Alkylcobalamins and Alkylcobaloximes. Electronic Structure, Spectra, and Mechanism of Photodealkylation

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Abstract: Extended, self-consistent HMO calculations demonstrate a close similarity in the nature of the axial bonds involving the cobalt atom in vitamin B_{12} and in cobaloxime model compounds. In the optical spectra of alkylcobaloximes a characteristic low-energy charge-transfer band is observed and assigned to a transition between the highest bonding and lowest antibonding axial bond MO's. The photolysis of alkylcobaloximes and of alkylcobinamides is initiated by excitation of the Co–C bond and proceeds by a mechanism related to charge-transfer induced photoreduction reactions of Co(III) complexes. The rate of Co–C bond photolysis depends essentially on the energy and intensity of the Co–C CT transition both of which vary with the axial base attached to cobalt. Imidazole, ammonia, and other nitrogen bases render alkylcobaloximes and -cobinamides less light-sensitive by causing substantial shifts of the Co–C CT transition. Certain methylcobalt derivatives appear to be light stable on irradiation under anaerobic conditions. This is ascribed to an increase in the efficiency of the recombination $Co^{II} + CH_3 \cdot \rightarrow Co\text{–}CH_3$. The light stability of enzyme-bound methylcobalamin is explained on this basis. The available evidence indicates the Co–C bonds in organocobaloximes to be slightly more stable than in the corresponding cobalamin derivatives. Steric effects of the corrin and cobaloxime moieties are of comparable magnitude. A combination of inductive, steric, and conformational effects causes considerable labilization of the Co–C bond in secondary alkylcobalamins as exemplified by cyclohexylcobalamin, whose first successful preparation in solution is also described.

The photodealkylation of organocobalt derivatives of vitamin B_{12} and of bisdimethylglyoximatocobalt compounds ("cobaloximes") yields cobalt(II) derivatives of the parent chelates and alkyl radicals as the initial products.[2] Whereas the termination reactions of the alkyl radicals produced are now well understood, little if anything is known on the mechanism of the light-induced Co–C bond cleavage reaction. A detailed study of the photodealkylation of alkylcobalt derivatives of vitamin B_{12} and of cobaloximes was therefore performed to provide more information on the ground state and excited state properties of the Co–C bond in both types of compounds.

Another purpose of the present paper is to justify the use of cobaloximes as models of vitamin B_{12} by theoretical arguments. We shall for this reason first describe the electronic structure of cobaloximes and cobalamins in terms of an extended HMO treatment. The results of the semiempirical calculations will be used subsequently in the discussion of the nature of the axial bonding interactions, the analysis of the optical spectra, and to establish the mechanism of the primary processes in the photodealkylation.

The Electronic Structure of Alkylcobalamins and of the Cobaloxime Model Compounds

The remarkable chemical analogy between cobalamins and cobaloximes has been essentially attributed to the fortuitous identity of the in-plane coordinating strengths of the corrin and the bisdimethylglyoxime ligand systems,[3] a view which is directly supported by the results of an X-ray structural analysis[4] of a cobaloxime as well as by polarographic[5] and esr[6] data. The available experimental evidence thus suggests that the properties of the cobalt atom are not specifically dependent on the electronic structure of the vertical π-electron system of the in-plane ligands. The latter conclusion is not immediately obvious, however, and will be justified by the direct comparison of the electronic structures of alkylcobalamins and -cobaloximes as calculated by a variant of the extended, self-consistent HMO method (ω–β technique).[7–10] Details of the calculation are outlined in the Appendix. In Figure 1 the calculated π-electron charge distributions of the cobaloxime and the cobalamin models are shown; the results are directly comparable due to the identity of the parametrization. It appears that the cobaloxime has a slightly greater partial positive charge on cobalt and on the in-plane nitrogen atoms. The charge distribution in the axial ligands is virtually identical. The difference in the charge on cobalt could account for the known tighter binding of the axial bases in the cobaloximes and the lower kinetic reactivity of cobaloximes in axial ligand exchange reactions.[11,12] The interactions of the axial ligand MO's with the cobalt atom produces several new MO's and leads to the stabilization of others, as follows from the MO diagrams in Figures 2 and 3. The most important bonding and antibonding axial MO's are designated σ_1, π_1. Their

(1) (a) Predoctoral fellow, UCSD 1967–1970; (b) sponsored by the Petroleum Research Fund.
(2) G. N. Schrauzer, J. W. Sibert, and R. J. Windgassen, *J. Amer. Chem. Soc.*, **90**, 6681 (1968).
(3) G. N. Schrauzer, *Accounts Chem. Res.*, **1**, 97 (1968), and references cited therein.
(4) G. Lenhert, *Chem. Commun.*, 890 (1967).
(5) G. N. Schrauzer, R. J. Windgassen, and J. Kohnle, *Chem. Ber.*, **98**, 3324 (1965).
(6) G. N. Schrauzer and L. P. Lee, *J. Amer. Chem. Soc.*, **90**, 6541 (1968).
(7) The method of calculation has been employed previously for vitamin B_{12}[8] and nickel chelates of the type $NiS_4C_4R_4^{0,1-,2-}$.[9] It is similar to the iterative, extended HMO approximations developed by Nakajima[10] and Boyd and Singer.[11]
(8) G. N. Schrauzer, *Naturwissenschaften*, **53**, 459 (1966).
(9) G. N. Schrauzer and H. N. Rabinowitz, *J. Amer. Chem. Soc.*, **90**, 4297 (1968).
(10) T. Nakajima and S. Katagiri, *Mol. Phys.*, **7**, 149 (1963).
(11) G. V. Boyd and N. Singer, *Tetrahedron*, **18**, 1325 (1966).
(12) D. N. Hague and J. Halpern, *Inorg. Chem.*, **6**, 2059 (1967).

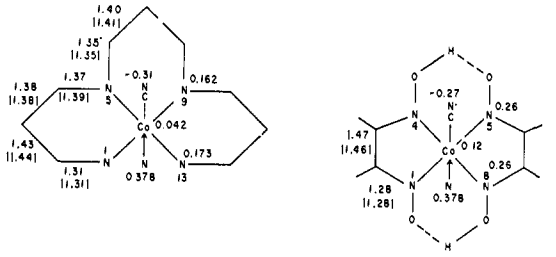


Figure 1. Calculated charges and calculated (observed) bond distances (in Å) of models of vitamin B_{12} and of "cyano(pyridine)-cobaloxime." Observed bond distances are average values.

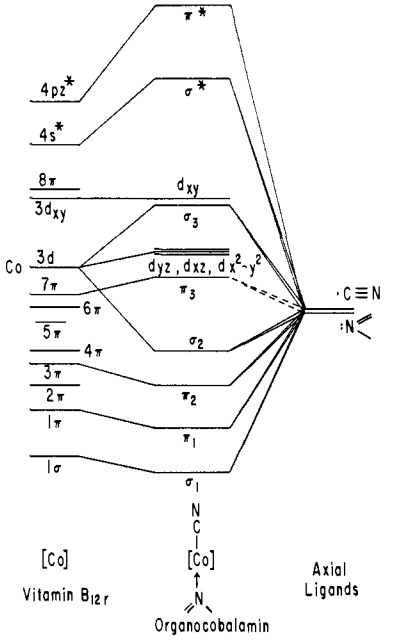


Figure 2. Schematic MO diagram depicting the effects of axial ligands on a model of vitamin B_{12r}. Only the most important orbitals are shown; MO's indicated on the left but not in the central portion of diagram remain essentially unaffected by the axial interactions. The π MO's of the axial ligands are not shown.

local symmetries are shown in Figure 4. The MO calculation reveals the eigenvalues and essential eigenvectors of the axial bond MO's in the cobalamin and the cobaloxime to be strikingly similar (Table I). This result provides a theoretical justification for the use of cobaloximes as vitamin B_{12} models. A difference between cobalamins and cobaloximes arises from the fact that certain of the cobalamin π MO's, mainly 7π, are labilized as a result of the axial interactions, producing a small ($\sim$0.5 eV) labilization of the axial bonds in the cobalamin. We conclude that the axial bonds in the cobaloxime model compounds are slightly more stable but otherwise identical with those in cobalamins. Axial ligands with unoccupied π or d orbitals attain some additional stabilization through π-back-bonding interactions. Since the $3d_{xz,yz}$ orbitals interact with the corrin π electron system only weakly, this type of "vertical conjugation"[13] has little if any direct spectroscopic consequences.[14]

(13) J. A. Elvidge and A. B. P. Lever, *J. Chem. Soc.*, 1257 (1961).
(14) This was shown by performing model calculations with and without including π-bonding axial interactions.

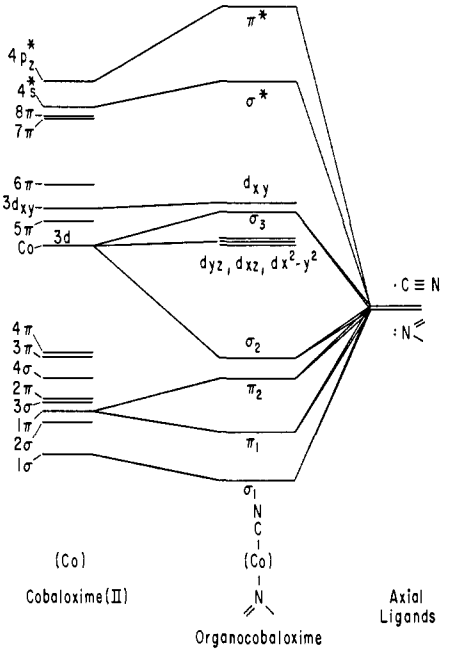


Figure 3. Effects of axial interactions on the MO of a planar cobaloxime(II). Note the principal similarity of the diagram with that in Figure 2 except the absence of the labilizing interaction π_3.

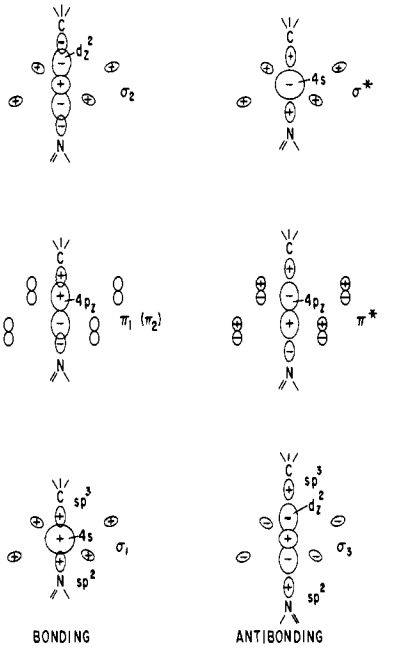


Figure 4. Local symmetries of the most important axial-bond MO's of a cobalamin and a cobaloxime. The local symmetry of π_2 is identical with that of π_1 in the cobaloxime. MO π_2 in the cobalamin has the same axial bond symmetry but two of the nitrogen MO's of the in-plane ligand are in a repulsive combination.

Co–C Bond Labilization through Steric Effects. Properties of Secondary Alkylcobalt Derivatives

The cobalt ion in vitamin B_{12} and in cobaloximes is sterically hindered to the extent that tertiary alkylcobalt derivatives, with few exceptions, are quite unstable and not isolable. Secondary alkylcobinamides are more labile than the corresponding cobaloxime derivatives as expected in view of the lower thermodynamic stability of the Co–C bonds in the vitamin B_{12} derivatives. Sec-

Table I. Eigenvalues and Cobalt and Axial Ligand Eigenvectors of the Axial Bond MO's $\pi_{1,2}$ and σ_{1-3} of a Model of Vitamin B_{12} (I) and a Cobaloxime (II). Ligands are CN^- and an Unsaturated Nitrogen Base

Orbital	$E(\beta)$		C_{CN}		C_N		$C_{3d_{z^2}}$		C_{4s}		C_{4p_z}	
	I	II	I	II	I	II	I	II	I	II	I	II
σ_1	−6.3353	−6.4404	−0.197	−0.200	0.361	0.351	0.035	0.039	−0.605	−0.603		
π_1	−5.7320	−5.8002	0.308	0.322	0.454	0.462					0.409	0.426
π_2	−5.1832	−5.0941	0.242	0.224	0.464	0.658					0.221	0.210
σ_2	−4.7237	−4.7911	−0.579	−0.599	0.375	0.356	−0.459	−0.465			−0.162	−0.168
σ_3	−2.7423	−2.9000	−0.289	−0.251	0.251	0.415	0.857	0.750			−0.108	−0.197

ondary alkyl cobalamins are not accessible by the usual synthesis routes because of the slower rates of alkylation of the Co(I) nucleophiles[15] and the sensitivity of the products to light, alkali, and excess reducing agent.[16,17] Using a special synthesis technique described in the Experimental Section, we have succeeded in preparing the very unstable compounds in solution. In Figure 5 the spectrum of cyclohexylcobalamin is shown. It is very similar to that of cyclohexylcobinamide,[18] suggesting that the 5,6-dimethylbenzimidazole ligand is not attached to cobalt. The compound is stable in acidic solution in the dark but slowly decomposes in neutral or alkaline medium. The absorption spectrum remains virtually unchanged upon the addition of excess imidazole or cyanide ion even though the compound decomposes faster in the presence of these ligands. This suggests that the coordination of a base in the axial position causes a further weakening of the Co–C bond, presumably by effecting a conformational change of the corrin system. In accord with a recent suggestion by Brodie[18] we believe that the cobinamide cobalt ion can bind secondary alkyl groups only with a concomitant conformational change of the corrin ring, placing the cobalt ion out of the plane of the four nitrogen atoms. Axial ligands would tend to reverse this effect and thus cause Co–C bond cleavage. The initial product of the Co–C bond cleavage in cyclohexylcobalamin is the cyclohexyl radical which terminates largely by cyclohexene formation. On reductive cleavage of cyclohexylcobalamin with dithioerythrol a mixture of cyclohexane and cyclohexene is produced in accord with the similar behavior of alkylcobaloximes.[2]

Spectroscopic Properties of Alkylcobalamins and -cobaloximes

Before discussing the mechanism of the photolysis reactions of the cobalt alkyl derivatives it is necessary to outline the spectroscopic properties of the compounds in some detail.

A. Alkylcobalamins. The optical properties of cobalamins are dominated by the inter-π transitions of the corrin chromophore. It consists of a 13-atom chain containing nitrogen in the positions 1, 5, 9, and 13, whose electronic structure has been treated by various authors.[8,20–22] Satisfactory correlations between calculated and observed transition energies have been obtained even with the complete neglect of the central metal and of the axial ligands.[20–22] Since the cobalt ion interacts with the vertical ligand π-electron system the main effects of the axial ligands may be traced back

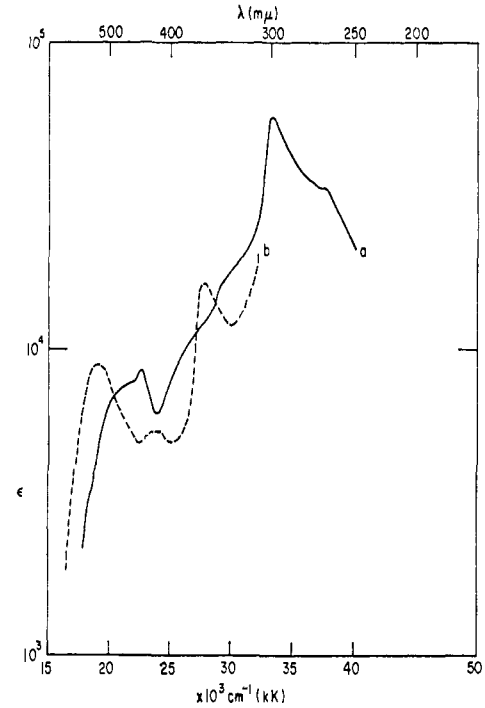


Figure 5. Spectra of cyclohexylcobalamin at pH 7: (a) before photolysis, (b) after photolysis. The spectrum of cyclohexylcobalamin in the presence of CN^- is essentially identical with (a).

to the change of the energy of 7π, the highest occupied π MO of the system, as a function of the axial ligands.[8] Its energy decreases almost linearly with increasing magnitude of the overlap integrals between the orbitals of the axial ligands and the $4p_z$ cobalt orbital.[8] Accordingly, all transitions involving 7π are shifted to lower energy if weakly interacting axial ligands are exchanged for strongly interacting ones, *e.g.*, water or OH^- by cyanide. π-Back-bonding interactions of the type discussed in the previous section are spectroscopically unimportant. The first inter-π transition is due to the excitation $^1\psi_7{}^8$ giving rise to a band between 580 and 450 mμ, commonly designated α. Its first vibrational fine structure is often resolved and known as β band. The next higher transitions could be $^1\psi_6{}^8$ or $^1\psi_7{}^9$, respectively. Their assignment is not unambiguous since often only one intense transition (γ band) is observable between 400 and 350 mμ. Two bands of moderate intensity are usually found in the

(15) G. N. Schrauzer and E. Deutsch, *J. Amer. Chem. Soc.*, **91**, 3341 (1969).
(16) Isopropylcobalamin was briefly mentioned by Firth, *et al.*,[17] as unstable, slowly decomposing in solution even in the dark.
(17) R. A. Firth, H. A. O. Hill, B. E. Mann, J. M. Pratt, and R. G. Thorp, *Chem. Commun.*, 1033 (1967).
(18) J. D. Brodie, *Proc. Nat. Acad. Sci. U. S.*, **62**, 461 (1969).
(19) H. Kuhn, *Fortschr. Chem. Org. Naturstoffe*, **17**, 404 (1959).
(20) H. Kuhn, H. Drexhage, and H. Martin, *Proc. Roy. Soc., Ser. A*, **288**, 348 (1965).
(21) B. H. Offenhartz, *ibid.*, **288**, 350 (1965).
(22) P. Day, *Theor. Chim. Acta*, **7**, 328 (1967).

Table II. Observed Co–C CT Transition Energies for a Variety of Organocobaloximes and Related Compounds in Alcohol–Water

R	In-plane ligand[a]	Axial base	λ_{max}, mμ (ε)
CH_3	Dmg	H_2O	448 (1.53 × 10³)
CH_3	Dmg	Py	438 (1.48 × 10³)
CH_3	Dmg	2-Picoline	450 (2.07 × 10³)
CH_3	Dmg	Benzimidazole	425 (1.2 × 10³)
CH_3	Dmg	Imidazole	410 (1.95 × 10³)
CH_3	Dmg	CNC_6H_{11}	425 (3.18 × 10²)
CH_3	Dmg	$P(C_6H_5)_3$	446 (1.37 × 10³)
CH_3	Dmg	$As(C_6H_5)_3$	446 (8.14 × 10²)
CH_3	Dmg	$Sb(C_6H_5)_3$	447.5 (2.48 × 10³)
CH_3	Dmg	NH_3	412.5 (1.09 × 10³)
C_6H_5	Dmg	Py	419 (1.3 × 10³)
p-$C_6H_4CH_3$	Dmg	Py	424 (1.3 × 10³)
p-$C_6H_4OCH_3$	Dmg	Py	423 (0.7 × 10³)
$-C\equiv C-C_6H_5$	Dmg	Py	370 (0.95 × 10³)
C_2H_5	Dmg	H_2O	456 (1.38 × 10³)
C_2H_5	Dmg	Py	448 (1.40 × 10³)
C_2H_5	Dmg	$P(C_6H_5)_3$	440 (0.46 × 10³)
C_2H_5	Dmg	$P(n\text{-}C_4H_9)_3$	428 (0.83 × 10³)
C_2H_5	Dmg	$As(C_6H_5)_3$	456 (1.14 × 10³)
C_2H_5	Dmg	$Sb(C_6H_5)_3$	458 (1.06 × 10³)
C_2H_5	Dmg	Benzimidazole	420 (1.15 × 10³)
C_2H_5	Dmg	Imidazole	405 (0.83 × 10³)
C_2H_5	Dmg	NH_3	412 (1.26 × 10³)
n-C_3H_7	Dmg	H_2O	455 (1.68 × 10³)
n-C_3H_7	Dmg	Py	454 (0.55 × 10³)
n-C_3H_7	Dmg	$P(C_6H_5)_3$	454 (1.07 × 10³)
n-C_3H_7	Dmg	$As(C_6H_5)_3$	455 (1.45 × 10³)
n-C_3H_7	Dmg	$Sb(C_6H_5)_3$	455 (1.51 × 10³)
n-C_3H_7	Dmg	Benzimidazole	414 (1.41 × 10³)
n-C_3H_7	Dmg	CNC_6H_{11}	406 (0.42 × 10³)
i-C_3H_7	Dmg	H_2O	455 (1.68 × 10³)
i-C_3H_7	Dmg	Imidazole	401 (1.48 × 10³)
$-CH_2-CH(CH_3)_2$	Dmg	H_2O	469 (1.01 × 10³)
c-C_6H_{11}	Dmg	Py	468 (1.84 × 10³)
$-CH(CH_3)CN$	Dmg	Py	428 (1.8 × 10³)
CH_2CH_2CN	Dmg	Py	406 (1.6 × 10³)
$CH_2CH{=}O$	Dmg	Py	435 (1.5 × 10³)
CH_2COOCH_3	Dmg	Py	429 (1.8 × 10³)
CF_3	Dmg	Py	335 (2.3 × 10³) (!)
CH_3	Glyoxime	Py	405 (1.27 × 10³)
CH_3	Chdioxime	Py	440 (1.2 × 10³)
CH_3	Dpg	H_2O	475 (2.1 × 10³)
CH_3	Dpg	Py	473 (3.16 × 10³)
CH_3	Dpg	$P(C_6H_5)_3$	470 (2.16 × 10³)
CH_3	Dpg	$P(n\text{-}C_4H_9)_3$	466 (1.37 × 10³)
CH_3	Dpg	Benzimidazole	455 (1.57 × 10³)
CH_3	Dpg	Imidazole	443 (1.57 × 10³)
CH_3	Dpg	CNC_6H_{11}	378 (1.45 × 10³)
CH_3	Dpg	NH_3	444 (2.6 × 10³)
C_2H_5	Dpg	H_2O	465 (1.68 × 10³)
C_2H_5	Dpg	Py	412.5 (1.72 × 10³)
C_2H_5	Dpg	Benzimidazole	430 (1.58 × 10³)
C_2H_5	Dpg	Imidazole	410 (1.97 × 10³)
C_2H_5	Dpg	NH_3	406 (1.68 × 10³)
CH_3	$Dmed^+$	H_2O	454 (2.1 × 10³)
C_2H_5	$Dmpd^+$	H_2O	463 (0.56 × 10³)
CH_3	Salen	H_2O	428 (2.2 × 10³)

[a] Dmg = dimethylglyoxime; Dpg, diphenylglyoxime; Chdioxime, 1,2-cyclohexanedione dioxime; $Dmed^+$, Schiff base derived from biacetyl monoxime and ethylenediamine; $Dmpd^+$ same as $Dmed^+$ except with propylenediamine; Salen, bis(salicylaldehyde)ethylenediimine.

spectra of cobalamins or cobinamides with weakly interacting ligands. If the ligands are cyanide, however, the intensity of one band is greatly enhanced at the expense of the other. This has been attributed[22] to configuration interaction between the two states $^1\psi_6{}^8$ and $^1\psi_7{}^9$. CI effects are negligible if the two states have sufficiently different energies, but become maximal if the energy differences are vanishingly small. On the basis of simple HMO calculations Day[22] concluded that the latter is the case if the ligands are cyanide. This is supported by the results of the extended HMO calculations reported here. The calculated energy difference between the two states becomes indeed very small for strongly interacting axial ligands such as CN^-. The CI produces an in-phase and an out-of-phase combination for which greatly different oscillator strengths are calculated.[22] In the spectra of alkylcobalamins CI is sufficiently small to permit the assignment of two bands as the almost pure $^1\psi_6{}^8$ and $^1\psi_7{}^9$ transitions. This leaves only one or two weaker bands unassigned,[22] none of which appears to be characteristic of the Co–C bond. The analysis of the spectra of alkylcobaloximes reveals that the expected Co–C CT transition is obscured by the intense α and β bands (see below). In

acid solution the spectra of alkylcobalamins resemble those of alkylcobinamides due to the protonation of the axial base, which is the main cause of the conspicuous "yellow-shift" of corrins.[23]

B. Alkylcobaloximes. The absence of extensive conjugation in the cobaloxime ligand π-electron system causes the energy of the inter-π transitions to be at high energy, the first at around 240 mμ (Figure 6). Between 400 and 250 mμ several unassigned ill-resolved bands with ϵ between 10^3 and 10^4 are located. Since the axial bases may absorb in this region these bands are of little diagnostic value so far as the cobaloxime moiety or the axial bonds are concerned. The important low-energy absorption of organo cobaloximes occurs between 400 and 500 mμ and is typical of the presence of covalent axial bonds. In view of the $\epsilon \sim 10^3$ it must be a charge-transfer band. We will present evidence for its assignment to the transition $\sigma_2 \rightarrow \sigma_3$ and will hereinafter designate it Co–C CT. Its energy depends sensitively on the axial base on cobalt, but also on inductive effects and the amount of 2s-character of the carbon residues attached. Examples for the various effects may be found in Table II. The Co–C CT transition is shifted to higher energy on changing the hybridization of the carbon residue from sp^3 to sp, and on varying the axial base component, in most cases in the sequence $H_2O \leq Sb(C_6H_5)_3 \leq As(C_6H_5)_3 < P(C_6H_5)_3 <$ Py < benzimidazole $\simeq$ CN–R < NH_3 < imidazole. With the exception of NH_3, this order is one of increasing σ-donor, π-acceptor character, which also mainly determines the thermodynamic stability of the axial base adducts.[24] Table II also contains λ_{max} values of alkylcobalt complexes of ligands other than Dmg. The energy of the transition increases with increasing donor power of the in-plane ligands. Stronger in-plane donors increase the charge density on cobalt and thus stabilize the Co–C bond. The effects of the axial bases are similar in the compound families of the same in-plane ligands although the magnitude of the Co–C CT band shifts may vary. As follows from Table II, the band shifts are greater for the weaker ligand Dpg than for Dmg, presumably because of the tighter binding of the axial base in the former.

In considering all available evidence the Co–C CT band is therefore assigned to transition $\sigma_2 \rightarrow \sigma_3$. For alkyl ligands the transition is predicted at around 3 eV on the basis of the extended HMO treatment, in satisfactory agreement with the observed range of 2.7–3.1 eV. In organocobaloximes with cobalt–metal bonds, R_3M–$Co(Dmg)_2B$, *e.g.*, M = Sn or Pb, a similar CT transition is observed between 500 and 450 mμ.[25] It was previously assigned to a d $\rightarrow \sigma^*$ transition but can now be assigned specifically to the $\sigma_2 \rightarrow \sigma_3$ transition. The corresponding Rh–C CT transition in organorhodoximes[26] is observed at higher energy in keeping with the greater stability of Rh–C relative to Co–C bonds. In methyl(aquo)rhodoxime, for example, the λ_{max} of the Rh–C CT transition is at 403 mμ (ϵ 7.30.10^2), in ethyl(aquo)rhodoxime at 410 mμ. On the basis of the MO bonding scheme (Figure 3) a second Co–C CT transition ($\sigma_2 \rightarrow d_{xy}$) should occur at slightly higher energy than the σ_2–σ_3 transition. This band appears to be observable in certain cases, *e.g.*, in one of the spectra in Figure 6, but is usually obscured.

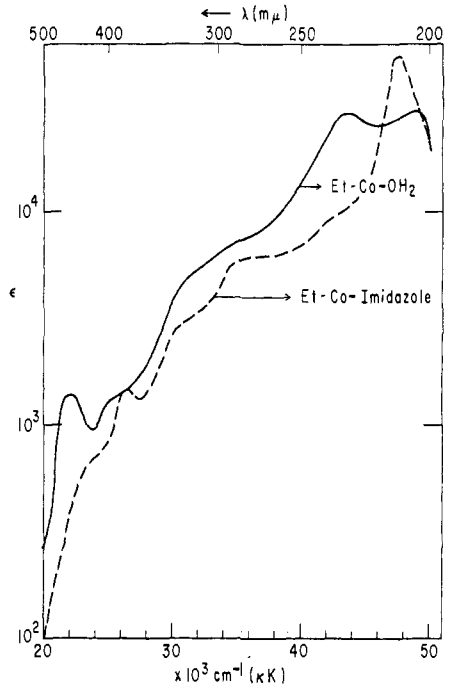
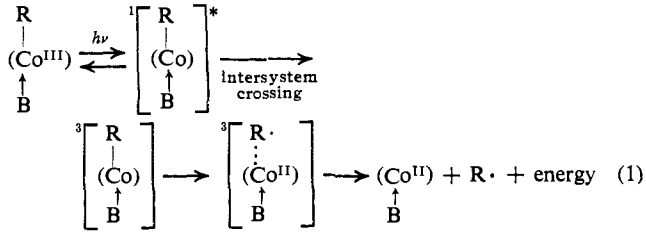


Figure 6. Absorption spectra of two alkylcobaloximes (both in water solvent).

The Mechanism of Co–C Bond Photolysis

The photochemical reaction preceding Co–C bond cleavage consists of the excitation of an electron from a bonding axial MO to an antibonding axial orbital. Since the Co–C CT transition $\sigma_2 \rightarrow \sigma_3$ occurs in the visible region it thus should be involved in the primary Co–C bond cleavage processes. This is supported by estimates of the minimum threshold energy of photolysis of alkylcobaloximes which coincides approximately with the Co–C CT transition energy. Thus, the aerobic photolysis of ethyl(aquo)cobaloxime is slow in monochromatic light of wavelengths greater than 480 mμ.

Orbital σ_2 is significantly localized in the axial ligand σ MO's, and σ_3 is composed largely of the antibonding $3d_{z^2}$ orbital (Figure 4). The Co–C bond excitation thus occurs by the transfer of a ligand electron to the metal and hence is directly related to known charge-transfer induced photoreduction reactions of Co(III) complexes (eq 1).[27] The rates of photolysis of alkyl-



cobaloximes are dependent on the efficiency of the recombination relative to the other radical termination reactions. The overriding factor influencing the pho-

(23) J. A. Hill, J. M. Pratt, and R. J. P. Williams, *J. Theor. Biol.*, 3, 423 (1962).
(24) G. N. Schrauzer and R. J. Windgassen, *J. Amer. Chem. Soc.*, 88, 3738 (1966).
(25) G. N. Schrauzer and G. Kratel, *Chem. Ber.*, 102, 2392 (1969).
(26) J. A. Weber and G. N. Schrauzer, *J. Amer. Chem. Soc.*, 92, 726 (1970).
(27) See E. L. Wehry, *Quart. Rev.*, 21, 213 (1967), for detailed discussion and references.

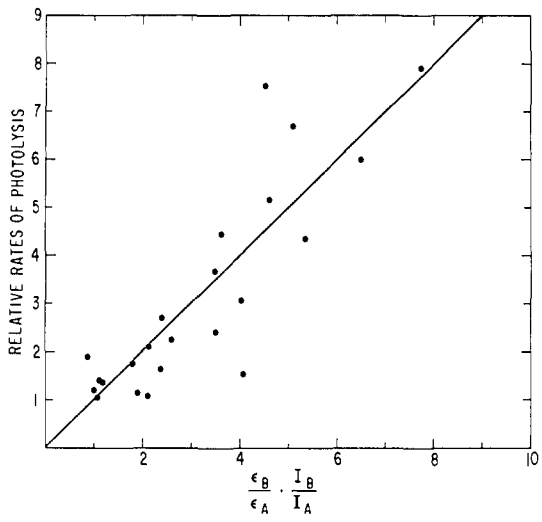


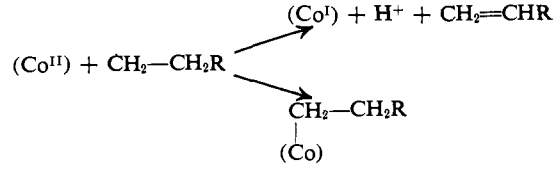
Figure 7. Correlation between the relative rates of photolysis of alkylcobaloximes with various axial bases and the product of the relative Co–C CT extinction coefficients and light source intensities at the wavelength of λ_{max} of the Co–C CT transition. All points relate to the photolysis rate of the corresponding aquocobaloxime with the same alkyl residue.

tolysis rates is the intensity of the radiation emitted by the light source in the region of λ_{max} of the Co–C CT transition, however. The relative rates of photolysis of alkylcobaloximes with the axial base B as compared to the aquo derivatives correlate satisfactorily with the quotient of the molar extinction coefficients ϵ and the relative light intensities I, $\epsilon_B I_B/\epsilon_A I_A$ (Figure 7). We emphasize that this correlation was obtained using aerobic photolysis rates. Under strictly anaerobic conditions all photodealkylations are slower due to more efficient recombination. This effect causes an anomalous stability of certain Co–methyl derivatives, as will be outlined below. The correlation in Figure 7 could probably be improved by using the relative oscillator strengths of the Co–C CT transition and average light intensity ratios. The use of the molar extinction coefficients is justified in view of the similarity of the Co–C CT band widths, however.

The relative aerobic photolysis rates of alkylcobaloximes with different axial bases decrease with decreasing λ_{max} and ϵ of the Co–C CT band. This implies a correlation between the thermodynamic stability of the Co–C bonds and the rate of photolysis. However, the alkylcobaloximes *seem* to become more light resistant with increasing energy of the Co–C CT transition *only* because of the light emission characteristics of the tungsten filament light source employed in the experiments.

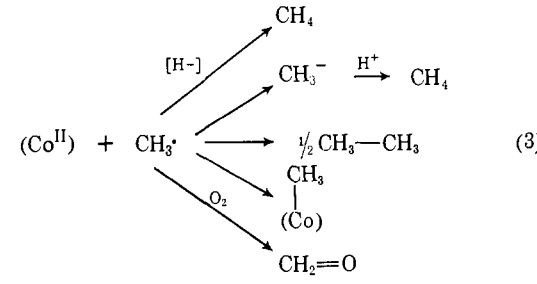
The Anomalous Photolysis Behavior of Methylcobaloximes

Higher alkyl radicals produced on photolysis of alkylcobaloximes terminate mainly either by recombination or olefin formation according to eq 2.[2] In view



(2)

of the efficiency of the olefin producing termination reactions the rates of photolysis are not very dependent on the nature of the solvent. The inability of the methyl radical to terminate by a mechanism related to eq 2 increases the importance of the recombination reaction.[2] Aerobically, methane and ethane are formed at low oxygen concentrations. The methane arises chiefly from ligand hydrogen abstraction, the ethane from methyl radical dimerization.[2] At high oxygen concentrations the methyl radicals are oxidized to formaldehyde.[2,24] The principal methyl radical termination reactions are summarized in eq 3. Anaerobically



(3)

a significant part of the methane is formed *via* methy radical reduction,[2] but the overall photolysis rates decrease considerably due to the increase of the efficiency of the recombination. Methylcobaloximes with pyridine, imidazole, or NH_3 as the axial bases become anomalously light resistant under anaerobic conditions. Thus, irradiation for 1 or 2 hr may indicate no change of the absorption spectrum whatsoever, suggesting that the complexes did not photodecompose at all. This remarkable behavior is not merely a consequence of the higher energy of the Co–C CT transition. It appears that the above-mentioned ligands modify the absolute energy of the Co $3d_{z^2}$ orbital to become essentially identical with that of the methyl radical. If this is verified the recombination could possibly reach a maximum efficiency. The stabilizing effect of the bases is only temporary. Photolysis usually does take place after prolonged irradiation; in the case of NH_3 there was evidence for a 2-hr induction period under our conditions of irradiation. This could be due to a slow displacement of the axial base by water, a process which could also be photoinduced,[27] but which in our systems has thus far not been studied in detail. We finally point out that the photolysis of all methylcobaloximes takes place readily in solvents containing abstractable hydrogen, *i.e.*, isopropyl alcohol.[2] Solvent H– abstraction evidently competes favorably with the recombination. Selected photolysis rate constants are listed in Table III.

Quantum Yields

The quantum yields of photodealkylation of a number of alkylcobaloximes were determined in the region of λ_{max} of the Co–C CT absorption. The magnitude of Φ observed (Table IV) is typical for charge-transfer induced excitation.[27] The photodealkylation reactions thus are related to CT photoreduction reactions of Co(III) chelates, *i.e.*, of the tris(ethylenediamine)cobalt(III) ion, for which a Φ of 0.070 was measured by Klein and Moeller.[28] Ligand field transitions are presumably

(28) D. Klein and C. W. Moeller, *Inorg. Chem.*, 4, 394 (1965).

Table III. Photolysis Rates of Alkylcobaloximes and -cobinamides in Water, Aerobic Conditions, Tungsten Light Source[a]

R	In-plane ligand	Axial base	Pseudo-first-order photolysis rate constants, sec^{-1}
CH_3	Dmg	H_2O	2.1×10^{-3}
CH_3	Dmg	Py	1.67×10^{-3}
CH_3	Dmg	Benzimidazole	1.72×10^{-3}
CH_3	Dmg	Imidazole	2.3×10^{-4}
CH_3	Dmg	NH_3	4.7×10^{-4}
CH_3	Dmg	CN^-	2.3×10^{-4}
CH_3	Dpg	H_2O	5.96×10^{-3}
CH_3	Dpg	Py	4.0×10^{-3}
CH_3	Dpg	Benzimidazole	3.52×10^{-3}
CH_3	Dpg	Imidazole	1.8×10^{-3}
CH_3	Dpg	NH_3	8.65×10^{-4}
CH_3	Dpg	CN^-	1.16×10^{-3}
CH_3	Cobinamide	H_2O	5.9×10^{-2}
CH_3	Cobinamide	Py	3.8×10^{-2}
CH_3	Cobalamin	Dimethylbenzimidazole	4.3×10^{-2}
CH_3	Cobinamide	Imidazole	3.46×10^{-2}
CH_3	Cobinamide	NH_3	1.8×10^{-2}
CH_3	Cobinamide	CN^-	2.0×10^{-2}
C_2H_5	Dmg	H_2O	5.8×10^{-3}
C_2H_5	Dmg	Py	3.5×10^{-3}
C_2H_5	Dmg	Benzimidazole	4.4×10^{-3}
C_2H_5	Dmg	Imidazole	1.0×10^{-3}
C_2H_5	Dmg	NH_3	0.72×10^{-3}
C_2H_5	Dmg	CN^-	1.22×10^{-3}
C_2H_5	Dmg	$P(C_6H_5)_3$	4.05×10^{-3}
C_2H_5	Dpg	H_2O	1.21×10^{-2}
C_2H_5	Dpg	Py	1.51×10^{-3}
C_2H_5	Dpg	Benzimidazole	2.06×10^{-3}
C_2H_5	Dpg	Imidazole	1.80×10^{-3}
C_2H_5	Dpg	NH_3	1.72×10^{-3}
C_2H_5	Dpg	CN^-	0.6×10^{-2}
C_2H_5	Dpg	Aniline	4.9×10^{-3}
C_2H_5	Dpg	$N(C_2H_5)_3$	2.62×10^{-3}
C_2H_5	Dpg	Piperidine	5.6×10^{-3}
C_2H_5	Dpg	CH_3CN	5.5×10^{-3}
C_2H_5	Cobinamide	H_2O	1.21×10^{-2}
C_2H_5	Cobinamide	Py	1.08×10^{-2}
$c\text{-}C_6H_{11}$	Cobalamin	Dimethylbenzimidazole	6.0×10^{-1}
C_2H_5	Cobalamin	Dimethylbenzimidazole	2.8×10^{-2}
C_2H_5	Cobinamide	Imidazole	1.33×10^{-2}
C_2H_5	Cobinamide	NH_3	1.31×10^{-2}
C_2H_5	Cobinamide	CN^-	2.64×10^{-2}
$(CH_3)_2CH\text{-}CH_2$	Dmg	H_2O	5.56×10^{-2}
$(CH_3)_2CH\text{-}CH_2$	Dmg	Py	1.44×10^{-2}
$(CH_3)_2CH\text{-}CH_2$	Dmg	Benzimidazole	2.3×10^{-3}
$(CH_3)_2CH\text{-}CH_2$	Dmg	Imidazole	7.48×10^{-3}

[a] The photolysis conditions were chosen to assure minimal (10%) absorbance of the incident light by the sample solutions. This was achieved by using an intense light source (300 W) and dilute solutions of the complexes with absorbances not exceeding 0.5 in the region of λ_{max} of the Co–C CT transition. The observed rate law was cleanly first order.

too inefficient to be in photoexcitation processes preceding Co–C bond cleavage but could possibly play a part in photoaquation reactions of our complexes. However, these effects require more detailed study. The quantum yield of aerobic photodemethylation of Co-methylcobaloximes is smaller than that of the Co-ethyl derivatives due to the greater efficiency of the recombination reaction in keeping with the greater light resistance of the Co-methyl derivatives (Table III).

Table IV. Quantum Yields of Aerobic Photodealkylations of Alkylcobaloximes in the Region of λ_{max} of the Co–C CT Transition (in H_2O, 27°)

R	In-plane ligand[a]	Axial base	Φ[b]	λ, mμ[c]
CH_3	Dmg	H_2O	0.0140	448
CH_3	Dmg	Py	0.00054	440
CH_3	Dmg	Benzimidazole	0.0497	420
CH_3	Dmg	NH_3	0.00282	420
CH_3	Dpg	H_2O	0.016	475
CH_3	Dpg	Py	0.00332	475
CH_3	Dpg	Benzimidazole	0.00429	455
CH_3	Dpg	Imidazole	0.00342	445
C_2H_5	Dmg	H_2O	0.0217	455
C_2H_5	Dmg	Py	0.0101	450
C_2H_5	Dmg	Benzimidazole	0.0209	420
C_2H_5	Dmg	Imidazole	0.00665	405
C_2H_5	Dpg	H_2O	0.0237	465
C_2H_5	Dpg	Py	0.0118	410
C_2H_5	Dpg	Benzimidazole	0.0158	430
C_2H_5	Dpg	NH_3	0.0575	405

[a] Dmg = dimethylglyoxime; Dpg = diphenylglyoxime. [b] Approximate error ±5%. [c] Wavelength of measurement.

The Photolysis of Alkylcobalamins and -cobinamides

The rates of aerobic photodealkylation of alkylcobalamins and -cobinamides are usually greater than those of the corresponding cobaloximes by about a factor of 10. Since the efficiency of intersystem crossing should not be greatly different this is attributed primarily to the lower strength of the Co–C bond in the vitamin B_{12} derivatives and to possible contributions from excitations other than $\sigma_2 \rightarrow \sigma_3$ in the initial energy absorption processes. Unfortunately, the Co–C CT transition is obscured by the α and β bands. The corrin ligand does not seem to greatly sensitize Co–C bond cleavage since the photodealkylation, *e.g.*, of ethylcobalamin becomes very slow at wavelengths greater than 500 mμ, even though the energy output of the light source and the intensity of the α and β bands reach a maximum in this region. A contributing factor to the greater rate of photolysis of the alkylcobalt derivatives of vitamin B_{12} could be the excitation $\pi_3 \rightarrow \sigma_3$. However, the photolysis rate difference between ethylcobinamide and ethylcobalamin suggests that this energy transfer process is of minor importance [methylcobalamin photolyzes at a slower rate than methylcobinamide (Table III), even though its $\pi_3 \rightarrow \sigma_3$ transition must be at lower energy]. The very fast rate of photolysis of cyclohexylcobalamin is undoubtedly a consequence of the weakness of the Co–C bond. Cyclohexyl(pyridine)cobaloxime similarly photolyzes faster than ethyl(pyridine)cobaloxime approximately by a factor of 10 (Table III). The effects of axial bases on the aerobic photolysis rate of methylcobaloximes and methylcobinamide are quite similar, as follows from Figure 8.

The effects of the axial bases are less pronounced in the cobinamide series presumably due to the weaker binding of the axial bases. The anaerobic photolysis rates are usually slower than the aerobic. The methylcobalt derivatives with 5,6-dimethylbenzimidazole,[29,30] imidazole, or NH_3 are anomalously light stable, how-

(29) The effect of oxygen on the photolysis rates of alkylcobalamins was first observed by A. W. Johnson and his coworkers.[30]

(30) D. Dolphin, A. W. Johnson, and R. Rodrigo, *Ann. N. Y. Acad. Sci.*, 112, 590 (1964).

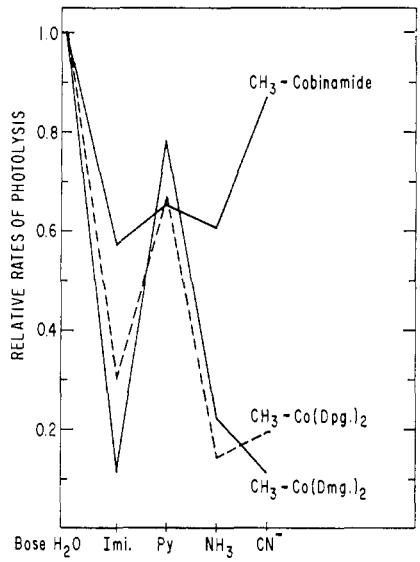


Figure 8. Effects of axial bases on the relative aerobic photolysis rates of methylcobinamide, and of two different Co-methylcobaloxime derivatives. (Dmg and Dpg denote the monoanions of dimethylglyoxime and diphenylglyoxime, respectively.)

ever, at least on irradiation with light of moderate intensity over a period of 1 to 3 hr. Methyl(aquo)-cobinamide photodecomposes slowly and the rates of photolysis decrease with increasing length of irradiation. It is possible that the initial photolysis occurs due to traces of oxygen present in the system.

These observations are of interest in view of the reported light stability of methylcobalamin in certain enzymes, *e.g.*, the 5′-methyltetrahydrofolatehomocysteine transmethylase of *Escherichia coli* B.[31] The holoenzyme is inactivated through reductive *n*-propylation but may be reactivated on exposure to light. Whereas the propylated cobinamide retains its photolability in the enzyme, the *methylated* derivative was found to be light stable on aerobic irradiation at 0°.[31] Pailes and Hogenkamp,[32] who independently studied effects of bases on the aerobic photolysis of methylcobinamide, suggested that the displacement of the 5,6-dimethylbenzimidazole ligand of methylcobalamin by the imidazole moiety of a histidine of the apoprotein could be responsible for the decrease in light sensitivity. The absorption spectrum of the methylated holotransmethylase shows bands of 470, 445, 405, and 355 mμ[33,34] and thus resembles methylcobinamide rather closely. Imidazole coordinated to the cobalt atom of methylcobinamide causes a shift of the α band to 524 mμ. It would appear, therefore, that histidine or any other base could only be weakly coordinated to cobalt, if at all, in the methylated holoenzyme.

Taylor and Weissbach[31] suggested that the light stability of the methylated holoenzyme is due to the local protection of the corrin to oxygen. We favor this interpretation in view of the demonstrated anomalous photostability of methylcobinamides under anaerobic conditions. Since many reactions requiring vitamin

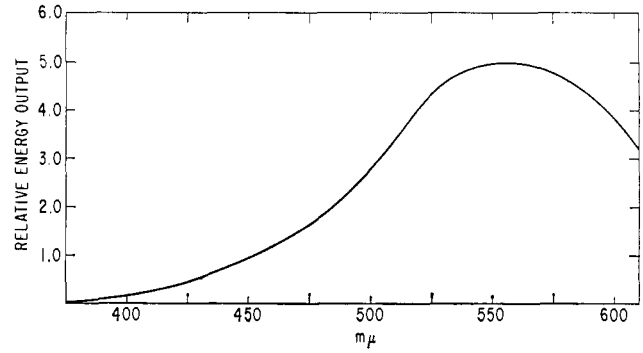


Figure 9. Relative energy output of a tungsten filament lamp used in the photolysis experiments as determined by measurement with a photomultiplier tube.

B_{12} or coenzyme B_{12} take place under reducing conditions one function of the apoprotein may be to protect the reduced cobamide cofactor against oxygen.

Experimental Section

Starting Materials. All reagents were reagent grade or better and commercially available. Vitamin B_{12a} and Factor B (cyanoaquocobinamide) were obtained from Merck Sharp and Dohme Research Laboratories, Rahway, N. J.

Organocobaloximes. All organocobaloximes were prepared by known methods[35-37] and of analytically established purity.

Organocobalt derivatives of cobalt chelates other than cobaloximes were prepared by reductive alkylation of the parent Co(III) or Co(II) chelates as outlined in ref 2.

Primary Alkylcobalamins and -cobinamides. Vitamin B_{12a} or Factor B was dissolved in deionized water. A drop of 0.1 *M* $CuSO_4$ solution was added and the solutions transferred into Pyrex glass vials equipped with rubber serum caps. The Co(I) nucleophiles were generated by adding fresh solutions of $NaBH_4$ in methanol to the solutions of the corrins under argon. Solutions of the alkyl halides in methanol were added in excess by means of a syringe. Upon completion of the alkylation reaction the excess of borohydride was destroyed with a few drops of acetone or acetaldehyde. The alkylcobalt derivatives were purified through phenol extraction as outlined in ref 38.

Cyclohexylcobalamin. To 10 mg of vitamin B_{12a} in 1 ml of water were added 2 ml of methanol and 1 drop of 0.1 *M* $CuSO_4$. The tube was sealed with a serum cap and deaerated by sweeping with argon for 5 min. A fresh solution of $NaBH_4$ was added and reduction to the Co(I) nucleophile occurred within 30 sec. An excess of purified bromocyclohexane was added and the tube was placed in the dark for approximately 5 min until the solution had become orange-red. The excess borohydride was destroyed by adding 1 ml of 0.2 *M* phosphate buffer (pH 5.5). All the operations involving the secondary corrinoids were performed under reduced light. Cyclohexylcobalamin decomposed in a few hours in the dark at room temperature but could be kept at −20° for several days.

Spectroscopic Measurements. All absorption spectra were obtained with a Beckman DK 2-A spectrophotometer under the conditions indicated in the text.

Photolysis Rates. If not stated otherwise, the photolysis rates of alkylcobalt compounds were determined by irradiating aqueous solutions of the organocobalt complexes with the unfiltered light generated by a 300-W GE projector spot lamp situated 40 cm from the measuring cuvette. The cuvettes were water-cooled to 27° during irradiation. The emission characteristics of the light source were determined by measuring the spectral energy output photometrically.

To assure spectral constancy of the light source the emission characteristics of the lamp were rechecked after 10, 20, and 50 hr of

(31) R. T. Taylor and H. Weissbach, *Arch. Biochem. Biophys.*, **123**, 109 (1968).
(32) W. H. Pailes and H. P. C. Hogenkamp, *Biochemistry*, **7**, 4160 (1968).
(33) R. T. Taylor and H. Weissbach, *Arch. Biochem. Biophys.*, **119**, 572 (1967).
(34) R. T. Taylor and H. Weissbach, *J. Biol. Chem.*, **242**, 1502 (1967).
(35) G. N. Schrauzer and J. Kohnle, *Chem. Ber.*, **97**, 3056 (1964).
(36) G. N. Schrauzer and R. J. Windgassen, *J. Amer. Chem. Soc.*, **89**, 143 (1967).
(37) G. N. Schrauzer, *Inorg. Syn.*, **11**, 61 (1968).
(38) H. A. Barker, R. D. Smyth, and H. P. C. Hogenkamp, *Biochem. Prep.*, **10**, 27 (1963).

lamp use. A typical light intensity distribution curve is given in Figure 9. The photolysis sample solutions were placed into quartz cells of 1-cm path length and approximately 5-ml volume. In the cobaloxime experiments the course of the photolysis was usually monitored at λ_{max} of the Co–C CT transition. In the experiments with the corrin compounds the measurements were carried out by following the changes of OD at 525 mμ. Using values of $OD_t - OD_\infty$ good first-order rate plots were obtained. The first-order rate constants given in Table III are accurate within ±2% and a reproducibility of ±5% under otherwise identical conditions. Axial bases were added, solubility permitting, in large (10^3-fold) excess, if the corresponding cobaloxime adduct was unavailable or unstable.

Quantum yields listed in Table IV were determined in aqueous solutions under aerobic conditions of irradiation with monochromatic light in the region of λ_{max} of the Co–C CT transition. The Φ values were calculated using the potassium ferrioxalate actinometer,[39] as described in ref 40; the monochromator was a commercial instrument (Bausch and Lomb). For the actual measurements the concentrations of the complexes and of the potassium ferrioxalate solutions were adjusted so as to have identical absorbancies at the wavelength selected for the quantum yield determination. The photolysis light source was 500 W.

Acknowledgment. This work was supported by Grant No. GP 12324 of the National Science Foundation.

Appendix. Method of Calculation

The ω–β technique combines the conventional ω technique with an iterative variation of the resonance integrals. The diagonal matrix elements are assumed to vary linearly with the charge, with $\omega = 1.4\beta_0$ ($\beta_0 = -3.000$ eV). The C–C and C–N bond distances are related to the calculated π-bond orders by the empirical equations[41]

$$r_{ij}(\text{C–C}) = 1.511 - 0.173p_{ij}$$

$$r_{ij}(\text{C–N}) = 1.478 - 0.208p_{ij}$$

The dependence of β_{ij} on the distance is described by an exponential function,[41] $\beta_{ij} = \beta_{ij}^0 \exp b(r_0 - r_{ij})$, with $b = 5.007$. The bond distance and bond order–bond distance relations were combined and for computational convenience expressed in a power series[42]

$$k_{ij} = k_0 + k_i p_{ij} + k_2 p_{ij}^2 + k_3 p_{ij}^3 + \ldots$$

The k_{ij}'s for C–C and C–N bonds are as follows.

	k_0	k_1	k_2	k_3
C–C	0.65074	0.4972	0.05142	0
C–N	0.74746	0.62140	0.07433	0

Only the C–C and C–N distances of the in-plane ligands were varied; the in-plane Co–N and the axial Co–ligand distances were kept constant and were chosen in accord with known experimental values.

Suitably calibrated values for the input Coulomb terms were selected for C and N and Co orbitals and were the same as in ref 8.

The off-diagonal elements were calculated assuming $\beta_{C=N} = 1.20\beta_{C=C}$. The H_{ij}'s involving cobalt orbitals were approximated by assuming direct proportionality to the overlap integrals.[43] The latter were calculated using Slater-type orbitals for N and C and with Richardson basis set orbitals for the 3d, 4s, and 4p cobalt orbitals. The in-plane Co–N distances were put at 1.90 Å, the N–Co–N angles were for the cobalamin: N_1–Co–N_5 = N_9–Co–N_{13} = 80°; N_5–Co–N_9 = N_1–Co–N_{13} = 100°; for the cobaloxime N_1–Co–N_4 = N_4–Co–N_8 = 80°; N_4–Co–N_5 = N_1–Co–N_8 = 100°, respectively. The axial bond distances Co–C and Co–N were 2.05 Å. Bond distances of the in-plane ligand were initially not specified (to save computing time the values are usually assumed to be intermediate between single and double bonds). "Self-consistency" is reached after 9–11 cycles; the final C–C and C–N distances agree closely with the experimental values.

(39) (a) C. A. Parker, *Proc. Chem. Soc., London*, **A220**, 104 (1953); (b) C. G. Hatchard and C. A. Parker, *ibid.*, **A235**, 518 (1956).

(40) J. G. Calvert and J. N. Pitts, "Photochemistry," John Wiley and Sons, Inc., New York, N. Y., 1966, p 783.

(41) R. L. Miller, P. G. Lykos, and H. N. Schmeising, *J. Amer. Chem. Soc.*, **84**, 4623 (1962).

(42) The ω–β program was written by Dr. J. A. Schachtschneider, Shell Development Co., Emeryville, Calif.

(43) K in $H_{ij} = KS_{ij}$ was assigned the value of 10.0, which approximately corresponds to the value calculated according to the familiar expression

$$H_{ij} = k\frac{H_{ii} + H_{jj}}{2}S_{ij}$$

for appropriate values of H_{ii} and H_{jj}, with $k \sim 1.0$.