Cobalt–Carbon Bond Cleavage in Substituted Alkylcobalamins and Alkylcobaloximes. Evidence for d-Orbital Participation and Olefin π Complexes of Cobalt(I) Nucleophiles

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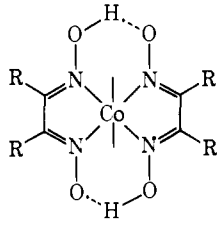
Abstract: Alkylcobaloximes and alkylcobalamins carrying inductively electron attracting substituents in the β position undergo β elimination with metal participation. The initial products in the cobaloxime reactions are shown to be π complexes of the Co(I) nucleophiles which are at equilibrium with the free cobaloximes(I) and the olefinic elimination product. Optical spectra and properties of solutions of the new π complexes are reported, including adducts of cobaloximes(I) with carbon monoxide. The new complexes are stabilized essentially through π back-bonding. The metal participation in the elimination reactions similarly involves interactions of the cobalt $3d_{xz}$ or $3d_{yz}$ orbitals with the antibonding π^* MO of the emerging olefin. The mechanism of the d-orbital-assisted β eliminations is discussed in relation to other cobalt–carbon bond cleavage reactions of cobaloximes and cobalamins. Nmr measurements suggest a reversible valence tautomerization in 1,2-dicyanoethyl(pyridine)cobaloxime and in related compounds.

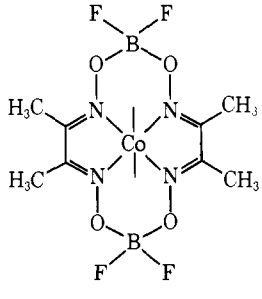
Reactions of organocobalt derivatives of vitamin B_{12} leading to the reversible cleavage of the carbon–cobalt bond are of interest concerning the function of the cobinamide cofactor in enzymatic reactions. Apart from coenzyme B_{12}, which recently was shown to undergo Co–C bond cleavage by an alkali-induced β elimination,[2] similar reactions have been described for a number of 2-substituted organocobaloximes[3,4] and -cobalamins.[5] In the present paper we report on the mechanism of these remarkable reactions. We will first outline the principal features of the system of Co(I) nucleophile-substituted olefins and discuss the properties of a class of novel π complexes whose existence was postulated previously[2] but which thus far have not been described in detail.

π-Complexes of Co(I) Nucleophiles

Formation and Properties. The addition of excess ethyl acrylate or acrylonitrile to aqueous solutions of the blue-green cobaloximes(I) (**1** and **2**) at pH 10 does not yield the substituted alkylcobaloximes directly. In a very rapid reaction red to purple complexes are formed first, which only subsequently undergo further chemical change to yield the organocobaloximes. In more strongly alkaline (0.1–1 *M* NaOH) solutions β-ethylcarbethoxycobaloximes are incapable of existence, and the ethyl acrylate–cobaloxime π complex is formed, as follows from spectroscopic measurements (Figures 1 and 2). The complex is not very stable and is at equilibrium with ethyl acrylate and the free Co(I) nucleophile. Accordingly, the olefinic ligand may be removed by merely passing a stream of oxygen-free argon through the solutions of the complex. The ethyl acrylate may also be displaced by other olefinic ligands, *e.g.*, acrylonitrile or fumaronitrile, or by coordinating ligands such as pyridine or alkylphosphines. With the exception of very strongly interacting ligands such as fumaronitrile the equilibria involving the displacement of π-bonded olefins are readily reversible. For example, the purple solution of the ethyl acrylate–cobaloxime(I) π complex turns green upon the addition of excess pyridine, but is regenerated on adding a large excess of ethyl acrylate. Since the free Co(I) nucleophile is at equilibrium with the π complex, formation of alkylcobaloximes occurs upon adding alkyl halides. The rates of alkylation are significantly diminished as compared to those of the free Co(I) nucleophiles and become very slow in the presence of excess of olefinic ligand. This indicates that the π complexes themselves are not reactive, and that the alkylation occurs only *via* the equilibrium amounts of free Co(I) nucleophile present. The characteristic red color of the cobaloxime(I)–ethyl acrylate π complex also appears on adding base to the originally yellow solutions of β-ethylcarbethoxy(pyridine)cobaloxime under anaerobic conditions. Subsequent experiments revealed that the properties of other β-substituted alkylcobaloximes closely resemble those of the ethylcarbethoxy derivative, whose principal properties and reactions are summarized in Scheme I. The analogous conversion of 2-carboxyethylcobaloximes into the π complex has not been observed even in hot 6 *M* NaOH, under conditions where



1a, Dmg; R = CH_3
b, Dpg; R = C_6H_5



2, $DmgB_2F_4$

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(2) G. N. Schrauzer and J. W. Sibert, *J. Amer. Chem. Soc.*, **92**, 1022 (1970).

(3) G. N. Schrauzer and R. J. Windgassen, *ibid.*, **89**, 1999 (1967).

(4) G. N. Schrauzer, *Accounts Chem. Res.*, 1, 97 (1968).

(5) R. Barnett, H. P. C. Hogenkamp, and R. H. Abeles, *J. Biol. Chem.*, **241**, 1483 (1966).

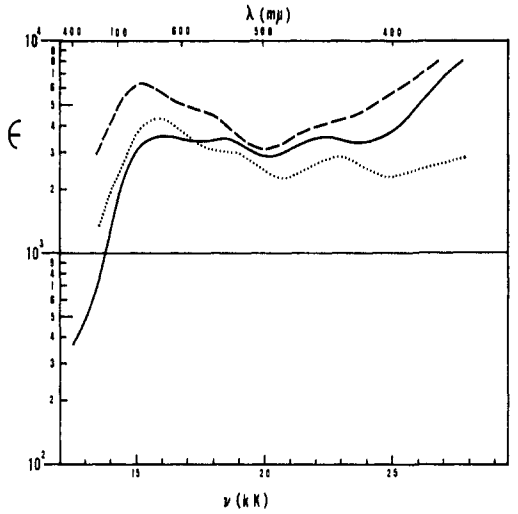


Figure 1. Absorption spectra of three Co(I) nucleophiles in 0.1 *M* methanolic NaOH: —, Co^{I}(Dmg)-Py; ···, $Co^{I}(DmgB_2F_4)$-Py; – – –, Co(Dpg)-Py.

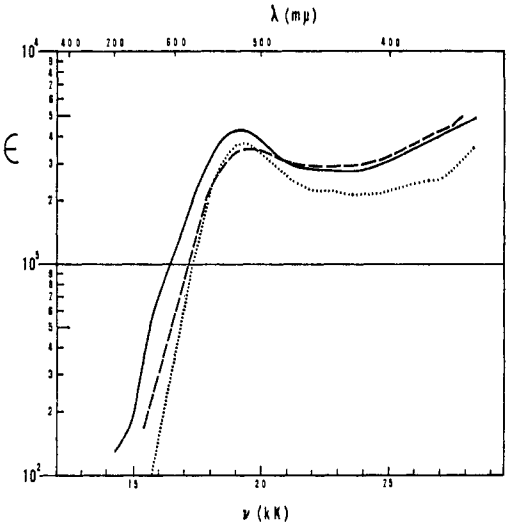
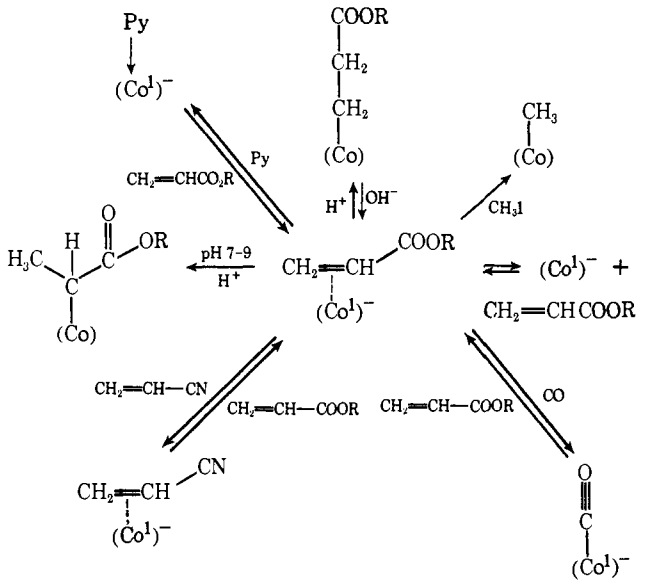


Figure 2. Absorption spectra of three cobaloxime(I) π complexes in methanolic NaOH. Olefinic ligands acrylonitrile (···), crotonitrile (—), and *p*-methoxycinnamonitrile (– – –) (axial base is pyridine at equilibrium with OH^-).

ethyl- and higher alkylcobaloximes undergo elimination with formation of olefins and the Co(I) nucleophile.

Scheme I. Reactions of the Cobaloxime(I)–Acrylic Ester π Complex[a]



[a] (Co) represents the $Co(Dmg)_2$ part of the cobaloxime (axial base not shown).

Spectra and Stability. The spectra of cobaloximes(I) exhibit characteristic low-energy bands which have been assigned[6,7] to the ligand-modified d–d transitions. The spectral changes on adding acrylonitrile, ethyl acrylate, fumaronitrile, and related olefins to solutions of the free cobalt(I) nucleophiles consist in a shift of the d–d transitions to higher energy. Typical absorption spectra of free cobaloxime(I) nucleophiles and of several π complexes are shown in Figures 1 and 2.

The first band, which is always the most intense, is shifted to shorter wavelengths with increasing π-acceptor strength of the olefinic ligand (Table I). It appears at longer wavelengths in complexes with diminished coordinating power of the in-plane ligands, *i.e.*, in the adducts with diphenylglyoxime (Dpg, **1b**) and the cobaloxime–BF_2 derivatives ($DmgB_2F_4$, **2**). Lowering the in-plane coordinating strength reduces the charge density on cobalt and causes a labilization of the π complexes. Whereas the complexes of the conventional cobaloximes with olefins such as acrylonitrile or ethyl acrylate have a stability constant K_{st} of $\gtrsim 10^6$, that of the acrylonitrile complex of $Co(DmgB_2F_4)$ is only $(3.3 \pm 0.5) \times 10^3$.

Axial bases with d or π^* orbitals available for backbonding were qualitatively noted to diminish the stability of the π complexes, which is reflected by their increased oxygen sensitivity. In the case of cyclohexylisocyanide, no π complex is formed even in the presence of a large excess of acrylonitrile. The complexes with the strong acceptor fumaronitrile, on the other hand, are much more stable than those of, *e.g.*, acrylonitrile, and on exposure to air decompose only very slowly over a period of hours. The tendency to react with alkylating agents also increases with decreasing stability of the complexes, as will be outlined below. The spectra of free cobaloxime(I) nucleophiles are not changed noticeably upon the addition of simple olefins, allylic compounds, vinyl ethers, or alkynes. Carbon monoxide, a sufficiently good acceptor, forms adducts with cobaloximes(I), the solution spectra of which are shown in Figure 3. The coordinated CO is readily displaced by olefinic ligands such as acrylonitrile or ethyl acrylate. The optical spectra of the complexes do not change significantly in the presence of excess olefin. There is no indication for the formation of adducts other than 1:1.

Rates of Alkylation. The π complexes of the cobaloxime(I) nucleophiles react with alkylating agents *via* the equilibrium amounts of the free nucleophiles as indicated in Scheme I. The rates of the alkylation (Table II) thus reflect the stability of the π complexes as well as the rate with which the equilibrium concentration of nucleophile is established. The reactions of the complexes with alkylating agents follow first-order rate laws best with slowly reacting alkylating agents, *e.g.*, ethyl bromide. Systematic deviation from pseudo-

(6) G. N. Schrauzer, R. J. Windgassen, and J. Kohnle, *Chem. Ber.*, **98**, 3324 (1965).
(7) G. N. Schrauzer, *Ann. N. Y. Acad. Sci.*, **112**, 526 (1968).

Table I. Absorption Spectra of Cobaloxime(I) Nucleophiles and Their π Complexes

π-Bonded ligand	In-plane ligand	Axial[b] base	Absorptions, kK (log ϵ)[a] ν_1	ν_2	ν_3
None[d]	Dmg	Pyridine	16.0 (3.56)	18.3 (3.54)	22.2 (3.54)
None[c]	Dpg	Pyridine	15.2 (3.80)	17.2 (3.68)	22.2 (3.61)
None[c]	$DmgB_2F_4$	Pyridine	15.9 (3.64)	18.3 (3.48)	22.8 (3.45)
CO[e]	Dmg	H_2O	17.6 (3.92)	22.2 (3.49)	27.0 (3.70)
CO[e]	Dmg	Pyridine	17.6 (3.82)	22.2 (3.40)	27.0 (3.58)
CO[e]	$DmgB_2F_4$	Pyridine	17.4[g]	19.1	23.3
CH_2=CHCN	Dmg	H_2O	19.5 (3.77)	22.7 (3.55)	
CH_2=CHCN[c]	Dmg	Pyridine	19.3 (3.57)	22.7 (3.34)	26.3 (3.39)
CH_2=CHCN[c]	Dmg	$(C_4H_9)_3P$	19.6[g]	20.8	25.6
CH_2=CHCN[c]	Dpg	Pyridine	17.9 (3.81)	22.7 (3.60)	
CH_2=CHCN[c]	$DmgB_2F_4$	Pyridine	18.3 (3.59)	22.7 (3.37)	
CH_2=CHCN[c]	Dmg	$(C_6H_5)_3P$	19.5 (3.60)	22.7 (3.43)	
CH_2=CHCN[c]	Dmg	$(C_6H_5)_3As$	19.4 (3.67)	22.5 (3.30)	
CH_2=$C(CH_3)CO_2CH_3$[d]	Dmg	Pyridine	18.8 (3.50)	22.2 (3.33)	26.3 (3.39)
CH_2=$CHCO_2C_2H_5$[d]	Dmg	Pyridine	19.0 (3.50)	22.2 (3.16)	25.0 (3.05)
CH_2=$C(CH_3)CN$[d]	Dmg	Pyridine	19.2 (3.50)	20.4 (3.33)	27.4 (3.32)
CH_3CH=CHCN[d]	Dmg	Pyridine	19.2 (3.27)	21.5 (3.44)	26.3 (3.36)
p-$CH_3O(C_6H_4)CH$=CHCN[c]	Dmg	Pyridine	19.4 (3.52)	22.2 (3.44)	26.7 (3.58)
C_6H_5CH=CHCN[e]	Dmg	Pyridine	19.7 (3.55)	22.7 (3.50)	
$C_2H_5O_2CCH$=$CHCO_2C_2H_5$	Dmg	Pyridine	20.8 (3.56)	18.7 (3.52)	
NCCH=CHCN[d]	Dmg	Pyridine	22.2 (3.46)		
Ethyl sorbate[e,f]	Dmg	Pyridine	19.6[g]		

[a] ϵ, l. mol^{-1} cm^{-1}. [b] Pyridine in equilibrium with OH^- as axial base in some cases. [c] Spectra in 0.1 M NaOH in methanol. [d] Spectra in 1 M NaOH in methanol. [e] Spectra in 2 M NaOH in methanol. [f] CH_3CH=CHCH=$CHCO_2C_2H_5$. [g] ϵ not obtained because of low stability.

first-order kinetics was observed with very reactive alkylating agents such as benzyl chloride or methyl iodide, presumably because equilibrium conditions for

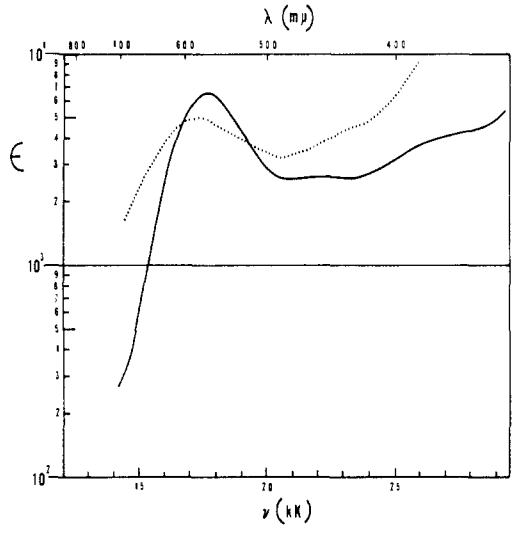
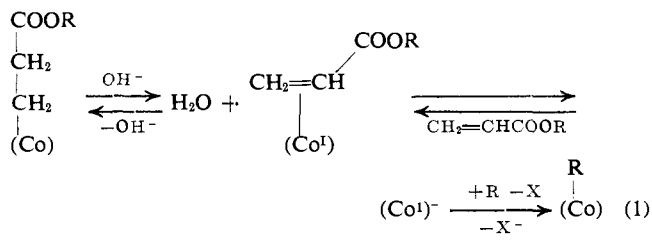


Figure 3. Absorption spectra of two adducts of cobaloximes(I) with carbon monoxide (in 2 M methanolic NaOH). Adduct with Co^I(Dmg) (—), with $Co^I(DmgB_2F_4)$ (···). Axial base is pyridine at equilibrium with OH^-. ϵ for the $Co^I(DmgB_2F_4)$ adduct is approximate.

the formation of the free Co(I) nucleophile according to eq 1 are not fulfilled. The alkylation rates are significantly diminished in the presence of excess of olefinic ligand, obviously due to the diminution of the equilibrium concentration of free nucleophile. In contrast to the behavior of the free Co(I) derivatives of cobaloximes[8] the rates of alkylation were found to increase with decreasing Co(I) nucleophilicity. For example, the acrylonitrile complex of the cobaloxime–BF_2 derivative is alkylated more rapidly than the analogous complex of the unsubstituted cobaloxime, in keeping with the diminished stability of the π complex in the BF_2 substituted derivative.



The Alkali-Induced Co–C Bond Cleavage of β-Substituted Alkylcobaloximes

Kinetic measurements of the σ–π conversion of substituted alkylcobaloximes were performed under standard conditions (0.1–1 M NaOH in CH_3OH at 25°) to establish the mechanism. The spectroscopically determined second-order rate constants k^{2nd} of the formation of the π complexes are given in Table III together with the Pearson nucleophilicities of the cobaloxime(I) leaving group. The rates *decrease* with *decreasing* Co(I) nucleophilicity. This is consistent with significant metal participation in the transition state, as will be outlined in the Discussion section. The rate of the σ–π conversion also depends on the nature of the alkyl substituents. It appears that inductive as well as steric effects affect the rate of π-complex formation in a composite fashion. The H–D effect on the rate of π-complex formation from β-cyanoethyl(pyridine)cobaloxime is 1.60 at 25°. For this experiment β-cyanoethyl(pyridine) cobaloxime-d_4 was synthesized by treating cobaloxime(I) with an excess of acrylonitrile in NaOD–D_2O–tetrahydrofuran. Under these conditions, complete deuteration of the acrylonitrile occurs. Since acrylonitrile did not undergo H–D exchange in alkaline medium in the absence of cobaloxime(I), this suggests

(8) G. N. Schrauzer and E. Deutsch, *J. Amer. Chem. Soc.*, 91, 3341 (1969).

Table II. Rates of Alkylation of Cobaloxime(I)–Olefin π Complexes at 25° [a]

π-Bonded olefin	In-plane ligand	Axial base	k_{MeI}^{2nd}	k_{BzCl}^{2nd}	k_{EtBr}^{2nd}
None	Dmg	H_2O	2.0×10^4	3.1×10^3	11.0
None	Dmg	Pyridine	9.1×10^3	1.8×10^3	5.9
None	Dmg	$P(n\text{-}C_4H_9)_3$	2300	440	1.6
None	$DmgB_2F_4$	Pyridine	88	17	0.063
$CH_2{=}CHCN$	Dmg	H_2O	65	1.0	0.10
$CH_2{=}CHCN$	Dmg	Pyridine	40	7.0	0.12
$CH_2{=}CHCN$	Dmg	$P(n\text{-}C_4H_9)_3$	Very fast	280	1.0
$CH_2{=}CHCN$	$DmgB_2F_4$	Pyridine	100	34	0.051
$CH_2{=}CHCOOC_2H_5$	Dmg	Pyridine	Very fast	120	0.26
$C_6H_5CH{=}CHCN$	Dmg	Pyridine	43	2.1	0.3
$H_5C_2O_2CCH{=}CHCO_2C_2H_5$ [b]	Dmg	Pyridine	0.9	0.3	0.04
$NCCH{=}CHCN$	Dmg	Pyridine	Very slow	0	0

[a] Most rates measured in 0.1 M NaOH in methanol; k^{2nd} in l. mol^{-1} sec^{-1}. [b] Rate measured in 1 M NaOH in methanol.

Table III. Rates of π-Complex Formation from Substituted Alkylcobaloximes and Alkylcobalamins at 25°, and Co(I) Pearson Nucleophilicities[a]

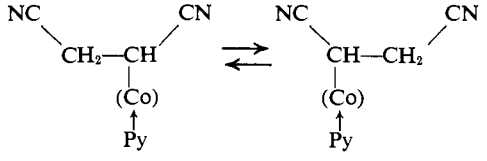
π-Bonded olefin generated	In-plane ligand	Axial base	k^{2nd}	Co(I) nucleophilicity[e]
$CH_2{=}CHCN$	Dmg	H_2O	0.48	14.3
$CH_2{=}CHCN$	Dmg	Pyridine	0.32	13.8
$CH_2{=}CHCN$	Dmg	$P(n\text{-}C_4H_9)_3$	0.12	13.3
$CH_2{=}CHCN$	Dpg	Pyridine	0.08	13.1
$CH_2{=}CHCN$	$DmgB_2F_4$	Pyridine	0.046	11.7
$CH_2{=}CHCO_2C_2H_5$	Dmg	Pyridine	0.16	13.8
$C_6H_5CH{=}CHCN$	Dmg	Pyridine	0.030	13.8
$H_5C_2O_2CCH{=}CHCO_2C_2H_5$	Dmg	Pyridine	0.0080	13.8
$NCCH{=}CHCN$	Dmg	Pyridine	0.12	13.8
$CH_2{=}CHCN$ [b]	Corrin	[c]	3.8 [d]	14.4
$CH_2{=}CHCO_2C_2H_5$ [b]	Corrin	[c]	0.32 [d]	14.4

[a] Most rates measured in 0.1–1.0 M NaOH in methanol; k^{2nd} in l. mol^{-1} sec^{-1}. [b] Rate measured in NaOH in water. [c] 5,6-Dimethylbenzimidazole. [d] π complexes unstable. [e] Reference 8.

that the reduced cobaloxime is actually catalyzing H–D exchange reactions, according to eq 1, as was also suggested in a previous paper.[2]

Valence Tautomerization of 1,2-Dicyanoethyl(pyridine)cobaloxime

The established reversibility of the σ–π conversion provides an interesting possibility for valence tautomerization. In 1,2-disubstituted ethylcobaloximes reversible rearrangement reactions such as formulated for the 1,2-dicyanoethyl derivative could occur.



(2)

Analyzing the nmr spectrum of 1,2-dicyanoethyl(tributylphosphine)cobaloxime, no evidence for valence tautomerization was observed in $CDCl_3$ as the solvent. The three protons of the substituted ethyl group gave rise to a typical AB_2 (or ABB′) pattern exhibiting no noticeable temperature dependence. The spectrum of 1,2-dicyanoethyl(tributylphosphine)cobaloxime shows additional splitting due to phosphorus which is readily accounted for on the basis of a nonfluctuating structure. The C–H, CH_2, as well as the dimethylglyoxime methyl signals are coupled to phosphorus with J = 5.1, 3.6, and 2.5 Hz, respectively, as has been proved by a spin-decoupling experiment (Figure 4). The spectrum is satisfactorily reproduced by assuming it to be AB_2, even though it is in fact ABB′. Analysis gives δ_{CH} 1.9 ppm, δ_{CH_2} 2.1 ppm (both from TMS), J_{HH} = 7.6 Hz. The nmr spectrum of 1,2-dicyanoethyl(pyridine)cobaloxime in $CDCl_3$, however, is anomalous in that the three protons of the dicyanoethyl group attached to cobalt give rise to only one sharp signal at 2.1 ppm, upfield relative to the dimethylglyoxime methyl protons. On cooling to −10° the signal begins to indicate fine structure

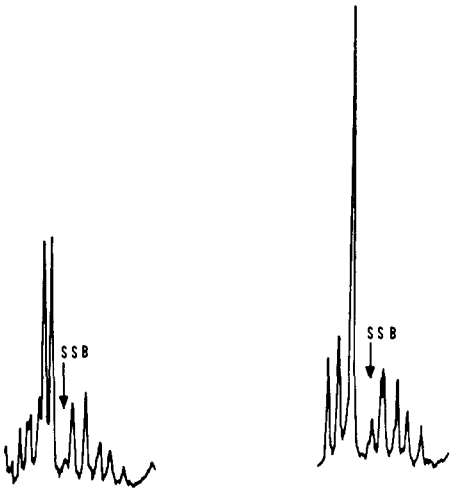


Figure 4. Sections of the ^1H nmr spectra of 1,2-dicyanoethyl(tri-*n*-butylphosphine)cobaloxime: (A) normal spectrum exhibiting the AB_2 (or ABB′) pattern of the three protons of the 1,2-dicyanoethyl group, coupled to phosphorus; (B) same spectrum after phosphorus spin decoupling (in $CDCl_3$, at 40°, measured with 100-Mc instrument; SSB = spinning side band).

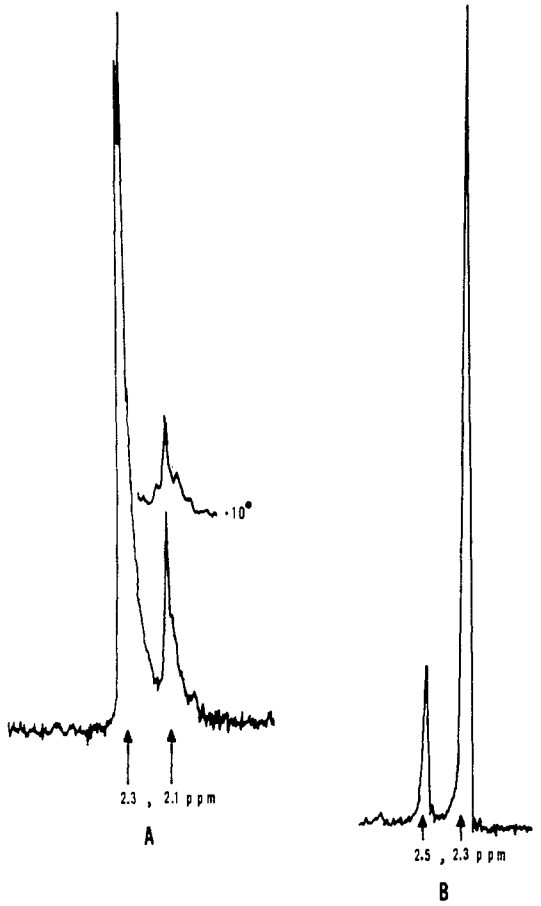


Figure 5. Section of the ^1H nmr spectrum of 1,2-dicyanoethyl(pyridine)cobaloxime: (A) in $CDCl_3$ at 25° and −10°, respectively; (B) in pyridine at 25°. The large peak is due to the Dmg methyl protons. The small signal corresponds to the three protons of the 1,2-dicyanoethyl moiety.

(Figure 5); unfortunately, the solubility is insufficient for work at lower temperature in this solvent. In pyridine at 25° the single signal of the dicyanoethyl protons is shifted to 2.5 ppm, downfield relative to the signal of the dimethylglyoxime methyl protons. This behavior is highly suggestive of the occurrence of some dynamic effect, *i.e.*, the valence tautomerization according to eq 2. Solvent participation in the process is indicated by the complete exchange of the 1,2-dicyanoethyl hydrogens upon addition of D_2O to pyridine solutions of the complex.[9]

Evidence for the valence tautomerization was obtained by cooling a $CDCl_3$–pyridine (3:1 mixture by volume) solution of 1,2-dicyanoethyl(pyridine)cobaloxime to −40°. Under these conditions the AB_2 pattern of the cyanoethyl protons is observable (triplet at 1.9 ppm, J = 7 Hz, doublet at 3.8 ppm; Figure 5). The full kinetic and thermodynamic parameters of the rearrangement process will be published elsewhere. The available evidence thus permits the conclusion that 1,2-dicyanoethyl(pyridine)cobaloxime undergoes reversible valence tautomerization in solution at room temperature. The corresponding complex with tributylphosphine behaves normally, possibly because of diminished π back-bonding (see Discussion section).

(9) Nmr analysis of diethylsuccinyl(pyridine)cobaloxime indicates similar anomalous behavior. The succinyl protons give rise to only one sharp solvent-dependent signal (observed at 2.9 ppm in pyridine and at 2.2 ppm in $CDCl_3$).

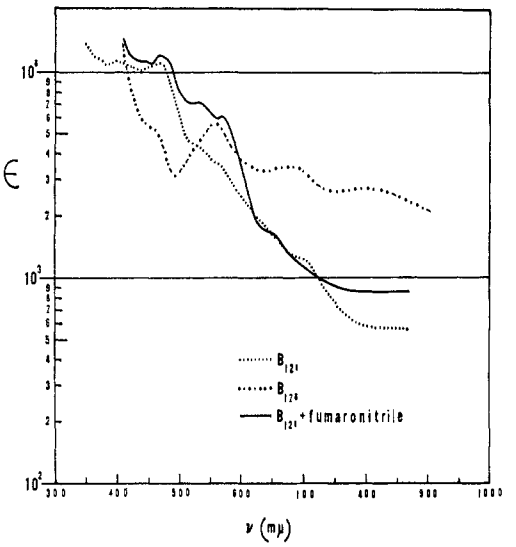


Figure 6. Absorption spectra of vitamin B_{12r} (···), vitamin B_{12s} (·-·-), and the vitamin B_{12s} fumaronitrile adduct (—).

Comparison with Vitamin B_{12}

The cobalt ion in vitamin B_{12} is sterically hindered to a greater extent than in the cobaloxime models. Accordingly, the olefin π complexes of vitamin B_{12s}, the Co(I) form of 5,6-dimethylbenzimidazolylcobalamin, are expected to be less stable than those of cobaloximes if at all capable of existence. Careful spectroscopic studies revealed little if any change of the low-energy absorptions in the spectrum of vitamin B_{12s} upon the addition of ethyl acrylate or acrylonitrile in 2 *M* NaOH, either at room temperature or at −10°. With excess fumaronitrile the *blue-green* solution of vitamin B_{12s} turns *brown-red* in the presence of excess reducing agent (*e.g.*, $NaBH_4$–Pd or copper-activated zinc). The absorption spectrum clearly differs from that of vitamin B_{12r} (Figure 6), suggesting that the solutions contain the π complex of vitamin B_{12s} with fumaronitrile. This is further supported by esr analysis, which indicates only traces of paramagnetic vitamin B_{12r}, and the fact that methylcobalamin is produced on addition of methyl iodide. We conclude, therefore, that vitamin B_{12s} forms a complex with fumaronitrile which is more labile than the corresponding complex of cobaloxime(I). We have been unable to detect π complexes of vitamin B_{12s} in the alkali cleavage of cyanoethyl- and ethylcarbethoxycobalamin. However, the results listed in Table IV indicate that the rates of alkylation of vitamin B_{12s} are significantly diminished in the presence of excess acrylonitrile and fumaronitrile. This is indicative of equilibria between vitamin B_{12s}, free olefin, and the corresponding π complexes. The close qualitative similarity between organocobaloximes and derivatives of vitamin B_{12} also follows from determinations of the rates of alkali cleavage of β-cyanoethyl- and 2-carbethoxyethylcobalamin. The cyanoethyl derivative decomposes at approximately ten times the rate of the cobaloxime; the 2-carboxyethyl complexes decompose at about the same rates, however (Table III). The qualitative conclusions drawn for cobaloximes are therefore valid also for cobalamins.

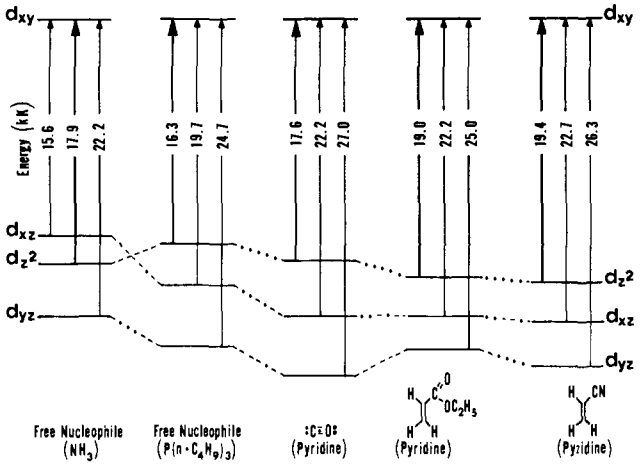


Figure 7. Experimental term-level schemes and suggested assignments for two cobaloxime(I) nucleophiles and complexes with various ligands (axial base in parentheses). The $3d_{x^2-y^2}$–d_{xy} transition is not resolved and therefore not included in diagram.

Discussion

Electronic Structure and Spectra of Cobaloxime(I)–Olefin π Complexes. The electronic structure of the cobaloxime(I)–olefin π complexes is readily described in terms of a conventional σ-donor–π-acceptor[10] bonding model. There can be no doubt that d_π–π^* back-bonding is the most important stabilizing interaction involving the lowest antibonding olefin π MO and the $3d_{xz}$ or $3d_{yz}$ cobalt orbital. Since the $3d_{z^2}$ orbital is filled, the σ-donor interactions are restricted to the ligand and the metal 4s and $4p_z$ orbitals, of which the latter two are strongly antibonding. The $3d_{z^2}$ orbital should become slightly stabilized due to the withdrawal of charge from cobalt through the π-back-bonding interactions. Since the first low-energy band in the spectra of the free Co(I) nucleophile is the most intense and particularly sensitive to the variation of the axial base component, it was previously assigned to the $3d_{z^2} \rightarrow 3d_{xy}$ transition.[6,7] We retain this assignment also for the first low-energy transition in the cobaloxime(I) π complexes, in view of its similar intensity. The remaining two bands could correspond to the transitions $3d_{xz} \rightarrow 3d_{xy}$ and $3d_{yz} \rightarrow 3d_{xy}$. As expected, they are shifted hypsochromically with respect to the free nucleophile. Experimental term-level schemes with the suggested assignments are given in Figure 7 for two free Co(I) nucleophiles and the CO– and two olefin π complexes. The assignments are empirically justified for the free Co(I) nucleophiles[6,7] and instructively reflect the effect of π-bonding axial ligands on the energy levels of the $3d_{xz}$ and $3d_{yz}$ orbitals. Carbon monoxide causes a stabilization of both of the two metal orbitals, but acrylonitrile and ethyl acrylate evidently stabilize one of the orbitals more than the other. This suggests that the π-bonded olefin adopts a preferred orientation relative to the cobaloxime moiety. Placing the coordinate axes as in Figure 8, the more stable structure of the complex is A. The $3d_{xz}$ orbital is more strongly antibonding than $3d_{yz}$ and hence produces stronger π back-bonding.

Table IV. Relative Rates of Alkylation in the Presence of π-Bonded Olefins at 25° [a]

π-Bonded olefin	Olefin–cobalt ratio	In-plane ligand	Rel rate
None	0	Dmg	1.0
CH_2=CHCN	1:1	Dmg	0.020
CH_2=CHCN	2000:1	Dmg	0.00071
None	0	$DmgB_2F_4$	1.0
CH_2=CHCN	1:1	$DmgB_2F_4$	0.82
CH_2=CHCN	500:1	$DmgB_2F_4$	0.024
CH_2=CHCN	2000:1	$DmgB_2F_4$	0.0082
None	0	Cobalamin	1.0
CH_2=$CHCO_2C_2H_5$	1000:1	Cobalamin	1.0
CH_2=CHCN	1000:1	Cobalamin	0.35
NCCH=CHCN	1000:1	Cobalamin	0.018

[a] Alkylation agent, ethyl bromide. Axial base is pyridine for cobaloximes and 5,6-dimethylbenzimidazole for cobalamins.

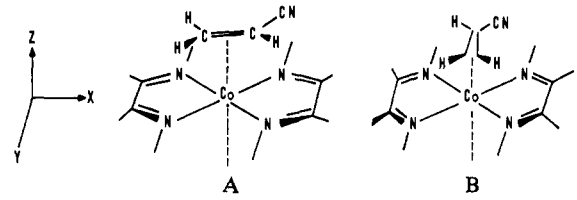
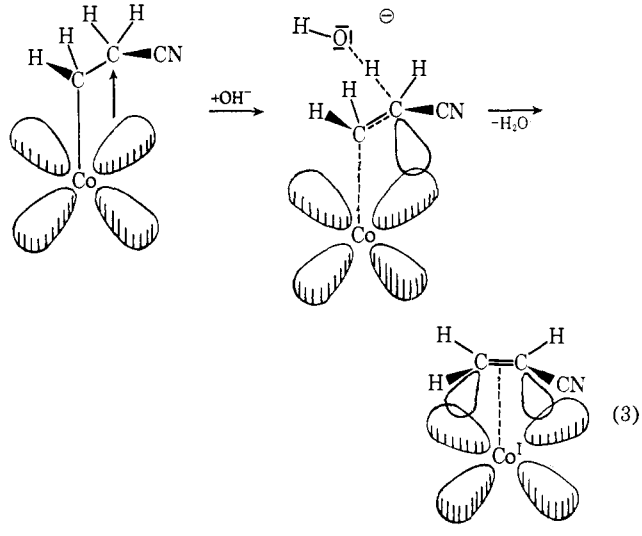


Figure 8. Possible structures of a cobaloxime π complex.

The Mechanism of the Cobalt–Carbon Bond Cleavage Reactions. The alkali-induced Co–C bond cleavage of β-substituted alkylcobaloximes and -cobalamins cannot be readily accommodated within existing classification schemes of organic 1,2-elimination reactions.[11] The observed σ–π rearrangement unambiguously indicates significant d-orbital participation in the transition state. The established importance of π back-bonding interactions in the π complexes, furthermore, leaves no question in that the participating d orbitals are either $3d_{xz}$ or $3d_{yz}$. The relatively small observed kinetic H–D effect (observed, 1.6) in the σ–π conversion of the β-cyanoethyl(pyridine)cobaloxime, finally, can only be interpreted to suggest that the complete C–H bond cleavage is a late event in the rate profile. The mechanism of the β elimination may thus be represented schematically according to eq 3. A mechanism oc-

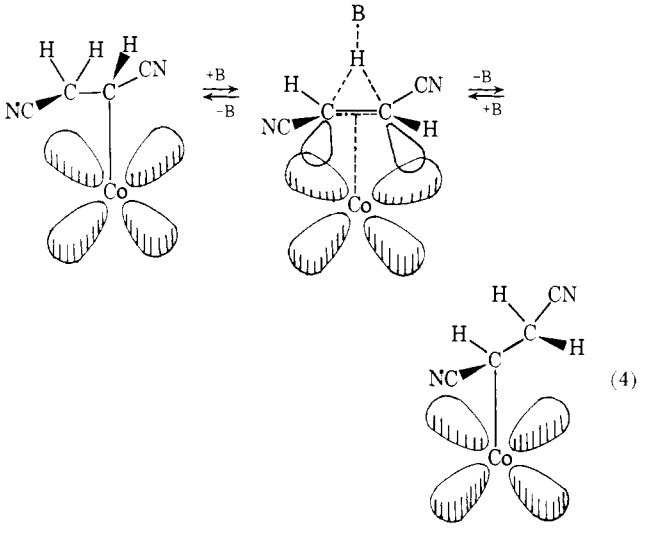


(3)

(10) (a) J. Chatt and L. M. Venanzi, *Nature (London)*, **177**, 852 (1956); (b) for acrylonitrile and related ligands, see G. N. Schrauzer, *Chem. Ber.*, **94**, 642 (1961).

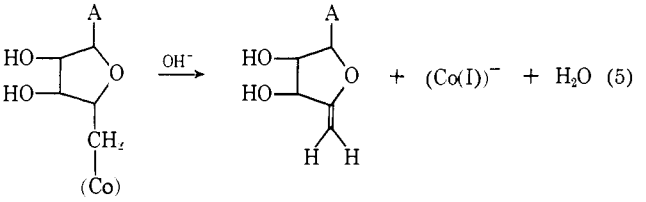
(11) See, for example, J. F. Bunnett, *Angew. Chem.*, **74**, 731 (1962); *Angew. Chem., Int. Ed. Engl.*, **1**, 225 (1962).

curring with the initial formation of a β-cyanoethylcobaloxime carbanion is clearly excluded on the basis of the low H–D effect and the lack of proton exchange in β-cyanoethylcobaloximes at neutral or mildly alkaline pH. The facile Co–C bond cleavage thus is a manifestation of a "β effect,"[12] which should indeed be strong in view of the high electron density on the cobaloxime-ligand-modified cobalt ion. The d-orbital effects are noticeable mainly in the transition state. Nmr measurements on several alkyl- and substituted-alkylcobaloximes reveal little indication of metal interactions with the β-carbon atom. However, it is conceivable that the repulsion of the β-carbon atom by the filled d orbital could cause a distortion of the angle of the Co–C bond with the *xy* plane. The results of the X-ray analysis of coenzyme B_{12}[13] and of a substituted alkylcobaloxime[14] indicate that this angle is ~95°. In addition to steric hindrance this distortion thus could be partly due to d-orbital repulsion effects. An interesting property of the cobaloxime(I) π complexes is their low residual nucleophilicity. In view of the enormous reactivity[8,15] of the complexed Co(I) ions it is surprising to find the relatively labile π complexes to be essentially unreactive with alkylating agents. Evidently, the $3d_{z^2}$ orbital is stabilized energetically as well as completely screened by the axial base and the π-bonded olefin. Another striking property of the cobaloxime(I) π complexes is the reversibility of Co–C bond formation. At pH around 10 the β-cyanoethyl derivative is formed from acrylonitrile–cobaloxime(I) π complexes in reverse of eq 3. At lower pH the α isomer is formed in an irreversible reaction presumably involving the cobaloxime hydride,[3] as will be outlined in a forthcoming publication. The valence tautomerism of 1,2-dicyanoethyl(pyridine)cobaloxime may be readily accounted for by the mechanism of the σ–π conversion. A scheme consistent with the available experimental evidence is given in eq 4. Substitution of the axially coordinated pyridine by acceptor ligands, such as phosphines, labilizes the Co(I) π complexes. The tributylphosphine adduct



(4)

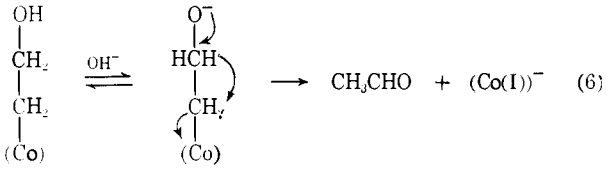
of 1,2-dicyanoethylcobaloxime, accordingly, does not appear to undergo valence tautomerization at room temperature presumably because of diminished metal participation in the σ–π transition state. This should have the effect of stabilizing the localized σ structure. The demonstrated "β-effect" in alkali-induced elimination reactions of organocobaloximes and -cobalamins undoubtedly also operates in the alkali cleavage of coenzyme B_{12} or the corresponding cobaloxime model compound[2] (eq 5), except that the olefinic sugar has



(5)

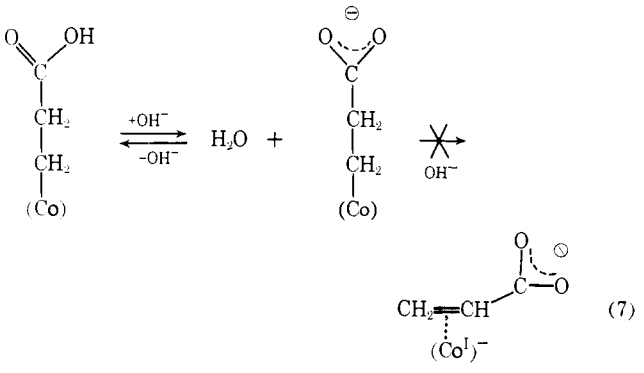
little, if any, tendency to π bond to the Co(I) ion on completion of the elimination process. The same must be the case in the alkali cleavage of higher alkylcobaloximes.[16] However, the detailed factors influencing these reactions will be discussed elsewhere.

Elimination with 1,2-Hydride Transfer. The alkali-induced cleavage of hydroxyethylcobaloximes to the Co(I) nucleophile and acetaldehyde, as well as related reactions, occur by a 1,2-hydride-shift mechanism, illustrated in the equation below.[2,17] One of the main



(6)

arguments against a β-elimination reaction involving vinyl alcohol as the intermediate is the complete alkali resistance of β-ethoxyethylcobaloximes. The tendency of the hydroxyethylcobalt compounds to undergo β elimination should be further diminished for electrostatic reasons; the vicinity of a negatively charged oxygen anion would make it difficult to approach a base close to the β protons to induce elimination. Inductive effects of a similar kind must also be held responsible for the observed alkali stability of the carboxyethylcobaloxime anion (eq 7). However, the large kinetic



(7)

(12) See, for example, M. L. H. Green, "Organometallic Compounds," Vol. II, 3rd ed, Methuen, London, 1968, p 215, for discussion of some aspects of the "β effect."

(13) D. Crowfoot-Hodgkin, *Proc. Roy. Soc., Ser. A*, **288**, 294 (1965).

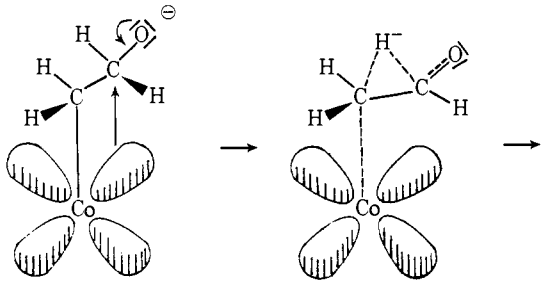
(14) G. Lenhert, *Chem. Commun.*, 980 (1967).

(15) G. N. Schrauzer, E. Deutsch, and R. J. Windgassen, *J. Amer. Chem. Soc.*, **90**, 2441 (1968).

(16) Higher alkylcobaloximes decompose in strong aqueous alkali with formation of olefins and the Co(I) nucleophile.

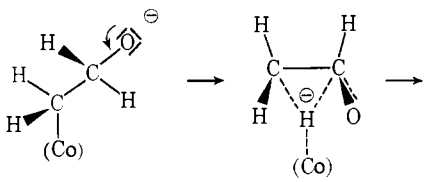
(17) G. N. Schrauzer and R. J. Windgassen, *J. Amer. Chem. Soc.*, **89**, 143 (1967).

H–D effect[2] of 5.5 for the reaction of eq 6 cannot be reconciled with a conventional 1,2 hydrogen transfer in which only C–H bending modes are activated.[18] It could be explained by assuming *increased hydride character of the migrating hydrogen, e.g.*, as represented in eq 8. The rehybridization of the β carbon during the



$$(Co^{I})^{-} + CH_3CH{=}O \quad (8)$$

C=O bond formation could be a driving force through which the migrating hydrogen atom attains increased hydride ion character. C–H bond breaking in the transition state could be facilitated by d-orbital participation as indicated in eq 8. A β-elimination mechanism related to the processes discussed above is excluded also by the different dependence of the reaction rates on the nucleophilicity of the Co(I) leaving group. In the β eliminations the rates decrease with decreasing Co(I) nucleophilicity, as has been outlined above. In the alkali decomposition of 2-hydroxyalkylcobaloximes the rates increase with decreasing nucleophilicity of the Co(I) leaving group.[2] The involvement of the metal in the hydride transfer, *e.g.*, according to eq 9, is further-



$$(Co^{I})^{-} + CH_3{-}CH{=}O \quad (9)$$

more unlikely in view of the established alkali stability of *trans*-hydroxycyclohexylcobaloxime,[2] even though the 2-hydrogen atom in this complex would be available for cis elimination according to eq 9. It thus appears that the β-elimination reactions of 2-substituted alkylcobaloximes and the elimination reactions with 1,2 hydride transfer may represent mechanisms unique to vitamin B_{12}-type compounds.

Experimental Section

Materials and Methods. All alkylcobaloximes and the corresponding derivatives of vitamin B_{12} were previously described and synthesized by published procedures.[2,3,5] Vitamin B_{12a} was obtained from Merck Sharp and Dohme Research Laboratories, Rahway, N. J. All other reagents were certified analytical grade and used without further purification. The argon used for the experiments under anaerobic conditions was 99.98% pure and a product from the National Cylinder Gas Co.; complete deoxygenation was achieved by passing the gas through an alkaline solution of pyrogallol. The carbon monoxide was "Pure" grade and used without additional purification.

(18) (a) K. B. Wiberg, "Physical Organic Chemistry," Wiley, New York, N. Y., 1963, pp 351–361; (b) K. B. Wiberg, *Chem. Rev.*, **55**, 713 (1955).

Spectra. All spectra were obtained using a Beckman DK 2A spectrometer.

Preparation of Solutions of Cobaloxime(I) Nucleophiles and π Complexes. A stock solution of 0.0327 g (7.91×10^{-5} mol) of hydroxyethyl(pyridine)cobaloxime in 10 ml of methanol was placed into a vial which was wrapped with aluminum foil to prevent excessive exposure to light and fitted with a rubber serum cap. The solution was deoxygenated by flushing with argon gas which was introduced and vented using 25-gauge syringe needles. A 3-ml uv cell containing 2.7 ml of 1 *M* NaOH in methanol was similarly deoxygenated. By means of a syringe 0.3 ml of the solution of hydroxyethyl(pyridine)cobaloxime was injected into the NaOH solution. Formation of the Co(I) nucleophile was complete in 3–5 min. This procedure can be modified by the use of chloro- or bromo(pyridine)cobaloxime or related complexes with bases other than pyridine. In this case an excess of $NaBH_4$ is dissolved in 0.1 *M* NaOH solution. To speed up generation of the Co(I) nucleophile a few drops of a 0.001% $K_2[PdCl_4]$ solution are added. The olefin π complexes were obtained by injecting the deoxygenated olefin in approximately 100-fold molar excess to the solutions of the Co(I) nucleophile. An alternative method consists in transferring a deoxygenated solution of the β-substituted alkylcobaloxime into the deoxygenated solution of methanolic NaOH; solutions of the π complexes generated according to the latter method may be stabilized by the addition of an excess of the olefinic ligand.

Equilibrium Constants. Most cobaloxime(I)–olefin π complexes are dissociated only to a minor extent, making it impossible to detect the presence of the equilibrium amounts of free Co(I) nucleophile by direct spectroscopic methods. The following procedure was applied to obtain a lower limit for the equilibrium constant.

To a uv cell of 3-cm³ capacity, fitted with a rubber serum cap, and containing 2.7 ml of a deoxygenated 0.1 *M* methanolic NaOH solution, 0.3 ml of a deoxygenated 0.0030 *F* solution of β-cyanoethyl(pyridine)cobaloxime in methanol was added. The red π complex formed immediately. By measuring the absorbance at 517 mμ, the concentration of the complex species was obtained. The absorbance remains constant for at least 5 min. During this time 4 μl (sevenfold molar excess) of deoxygenated acrylonitrile was injected, causing a slight increase of the absorbance at 517 mμ. The increase ΔA was taken as proportional to the concentration of free cobaloxime(I) under the initial equilibrium conditions. From these data, together with the known absorbance before addition of acrylonitrile (A_0) and the known molar extinction coefficient ϵ for the π complex, K was obtained according to

$$K = \frac{[\text{complex}]}{[\text{Co(I)}][\text{olefin}]} = \frac{A_0/\epsilon_{\text{complex}}}{(\Delta A/\epsilon_{\text{complex}})^2} \quad (10)$$

The formation constant for the acrylonitrile complex of Co(Dmg-B_2F_4) was determined analogously, except that the absorbances were monitored at 630 and 540 mμ (this complex is sufficiently unstable to permit direct detection of the equilibrium amounts of free Co(I) nucleophile at 630 mμ).

Kinetic Measurements. The rate determinations were performed spectrophotometrically at 25° using the Beckman DK 2A instrument. All runs were measured under strictly anaerobic conditions. The rates of formation of the π complexes from the β-substituted alkylcobaloximes were determined by following the increase of absorbance near 550 mμ in 0.1–1 *M* methanolic NaOH, depending on the complex. Since the rates are linearly dependent on the [OH^-] the pseudo-first-order rate constants were divided by [OH^-] to yield the k^{2nd} values listed in Table III. The alkylation experiments were done in 0.1 *M* NaOH in methanol, except for the 1,2-dicyanoethyl(pyridine)cobaloxime and the dicarbethoxyethyl derivatives, for which 1 *M* NaOH was employed (Table II). The experiments with vitamin B_{12s} (see data listed in Table IV) were performed in 1 *M* NaOH in 1:1 (v/v) water–methanol. The rates of alkali decomposition of β-cyanoethylcobalamin and of the corresponding β-carbethoxyethyl derivative were determined by following the change of the absorbance near 550 mμ (anaerobic conditions) or at 355 mμ (aerobic conditions) in pH 11 buffer or in 0.0100–0.0200 *M* aqueous NaOH (Table III).

Synthesis of β-Cyanoethyl(pyridine)cobaloxime-d_4. A mixture of 5 ml of tetrahydrofuran and 5 ml of 1 *M* NaOD in D_2O was deoxygenated prior to the addition of 0.6 g of β-cyanoethyl(pyridine)-cobaloxime. A small amount of $NaBD_4$ was added to prevent yield losses through oxidation of the π complex. The resulting deep red solution was maintained at 40° for 10 min. To regenerate the σ complex, CO_2 was passed through the solution until the red color of the π complex turned yellow-brown. The resulting solu-

tion was poured into 30 ml of water, yielding yellow crystals of the deuterated complex. These were collected by filtration, washed with water, and dried in a vacuum desiccator. The nmr spectrum of the complex in $CDCl_3$ revealed the presence of the dimethylglyoxime methyl protons but was free of signals due to undeuterated β-cyanoethyl(pyridine)cobaloxime. No incorporation of deuterium was observed under similar conditions at pH <12.5.

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Spectral and Calorimetric Studies of Hydrogen Bonding with Pyrrole

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Contribution from the W. A. Noyes Laboratory, University of Illinois, Urbana, Illinois 61801. *Received April 6, 1970*

Abstract: The N–H frequency shifts and the enthalpies of hydrogen-bonding interactions between pyrrole and selected Lewis bases were experimentally determined. E and C values for pyrrole were calculated and used to estimate the enthalpies of adduct formation for pyrrole with other Lewis bases which are too weak to measure accurately. Comparison of the data for pyrrole with previously studied hydrogen-bonding hydroxy acids indicates that the ratios of the E and C parameters for all these hydrogen-bonding systems are similar. Pyrrole is a weaker acid than the phenols and 1,1,1,3,3,3-hexafluoro-2-propanol, but is stronger than *tert*-butyl alcohol. For the donors studied, the plot of $-\Delta H$ *vs.* $\Delta\nu_{N-H}$ (the change in N–H stretching frequency upon adduct formation) is found to be linear, as in the case of the hydroxy acids, and obeys the quantitative relationship: $-\Delta H = (0.0123 \pm 0.0006) \cdot \Delta\nu_{N-H} + 1.8\ (\pm 0.1)$. The enthalpy and spectral changes accompanying adduct formation are considered in the light of other reported relationships from this and other laboratories pertaining to hydrogen bonding by alcohols.

The general area of hydrogen bonding has attracted considerable interest in recent years in part owing to its importance in biological processes. Several articles[1–6] from this laboratory have been concerned with establishing correlations between the enthalpy of adduct formation and changes in the O–H stretching frequency of the hydrogen-bonding acid (various phenols and *tert*-butyl alcohol) upon complexation. The existence of such correlations is significant as a means of readily evaluating the magnitude of interactions, and the existence or lack of correlations provides insight into the fundamentals of the spectroscopic procedures employed. The studies from this laboratory have recently been extended[7,8] to provide similar relationships with the alcohols 1,1,1,3,3,3-hexafluoro-2-propanol and 2,2,2-trifluoroethanol. The correlations reported to date have been limited to alcohols interacting with various types of oxygen and nitrogen donors. It has been found recently that sulfur donors[9] do not obey the correlations of enthalpy *vs.* O–H infrared frequency shift found for the oxygen and nitrogen donors. This is consistent with an earlier claim that alkyl halides gave an incorrect trend[10,11] and suggests that caution must be employed in incorporating donors from different rows in the periodic table into our infrared correlations. We are most interested in ascertaining the limitations, if any, on the type of hydrogen bonding acid that will provide linear enthalpy–frequency shift correlations.

In biological systems, the Lewis acid involved in the hydrogen bonding system is very often an N–H functional group, as in the nucleic acids. Accordingly, we became very much interested in extending the correlations found for the alcohols to an acid with an N–H functional group. In this article, we report a successful extension of our spectroscopic correlations to the Lewis acid pyrrole.

Hydrogen bonding and other Lewis acid–base enthalpies of adduct formation have been incorporated into the general equation[12]

$$-\Delta H = C_A C_B + E_A E_B \qquad (1)$$

Empirically determined E_A and E_B, C_A and C_B parameters can be substituted into this equation to reproduce most of the known enthalpies determined in the gas phase or in poorly solvating media. It was of interest to incorporate an N–H-type functional group into this correlation and compare the E_A and C_A values for this type of acid with the alcohols.

Experimental Section

Purification of Chemicals. Reagent grade cyclohexane and carbon tetrachloride were dried over fresh Linde 4-A molecular sieves

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(1) M. D. Joesten and R. S. Drago, *J. Amer. Chem. Soc.*, **84**, 3817 (1962).
(2) D. P. Eyman and R. S. Drago, *ibid.*, **88**, 1617 (1966).
(3) T. D. Epley and R. S. Drago, *ibid.*, **89**, 5770 (1967).
(4) R. S. Drago and T. D. Epley, *ibid.*, **91**, 2883 (1969).
(5) W. Partenheimer, T. D. Epley, and R. S. Drago, *ibid.*, **90**, 3886 (1968).
(6) R. S. Drago, N. O'Bryan, and G. C. Vogel, *ibid.*, **92**, 3924 (1970).
(7) K. F. Purcell, J. A. Stikeleather, and S. D. Brunk, *ibid.*, **91**, 4019 (1969).
(8) A. D. Sherry and K. F. Purcell, private communication.
(9) G. C. Vogel and R. S. Drago, *J. Amer. Chem. Soc.*, **92**, 5347 (1970).
(10) R. West, D. L. Powell, L. S. Whatley, M. K. T. Lee, and P. v. R. Schleyer, *ibid.*, 84, 3221 (1962).
(11) D. A. K. Jones and J. G. Watkinson, *J. Chem. Soc.*, 2366 (1964).
(12) R. S. Drago and B. B. Wayland, *J. Amer. Chem. Soc.*, **87**, 357 (1965).