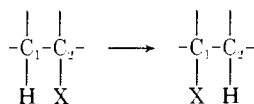# Diol Dehydrase Model Studies. The Acid Catalyzed Rearrangement of β-Hydroxyisopropylcobaloxime[1]
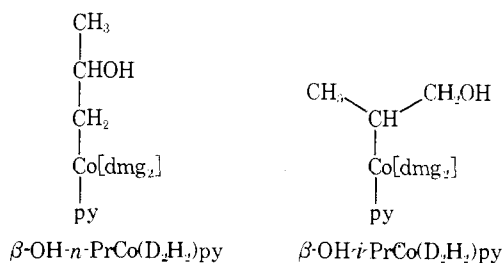
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Abstract: Two isomeric organocobalt complexes, β-hydroxyisopropyl(pyridine)cobaloxime (β-OH-*i*-PrCo(D_2H_2)py) and β-hydroxy-*n*-propyl(pyridine)cobaloxime (β-OH-*n*-PrCo(D_2H_2)py), have been synthesized and characterized by nmr spectroscopy and glpc analysis of anaerobic photolysis products. A mechanism is proposed to account for the photolysis products. When β-OH-*n*-PrCo(D_2H_2)py is stirred with a strongly acidic ion exchange resin the corresponding aquo complex is formed, but when β-OH-*i*-PrCo(D_2H_2)py is similarly treated it rearranges to the *n*-propyl derivative as confirmed by nmr measurements as well as product analysis of photolyzed rearrangement mixtures. When small aliquots of acid are added to separate solutions of the two isomeric aquo complexes in D_2O, nmr spectra show that both isomers decompose stoichiometrically but β-OH-*i*-PrCo(D_2H_2)HOH rearranges to β-OH-*n*-PrCo(D_2H_2)HOH as well. The results are consistent with the intermediacy of an olefin–cobaloxime(III) π-complex and provide model system evidence for a proposed diol dehydrase mechanism which proceeds through such an intermediate.

The enzymatic reactions in which vitamin B_{12} participates in the coenzyme form have been shown to proceed *via* apparent intramolecular 1,2-rearrangements of substrates in which a hydrogen and an electronegative group on neighboring carbon atoms exchange places[3] (eq 1). Numerous

$$-\underset{\underset{H}{|}}{\overset{|}{C_1}}-\underset{\underset{X}{|}}{\overset{|}{C_2}}- \longrightarrow -\underset{\underset{X}{|}}{\overset{|}{C_1}}-\underset{\underset{H}{|}}{\overset{|}{C_2}}-$$

mechanisms have been proposed for these rearrangements (see, for example, ref 3d, 3e, and 4). In order to attempt to model the rearrangement known to occur during the catalysis of the formation of aldehydes from 1,2-diols by the coenzyme B_{12} requiring enzyme diol dehydrase, we have synthesized two isomeric alkylcobaloximes,[5] β-hydroxy-*n*-propyl(pyridine)cobaloxime (β-OH-*n*-PrCo(D_2H_2)py) and β-hydroxyisopropyl(pyridine)cobaloxime (β-OH-*i*-PrCo-

CH₃ diagram:

```
CH₃
|
CHOH
|                    CH₃    CH₂OH
CH₂                    \   /
|                       CH
Co[dmg₂]                |
|                       Co[dmg₂]
py                      |
                        py
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β-OH-*n*-PrCo(D_2H_2)py   β-OH-*i*-PrCo(D_2H_2)py

(D_2H_2)py). The present paper deals with the synthesis and identification of these organocobalt complexes as well as the demonstration of an acid catalyzed rearrangement of β-OH-*i*-PrCo(D_2H_2)L to β-OH-*n*-PrCo(D_2H_2)L which must be considered as a highly relevant model for the rearrangement steps of the diol dehydrase reaction.

Experimental Section

Materials. Propionic acid, triethanolamine hydrochloride, bromine, dimethylglyoxime, benzoyl chloride, silica gel, organic solvents, and inorganic salts and acids were obtained in the highest purity commercially available and used without further purification.

Propylene oxide was purified according to ref 6 and spectral grade pyridine (Eastman) was dried over "Linde" type 4A molecular sieve. Deuterated solvents were obtained from Bio-Rad. Bio-Rad AG50W-X8 cation exchange resin was cycled four times between its proton and sodium forms with extensive washing between cycles. Triethanolamine was dried over KOH and redistilled at 0.5 Torr and stored in the dark, under argon in the cold. Chromatogra-

phy grade acetone (MCB) and reagent grade isopropyl alcohol were used without further purification as glpc standards. Allyl alcohol and propionaldehyde were purified according to ref 6, and propionaldehyde was subsequently redistilled daily for use as glpc standards. α-Chloropropionic acid was purified according to ref 6, and its acid chloride was synthesized according to the method of Brown.[7] 2-Chloro-1-propanol was obtained by $LiAlH_4$ reduction of α-chloropropionyl chloride.[8] Allyl chloride was purified according to ref 6 and hydrated in concentrated H_2SO_4 to 1-chloro-2-propanol.[9] Bromoacetone was prepared by the method of Catch, *et al.*,[10] and reduced with $LiAlH_4$ to 1-bromo-2-propanol.[11] Propionyl chloride was synthesized from propionic acid and benzoyl chloride.[7] α-Bromopropionyl bromide was either obtained commercially (K & K) or synthesized by bromination of propionyl chloride[12] and fractionally redistilled at 20 Torr before reduction to 2-bromo-1-propanol with $LiAlH_4$.[8] Deionized water of $>2 \times 10^5$ ohm cm specific resistance was used throughout.

Methods

Syntheses. The numerous attempts to synthesize the desired alkylcobaloximes (Table I) were all by standard techniques[13-15] with the exception of the final synthesis of β-OH-*i*-PrCo(D_2H_2)py which was carried out as follows. Pyridinecobaloxime(II) (0.5 mol) was prepared by the usual method[14b] in 150 ml of methanol in a three-necked 1-l. flask maintained under an argon atmosphere. A mixture of 19.4 g (0.13 mol) of triethanolamine plus 3.71 g (0.02 mol) of triethanolamine hydrochloride in sufficient water–methanol to dissolve was added, followed by 20.2 ml of pyridine and 27.2 g (0.196 mol, 3.9-fold excess) of 2-bromo-1-propanol. The argon atmosphere was replaced by hydrogen. After 50 hr of vigorous stirring 4.8 l. of hydrogen had been taken up. The reaction mixture was filtered, concentrated to *ca.* 50 ml on a rotary flash evaporator, and diluted with 100 ml of water. Generally, further flash evaporation and cooling of this solution were required to produce *ca.* 14 g of crude material. This material was either recrystallized from methanol–water (poor yield) or stirred with a small volume of chloroform, the insoluble (unalkylated) material filtered off, and the solution applied to a large silica gel column eluting with acetone and collecting the single migrating band (unalkylated material remains at the origin). Flash evaporation of the solvent provides 4.8 g (21%) of pure β-OH-*i*-PrCo(D_2H_2)py. β-OH-*n*-PrCo(D_2H_2)py was also obtained analogously by substituting 1-bromo-2-propanol as the alkylating agent (yield 13.5 g (63%)).

Formation and purity of alkylcobaloximes were assayed both by their migration as single, photolabile spots on silica gel thin-layer plates eluted with three different solvents (methanol, acetone, and ethyl acetate) and by nmr spectrometry (Varian A-60-A 60-MHz nmr spectrometer).

Anaerobic Photolysis and Product Identification. Alkylcobaloximes were further identified by analysis of the products of their anaerobic photolysis. Samples to be photolyzed (*ca.* 5×10^{-3} *M* in

Table I. Synthesis Conditions and Products from the Attempted Syntheses of the Two Isomers of
β-Hydroxypropyl(pyridine)cobaloxime

Alkylating agent	Conditions	Reductant	Product[a]	Ref
Propylene oxide	Neutral	H_2	β-OH-n-PrCo(D_2H_2)py	13, 14
Propylene oxide	Basic	$NaBH_4$	β-OH-n-PrCo(D_2H_2)py	13
1-Chloro-2-propanol	Basic	$NaBH_4$	β-OH-n-PrCo(D_2H_2)py	13, 14
2-Chloro-1-propanol	Basic	$NaBH_4$	β-OH-n-PrCo(D_2H_2)py	13, 14
Allyl alcohol	Neutral	H_2	No product	15
2-Bromo-1-propanol	Basic	$NaBH_4$	b	13, 14
1-Bromo-2-propanol	Buffered neutral[c]	H_2	β-OH-n-PrCo(D_2H_2)py	This work
2-Bromo-1-propanol	Buffered neutral[c]	H_2	β-OH-i-PrCo(D_2H_2)py	This work

[a] Product identified by nmr spectra of pyridine complex in $CDCl_3$. [b] Product contained 83% β-OH-n-PrCo(D_2H_2)py and 17% β-OH-i-PrCo(D_2H_2)py. [c] Buffered with 0.15 mol of triethanolamine buffer, 87% free base, pH ≈8.0 throughout the course of the reaction.

alkylcobaloxime, 0.1 M in phosphate buffer) were made anaerobic in Thunberg tubes and exposed to the intense light of a Xenon arc lamp (XTL projection illuminator) for varying lengths of time while being cooled in a stream of air. After photolysis *ca.* 2-μl samples were injected into a Varian Aerograph Series 1200 gas chromatograph equipped with a 10 ft by ⅛ in. stainless steel column of Porapak T; injector T 200°, detector T 300°, column T 135°, with N_2 carrier gas flow *ca.* 36 ml/min. Approximate retention times were: propionaldehyde, 11 min; acetone, 13 min; isopropyl alcohol, 15.5 min; allyl alcohol, 25 min. All photolysis products were positively identified by coinjection with authentic materials.

Hydrolysis and Rearrangement. Hydrolysis of β-OH-n-PrCo(D_2H_2)py to the corresponding aquo complex was accomplished by dissolving 5.0 g (0.0117 mol) of the complex in 900 ml of water and stirring rapidly with 8.6 g (3.75-fold excess of sites) of AG50W-X8 cation exchange resin (H^+ form) for 4.5 min. After rapid filtration of the resin the supernatant was evaporated to dryness on a rotary flash evaporator and the residue was dissolved in 10 ml of $CHCl_3$. applied to a small silica gel column, and rapidly eluted with acetone. After evaporation of the solvent the eluted material was dried under vacuum over P_2O_5, yield 1.0 g, 23%.

β-OH-i-PrCo(D_2H_2)py was similarly hydrolyzed by stirring 1.40 g of material with 2.39 g (3.75-fold excess of sites) of AG50W-X8 for either 2.5 min (hereafter referred to as the 2.5 min hydrolyzate, yield 0.75 g, 63%) or for 30 sec (30 sec hydrolyzate, yield 0.91 g, 77%) and then treated as above. Although silica gel chromatography was not necessary for purification, half of the 30 sec hydrolyzate was subjected to silica gel chromatography (rapid elution with 10% methanol–90% $CHCl_3$ (v/v), the second band being collected) to separate β-OH-i-PrCo(D_2H_2)HOH from the mixture of the two isomers.

Results

Syntheses. Table I shows the results of the several syntheses performed. It can be seen that under basic conditions the alkylating agents 1-chloro-2-propanol and 2-chloro-1-propanol yield *only* β-OH-n-PrCo(D_2H_2)py, and 2-bromo-1-propanol yields mainly this isomer (83%). Furthermore, cobalt(1) nucleophiles add to the primary carbon of propylene oxide in both basic and neutral solution. Although 2.8 l. of H_2 was taken up in 19 hr by the neutral synthesis mixture containing allyl alcohol, only a trace of alkylcobaloxime could be detected by tlc.

Figure 1 shows the nmr spectra of the two isomeric β-hydroxypropyl(pyridine)cobaloximes in $CDCl_3$ and 50% pyridine-d_5–D_2O (v/v).

Hydrolysis. Figure 2 shows the nmr spectra of the products of the three cation exchange resin hydrolyses of the alkyl(pyridine)cobaloximes, in 50% pyridine-d_5–D_2O (v/v) (Figure 2A–C) as well as that of β-OH-i-PrCo(D_2H_2)-HOH (Figure 2D) obtained from silica gel chromatography of the 30 sec hydrolyzate (see Experimental Section) of the corresponding pyridine complex. All of these hydrolyzed alkyl(aquo)cobaloximes were found to be free of pyridine by nmr in DMSO-d_6.

The spectra in Figure 2 are all quite clean indicating a high degree of purity with the exception of the spectrum of
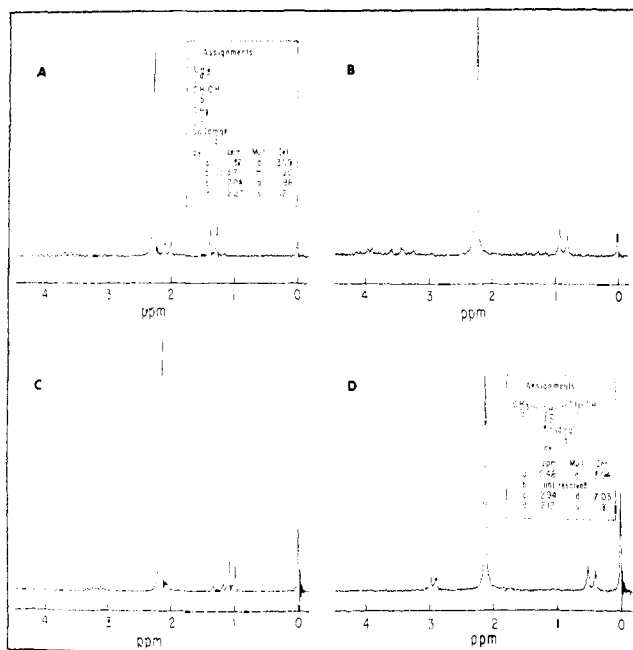

Figure 1. Nmr spectra of β-hydroxypropyl(pyridine)cobaloximes: (A) β-OH-n-PrCo(D_2H_2)py in 50% pyridine-d_5-D_2O (v/v) (inset, assignments); (B) β-OH-i-PrCo(D_2H_2)py in 50% pyridine-d_5-D_2O (v/v); (C) β-OH-n-PrCo(D_2H_2)py in $CDCl_3$; (D) β-OH-i-PrCo(D_2H_2)py in $CDCl_3$ (inset, assignments).

β-OH-i-PrCo(D_2H_2)HOH (Figure 2D) which has an impurity peak at 3.55 ppm and smaller impurities at 1.1–1.5 ppm (some of which are due to contaminating β-OH-n-PrCo(D_2H_2)HOH, see below).

The spectra in Figure 2A and 2D are essentially identical with those of the parent compounds in Figures 1A and B, respectively, with the exception of the impurities evident in Figure 2D. The spectra in Figure 2B and C can be seen to be due to mixtures of the two isomers.

The nmr spectra of the aquo complexes of both isomers in D_2O, before and after the addition of small quantities of DCl, are shown in Figure 3.

Photolysis. The results of the photolysis experiments are shown in Table II. The only photolysis products obtained were propionaldehyde, acetone, isopropyl alcohol (in small amounts), and allyl alcohol. Samples containing only β-OH-n-PrCo(D_2H_2)L produced mostly acetone with minor amounts of isopropyl alcohol, while those containing mostly β-OH-i-PrCo(D_2H_2)L produced mostly allyl alcohol and propionaldehyde with small amounts of acetone and isopropyl alcohol.

Discussion

Synthesis and Identification of β-Hydroxypropyl(pyridine)cobaloximes. As seen in Table I, alkylation of $Co^I(D_2$-

Table II. Summary of the Product Analyses from the Anaerobic Photolysis of β-Hydroxypropylcobaloximes in 0.1 M Aqueous Phosphate Buffer

Sample	Photolysis conditions $10^3 \times$ [Sample] M	pH	Time, hr	10^3[Products],[a] M Prop	Ace	i-PrOH	AllylOH	[AllylOH]/[Prop]	Total yield $\times 10^3$ (M) (% theory)	% β-OH-n-PrCo(D₂H₂)L in sample By nmr[b]	By glpc[c]
β-OH-n-PrCo(D₂H₂)py	5.00	7.16	23.0		4.62	Trace[d]			4.62 (92.3)	100	100
β-OH-i-PrCo(D₂H₂)py	5.00	7.16	29.5	1.11	0.192	Trace[d]	2.98	2.68	4.28 (85.6)	0	4.5
β-OH-i-PrCo(D₂H₂)py	5.00	7.55	38.8	1.22	0.117	0.108	3.08	2.52	4.53 (91.0)	0	5.0
β-OH-n-PrCo(D₂H₂)HOH	5.00	6.97	22.7		4.55	0.471			5.02 (100)	100	100
β-OH-n-PrCo(D₂H₂)HOH	4.49	7.05	3.25		4.29	Trace[d]			4.29 (97.0)	100	100
β-OH-i-PrCo(D₂H₂)HOH[e]	5.00	7.00	23.2	1.35	0.348	Trace[d]	2.79	2.07	4.49 (89.7)	0	8.0
β-OH-i-PrCo(D₂H₂)HOH[e]	4.69	6.97	3.75	1.24	0.298	Trace[d]	2.57	2.07	4.11 (87.7)	0	7.0
β-OH-i-PrCo(D₂H₂)py 30 sec hydrolyzate[f]	5.00	7.43	3.50	1.10	0.657	0.176	2.37	2.15	4.31 (86.3)	19	19.3
β-OH-i-PrCo(D₂H₂)py 2.5 min hydrolyzate[f]	5.00	7.49	3.50	0.557	1.41	0.147	1.19	2.12	3.31 (66.2)	47	47.2
β-OH-i-PrCo(D₂H₂)py 2.5 min hydrolyzate[f]	5.00	7.38	3.30	0.556	1.48	0.344	1.20	2.12	3.59 (72.0)	47	50.7

[a] Prop = propionaldehyde, Ace = acetone, i-PrOH = isopropyl alcohol, AllylOH = allyl alcohol. [b] Calculated from integration of the nmr spectra in Figures 1 and 2. [c] See text for method of calculation. [d] Less than 5% of total yield. [e] Isolated from 30 sec hydrolyzate of β-OH-i-PrCo(D₂H₂)py by silica gel chromatography (see Experimental Section). [f] See Experimental Section.
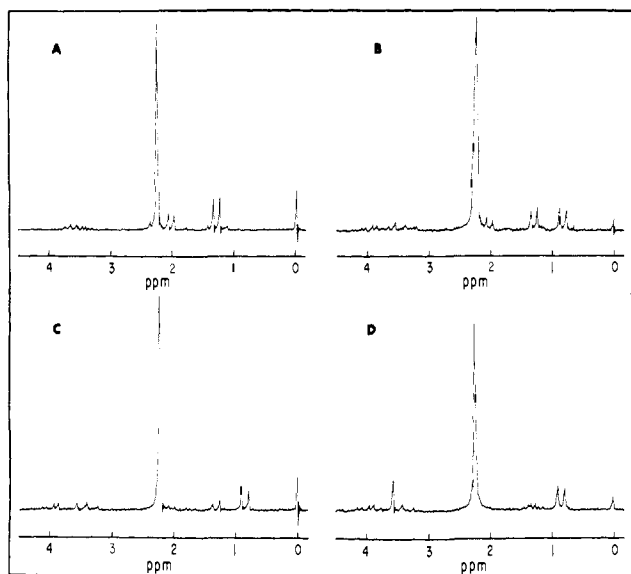

Figure 2. Nmr spectra of β-hydroxypropyl(aquo)cobaloximes in 50% pyridine-d_5–D₂O (v/v): (A) β-OH-n-PrCo(D₂H₂)HOH; (B) 2.5 min hydrolyzate of β-OH-i-PrCo(D₂H₂)py (see Experimental Section); (C) 30 sec hydrolyzate of β-OH-i-PrCo(D₂H₂)py (see Experimental Section); (D) β-OH-i-PrCo(D₂H₂)HOH purified from 30 sec hydrolyzate by silica gel chromatography (see Experimental Section).

Figure 3. (A) Nmr spectrum of β-OH-n-PrCo(D₂H₂)HOH in D₂O; (B) same as A plus 2.3 μl of 20% DCl in D₂O; (C) nmr spectrum of β-OH-i-PrCo(D₂H₂)HOH in D₂O, upper scan twofold amplification of lower scan; (D) same as C plus 1.1 μl of 20% DCl in D₂O, upper scan twofold amplification of lower scan; (E) same as D plus 1.0 μl 20% DCl in D₂O, upper scan 1.56-fold amplification of lower scan.

H₂)py⁻ with either of the chlorohydrins of propylene under basic conditions yields only β-OH-n-PrCo(D₂H₂)py. This result is completely consistent with the work of Clarke, et al.,[16] who found that alkylation of reduced cobalt(I) etioporphyrin I with 2-bromo-1-propanol yielded only the β-hydroxy-n-propylcobalt derivative. This was presumed to be due to formation of propylene oxide from the bromohydrin under the basic conditions employed, followed by addition of the cobalt(I) nucleophile to the least hindered carbon of propylene oxide. This explanation is consistent with the present results which indicate that addition of Co¹(D₂H₂)py⁻ to propylene oxide also occurs at the pri-
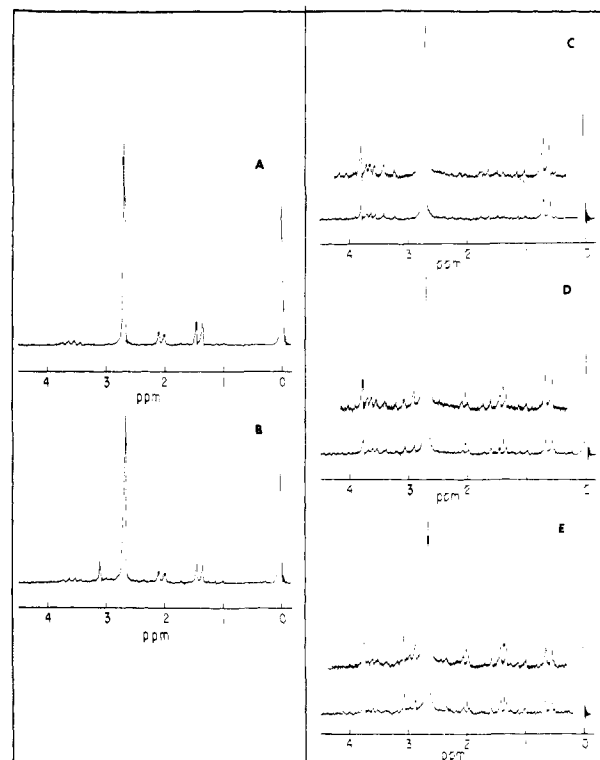
mary carbon. The fact that alkylation of Co¹(D₂H₂)py⁻ with 2-bromo-1-propanol does produce a small amount of β-OH-i-PrCo(D₂H₂)py is not inconsistent with the results of Clarke, et al.,[16] who employed significantly different conditions.

It is interesting to note that the mode of addition of cobaloxime(I) nucleophile to propylene oxide remains the same under neutral and basic conditions (*i.e.*, addition of $HCo^I(D_2H_2)py$[15,17] or $Co^I(D_2H_2)py^-$ nucleophile, respectively) while the mode of addition to substituted olefins has been shown to change from β-addition in base to α-addition in neutral solution.[15] Interestingly, Naumberg, *et al.*,[18] have shown that $Co^I(D_2H_2)py^-$ adds only to the more hindered, secondary carbon of styrene oxide in basic solution.

The successful synthesis of β-OH-*i*-$PrCo(D_2H_2)py$ under buffered neutral conditions from 2-bromo-1-propanol may well be the first synthesis of this complex. A previously reported synthesis by Schrauzer and Windgassen,[13] although lacking in experimental detail and devoid of structural information, seems to have been carred out in base with a 2-halo-1-propanol as alkylating agent—conditions which clearly could not have yielded a very pure sample of this isomer. A similar synthesis attempt by Yamazaki and Hohokabe[19] probably also produced principally the *n*-propyl isomer (again structural information was not presented).

The large excess of hydrogen taken up during the synthesis of β-OH-*i*-$PrCo(D_2H_2)py$ (see Experimental Section) may be due to the reductive elimination of bromide from the bromohydrin alkylating agent under the influence of hydrido(pyridine)cobaloxime(I) analogous to the known elimination of bromide during the reduction of *p*-bromophenacyl bromide to α-(*p*-bromophenyl)ethanol in excess $LiAlH_4$.[20]

Although we do not completely understand the anomalies seen in the nmr spectra of β-OH-*n*-$PrCo(D_2H_2)py$ in $CDCl_3$ (Figure 1C) and β-OH-*i*-$PrCo(D_2H_2)py$ in 50% pyridine-d_5–D_2O (v/v) (Figure 1B), it is clear from the spectra in Figure 1A and 1D, as well as the photolysis results (below) that both isomers have indeed been obtained.

Photolysis of β-Hydroxypropylcobaloximes. The anaerobic photolysis of β-OH-*n*-$PrCo(D_2H_2)py$ produces acetone in high yield with a trace of isopropyl alcohol, while β-OH-*i*-$PrCo(D_2H_2)py$ photolysis produces most allyl alcohol and propionaldehyde (ratio of allyl alcohol:propionaldehyde = 2.60) with minor amounts of acetone and isopropyl alcohol (Table II). These results are in accord with those of Clarke, *et al.*,[16] and Schrauzer and Windgassen[13] who found acetone to be the photolysis product of β-hydroxy-*n*-propylcobalt etioporphyrin I and β-OH-*n*-$PrCo(D_2H_2)py$, respectively. Scheme I presents a mechanism which accounts for
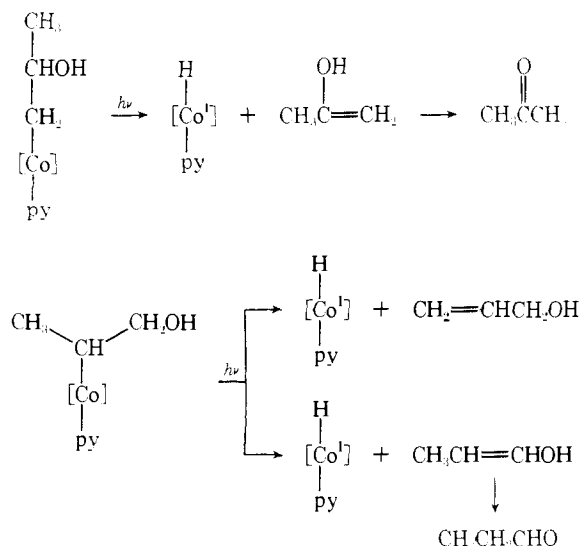
these products and is consistent with the recent work of Duong, *et al.*,[21] who showed that substituted alkylcobaloximes containing at least one β-proton undergo a concerted β-elimination when photolyzed (or thermolyzed) anaerobically to produce hydridocobaloxime(I) and an olefinic derivative of the alkyl ligand. Thus the anaerobic photolysis of β-OH-*n*-$PrCo(D_2H_2)py$ should yield only the enol of acetone (and hence acetone as the final product) while β-OH-*i*-$PrCo(D_2H_2)py$, which has two proton bearing β-carbons, should produce both allyl alcohol and the enol of propionaldehyde. Furthermore, the magnitude of the product ratio allyl alcohol:propionaldehyde from the photolysis of the latter complex is seen to be the consequence of the greater ease of elimination of hydride ion from the methyl carbon than from the hydroxymethyl carbon of β-OH-*i*-$PrCo(D_2H_2)py$. The appearance of small amounts of isopropyl alcohol during the photolysis of samples containing β-OH-*n*-$PrCo(D_2H_2)py$ (Table II) is thought to be due to the secondary process of reduction of acetone by $HCo^I(D_2H_2)py$ produced during the photolysis analogous to the known catalysis of the reduction of olefins by molecular hydrogen by Co(II) chelates.[22] This assumption is supported by the apparent increase in the ratio isopropyl alcohol:acetone with increasing photolysis time (Table II). The appearance of small amounts of acetone (and hence isopropyl alcohol) in the photolyzate of β-OH-*i*-$PrCo(D_2H_2)py$ is attributed to the contamination of this complex with a small amount (*ca.* 5%) of the *n*-propyl isomer which could be due to slow epoxide formation from 2-bromo-1-propanol during the protracted synthesis of β-OH-*i*-$PrCo(D_2H_2)py$ despite the near neutral conditions. Consequently, the product analysis of the anaerobic photolysis of samples of β-hydroxypropylcobaloximes can be used to determine the composition of the samples assuming that acetone and traces of isopropyl alcohol are the only products from the *n*-propyl isomer, while allyl alcohol and propionaldehyde are the only products produced by the isopropyl isomer.

An alternative photolysis mechanism, consistent with the prevailing opinion on the nature of photoinduced carbon-cobalt bond cleavage (see, for example, ref 3e), involves the production of organic radicals due to carbon–cobalt bond homolysis followed by elimination of a β-hydrogen atom from the radicals thus produced. While this mechanism accounts for the products as well as the magnitude of the product ratio from β-OH-*i*-$PrCo(D_2H_2)py$, it is inconsistent with the observation (Table II) that the product ratio from β-OH-*i*-$PrCo(D_2H_2)L$ photolysis seems to depend on the nature of the axial ligand. This observation clearly warrants a concerted mechanism such as the one depicted in Scheme I.

Hydrolysis of the β-Hydroxypropyl(pyridine)cobaloximes and the Rearrangement of β-OH-*i*-$PrCo(D_2H_2)py$. When β-OH-*n*-$PrCo(D_2H_2)py$ is treated with a strongly acidic cation exchange resin for 4.5 min (see Experimental Section) the corresponding aquo complex is obtained, as seen by comparison of its nmr spectrum (Figure 2A) and its photolysis products (Table II) with those of the parent pyridine complex (Figure 1A, Table II). The poor yield for this hydrolysis (see Experimental Section) is unquestionably due to the known acid lability of β-hydroxyalkylcobaloximes[13] which decompose to olefins and cobaloximes(III). However, when β-OH-*i*-$PrCo(D_2H_2)py$ is similarly treated for 2.5 min, the material isolated is clearly seen to be a mixture of the two isomeric aquo complexes (Figure 2B). Integration of the nmr spectrum leads to the conclusion that the sample contains 47% β-OH-*n*-$PrCo(D_2H_2)HOH$ after 2.5 min hydrolysis (Table II). Analysis of the photolysis products of this rearranged sample confirms this conclusion (calculated to be 49.0% β-OH-*n*-$PrCo(D_2H_2)HOH$, Table II). If the

Scheme I

resin treatment of β-OH-i- PrCo(D₂H₂)py is limited to 30 sec the sample is seen to contain 19% β-OH-n- PrCo(D₂-H₂)HOH by nmr (Figure 2C) and 19.3% by analysis of photolysis products (Table II). Slightly impure β-OH-i-PrCo(D₂H₂)HOH (Figure 2D) isolated from this latter sample by silica gel chromatography is seen to be contaminated with 7.5% β-OH-n- PrCo(D₂H₂)HOH by analysis of its photolysis products (Table II).

Confirmation of this apparent acid catalyzed rearrangement is obtained from the experiment shown in Figure 3. The nmr spectrum of β-OH-n- PrCo(D₂H₂)HOH in D₂O (Figure 3A) is characterized by a three-proton doublet at *ca.* 1.40 ppm and a two-proton doublet at *ca.* 2.00 ppm, as well as the other expected peaks (see Figure 1A). Addition of 2.3 μl of 20% DCl in D₂O (Figure 3B) causes little change in the spectrum except for the appearance of a new singlet at 3.07 ppm attributed to the 12-proton equatorial ligand peak of dealkylated cobaloxime(III) corresponding to *ca.* 13% acid cleavage of the alkylcobaloxime. The spectrum of β-OH-i- PrCo(D₂H₂)HOH in D₂O (Figure 3C) is characterized by a high field three-proton doublet at *ca.* 0.62 ppm as well as other expected peaks (see Figure 1B) including the above mentioned impurity peaks which now appear at 3.78 ppm and in the 1.0-2.0 ppm region. Addition of 1.1 μl of 20% DCl in D₂O (Figure 3D) causes *ca.* 7% decomposition but also causes the appearance of doublets (arrows) at 2.0 and 1.4 ppm (with concomitant decrease in intensity of the 0.62 ppm doublet) indicative of β-OH-n-PrCo(D₂H₂)HOH, which can be clearly seen despite the small impurity peaks in this region. Integration shows this sample to be 30% β-OH-n- PrCo(D₂H₂)HOH (*i.e.,* 22.5% rearranged, since the starting β-OH-i- PrCo(D₂H₂)HOH sample contained 7.5% of the n- propyl isomer (Table II)). Further addition of 1.0 μl of 20% DCl in D₂O (Figure 3E) leads to a sample which is *ca.* 15% decomposed and shows clean doublets at 2.0 and 1.4 ppm (arrows) indicative of 42% rearrangement (calculated as above).

We conclude that under acid conditions net rearrangement of β-OH-i- PrCo(D₂H₂)HOH to β-OH-n- PrCo(D₂-H₂)HOH occurs. In light of the known decomposition of β-hydroxyalkylcobaloximes to olefins and cobaloximes(III) in acid,[13] it seems reasonable that the rearrangement proceeds through an olefin-cobaloxime(III) π-complex as shown in Scheme II.

Abundant evidence in the recent literature on the solvolytic reactions of β-substituted alkylcobaloximes[23-25] and the thermal reactions of allylcobaloximes[26] supports the existence in solution of such olefin-Co(III) π-complexes as depicted in Scheme II. In fact, such complexes have been predicted as intermediates in the acid cleavage of β-hydroxyalkylcobaloximes.[23a] The only direct evidence for the formation of such intermediates comes from the elegant work of Silverman and Dolphin[25b,27] who demonstrated net synthesis of β-substituted alkyl cobaloximes and cobalamins from olefins, appropriate cobalt(III) complexes, and ambient nucleophiles. Although no such direct evidence for the intermediate formation of an olefin-Co(III) π-complex in the acid catalyzed rearrangement of β-OH-i- PrCo(D₂H₂)-HOH is presented here, work is in progress to provide such evidence.

In conclusion, the net rearrangement of β-OH-i-PrCo(D₂H₂)HOH to β-OH-n- PrCo(D₂H₂)HOH under acidic conditions demonstrated above must be considered as a highly relevant model reaction for the rearrangement steps of the diol dehydrase mechanism recently proposed by Silverman and Dolphin.[25b]

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Scheme II
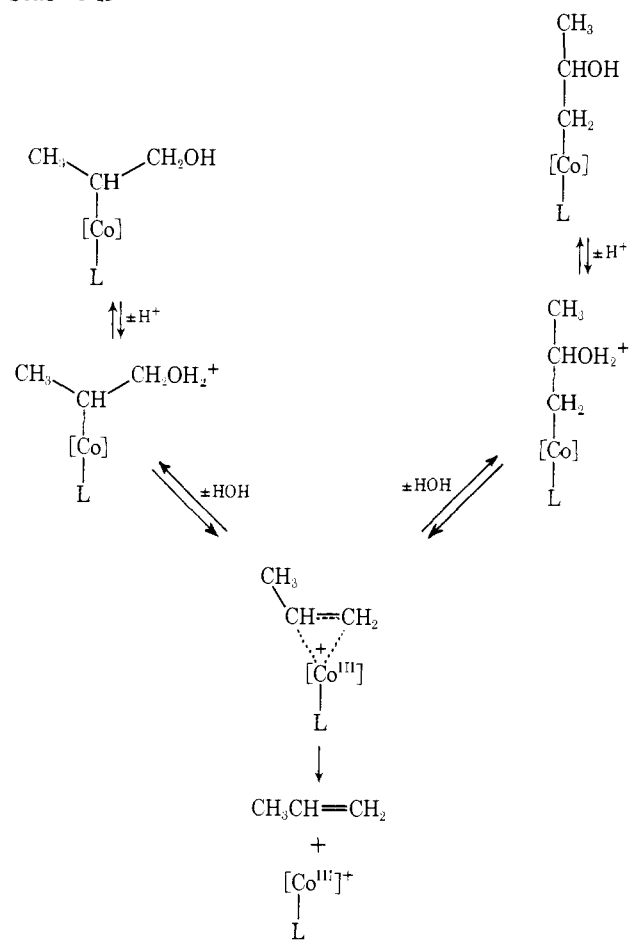
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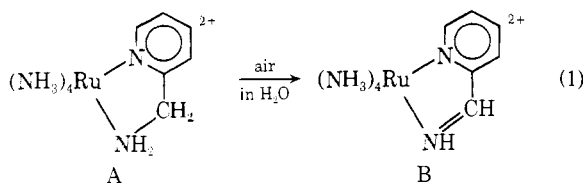(27) R. B. Silverman and D. Dolphin, submitted for publication in *J. Amer. Chem. Soc.*

Synthesis and Properties of Some Tetraammineruthenium(II) Complexes of Bidentate Ligands, cis-Ru(NH₃)₄(X–Y)²⁺

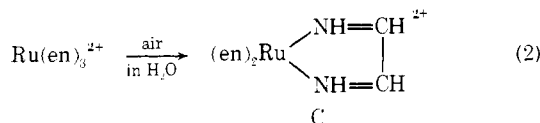Vincent E. Alvarez,[1a] Rebecca J. Allen, Tadashi Matsubara, and Peter C. Ford*[1b]

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Abstract: Reported are the syntheses and spectral characterizations of a series of ruthenium(II) complex ions of the type $Ru^{II}(NH_3)_4(X-Y)$, where X–Y is a bidentate ortho-substituted pyridine such as 2-aminomethylpyridine, 2-pyridinalimine, 2-pyridinecarboxaldehyde, or bipyridine. The 2-pyridinalimine complex is formed by facile and quantitative air oxidation of the 2-aminomethylpyridine complex, while the 2-pyridinecarboxaldehyde complex is formed by reaction of the free ligand with either $Ru(NH_3)_5H_2O^{2+}$ or cis-$Ru(NH_3)_4(H_2O)_2^{2+}$ in aqueous solution. In aqueous solution the aldehyde complex exists entirely in the nonhydrated carbonyl form in contrast to the free ligand which is largely hydrated under similar conditions. The $Ru(NH_3)_4(2$-pyridinecarboxaldehyde$)^{2+}$ complex does react reversibly with aqueous hydroxide to give the aldehyde hydrate anion, and the equilibrium constants for this reaction and the analogous reaction of aqueous hydroxide with $Ru(NH_3)_5(4$-pyridinecarboxaldehyde$)^{2+}$ have been evaluated. In addition, the reduction potentials for the $Ru(III)/Ru(II)$ couples for a number of these complexes are reported. These data are interpreted in terms of the special stability of unsaturated metallocyclic complexes formed between $Ru(II)$ and a π-unsaturated bidentate ligand.

Recent research in these laboratories has focused on the reactions and properties of monodentate ligands coordinated in the pentaammine and tetraammine complexes of the group VIII metal ions: ruthenium(II), ruthenium(III), and rhodium(III).[2-5] This work has established the metal-to-ligand back-bonding which characterizes Ru(II) complexes of monodentate, π-unsaturated organic ligands, as well as other differences in the abilities of the various ions to affect the electronic character of coordinated ligands. In the course of studying ligand substitution rates of related complexes,[6] it was discovered that the ruthernium(II) 2-aminomethylpyridine complex, A, undergoes facile air oxidation in aqueous solution to a product proposed to be the ruthenium(II) imino species B (eq 1). This reaction is analo-

$$(\text{NH}_3)_4\text{Ru} \overset{\text{air}}{\underset{\text{in H}_2\text{O}}{\longrightarrow}} (\text{NH}_3)_4\text{Ru} \qquad (1)$$

$$\text{A} \qquad\qquad\qquad \text{B}$$

gous to air oxidation reported for Ru(en)₃²⁺ to form the α-diamine complex C (eq 2).[7,8] Complexes such as B and C

$$\text{Ru(en)}_3^{2+} \overset{\text{air}}{\underset{\text{in H}_2\text{O}}{\longrightarrow}} (\text{en})_2\text{Ru} \begin{matrix} \text{NH}=\text{CH} \\ | \\ \text{NH}=\text{CH} \end{matrix}^{2+} \qquad (2)$$

$$\text{C}$$

where the π-unsaturated bidentate ligand forms a cyclic configuration including the metal potentially have substantially different metal–ligand interactions than do complexes of monodentate ligands. Here we report the synthesis and properties of several complexes of ortho-substituted pyridine ligands (including B) which can form such unsaturated

metallo ring systems with the goal of comparing these to the analogous monodentate pyridine complexes. In a subsequent paper we shall report on kinetics studies regarding certain reactions relating to the formation of these complexes.

Experimental Section

Materials. Chloropentaammineruthenium(III) dichloride,[9] [Ru(NH₃)₅Cl]Cl₂, and cis-dichlorotetraammineruthenium(III) chloride,[10] cis-[Ru(NH₃)₄Cl₂]Cl, were prepared according to literature procedures. Organic ligands used in syntheses of complexes were purchased from Aldrich and were purified by vacuum distillation. Water used in these studies was redistilled from alkaline permanganate. Argon used to entrain air from reaction solutions was deoxygenated by passing through chromous solution in gas scrubbing bottles. Standard sodium hydroxide solutions were prepared from commercial solution concentrates (Dilut-lt).

Syntheses. Tetraammine(2-aminomethylpyridine)ruthenium(II) Tetrafluoroborate, [Ru(NH₃)₄(2-NH₂CH₂C₅H₄N)][BF₄]₂. A deaerated solution (3.0 ml) of cis-Ru(NH₃)₄(H₂O)₂²⁺, generated[11] by Zn(Hg) reduction of aqueous cis-[Ru(NH₃)₄Cl₂]Cl (0.20 g, 7.2 × 10⁻⁴ mol) was added to a fivefold molar excess of deaerated 2-aminomethylpyridine (~0.2 g), and the reaction was allowed to proceed under an argon atmosphere for 30 min. Subsequently, the reaction mixture was filtered, and upon addition of 2 ml of saturated aqueous NaBF₄, a yellow precipitate, [Ru(NH₃)₄(NH₂CH₂C₅H₄N)][BF₄]₂, formed. The solid was separated by filtration and washed with 2 ml each of cold ethanol–H₂O (2:1 v/v), ethanol, ethanol-ether (1:1 v/v), and ether. Recrystallization was from hot water under deaerated conditions to prevent air oxidation of the ruthenium(II) complex. The recrystallized solid was washed with ice-cold deaerated water (1 ml) then 2 ml each of cold ethanol-H₂O (2:1 v/v), ethanol, ethanol-ether (1:1 v/v), and ether. The yellow crystals were dried under a vacuum at room temperature, yield 0.130 g, 80%. *Anal.* Calcd for C₆H₂₀N₆B₂F₈Ru: C, 15.87; H, 4.47; N, 18.64; Ru, 22.41. Found: C, 15.65; H, 4.53; N, 18.74; Ru, 21.90.