-fold more reactive than the base-off species, depending on R. In addition, the reactivity is seen to be substantially dependent on the nature of R, the values of k_{on} varying by 40-fold across the series while those of k_{off} vary by 31-fold. The order of reactivity for the base-on species is R = H > C_6H_5 > $(CH_3)_2CH$ > CH_3 > CH_3CH_2 > CF_3CH_2, although the variation for R = $(CH_3)_2CH$, CH_3, and CH_3CH_2 is quite small (1.6-fold). These values of k_{off} follow a similar order except that β-$(CH_3)_2CHOCH_2CH_2Cbl$ (**1c**) is slightly more reactive than β-$C_6H_5OCH_2CH_2Cbl$ (**1b**). These results are again in contrast to those previously obtained for the (alkoxyethyl)cobaloximes where the reactivity of $CH_3CH_2OCH_2CH_2Co(D_2H_2)OH_2$ exceeded that of $C_6H_5OCH_2CH_2Co(D_2H_2)OH_2$ by 2-fold under similar conditions.[11,12] Neither the values of k_{on} nor of k_{off} correlate with the solution[82-84] or gas-phase[85] acidities of the leaving group alcohols or the analogous alkyl ethyl ethers, $ROCH_2CH_3$,[85] the solution basicity of the analogous alkyl methyl ethers, $ROCH_3$,[86] or the inductive substituent constant, σ_I, for R.[87] Both k_{on} and k_{off} do, however, roughly correlate with $pK_{base\text{-}off}$.[88]

The β-$ROCH_2CH_2Cbi$'s also showed first-order, isosbestic spectral changes in acid leading to the spectrum of

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(81) For the most reactive compound, β-$HOCH_2CH_2Cbl$, the half-time for decomposition at pH 1.0 was 32 min.

(82) Takahishi, S.; Cohen, L. A.; Miller, H. K.; Peake, E. G. *J. Org. Chem.* **1971**, *36*, 1205.

(83) Murto, J. *Acta Chem. Scand.* **1964**, *18*, 1403.

(84) Ballinger, P.; Long, F. A. *J. Am. Chem. Soc.* **1959**, *81*, 1050; **1960**, *82*, 795.

(85) Gasteiger, J.; Hutchings, M. G. *J. Am. Chem. Soc.* **1984**, *106*, 6489.

(86) Levitt, L. S.; Levitt, B. W. *Z. Naturforsch.* **1979**, *34B*, 614.

(87) Charton, M. *Prog. Phys. Org. Chem.* **1981**, *13*, 119.

(88) For plots of log k_{on} vs $pK_{base\text{-}off}$, intercept = −18.8 ± 3.1, slope = 5.3 ± 0.9, r^2 = 0.89. For log k_{off} vs $pK_{base\text{-}off}$, intercept = −17.3 ± 4.3, slope = 4.3 ± 1.3, r^2 = 0.73.

diaquocobinamide. First-order rate constants, k_{obs}, for the decomposition of these compounds were obtained as above, from semilogarithmic plots of the increase in absorbance at 350 nm. The dependence of k_{obs} on pH for these complexes was, however, strictly first-order, as shown in Figure 4 for representative compounds. Thus, in the absence of a pendent nucleotide which can coordinate, the decomposition of the β-ROCH$_2$CH$_2$Cbi's follows the simple rate law of eq 6. The second-order rate constants, k_2, were

$$\text{rate} = k_2[\beta\text{-ROCH}_2\text{CH}_2\text{Cbi}][\text{H}^+] \qquad (6)$$

determined from the slopes of plots of k_{obs} vs [H$^+$] (eq 7) and are listed in Table II. Plots of log k_{obs} vs pH (as in Figure 4) had slopes which varied from −0.96 to −0.99 and correlation coefficients, r^2, which in all cases exceeded 0.996.

$$k_{obs} = k_2[\text{H}^+] \qquad (7)$$

The second-order rate constants, k_2, for the acid-induced decomposition of the β-ROCH$_2$CH$_2$Cbi's can be seen to vary with R in the same order as the values of k_{on} for the β-ROCH$_2$CH$_2$Cbl's and span a range of 36-fold. However, in every case the value of k_2 slightly (24–55%), but significantly, exceeds that of k_{off} for the base-off form of the analogous β-ROCH$_2$CH$_2$Cbl. We have previously noted[68] that substantial ^{13}C chemical differences exist (some >1.0 ppm) between the base-off form of AdoCbl[64] and AdoCbi[65] for numerous corrin ring carbons and side-chain methylene carbons. These differences have been attributed to an effect of the pendent, but uncoordinated, nucleotide on the corrin ring conformation,[68] which has also been invoked to explain small, but finite, chemical shift differences between alkylcobinamides and base-off alkylcobalamins enriched in ^{13}C in the α-carbon of the organic ligand. This conformational effect is evidently responsible for the differential reactivity of the β-ROCH$_2$CH$_2$Cbi's and base-off β-ROCH$_2$CH$_2$Cbl's, to our knowledge the first such demonstration of the effect of this conformational difference on carbon–cobalt bond reactivity.

The decomposition of representative β-ROCH$_2$CH$_2$Cbl's (R = H (**1a**), CH$_3$CH$_2$ (**1e**), CF$_3$CH$_2$ (**1f**)) was also studied in sulfuric acid/water mixtures using the generalized acidity function of Cox and Yates[58] (eq 8). In this func-

$$-H = m^*X + \log C_{\text{H}^+} \qquad (8)$$

tion, X is the "excess" acidity of sulfuric acid, C_{H^+} is the molar concentration of hydrogen ion, and m^* is an adjustable parameter characteristic of the weak base being protonated and indicative of the fact that all known acidity functions are linearly related.[58] Using appropriate values of m^* (vide infra), the dependence of k_{obs} on hydrogen ion activity was found to be first order (eq 9) at acidities

$$k_{obs} = k_{off}a_{\text{H}^+} \qquad (9)$$

sufficiently high ($H < 0.5$) to ensure that only the base-off species contributed significantly to the rate,[89] as shown in Figure 5. Under these conditions, eqs 8 and 9 can be combined to yield eq 10 (since $a_{\text{H}^+} = 10^{-H}$) which allows

$$\log k_{obs} - \log C_{\text{H}^+} = m^*X + \log k_{off} \qquad (10)$$

determination of m^* and k_{off} from the slopes and intercepts of plots of log k_{obs} − log C_{H^+} vs X. Such plots are shown in the inset to Figure 5, from which the values of k_{off} = (1.97 ± 0.04) × 10^{-3} M^{-1} s^{-1}, (3.33 ± 0.13) × 10^{-4} M^{-1} s^{-1}, and (5.24 ± 0.23) × 10^{-5} M^{-1} s^{-1}, and m^* = 0.735, 0.828, and 0.791, for R = H (**1a**), CH$_3$CH$_2$ (**1e**), and CF$_3$CH$_2$ (**1f**), respectively, were obtained. These second-order rate constants are somewhat smaller than the values of k_{off} for these complexes obtained in water at ionic strength 1.0 M, evidently a medium effect. This effect is in the expected direction since the higher ionic strength in the aqueous studies would be expected to stabilize the transition state for this ionic reaction.

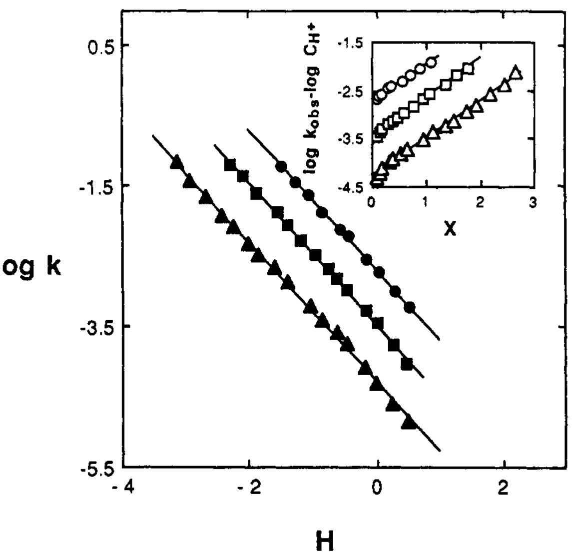

Figure 5. Dependence of the observed rate constant, k_{obs}, for the acid-induced decomposition of representative β-ROCH$_2$CH$_2$Cbl's in H$_2$SO$_4$/H$_2$O, on H, the generalized acidity function: (●) R = H (**1a**), slope = −0.998 ± 0.008, r^2 = 0.999; (■) R = CH$_3$CH$_2$ (**1e**), slope = −1.020 ± 0.012, r^2 = 0.998; (▲) R = CF$_3$CH$_2$ (**1f**), slope = −0.998 ± 0.11, r^2 = 0.998. The solid lines were calculated from eqs 8 and 9 using the rate constants, k_{off}, and m^* values (eq 8) 1.97 ± 0.04 × 10^{-3} M^{-1} s^{-1} and 0.735 for R = H, 3.33 ± 0.13 × 10^{-4} M^{-1} s^{-1} and 0.828, for R = CH$_3$CH$_2$, and 5.24 ± 0.23 × 10^{-5} M^{-1} s^{-1} and 0.791 for R = CF$_3$CH$_2$. Inset: Plots of log k_{obs} − log C_{H^+} vs X (eq 10) for representative β-ROCH$_2$CH$_2$Cbl's. Key: (○) R = H (**1a**), slope = 0.735 ± 0.016, r^2 = 0.996; (□) R = CH$_3$CH$_2$ (**1e**), slope = 0.825 ± 0.019, r^2 = 0.994; (△) R = CF$_3$CH$_2$ (**1f**), slope = 0.791 ± 0.014, r^2 = 0.995. The solid lines were calculated from eq 10 using the stated m^* values (i.e., the slopes of these plots) and the rate constants, k_{off}, listed above.

The strictly first-order dependence of k_{off} on a_{H^+} for these β-ROCH$_2$CH$_2$Cbl's is again in contrast to results previously obtained for the analogous cobaloximes.[12] For the ROCH$_2$CH$_2$Co(D$_2$H$_2$)OH$_2$'s, the first-order dependence on a_{H^+} was punctuated by a downward inflection at $H \sim 0.5$ attributable to the first equatorial protonation of the cobaloxime moiety. This difference between the cobaloximes and cobalamins is not surprising, however, as the only known equatorial protonation of the corrin macrocycle occurs at much higher acidities.[90,91] However, for the cobaloximes, a leveling off of the H–rate profiles occurs at $H \sim -1.0$ due to achievement of equilibrium protonation of the β-oxygen atom. No such leveling off is seen in the H–rate profiles for the β-ROCH$_2$CH$_2$Cbl's despite the fact that the reactions were studied to as high an acidity as possible (i.e., until $t_{1/2} \sim 10$ s and H = −1.48, −2.29, and −3.10 for R = H, CH$_3$CH$_2$, and CF$_3$CH$_2$, respectively). Hence, the alkoxyethyl ligands of the ROCH$_2$CH$_2$Cbl's must be substantially weaker bases than those of the ROCH$_2$CH$_2$Co(D$_2$H$_2$)OH$_2$'s. Finally, in the case of the cobaloximes, at even higher acidities the first-order decomposition was preceded by a "burst" of absorbance change with the subsequent first-order spectral changes

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(89) At lower acidities (i.e., $H > 0.5$), values of k_{obs} deviated positively from the first-order dependence on a_{H^+}, as expected due to significant participation by the base-on species.

(90) Brown, K. L.; Peck, S. *Inorg. Chem.* **1987**, *26*, 4143.

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Table III. Rate Constants for the Acid-Induced Decomposition of the (α-Alkoxyethyl)cobalamins and Cobinamides[a]

R	10^4k_2,[b] M^{-1} s^{-1}		$k_2^{\alpha\text{-Cbi}}/k_2^{\alpha\text{-Cbl}}$	$k_2^{\beta\text{-Cbi}}/k_2^{\alpha\text{-Cbi}}$	$k_{off}^{c}/k_2^{\alpha\text{-Cbl}}$
	α-Cbl	α-Cbi			
H	19.8 ± 0.1	28.4 ± 0.1	1.43	1.56	1.44
C_6H_5	5.87 ± 0.18	12.4 ± 0.1	2.11	0.94	1.28
$(CH_3)_2CH$	4.04 ± 0.07	6.00 ± 0.13	1.49	1.63	1.95
CH_3	4.13 ± 0.04	3.95 ± 0.17	0.96	2.12	1.47
CH_3CH_2	2.12 ± 0.06	3.42 ± 0.05	1.61	2.22	2.55
CF_3CH_2	0.606 ± 0.022	1.25 ± 0.07	2.06	0.98	1.51

[a] 25.0 ± 0.1 °C, ionic strength 1.0 M (KCl). [b] Equation 6. [c] Equation 1 and Scheme II.

identical for all R groups. These kinetic features are consistent with the accumulation of an intermediate at high acidity (and low water activity[28-30]), as indicated in Scheme I. However, no such deviations from first-order behavior nor any tendency for the first-order rate constants to become the same for the various β-$ROCH_2CH_2Cbl$'s is seen with the cobalamins.

(α-Alkoxyethyl)cobalt Corrinoids. The α-$ROCH_2CH_2Cbl$'s (**2a–f**) and the α-$ROCH_2CH_2Cbi$'s (**4a–f**) also decomposed in acid with strictly isosbestic and first-order spectral changes. For **2a–f** the final spectrum and HPLC retention time were identical to those of H_2OCbl while **4a–f** generated $(H_2O)_2Cbi$ by the same criteria. First-order rate constants, k_{obs}, for the decomposition of **2a–f** and **4a–f** were strictly first order in $[H^+]$, as shown in Figure 6 for representative compounds. The second-order rate constants, k_2, were determined from plots of eq 7, as for the β-$ROCH_2CH_2Cbi$'s, and are listed in Table III.

The second-order rate constants for the acid-induced decomposition of the α-$ROCH_2CH_2Cbl$'s and α-$ROCH_2CH_2Cbi$'s vary with R in essentially the same order as the values of k_{on} for the β-$ROCH_2CH_2Cbl$'s and k_2 for the β-$ROCH_2CH_2Cbi$'s and span a range of 33-fold and 23-fold, respectively. With the exception of the methoxyethyl compounds, for which k_2 is identical for the α-Cbl (**2d**) and the α-Cbi (**4d**), the α-$ROCH_2CH_2Cbi$'s are slightly more reactive (1.4–2.1-fold) than the α-$ROCH_2CH_2Cbl$'s (Table III). Except for the $C_6H_5OCH_2CH_2$- (**3b** and **4b**) and the $CF_3CH_2OCH_2CH_2Cbi$'s (**3f** and **4f**) the β-diastereomers of the $ROCH_2CH_2Cbi$'s are more reactive (by 1.6–2.2-fold) than the α-diastereomers. As seen in Table III, this order of reactivity also holds for the $ROCH_2CH_2Cbl$'s in which the base-off species of the β-$ROCH_2CH_2Cbl$'s are 1.3–2.6-fold more reactive than the α-$ROCH_2CH_2Cbl$'s. To our knowledge, these data represent the first such comparisons of the carbon–cobalt bond reactivity of the α- and β-diastereomers of alkylcobalt corrinoids.

Mechanism of the Acid-Induced Decomposition of the (Alkoxyethyl)cobalt Corrinoids. The kinetics of the acid-induced decomposition of the (alkoxyethyl)cobalt corrinoids reveal several important differences between this reaction and the analogous decomposition of the $ROCH_2CH_2Co(D_2H_2)OH_2$'s. For the cobaloximes, at all acidities below about 6 M H_2SO_4, only $HOCH_2CH_2Co(D_2H_2)OH_2$ decomposed in a strictly first-order fashion.[11,12] The $ROCH_2CH_2Co(D_2H_2)OH_2$'s (R = CH_3CH_2 and C_6H_5), in contrast, displayed a distinct lag prior to first-order behavior, indicative of the approach to a steady state as indicated in Scheme I.[11,12] No such deviation from first-order kinetic behavior is observed for any of the (alkoxyethyl)cobalt corrinoids under any of the conditions studied here. In addition, under the conditions described above, the order of reactivity for the $ROCH_2CH_2Co(D_2H_2)OH_2$'s (R = CH_3CH_2 > C_6H_5, 2:1)[11,12] was inverted from that observed for the analogous (alkoxyethyl)cobalt corrinoids, where the phenoxy compounds (**1b–4b**) are more reactive than the ethoxy compounds (**1e–4e**) by 1.4–3.6-fold, depending on the cobalt corrinoid. The behavior of the $ROCH_2CH_2Co(D_2H_2)OH_2$'s and (alkoxyethyl)cobalt corrinoids at high acidity is also substantially different. The cobaloximes display complex H–rate profiles showing evidence of equatorial ligand protonations and achievement of equilibrium protonation of the β-oxygen atom.[12] Most importantly, at acidities greater than ca. 7.3 M H_2SO_4 (H < ca. −3) a distinct "burst" was seen in the kinetis of the decomposition of the $ROCH_2CH_2Co(D_2H_2)OH_2$'s, followed by a first-order decay with an identical rate constant for all three complexes.[11,12] This behavior is indicative of the accumulation of an intermediate (Scheme I) which proved to be sufficiently stable in strongly acidic media to permit its characterization as the ethylcobaloxime carbonium ion shown in Scheme I. In contrast, no such deviations from a strictly first-order dependence of the rate constants for acid-induced decomposition of representative β-$ROCH_2CH_2Cbl$'s on a_{H^+} has been observed (Figure 5).

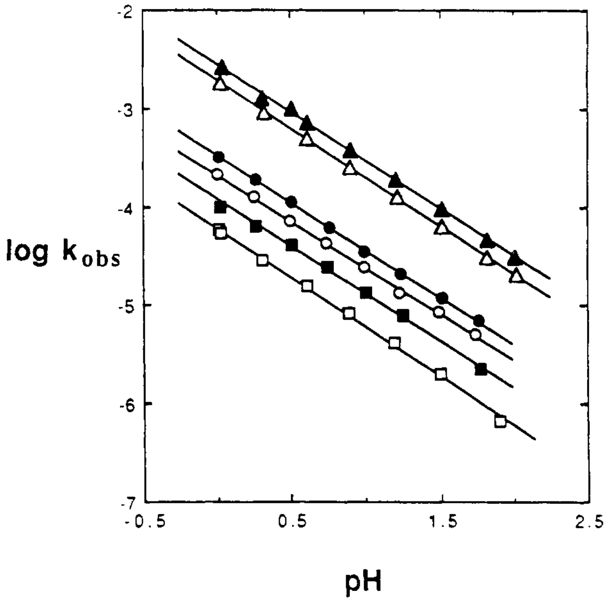

Figure 6. Dependence of the observed rate constants, k_{obs}, on pH for the acid-induced decomposition of representative α-$ROCH_2CH_2Cbl$'s (open symbols) and α-$ROCH_2CH_2Cbi$'s (solid symbols), 25.0 ± 0.1 °C, ionic strength 1.0 M (KCl): (○, ●) R = CH_3CH_2 (**2e** and **4e**); (□, ■) R = CF_3CH_2 (**2f** and **4f**): (△, ▲) R = H (**2a** and **4a**). The solid lines were calculated from eq 7 and the rate constants in Table III.

In the case of (phenoxyethyl)- and (ethoxyethyl)cobaloximes, the steady state observed at acidities below 6.0 M H_2SO_4 was found to be due to accumulation of $HOCH_2CH_2Co(D_2H_2)OH_2$, the equilibrium (Scheme I) between this species and the intermediate, $CH_2CH_2Co(D_2H_2)OH_2^+$, being displaced toward the intermediate only in highly acidic media where the activity of water is reduced. Consequently, under more mildly acidic conditions,

$HOCH_2CH_2Co(D_2H_2)OH_2$ could be detected during the decomposition of $CH_3CH_2OCH_2CH_2Co(D_2H_2)OH_2$ and $C_6H_5OCH_2CH_2Co(D_2H_2)OH_2$ and could be purified from reaction mixtures in which the (alkoxyethyl)cobaloximes were partially decomposed. Similar experiments were consequently attempted for the β-$ROCH_2CH_2Cbl$'s. Each of the six compounds (**1a–f**) was decomposed for 1 half-time in 1.0 M HCl, neutralized with K_2HPO_4, desalted by chromatography on Amberlite XAD resin, and analyzed by HPLC, as all six of the complexes are cleanly separated by the HPLC methodology described above. The chromatograms from each sample contained peaks for the unreacted starting material and for H_2OCbl, but no β-$HOCH_2CH_2Cbl$ (**1a**) could be detected in the samples from any of the other five β-$ROCH_2CH_2Cbl$'s (**1b–1f**). By overinjection of the samples resulting from the partial decomposition of **1b–f** and comparison of the chromatograms to those of samples which were spiked with varying amounts of **1a**, a detection limit of 0.05% could be set for **1a** in such mixtures of **1b–f** and H_2OCbl. Thus, if **1a** is formed during the decomposition of **1a–f**, it is present at less than 0.05% of the total cobamide during these reactions.

In the absence of any evidence whatsoever for the formation of an intermediate in the acid-induced decomposition of the $ROCH_2CH_2Cba$'s, the simplest mechanism which accounts for all of the observations is a concerted elimination of the alcohol, ROH, and the dealkylated cobalt corrinoid from the β-oxygen-protonated species formed in a rapid preequilibrium. For such a mechanism, achievement of equilibrium β-oxygen protonation (i.e., a leveling of the *H*–rate profiles) would be expected to occur at some acidity. Our failure to observe such a leveling of the *H*–rate profiles of representative β-$ROCH_2CH_2Cbl$'s at *H* values as low as −3.0 (Figure 5) indicates that the β-oxygens of the (alkoxyethyl)cobalt corrinoids are very weak bases indeed.

Summary. An extensive series of (alkoxyethyl)cobalt corrinoids has been prepared, including the α- and β-diastereomers of the cobalamins and cobinamides as well as the deuterated analogue of (2-hydroxyethyl)cobalamin and the ^{13}C-enriched analogues of the four (hydroxyethyl)cobalt corrinoids. These complexes have been thoroughly characterized by ^1H, ^2H, ^{13}C, ^{19}F, and ^{13}C edited ^1H NMR spectroscopy, UV–visible spectroscopy, and mass spectrometry. As was the case with the analogous (hydroxyethyl)cobaloximes, these complexes undergo an acid-induced decomposition to yield a cobalt(III) product, ethylene, and the alcohol derived from the alkoxy moiety. However, unlike the cobaloximes, which decompose via a two-step mechanism involving a σ-bonded ethylcobaloxime carbonium ion intermediate which accumulates in strongly acidic media and has been directly observed by ^1H and ^{13}C NMR spectroscopy, the (alkoxyethyl)cobalt corrinoids appear to decompose via a concerted elimination from the β-oxygen-protonated species.

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Synthesis and Structure of a Novel Bicyclic Cobalt Dithiolene: Formation of a Five-Membered CoS_2C_2 Ring from a CoSCNC Precursor and Elemental Sulfur as a Substrate[1]

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The cobalt isocyanide complex $C_5H_5Co(PMe_2Ph)(CNMe)$ (**3**), prepared from $C_5H_5Co(PMe_2Ph)_2$ (**2**) and CNMe by ligand exchange, reacts with methyl iodide to form the imidoylcobalt compound $[C_5H_5Co(PMe_2Ph)(CH_3CNMe)]I$ (**4**), which on further treatment with CS_2 in the presence of sodium methoxide gives the metallaheterocycle $C_5H_5(PMe_2Ph)\overline{CoC({=}CH_2)N(CH_3)C({=}S)S}$ (**5**). The X-ray crystal structure of **5** has been determined: monoclinic, space group $P2_1/n$ (No. 14), $a = 8.461$ (1) Å, $b = 13.885$ (3) Å, $c = 15.187$ (1) Å, $\beta = 93.57$ (1)°, $Z = 4$. The reaction of **5** with S_8 leads to the elimination of the phosphine ligand and affords the novel bicyclic cobalt dithiolene complex $C_5H_5Co[\eta^2\text{-}S_2C_2(SC({=}S)NCH_3)]$ (**6**) in 50% yield. The X-ray structure analysis of **6** (monoclinic, space group $P2_1/n$ (No. 14), with $a = 13.757$ (4) Å, $b = 12.614$ (2) Å, $c = 14.555$ (4) Å, $\beta = 112.69$ (1)°, and $Z = 8$) reveals an almost exactly planar bicyclic system in which partial electron delocalization is to be expected. From labeling studies with $^{12}CH_3I$ it is found that the second carbon atom of the C=C bond in **6** stems from the exocyclic CH_2 group of the heterocyclic ring system in **5**.

The reactivity of transition-metal complexes toward small molecules containing a carbon-to-element double bond or triple bond continues to arouse much attention.[2] We have recently shown that cyclopentadienylcobalt