Cobalamin Model Compounds. Preparation and Reactions of Substituted Alkyl- and Alkenylcobaloximes and Biochemical Implications

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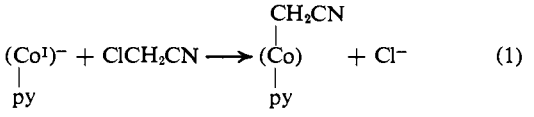
Abstract: Fifty organometallic derivatives of bisdimethylglyoximatocobalt containing substituted alkyl and alkenyl groups directly linked to the cobalt atom were prepared by reactions similar to those employed previously for the preparation of simple alkylcobaloxime derivatives. The reactions of olefinic and acetylenic compounds with reduced cobaloxime species were examined in greater detail. The reaction of the reduced cobaloximes with substituted olefins and acetylenes was found to depend on the pH of the solution. In near to neutral medium only the α-substituted cobaloximes were formed, for instance, $Co(D_2H_2)\cdot 2H_2O + 0.5H_2 + CH_2{=}CHCN + py = CH_3CH(CN)Co(D_2H_2)py + 2H_2O$. In alkaline solution, however, addition in the β position takes place: $Co(D_2H_2)\cdot 2H_2O + 0.5H_2 + CH_2{=}CHCN + py = NCCH_2CH_2Co(D_2H_2)py + 2H_2O$. The β-substituted ethylcobaloximes carrying activating substituents are less stable than the α isomers and may be rearranged into the latter under appropriate conditions. On the basis of these findings the mechanism for the cobalamin-dependent enzymic rearrangement of succinyl-CoA to methylmalonyl-CoA is discussed. The properties of several reported organocobalamins are qualitatively similar to those of the corresponding organocobaloximes.

Bisdimethylglyoximatocobalt complexes uniquely reproduce the basic metal reactions of cobalamins and thus are excellently suited for the study of the mechanisms of vitamin B_{12} catalyzed biochemical processes.[2-4] Whereas simple alkylcobaloximes were found to be unusually stable, a surprising variation of the reactivity of the Co–C bond results on introduction of substituents to the cobalt-bound alkyl group. For instance, methyl- or ethylcobaloximes are very stable toward acids or bases; β-hydroxyethylcobaloximes, on the other hand, readily decompose both in mildly acidic or basic media.[3] In order to obtain additional information on the effects of substituents on the stability of the Co–C bond in cobaloximes, we have prepared various substituted alkylcobaloximes. Several alkenylcobaloximes were also made and will be described as well. In the course of this work, interesting rearrangement reactions were observed which may have important biochemical implications.

Preparation of Substituted Alkylcobaloximes *via* Alkyl Halide Derivatives. The methods previously described for the preparation of alkylcobaloximes[2] are generally applicable. Three pertinent examples are given in eq 1–3. The reaction conditions must be modified in certain cases to accommodate the instability of the starting materials and products. In particular, reductive cleavage of the Co–C bond occurs more readily than in the case of simple alkylcobaloximes; appropriate experimental procedures are described in the Experimental Section.



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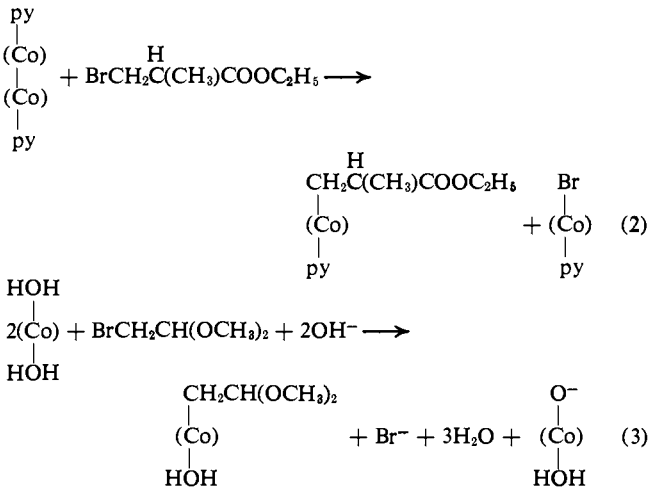

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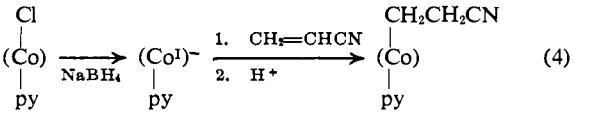
Preparation from Substituted Olefins. It was previously reported[2] that most unsubstituted olefins do not react with reduced cobaloximes to form the expected alkylcobaloximes. So far only propylene was found to behave exceptionally, affording isopropylcobaloxime in low yield[2] under special conditions (reaction of the dimeric pyridinatocobaloxime with excess propylene in ethanol in the presence of hydrogen). No reaction occurred in alkaline medium with cobaloximes. Under these conditions only electronegatively substituted olefins react with the nucleophilic cobalt atom, to produce β-substituted ethylcobaloximes. For example, acrylonitrile affords β-cyanoethylcobaloxime[5] (eq 4).



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A significant change in the mode of addition of the cobalt species to the double bond takes place in neutral or only slightly alkaline solution. Here the α-substituted alkylcobaloxime is formed exclusively (eq 5).

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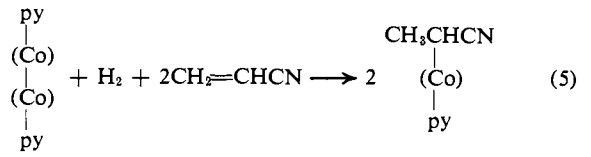
(2) G. N. Schrauzer and R. J. Windgassen, *J. Am. Chem. Soc.*, 88, 3738 (1966), and references cited therein.

(3) G. N. Schrauzer and R. J. Windgassen, *ibid.*, 89, 143 (1967).

(4) G. N. Schrauzer and R. J. Windgassen, *ibid.*, in press.

(5) G. N. Schrauzer and J. Kohnle, *Chem. Ber.*, 97, 3056 (1964).



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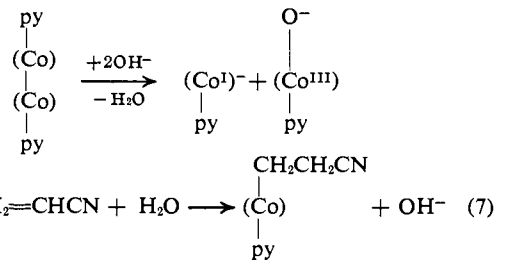

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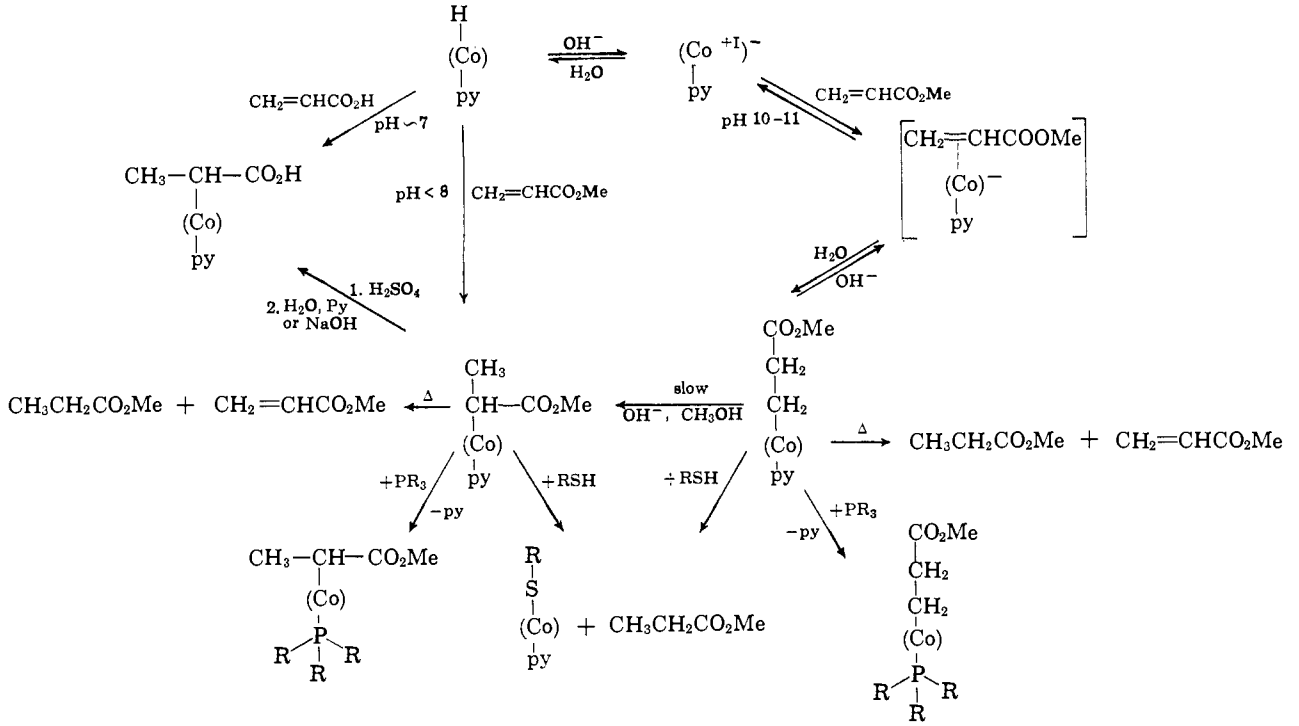
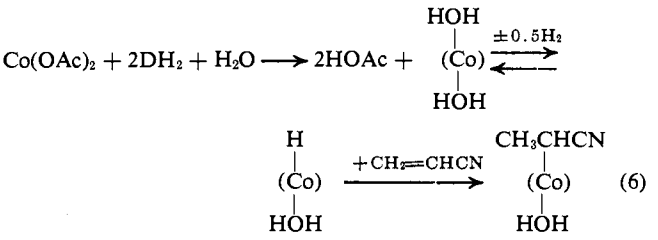
In Scheme I the observed reactions of α- and β-carbomethoxyethylcobaloximes obtained from methyl acrylate are shown. For the synthesis of the α-substituted organocobaloximes it is possible and preferable to simply stir together cobaltous acetate, dimethylglyoxime, and a solution of the olefinic substrate in methanol under 1 atm of hydrogen (eq 6). To explain

Scheme I. Reactions of Carbomethoxyethylcobaloximes (dioxime ligands symbolized by parentheses)





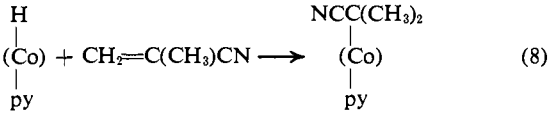
(6)

this "reverse" addition to the olefinic substrate, it is reasonable to assume that the actually reacting cobaloxime species is a cobalt(I) "acid" which on interaction with the olefin transfers the proton to the β-carbon atom of the substituted olefin. To prepare the β-substituted ethylcobaloximes a similar one-step procedure may be applied. The β-cyanoethylcobaloxime, for instance, is obtained from cobaltous chloride, dimethylglyoxime, hydrogen, and excess acrylonitrile by adding NaOH up to the pH of about 10–11. Since cobaloximes(II) disproportionate in alkaline solution, the molecular hydrogen may also be omitted if an essentially quantitative yield of product is not desired. In eq 7 this variant of the general procedure is described using the dimeric pyridinatocobaloxime(II) as the metal-containing starting material. In alkaline solution the reduced cobaloxime is essentially present as the strongly nucleophilic anion $(Co^{I})^{-}$, the corresponding base of the hypothetical acid (HCo). Therefore, the normal nucleophilic addition to the olefin may take place (Scheme I), possibly *via* an initial π complex formed between the olefinic double bond and the metal as indicated.

It is of interest to note that the reaction product of styrene with cobaloxime(I) is not the β- but rather the α-phenylethylcobaloxime derivative; it is formed both under alkaline and neutral conditions. The β isomer could be obtained only from β-bromoethylbenzene and was found to behave just like a simple alkylcobaloxime, especially with respect to its stability to acids or bases. The α-phenylethylcobaloxime, on the other hand, is a relatively unstable material which slowly decomposes on storage and is readily cleaved in mildly alkaline or acidic solution. We ascribe the instability of this compound to a steric effect. It is of interest that vitamin B_{12s} was reported not to react with styrene.[6] This may be due to steric effects, which would favor the formation of the β isomer. Since the latter could not be obtained even with the cobaloximes, it is not surprising that it does not form with the corresponding cobalamin species. The yields of product isolated in general strongly depend on the nature and number of the substituents on the olefinic substrate; both electronic and steric effects operate. Normally, the olefinic substrate must be employed in excess to counteract yield losses

(6) E. Lester Smith, L. Mervyn, P. W. Muggleton, A. W. Johnson, and N. Shaw, *Ann. N. Y. Acad. Sci.*, 112, 565 (1964).

through the reductive cleavage of the Co–C bond, which is the major side reaction. Only with highly reactive olefins is reduction of the organocobalt products sufficiently small to be neglected. In all other instances substituted ethanes are formed in appreciable quantity. The reductive cleavage is apparently catalyzed by unreacted cobaloxime(I). Thus, we have previously reported the observation that cobaloxime(I) slowly reacts with methylaquocobaloxime to produce cobaloxime(II) and methane.[2] An analogous reaction may be responsible for the reduction in other cases and could, for instance, explain the low yield of isopropylcobaloxime from propylene, since it is accompanied by a significant formation of propane. When diethyl maleate was allowed to react with the reduced cobaloximes, the main side reaction was the reduction to succinate, and the rest was isomerized to fumarate. Alkyl substituents on the olefinic substrate generally introduce lability, probably both for steric and electronic reasons. Thus, methyl methacrylate or crotonate undergo reduction to the saturated esters without allowing the isolation of organocobalt intermediates. Methylacrylonitrile under neutral conditions gives high yields of α-cyanoisopropylcobaloxime (eq 8). In alkaline

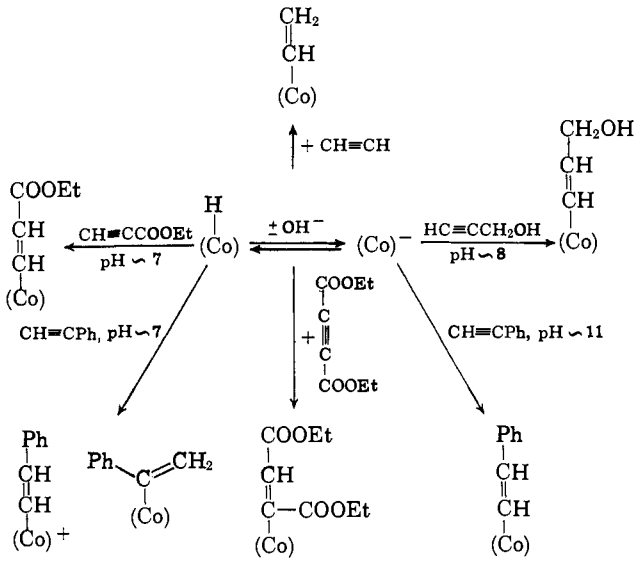


(8)

solution no product was obtained, indicating that the inductive effect of the methyl group lowers the electrophilicity of the olefinic system sufficiently to prevent the formation of the Co–C bond. Crotonitrile gives small yields of α-cyanopropylcobaloxime under neutral conditions, but mainly butyronitrile in alkaline medium. Owing to both steric and electronic effects of the carbomethoxy substituent, methyl methacrylate in neutral solution is similarly reduced to methyl isobutyrate, and no organocobaloxime could be isolated even when the reaction was interrupted prior to complete utilization of the olefinic substrate. In alkaline solution small amounts of the β-addition products were isolated, however. Vinyl acetate afforded small yields of acetoxyethylcobaloxime, but vinyl ethyl ether and α-methylstyrene were unreactive.

Reaction of Alkynes with Reduced Cobaloximes. We have already reported that acetylene reacts with reduced cobaloximes readily to form vinylcobaloxime.[2] Monosubstituted alkynes were found to form α- and β-substituted alkenylcobaloximes under conditions similar to those employed for the preparation of substituted alkyl derivatives. Phenylacetylene, for example, in alkaline solution gives excellent yields of β-phenylvinylcobaloxime. In approximately neutral solution about equal amounts of the α- and β-isomeric phenylvinylcobaloximes are formed and may be readily identified by nmr measurements. Ethyl propiolate, under neutral conditions, only yields the β-substituted product. Among disubstituted acetylenes dimethyl acetylenedicarboxylate gave 1,2-dicarbomethoxyvinylcobaloxime under all conditions. The observed reactions are summarized in Scheme II. Formation of the β-substituted vinylcobaloximes from alkynes requires *cis* addition to the triple bond since the final product must have *trans* configuration. Acetylene itself reacts with cobaloxime(II) to form a dimeric cobaloxime of composition B—(Co)—CH=CH—(Co)—B (B, *e.g.*, is pyridine or H_2O). This compound must contain the cobalt atoms attached to the ethylenic system in the *trans* position to be strain-free. Mono- or disubstituted alkynes did not yield such dimeric cobaloximes under similar conditions.

Scheme II. Reactions of Alkynes with Reduced Cobaloximes (base component is not included)



Reactions and properties of these alkenylcobaloximes have not yet been studied in detail and will be reported in forthcoming papers. The Co–C bond in them is not easily cleaved by acids or bases. Heating with concentrated hydrochloric acid is required, for example, to decompose β-phenylvinylcobaloxime.

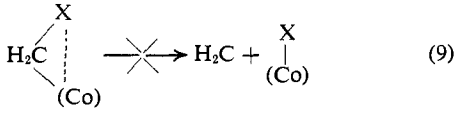
Properties and Reactions of Substituted Alkylcobaloximes. Thermal Decomposition. The behavior of simple alkylcobaloximes during thermal decomposition was reported previously.[2] The products of the cleavage of the Co–C bond are unrearranged paraffins and olefins, olefins being formed only when β-hydrogen is present.[2] The results are consistent with cobalt–carbon bond homolysis followed by prompt reaction of the organic radical with the cobaloxime(II) during the initial stage of the thermal cleavage. Under these conditions the lifetime of the organic radicals is short and hydrogen abstraction or addition to produce olefins, or paraffins, respectively, takes place preferentially. However, radical dimerization products (*e.g.*, ethane from $CH_3\cdot$) were detected, at least in a few instances. The pyrolysis of several functionally substituted cobaloximes has also been described.[3] Allylcobaloximes, for instance, form propylene, and β-hydroxyethylcobaloxime forms ethylene, both at lower temperature than the corresponding alkylcobaloximes. The decomposition temperature of substituted alkylcobaloximes appears to depend on electronic as well as steric factors. Thus, all α-substituted derivatives of ethylcobaloximes decomposed at lower temperature than the corresponding β-substituted derivatives. Isopropylpyridinatocobaloxime and *n*-propylpyridinatocobaloxime evolve propylene at 145 and 175–180°, respectively. Additional examples are shown in Table I. Particularly striking is the difference in thermal stability between α- and β-phenylethylcobaloximes. The α isomer decomposes around 90°, the β compound around 175°.

Table I. Approximate Pyrolysis Temperatures and Products of Various Alkylcobaloximes[a]

R	Approx dec temp, °C	Products[b]
CH_3	215–220	CH_4 (C_2H_6)
C_2H_5	185–190	C_2H_4 (C_2H_6)
CH_2CH_2CN	210–215	CH_2=$CHCN$, CH_3CH_2CN
$CH(CH_3)CN$	179–185	CH_2=$CHCN$, CH_3CH_2CN
CH_2CN	207	CH_3CN
CH_2Cl	210–220	CH_3Cl
$CH(CH_3)C_6H_5$	90	C_6H_5CH=CH_2 ($C_6H_5C_2H_5$)
$CH_2CH_2C_6H_5$	175	C_6H_5CH=CH_2 ($C_6H_5C_2H_5$)
CH_2COOH	200–210	CH_3COOH (CH_4,CO_2)
CH_2CH=O	180	CH_3CHO

[a] Base component, pyridine; solid complex *in vacuo*. [b] Products detected in small amounts are placed in parentheses.

Both saturated and unsaturated products are isolated from the decomposition of the substituted α- and β-ethylcobaloximes. This is apparently due to higher stabilization of the radicals produced, and these can undergo subsequent reactions such as hydrogen abstraction. The ratio of olefin:saturate can vary considerably from cobaloxime to cobaloxime for reasons which may be different in each individual case; for instance, secondary degradation or polymerization or hydrogen abstraction from other reaction fragments may take place. The photolytic behavior parallels, in essence, the results of the thermal decomposition. This clearly indicates that the primary step in both photolysis and pyrolysis must be the cleavage of the Co–C bond. Substitution of one proton in methylcobaloxime by Cl, COOH, $COOCH_3$, or CN does not significantly affect the thermal stability. We have tried to utilize α-halomethylcobaloximes as possible sources of methylene (eq 9). However, the suggested elimination reac-



(9)

tion is not favored at low reaction temperatures. The thermal decomposition of the carboxyl-, carbomethoxy-, and chloro- or cyanomethylcobaloximes yielded the respective acids, esters, CH_3Cl, or CH_3CN, respectively, and did not produce detectable quantities of products arising from radical dimerization reactions (Table I). Only small amounts of CH_4 and CO_2 were formed during the decomposition of the carboxymethylcobaloxime.[7] This indicates that the cobaloxime moiety does not enhance decarboxylation reactions.

Infrared Spectra and pK_a Values of Organocobaloxime Carboxylic Acids. Whereas the infrared spectra of most substituted organocobaloximes did not show any particularly striking features, we have found that the carbonyl stretching frequency of the organocobaloxime carboxylic acids is markedly affected by the proximity of the cobaloxime moiety. Thus, β-carbomethoxyethylpyridinatocobaloxime exhibits a band at 1711 cm^{-1} which is assigned to the perturbed carbonyl stretch. This band is shifted in the α-carbomethoxymethylpyridinato derivative to 1673 cm^{-1}. The corresponding acids show a similar shift (β = 1677, α = 1648 cm^{-1}). The same proximity effect of the cobaloxime moiety also affects the pK_a values of the acids. The β-carboxyethylpyridinatocobaloxime is a stronger acid (pK_a = 5.70; propionic acid, 4.87, both at 25°) than the α isomer (pK_a = 7.14). The axial base component was found to be of little effect on the acid strength. Finally, carboxymethyl(pyridinatocobaloxime) has the same pK_a as the α-carboxyethylcobaloxime derivative (pK_a = 7.14 at 25°). The β-carbethoxyvinyl- and the α,β-dicarbomethoxyethylene–pyridinatocobaloximes (pyCoCH=CHCOOEt and pyCoC(COOMe)=CHCOOMe) exhibited C=O stretching frequencies at 1714 and 1715–1689 cm^{-1}, respectively, thus in the general range of the saturated cobaloxime derivatives. It is apparent that the *trans* nature of these cobaloximes largely eliminates interactions of the ester group with the cobaloxime moiety. A particularly strong interaction seems to occur in α-acetylethylpyridinatocobaloxime (pyCoCH(CH_3)$COCH_3$), the reaction product of vinyl methyl ketone with reduced cobaloximes. The C=O stretch is observed in this case at 1638 cm^{-1}, indicating a rather significant lowering of the C=O π-bond order. It is not inconceivable that the carbonyl oxygen actually forms a weak hydrogen bridge with one of the oxime protons. In both α- and β-substituted cyanoalkylcobaloximes no significant shift in the nitrile stretching frequencies was observed. The bands attributable to the dimethylglyoximato ligands in the substituted alkylcobaloximes were found to vary somewhat with the nature of the axial base component; the effects, however, were similar to those observed in simple alkylcobaloximes.[2]

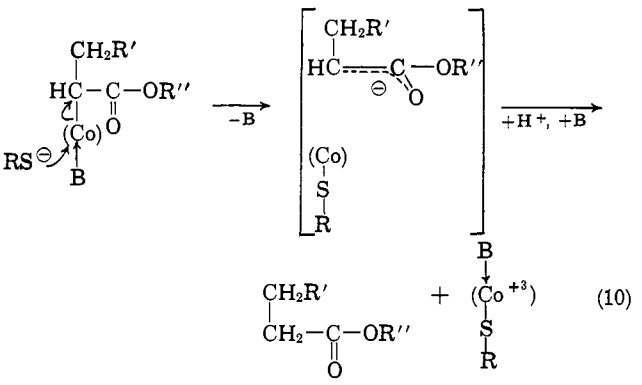
Nmr Spectra. The nmr spectra of all compounds reported were recorded and used as important evidence for the assigned structures. Because of the wide variety of compounds reported and the relative ease of interpretation, no attempt will be made to report or discuss the spectra of individual compounds in detail. In cobaloximes of the type $CH_3CH(X)$–$Co(D_2H_2)py$, the methyl protons appear as the expected doublet (J = 7 cps) at positions varying with the nature of X (X = $COCH_3$, 9.72; COOH, 9.64; COOEt, 9.61; CN, 9.43; C_6H_5, 9.40 ppm). The axial base also causes shifts; *e.g.*, $CH_3CH(COOEt)$–$Co(D_2H_2)py$ shows the methyl doublet at 9.61 and the corresponding aquocobaloxime at 9.91 ppm. The quartet of the tertiary proton is usually masked by the ligand methyl singlet but may be clearly seen in organocobalt derivatives of diphenylglyoxime. The protons of the attached base component, *e.g.*, pyridine, may readily be identified but do not show significant shifts on variation of the Co organyl group. In the organocobaloximes with strongly bound alkyl- or arylphosphine ligands, splitting of the proton signals due to interaction with ^{31}P has been observed.[2] It is of interest that even the protons of the dimethylglyoxime methyl groups show a small splitting of approximately 3 cps. We attribute this to the high degree of covalency in the Co–P, Co–C, and Co–N bonds in these complexes.

Polarographic Reduction. The results of polarographic measurements on simple alkylcobaloximes may be interpreted by the initial cleavage of the Co–C bond during the addition of the first electron.[2] Hence, the first polarographic wave is irreversible; it occurs in

(7) In the anaerobic photolysis of carboxymethylcobalamin, acetic acid (48%) is the main product; small amounts of succinic acid (5%) and CO_2 (13%) were also detected: L. Ljungdahl and E. Irion, *Biochemistry*, 5, 1846 (1966).

simple alkylcobaloximes around −1.7 v (relative to the Ag|0.10 *M* $AgNO_3$ electrode at 25°, in acetonitrile solution). The next wave appears at about −2.42 v and corresponds to the reduction of the cobaloxime(I) species to a zerovalent derivative. Beyond this point reduction of the ligands is observed. Frequently an additional band at around −2.8 v is found which probably is indicative of the reduction of dimethylglyoxime present in the solution. At about −3.0 v, reduction of the pyridine ligand occurs. The substituted organocobaloximes show a basically similar behavior. The first cathodic wave is somewhat substituent dependent and occurs in the range between −1.4 and −1.8 v. It is followed by a second wave which is usually not observed in the simple alkylcobaloximes. This wave is tentatively attributed to the reduction of the organic product formed from the cleavage of the Co–C bond. The remaining waves correspond to the reduction of the Co^I to the Co^0 species (at about −2.42 v), followed by dimethylglyoxime and pyridine reduction at −2.7 and −3.04 v, respectively. Molecular orbital calculations indicate that the lowest antibonding orbital in both cobaloximes and cobalamins with axial substituents is essentially the antibonding component of the combination of the d_{z^2} orbital with the σ-bonding orbitals of the axial ligands. This orbital does not appreciably interact with the vertical π-electron system of the ligands. According to the calculations, this orbital lies about 1.4 ev above the essentially nonbonding filled cobalt d orbitals, which is in accord with the polarographic data and the observed photosensitivity of both alkylcobaloximes and alkylcobalamins. The photochemical cleavage of the Co–C bond most likely occurs *via* the excitation of metal d electrons into the lowest antibonding orbital. Finally we wish to mention the exceptional behavior of two organocobaloximes on polarographic reduction. In the complexes RCo(D_2H_2)py, with R = CH=CHCOOEt or CH=CHPh, the first two cathodic waves occur in the normal range, but the two waves at −2.42 and −2.76 v were not detected. The fact that abnormal polarographic behavior was observed only in cobaloximes with unsaturated substituents R attached to the cobalt suggests that the substituents may act as electron traps preventing further reduction and decomposition of the resulting anionic organocobaloxime species.

Reactions of Substituted Alkylcobaloximes. The Co–C bond in alkylcobaloximes and -cobalamins may be cleaved reductively, and the same of course is also the case for the compounds carrying substituted alkyl groups. In fact, the latter are usually more readily cleaved than simple alkylcobaloximes. Of particular importance is the observation that thiols may be used as the cleaving agents, although they were found to be ineffective with alkylcobaloximes. The relative rate of reduction decreases in the order $CoCH(CH_3)COOR > CoCH_2CH_2COOR > CoCH(CH_3)CN > CoCH_2CH_2CN$. All α-carboxylic alkylcobaloximes are rapidly and nearly quantitatively reduced, which suggests that the carbonyl group assists the reduction (eq 10). The reduction is not accompanied by ester exchange. The α-substituted organocobaloximes are stable in 1 *N* HCl. Surprisingly, the α-organocobalt carboxylic esters are not even saponified under these conditions. For the saponification of the α-carbomethoxyethylcobaloxime, for example, treatment with warm, concentrated H_2SO_4 (!) followed by addition of water was necessary. This behavior apparently results from the hindrance of the equatorial ligands of the cobaloxime moiety. Although protonation of the ester methoxy group is possible, subsequent SN2 displacement of methanol by water is apparently severely inhibited for steric reasons. The carbomethoxymethylcobaloxime is also saponified by the sulfuric acid treatment, with little degradation. In contrast, β-carbomethoxyethylcobaloxime is quantitatively saponified in 1 *N* HCl, and 1,2-dicarboethoxyethylcobaloxime is selectively hydrolyzed to the α-monoester.



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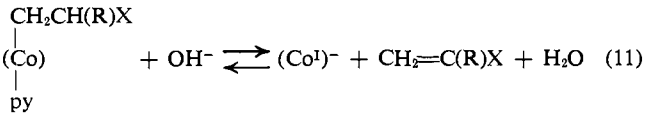
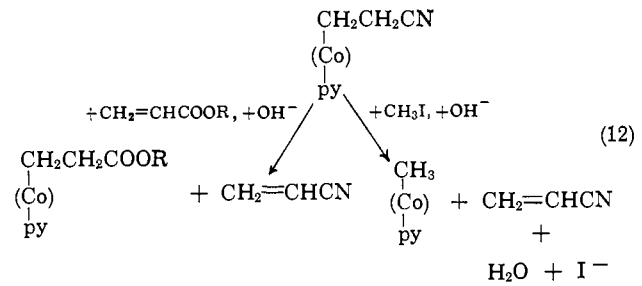
With alkaline reagents β-substituted alkylcobaloximes undergo elimination to the substituted olefin and cobaloxime$_s$ by a reversal of the formation reaction (eq 11). Under carefully controlled alkaline conditions



(11)

a slow rearrangement of the β-substituted ethylcobaloximes into the α isomers was also noted. The facile cleavage of the Co–C bond to form the nucleophilic cobalt species may also be utilized for organyl group exchange reactions (eq 12). The reactivity of



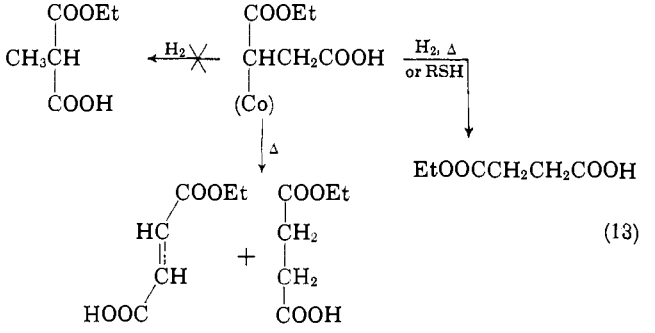
(12)

the α-substituted organylcobaloximes toward alkali varies. For instance, α-acetylethylcobaloxime is readily cleaved to methyl ethyl ketone and cobaloxime(III); in this case, only small amounts of cobaloxime(I) and the parent vinylog, methyl vinyl ketone, are formed which clearly indicates how sensitively the nature of the organyl group attached to the cobalt affects the reactivity and product distribution. The α-carbomethoxyalkylcobaloximes, on the other hand, are soluble in aqueous alkali without decomposition or saponification.

Biochemical Implications

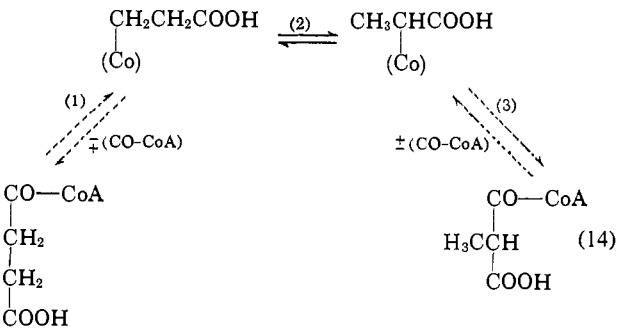
Among the reactions described in this paper, the unusual formation and isomerization of α- and β-sub-

stituted ethylcobaloximes may have biochemical implications. An isomerization of this type could be involved in the cobalamin-dependent rearrangement of succinyl-CoA to methylmalonyl-CoA.[8] To explain the mechanism of this unusual and enigmatic reaction it must be assumed that the carboxy-CoA group becomes significantly labilized or even temporarily detached from the remaining propionic acid moiety. Although we have not yet obtained positive evidence for this labilization from model experiments, it is at least established that the cobalt atom does not facilitate decarboxylation reactions or carboxyl group migration in α- or β-carboxylalkylcobaloximes. We have pointed out previously that the decarboxylation during the thermal decomposition of carboxymethylcobaloxime is a minor side reaction which only occurs at high reaction temperature. To see if the migration of a carboxyl group could take place, we have prepared the 1,2-dicarboethoxyethylcobaloxime and saponified it to the α-monoester. Subsequent degradation under various conditions gave no decarboxylation or carboxyl group migration, even in the presence of thiols (eq 13).



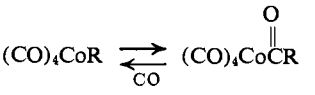
(13)

It is of interest to note, furthermore, that the 1,2-dicyanoethylcobaloxime obtained from fumaronitrile and reduced cobaloxime exhibits an unusual nmr spectrum in which only one signal of the $>CHCH_2-$ protons is present besides the signal of the dimethylglyoxime methyl protons. In principle, the absence of the AB_2 pattern in the nmr could, however, be compatible with the rearranged structure $CH_3C(CN)_2Co$ of the Co organyl moiety. The complex was therefore carefully degraded under various conditions. The only products were succinonitrile and fumaronitrile, and not even a trace of methylmalononitrile could be detected. We conclude that the succinic–methylmalonic mutase reaction must involve the reversible removal of the CO–CoA group, functioning in close connection with the cobalamin. If this view is accepted, the succinic–methylmalonic rearrangement may be formulated as follows: (1) temporary removal of the CO–CoA group, leading to the formation of carboxyethylcobalamin; (2) isomerization of the carboxyethylcobalamin; (3) reattachment of the CO–CoA group and formation of methylmalonyl-CoA. The mechanism is summarized in eq 14. The key step (2) corresponds to the mechanism proposed by Whitlock,[9a] which was based on reactions of cobalt carbonyls in hydroformylation. Hydrocarbonylation of methyl acrylate with cobalt hydrocarbonyl at 0° followed by methanolysis



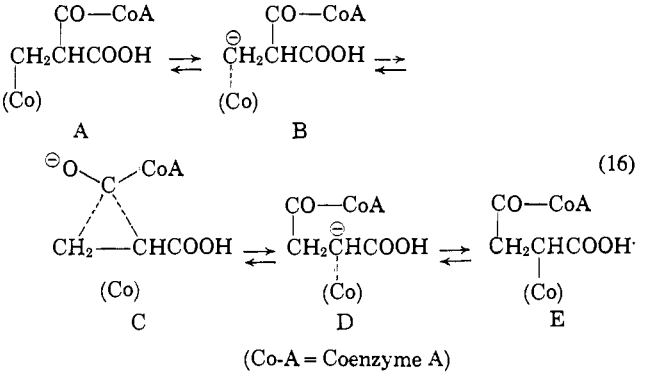
(14)

afforded a 5:1 mixture of methyl malonate and methyl succinate.[9b] Although it is very tempting to draw this analogy, it should not be carried too far. The Co–C bond in alkylcobalt tetracarbonyls is much more reactive than that in alkylcobalamins (or -cobaloximes). Whereas the former readily undergo reversible CO insertion (eq 15), no such reaction was observed with



(15)

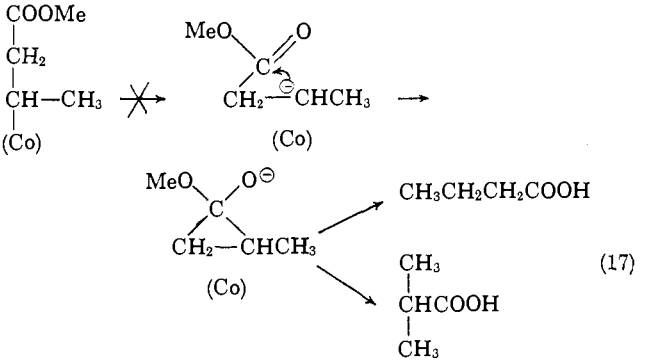
various substituted and unsubstituted alkylcobaloximes. A difficulty with this mechanism is the way in which it is assumed that the carbon monoxide remains attached to the cobalamin in the course of the reaction. A mechanism was proposed by Ingraham[10] in which the cobalamin was mainly seen to facilitate the formation of a carbanion which would subsequently rearrange *via* a cyclic three-membered intermediate. This mechanism, shown in slightly modified form in eq 16,



(16)

(Co-A = Coenzyme A)

invokes ring opening of a cyclopropanone hemiketal (C) which is supported by the observed base-catalyzed reactions of cyclopropanone derivatives.[11] We have therefore tried to generate carbanions resembling **B** or **D** by decomposing the cobaloxime shown in eq 13, as well as the carbomethoxyisopropylcobaloxime of eq 17



(17)

(8) See *Ann. N. Y. Acad. Sci.*, 112 (1964), for detailed discussion and literature references.

(9) (a) H. W. Whitlock, *ibid.*, 112, 721 (1964); (b) R. F. Heck and D. S. Breslow, *J. Am. Chem. Soc.*, 83, 4023 (1961).

(10) L. L. Ingraham, *Ann. N. Y. Acad. Sci.*, 112, 713 (1964).

(11) P. Lipp, J. Buchkremer, and H. Seeles, *Ann.*, 499, 1 (1932).

Table II. Analyses and Synthesis Conditions of Substituted Alkylcobaloximes

Product, $RCo(D_2H_2)B$					Calcd, %			Found, %		
R	B	Olefin	Conditions employed	Molecular formula	C	H	N	C	H	N
$CH_2(OAc)CH_3$	C_5H_5N	Vinyl acetate	Neutral	$C_{17}H_{26}N_5O_6Co$	44.83	5.76	15.38	45.71	6.02	14.91
$CH(CH_3)COOH$	H_2O	Acrylic acid	Neutral	$C_{11}H_{21}N_4O_7Co$	34.73	5.57	14.74	34.53	5.69	14.45
$CH(CH_3)COOH$	C_5H_5N	Acrylic acid	Neutral	$C_{16}H_{24}N_5O_6Co$	43.53	5.48	15.87	43.72	5.68	15.76
$CH(CH_3)COOMe$	H_2O	Methyl acrylate	Neutral	$C_{12}H_{23}N_4O_7Co$	36.55	5.88	14.21	36.25	6.21	14.65
$CH(CH_3)COOMe$	C_5H_5N	Methyl acrylate	Neutral	$C_{17}H_{26}N_5O_6Co$	44.83	5.76	15.38	44.97	5.82	15.28
$CH(CH_3)COOMe$	$(C_4H_9)_3P$	Methyl acrylate	Neutral	$C_{24}H_{48}N_4O_6CoP$	49.79	8.36	9.68	50.03	8.54	9.77
CH_2CH_2COOMe	C_5H_5N	Methyl acrylate	Alkaline	$C_{17}H_{26}N_5O_6Co$	44.83	5.76	15.38	44.49	5.95	15.44
$CH(CH_3)COOEt$	C_5H_5N	Ethyl acrylate	Neutral	$C_{18}H_{28}N_5O_6Co$	45.66	5.96	14.80	45.78	6.19	14.93
CH_2CH_2COOEt	C_5H_5N	Ethyl acrylate	Alkaline	$C_{18}H_{28}N_5O_6Co$	45.66	5.96	14.80	45.42	5.80	14.71
$CH_2CH(CH_3)COOMe$	C_5H_5N	Methyl methacrylate	Alkaline	$C_{18}H_{28}N_5O_6Co$	45.66	5.96	14.80	47.45	6.26	

Table III. Analyses and Synthesis Conditions of Substituted Alkylcobaloximes

Product, $RCo(D_2H_2)B$					Calcd, %			Found, %		
R	B	Olefin	Conditions employed	Molecular formula	C	H	N	C	H	N
$CH(CH_3)COCH_3$	C_5H_5N	Methyl vinyl ketone	Neutral	$C_{17}H_{26}N_5O_5Co$	46.47	5.96	15.94	46.19	5.92	15.97
$CHCH_2COOEt$ $COOEt$	H_2O	Diethyl maleate or fumarate	Neutral	$C_{16}H_{29}N_4O_9Co$	34.36	5.23	10.02	34.53	5.43	10.11
$CHCH_2COOEt$	C_5H_5N	Diethyl maleate or fumarate	Neutral	$C_{21}H_{32}N_5O_8Co$	46.58	5.96	12.94	46.44	6.19	13.24
$CH(CH_3)CN$	C_5H_5N	Acrylonitrile	Neutral	$C_{16}H_{23}N_6O_4Co$	45.50	5.49	19.90	45.77	5.58	19.99
$CH(CH_3)CN$	$(C_4H_9)_3P$	Acrylonitrile	Neutral	$C_{25}H_{45}N_5O_4CoP$	50.53	8.30	12.81	50.79	8.06	12.77
$CH(CH_3)CN$	$C_6H_5NH_2$	Acrylonitrile	Neutral	$C_{17}H_{25}N_6O_4Co$	46.79	5.77	19.26	46.73	5.88	19.11
CH_2CH_2CN	C_5H_5N	Acrylonitrile	Alkaline	$C_{16}H_{23}N_6O_4Co$	45.50	5.49	19.90	45.84	5.58	19.56
$CH_2CH(CH_3)CN$	C_5H_5N	Methacrylonitrile	Neutral	$C_{17}H_{25}N_6O_4Co$	46.79	5.78	19.27	46.83	5.57	18.93
$CH_2CH(CH_3)CN$	$C_6H_5NH_2$	Methacrylonitrile	Neutral	$C_{18}H_{27}N_6O_4Co$	48.00	5.60	18.66	47.59	6.41	18.44
$CH(CN)CH_2CH_3$	C_5H_5N	Crotonitrile	Neutral	$C_{17}H_{25}N_6O_4Co$	46.79	5.78	19.27	46.88	6.03	19.35
$CH(CN)CH_2CN$	C_5H_5N	Fumaronitrile	Neutral	$C_{17}H_{22}N_7O_4Co$	45.65	4.96	21.92	45.34	5.19	21.88

in alkaline solution, but the failure to detect a mixture of *n*-butyric and isobutyric acids after saponification (only *n*-butyric acids was formed) suggests that formation of the cyclopropanone hemiketal evidently did not take place. (See reaction series in eq 17.) We therefore do not further specify the detailed fashion in which the CO-CoA group migrates until further experimental evidence becomes available. It seems to be clear, however, that the mutase must be rather highly specialized and relatively complicated. In addition, it is possible that the cobamide cofactor is not as centrally involved in the rearrangement as has been assumed. We have so far not been able to verify the conversion of β-substituted ethylcobalamins into the α isomers, primarily because the secondary organyl cobalamins are rather unstable. This, of course, does not mean that such rearrangements cannot occur, but demonstrates some of the difficulties that arise in studying model reactions with the vitamin itself.

In the meantime the properties of the Co-C bond in several substituted alkylcobalamins (RCo) were reported for R = CH_2COOH, CH_2COOCH_3, CH_3, CH_2CH_2CN, CH_2CH_2OH, $CH_2CH_2OCH_3$, CH_2CH_2COOH, $CH_2CH_2COOCH_3$, $CH_2CH_2CH_3$, and CH_2CH_3.[12,13] All corresponding cobaloximes are known and exhibit similar reactivities. For instance, only the β-hydroxyethyl- and the β-methoxyethylcobalamins in the above series were found to be sensitive to acid, in agreement with the properties of the respective cobaloxime derivatives.[3] With cyanide, the β-cyanoethyl- as well as the β-carbomethoxyethylcobalamin were initially reported to react rather rapidly in dilute solution,[12] which contradicts our observations on the cobaloximes. It was later shown,[13] however, that it was the OH^- and not the cyanide ion which had actually reacted. The base cleavage of the Co-C bond in β-cyanoethylcobalamin also produces the nucleophilic Co(I) species as was shown by a *trans*-alkylation reaction analogous to eq 12.[13] It will be of interest to compare the reaction rates of alkylcobalamins with those of alkylcobaloximes. Qualitative experiments indicate that the alkylcobalamins are somewhat more labile than the corresponding cobaloximes. This may be due in part to slight differences in the effective strength of the corrin and the dimethylglyoxime ligands, but even more to the greater steric effect of the corrin ligand system.

Experimental Section

Preparation of Substituted Alkylcobaloximes. In view of the many derivatives prepared, a detailed description of the procedures employed will be limited to several specific examples.[14] Information regarding the preparation of cobaloximes may be drawn also from the attached Tables II–VI. Decomposition points are reported only in a few cases; they are usually of little diagnostic value. When heated near the decomposition temperature certain of the cobaloximes decompose violently and the use of proper safety equipment is advisable.

α-Cyanoethylpyridinatocobaloxime. To a 1.5-l. flask purged with nitrogen there was added 50.0 g of cobalt acetate (0.2 mole) and 46.4 g (0.4 mole) of dimethylglyoxime. Then 750 ml of metha-

(12) H. P. C. Hogenkamp, J. E. Rush, and C. A. Swenson, *J. Biol. Chem.*, 240, 3641 (1965).

(13) R. Barnett, H. P. C. Hogenkamp, and R. H. Abeles, *ibid.*, 241, 1483 (1966).

(14) A number of convenient laboratory procedures will be published in a forthcoming volume of *Inorganic Syntheses*.

Table IV. Analyses and Synthesis Conditions for Substituted Alkyl- and Alkenylcobaloximes

Product, $RCo(D_2H_2)B$ R	B	Olefin	Conditions employed	Molecular formula	Calcd, % C	H	N	Found, % C	H	N
$CH(CH_3)C_6H_5$	H_2O	Styrene	Alkaline or neutral	$C_{16}H_{24}N_4O_5Co$	46.61	6.13	13.59	46.77	6.31	13.17
$CH(CH_3)C_6H_5$	C_5H_5N	Styrene	Alkaline or neutral	$C_{21}H_{27}N_5O_4Co$	53.28	5.96	14.80	52.89	6.17	15.11
$CH{=}CHCOOEt$	H_2O	Ethyl propiolate	Neutral	$C_{13}H_{23}N_4O_7Co$	38.43	5.71	13.79	38.51	5.79	13.58
$CH{=}CHC_6H_5$	H_2O	Phenylacetylene	Alkaline	$C_{16}H_{23}N_4O_5Co$	46.83	5.65	14.00	47.30	5.92	13.71
$CH{=}CHC_6H_5$	C_5H_5N	Phenylacetylene	Alkaline	$C_{21}H_{26}N_5O_4Co$	53.50	5.56	15.86	53.84	5.68	15.49
COOMe | $C{=}CHCOOMe$	C_5H_5N	Dimethyl acetylene-dicarboxylate	Alkaline or neutral	$C_{19}H_{26}N_5O_8Co$	44.62	5.12	13.70	44.66	5.27	14.06

Table V. Analyses and Synthesis Conditions for Substituted Alkyl- and Alkenylcobaloximes

Product, $RCo(D_2H_2)B$ R	B	Preparation of starting material or method	Molecular formula	Calcd, % C	H	N	Found % C	H	N
CH_2Cl	H_2O	CH_2Cl_2	$C_9H_{18}N_4O_5CoCl$	30.31	5.09	15.71	30.62	5.28	15.66
CH_2Cl	C_5H_5N	CH_2Cl_2	$C_{14}H_{21}N_5O_4CoCl$	40.25	5.06	16.77	40.45	5.32	17.01
CH_2Cl	None	Dehydration of aquo compound	$C_9H_{16}N_4O_4CoCl$	31.91	4.76	16.54	31.81	4.93	16.22
CH_2Cl	$(CH_3)_2S$	CH_2Cl_2	$C_{11}H_{22}N_4O_4CoClS$	32.96	5.53	13.98	33.28	5.66	14.09
CH_2I	C_5H_5N	CH_2I_2	$C_{14}H_{21}N_5O_4CoI$	33.02	4.16	13.76	33.28	4.29	13.31
$CH_2C_6H_5$	$P(C_6H_5)_3$	$C_6H_5CH_2Cl$	$C_{33}H_{36}N_4O_4PCo$	61.68	5.65	8.72	61.44	5.49	8.59
$CH{=}CH_2$	C_5H_5N	$CH_2{=}CHBr$	$C_{15}H_{22}N_5O_4Co$	45.58	5.61	17.72	45.92	5.66	17.70
$CH_2CH(OMe)_2$	C_5H_5N	$BrCH_2CH(OMe)_2$	$C_{17}H_{28}N_5O_6Co$	44.64	6.18	15.32	44.77	6.26	15.28
CH_2CHO	C_5H_5N	Acid hydrolysis of acetal	$C_{15}H_{22}N_5O_5Co$	43.80	5.39	17.03	43.92	5.34	17.00
CH_2CN	C_5H_5N	$ClCH_2CN$	$C_{15}H_{21}N_6O_4Co$	44.12	5.18	20.59	44.28	5.36	20.37
CH_2COOMe	C_5H_5N	$ClCH_2COOMe$	$C_{16}H_{24}N_5O_6Co$	43.54	5.48	15.87	43.52	5.57	15.79
CH_2COOMe	Benzimidazole	Base displacement of pyridine	$C_{18}H_{25}N_6O_6Co$	45.00	5.25	17.50	45.11	5.31	17.22
CH_2COOH	C_5H_5N	Acid hydrolysis of ester	$C_{15}H_{22}N_5O_6Co$	42.16	5.19	16.39	42.32	5.22	16.18
$CH(CH_3)CH_2COOMe$	C_5H_5N	$CH_3CHBrCH_2COOMe$ and cobaloxime(II)	$C_{18}H_{28}N_5O_6Co$	45.66	5.96	14.80	45.76	6.18	15.00

Table VI. Analyses and Synthesis Conditions for Substituted Alkyl- and Alkenylcobaloximes

Product, $RCo(D_2H_2)B$ R	B	Preparation of starting material or method	Molecular formula	Calcd, % C	H	N	Found, % C	H	N
$-CH{=}CH-$	H_2O	Acetylene + $Co(D_2H_2)\cdot 2H_2O$	$C_{18}H_{36}N_8O_{11}\text{-}Co_2\cdot H_2O$	32.84	5.52	17.02	32.66	5.63	16.74
$-CH{=}CH-$	C_5H_5N	Acetylene + $[Co(D_2H_2)\cdot C_5H_5N]_2$	$C_{14}H_{20}N_5O_4Co$	44.09	5.29	18.11	44.11	5.07	18.32
CH_2CH_2COOMe	$(C_4H_9)_3P$	Base displacement in acetic acid-methanol	$C_{24}H_{48}N_4O_6CoP$	49.79	8.36	9.68	50.01	8.24	9.44
CH_2CH_2COOH	C_5H_5N	Acid hydrolysis of ester	$C_{16}H_{24}N_5O_6Co$	43.53	5.48	15.87	43.41	5.78	15.66
$CH(CH_3)COOEt$	NH_3	Displacement of pyridine base in concentrated NH_3	$C_{13}H_{26}N_5O_6Co$	38.33	6.44	17.20	38.23	6.39	16.89
COOEt | $CHCH_2COOH$	C_5H_5N	Acid hydrolysis of ester	$C_{19}H_{30}N_5O_9Co$ (hydrate)	42.94	5.69	13.18	43.32	5.61	13.41
$CH_2C(CH_3)COOEt$	C_5H_5N	$BrCH_2C(CH_3)COOEt$	$C_{19}H_{30}N_5O_6Co$	47.20	6.25	14.49	46.92	5.95	14.73
COC_6H_5	$(C_4H_9)_3P$	$ClCOC_6H_5$	$C_{27}H_{46}N_4O_4CoP$	55.75	7.97	9.64	55.64	8.13	9.68
$CH_2COC_6H_5$	C_5H_5N	$BrCH_2COC_6H_5$	$C_{21}H_{26}N_5O_5Co$	51.75	5.38	14.37	51.70	5.41	14.35
$CH_2CH_2C_6H_5$	C_5H_5N	$BrCH_2CH_2C_6H_5$	$C_{21}H_{27}N_5O_4Co$	53.28	5.96	14.80	53.63	6.02	14.46

nol was added and the suspension stirred until all dimethylglyoxime was dissolved and formation of $Co(D_2H_2)\cdot 2H_2O$ was complete. Next 13.5 g (0.25 mole) of acrylonitrile was added and the flask purged with hydrogen. On stirring at 20–25°, 2.5 l. of hydrogen was absorbed, which ceased as the solution became homogeneous. The solution was filtered, diluted with two volumes of water, and stirred. On addition of 16 g (0.2 mole) of pyridine the desired product crystallized and was collected by filtration, washed with water, and air dried, yield 76.0 g (90%).

Products with bases other than pyridine result when the solution of α-cyanoethylaquocobaloxime is treated with aniline, tributylphosphine, etc. The base may also be added prior to the hydrogenation.

The procedure may be modified for use with cobalt chloride, but stoichiometric amounts of alkali must be employed.

β-Cyanoethylpyridinatocobaloxime. A suspension of 95.2 g (0.4 mole) of $CoCl_2\cdot 6H_2O$ and 92.8 g (0.8 mole) of dimethylglyoxime in 1500 ml of methanol was stirred until the cobalt chloride had dissolved and then, under nitrogen, 32.0 g (0.8 mole) of NaOH in 100 ml of water was added, followed by 32 g (0.4 mole) of pyridine. The suspension was stirred and cooled to room temperature when 27 g (0.5 mole) of acrylonitrile was added. Over 5 min a solution of 4.0 g (0.1 mole) of NaOH in 25 ml of water was added. The flask was flushed with hydrogen and after 20 min, 5.1 l. of hydrogen had been absorbed and the rate of absorption had decreased to about one-third the maximum rate. The suspension of yellow

crystals was poured into 2 l. of water, and then 10 ml of acetic acid was added and the suspension stirred under air to oxidize traces of $[pyCo(D_2H_2)]_2$. The crystals were then filtered, washed with water, and air dried, yield 117 g (70%). The product was recrystallized from methanol–water.

Methylpyridinatocobaloxime from β-Cyanoethylpyridinatocobaloxime. To a suspension of 12.7 g (0.03 mole) of β-cyanoethylpyridinatocobaloxime in 75 ml of methanol and 5 ml of methyl iodide, there was added with stirring 2.0 g (0.05 mole) of NaOH in 10 ml of water. The solution soon became homogeneous and shortly after crystals of methylpyridinatocobaloxime formed. The yield was 9.2 g (80%).

β-Carboethoxyethylpyridinatocobaloxime. A suspension of 47.6 g (0.2 mole) of $CoCl_2 \cdot 6H_2O$ and 46.4 g (0.4 mole) of dimethylglyoxime in 800 ml of ethanol was stirred until the cobalt chloride had dissolved, and then 16 g (0.4 mole) of NaOH in 100 ml of water was added, followed by 16 g (0.2 mole) of pyridine. When complex formation was complete 20 g (0.2 mole) of ethyl acrylate was added, followed by 4.0 g (0.1 mole) of NaOH in 25 ml of water. After 5 min the solution was homogeneous and was added to 2 l. of water containing 10 ml of acetic acid. The solution was filtered and the filtrate extracted with methylene chloride. From the methylene chloride concentrate, on recrystallization from water–methanol, there was obtained 21 g (45%) of orange plates.

Vinylpyridinatocobaloxime. A suspension of 0.1 mole of $[pyCo(D_2H_2)]_2$ in 750 ml of methanol was prepared as described above from cobalt chloride. The suspension was kept saturated with vinyl chloride while 8.0 g (0.2 mole) of NaOH in 50 ml of water was added. The solution was filtered, concentrated to 400 ml, and diluted with 1 l. of water, affording 28.2 g (71%) of yellow crystals.

Chloromethylpyridinatocobaloxime. This product is formed very readily by any of the procedures utilized for preparing alkylcobaloximes. Consequently it is occasionally encountered as an undesirable product during extractions when traces of Co^{II} or Co^{I} are present, *e.g.*, alkaline solutions of β-cyanoethylcobaloxime.

β-Phenylvinylaquocobaloxine. To a stirred suspension of 0.2 mole of $Co(D_2H_2) \cdot 2H_2O$ in 700 ml of methanol there was added 10.2 g of phenylacetylene, and this was then stirred for 5 min with 4.0 g (0.1 mole) of NaOH in 20 ml of water. After filtering the solution and dilution with 1 l. of H_2O there was obtained 24.6 g (63%) of yellow crystals.

Carboxymethylpyridinatocobaloxime. To 70 ml of concentrated sulfuric acid there was added with stirring 20 g of carbomethoxymethylpyridinatocobaloxime in small portions (safety shield). The acid was warmed to about 40° to aid solution and, after 1 hr of standing, poured into 2 l. of water. This solution was made alkaline with KOH, then acidified with acetic acid and cooled, yielding 13.5 g (69%) of orange platelets. The product is purified by dissolving in dilute $NaHCO_3$ and reprecipitating with acetic acid.

2,2-Dimethoxyethylpyridinatocobaloxime. To a suspension of 65.0 g (0.2 mole) of $(Co(D_2H_2) \cdot 2H_2O$ prepared in 700 ml of methanol, there was added, at 0°, 25.4 g (0.15 mole) of bromoacetaldehyde dimethyl acetal, followed by 8.0 g (0.2 mole) of NaOH in 50 ml of water over 10 min. The resulting solution was diluted with water and extracted with methylene chloride containing pyridine. The product was recrystallized from methanol–water, yield 6.4 g (14%) of yellow crystals. If alkaline conditions are not present during all stages, brown crystals of the corresponding aldehyde are isolated.

Conversion of β-Cyanoethylcobaloxime into the α Isomer. A suspension of 3 g of β-cyanoethylpyridinatocobaloxime in 25 ml of methanol–water (1:1) was stirred in an atmosphere of hydrogen while a 1 *N* solution of NaOH was slowly added until the pH of the solution was approximately 11. After 5 hr of continued stirring 1 *N* hydrochloric acid was slowly added up to a pH of about 7. The reaction mixture was subsequently poured into 100 ml of water and filtered. The yellow product was washed with water and dried. Examination of the nmr spectrum revealed that it consisted of a mixture (approximately 1:2.5) of α-cyanoethylcobaloxime and the β isomer. The α derivative is readily recognized by the methyl doublet at 9.43 ppm, $J = 7$ cps, and by the fact that it is stable in 20% KOH solution.

Reactions of Substituted Alkylcobaloximes. The reactions of the organocobaloximes were carried out as indicated in the text; the procedures were straightforward in all cases and need not be described in this section. The products of the various cleavage reactions were identified by usual methods (gas–liquid chromatography infrared, nmr, and mass spectroscopy.

The polarographic measurements were carried out by Dr. D. C. Olson on an ORNL controlled potential instrument, Model Q-1988 A, using a Varian F-80 X–Y recorder. The pyrolysis experiments were performed without solvent *in vacuo* at the temperatures given in the text. The volatile products were collected by vacuum condensation and identified as indicated above. Gaseous products were transported into a gas-sample tube and analyzed mass spectrographically.

Attempted Rearrangement Reactions. Samples of the pyridinatocobaloximes, $RCo(D_2H_2)py$ with $R = EtOOC\dot{C}HCH_2COOH$, were decomposed without solvent *in vacuo* at about 200°. The volatile products consisted of a mixture of monoethyl fumarate and monoethyl succinate. Decomposition in the presence of H_2 (10 atm) afforded only monomethyl succinate. The complex (5 g in 50 ml of ethanol) was allowed to stand in the dark in the presence of 5 ml of CH_3SH for 1 week. Glpc analysis of the remaining solution indicated the presence of monoethyl succinate and a trace of monoethyl fumarate. Similar experiments were also carried out with the cobaloximes with $R = NC\dot{C}HCH_2CN$ and $R = CH_3CHCH_2COOCH_3$. Rearrangement products (*e.g.*, methylmalononitrile or isobutyric ester) could not be detected. Similarly, no rearrangement occurred in alkaline (pH 11) solutions of mercaptans.

The Infrared Spectra and Structure of Methylamine Complexes of Platinum(II)

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Abstract: The infrared spectra of the complexes *cis*-$[Pt(CH_3NH_2)_2X_2]$, *trans*-$[Pt(CH_3NH_2)_2X_2]$, $[Pt(CH_3NH_2)_4]X_2$, and $[Pt(CH_3NH_2)_4][PtX_4]$ ($X = Cl^-, Br^-$) have been measured and assignments made in the region 200–4000 cm^{-1}. The structure of each complex has been elucidated through a group theoretical treatment of the observed spectra of the crystalline complexes.

In order to interrelate the vibrational assignments for the ammonia[1] and ethylenediamine[2,3] complexes of platinum(II), the infrared spectra of certain methylamine complexes have been studied; the results are reported here.

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