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Structural Properties of Organocobalt Coenzyme B_{12} Models

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1 Introduction

Homolysis of the Co–C bond of coenzyme B_{12} (5′-deoxyadenosylcobalamin, Figure 1) is generally accepted to be an essential step in the enzymatic reactions for which coenzyme B_{12} is a cofactor.[1–6] Cobalamins (Cbls) are a class of compounds with the cobalt(III) coordinated in the equatorial plane by four corrin N atoms and in the axial position by a 5,6-dimethylbenzimidazole nucleotide. If the nucleotide is missing, the molecules are called cobinamides. The seminal experiments and some of the key conceptual contributions in this field have recently been reviewed in this journal.[4] In that review, the rate of Co–C bond homolysis was estimated to be increased by $\approx 10^5$ on binding of coenzyme B_{12} to the protein, and by a further factor of $\approx 10^5$ by substrate binding. More recent studies document a $\geqslant 10^{13}$ increase in the rate of the coenzyme B_{12} Co–C bond cleavage in the holoenzyme compared to cleavage of this bond in the absence of enzyme in solution.[5] The manner in which the enzyme accomplishes this rate enhancement remains a mystery, although it is likely that the enzyme must use its cofactor·enzyme intrinsic binding energy[5] to weaken the Co–C bond or otherwise 'trigger' the Co–C bond homolysis step. The molecular level details of this process are of considerable interest. Specifically, B_{12}-cofactor-localized mechanisms that have been postulated to account for the enzyme-accelerated Co–C bond homolysis include:[3] (a) a distortion in the corrin ring increasing the steric interaction with the adenosyl moiety (the 'butterfly' bending or upward conformational theory);[3,5,7] (b) a direct lengthening or angular distortion[4] of the Co–C bond by the protein; and (c) an alteration in the position or Co–N bond

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length[8] of the axial 5,6-dimethylbenzimidazole (bzm) ligand. U.v. spectral data have been used to suggest that the Co–bzm bond is broken during catalysis, giving the so-called base-off (benzimidazole-unprotonated) form of the coenzyme,[9] and several studies exist claiming that axial base-free 5′-deoxyadenosylcobinamide (Ado-Cbi^+) is still a partially active cofactor.[5]

The adenosyl–cobalt bond in coenzyme B_{12} is relatively stable when compared to other alkyl–cobalt bonds. Coenzyme B_{12} and Ado-Cbi^+ not only exhibit the largest $\Delta H_h^{\ddagger}$ (Co–C bond homolysis activation enthalpy) for an alkyl-Cbl (20—27 kcal mol^{-1})[10] or an alkyl-Cbi^+ (27—32 kcal mol^{-1}),[10] respectively, but Ado-Cbi^+ also exhibits the largest $\Delta H_h^{\ddagger}$ value reported[5] to date, 37.5 kcal mol^{-1}, when compared to all literature values (17—37.5 kcal mol^{-1}).[5,6,10–17] Since the essential, and perhaps only, role of coenzyme B_{12} in the holoenzyme is thought to be the homolysis of the Co–C bond,[2,4,18–20] comparison of the rates of thermally induced Co–C bond homolysis and Co–N bond dissociation rates to structures of both models and Cbls is of special significance and is the subject of this review. Particular emphasis will be placed on cobaloxime models which contain dioximate ligands in the equatorial plane (*vide infra*).

2 Cobalamins

Cbls contain a corrin ring, which is similar in structure to a porphyrin ring with one bridge atom missing and with saturated β-positions on the five-membered rings A and D (Figure 1). Seven amide chains are attached to the corrin. One of the amides is linked by a 2-aminopropanol group to a 5,6-dimethylbenzimidazole nucleotide. These side chains, as well as the eleven ring-methyl substituents, limit the flexibility of the corrin and, when axially projected from the rings, serve to 'protect' the axial Co–C bond. The axial R ligand, coordinated to the upper or β-site of the corrin ring, is 5′-deoxyadenosyl in B_{12} coenzyme (Ado-Cbl), CN in vitamin B_{12} (CN-Cbl), and an alkyl group in alkylcobalamins (alkyl-Cbl). The benzimidazole residue is coordinated to cobalt in the lower or α-site. A second organocobalamin, Me-Cbl, is also an important cofactor for many enzymic processes. CN-Cbl serves as a metabolic precursor for both coenzymes. Their

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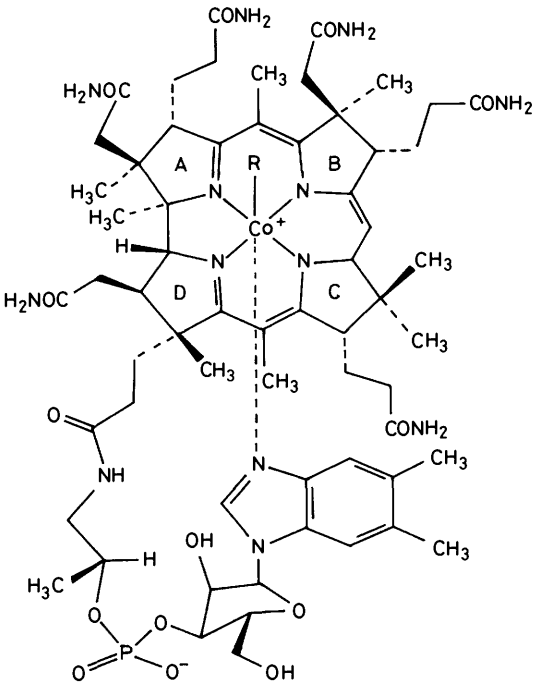

Figure 1 *Atomic model of cobalamins*

biological aspects have been reviewed extensively,[1] and the need for understanding the structural factors influencing the Co–C bond homolysis in Ado-Cbl has been emphasized.[2–4,21]

A. *X*-Ray Structures.—The results of *X*-ray structure analyses of Cbls and related compounds were thoroughly reviewed in 1981.[22] Surprisingly, the only structural results available then for Co–C bonded systems were for different forms of CN-Cbl in addition to the first determination of CN-Cbl done by Dorothy Hodgkin in 1950s,[22] and the only organocobalamin structure was for Ado-Cbl. Since then, only a few more structure analyses have been reported. Among them, the Me-Cbl structural analysis finally appeared.[23] Except for the axial group, the structure of this coenzyme is very similar to those previously reported, although there is some

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Table 1 *Coordination geometry in cobalamins*

R	Co–N(ax) (Å)	Co–C (Å)	Co–N(eq) (Å)	N(ax)–Co–C (°)	Co–Cα–Cβ (°)	*Ref.*
CN	2.03(2)	1.91(3)	1.91—1.94(2)	175.0(9)	176(3)	*a*
P(O)F(OMe)	2.09(2)	—	1.88—1.92(1)	—	—	*b*
Me	2.19(2)	1.99(2)	1.88—1.97(2)	171(2)	—	*c*
$PO(OMe)_2$	2.20(1)	—	1.91—1.96(1)	—	—	*b*
Ado (neutron)	2.24(1)	2.04(1)	1.82—1.96(1)	169.0(8)	121.0(8)	*d*
Ado (*X*-ray)	2.24(1)	2.00(1)	1.87—1.91(1)	173.0(5)	124.0(5)	*d*
(*R*)-Dhp	2.27(2)	2.00(2)	1.84—1.95(2)	169.1(9)	120(2)	*e*
(*S*)-Dhp	2.36(3)	2.08(3)	1.89—1.98(3)	172(1)	114(2)	*e*

[a] Ref. 25. [b] Ref. 26. [c] Ref. 23. [d] Ref. 27. [e] Ref. 24, Dhp = 2,3-dihydroxypropyl.

disorder in the area of the phosphate group. A careful comparison of the benzimidazole orientation and the side-chain conformation in both Me-Cbl and CN-Cbl revealed a remarkable similarity, with the exception of the orientation of the side-chain terminal amide groups. The coordination bond lengths are given in Table 1, together with the axial N–Co–C and the Co–Cα–Cβ angles. More recently, the crystal structures[24] of two isomers (*R*) and (*S*) of 2,3-dihydroxypropylcobalamin (Dhp-Cbl) gave the geometrical data reported in Table 1. The cobalamin portion of both molecules is very similar to that of Ado-Cbl. The alcohol residue, which adopts a similar conformation in the (*R*)- and (*S*)-isomers, uses in the latter a channel between C and D corrin rings to locate its Cβ-CH_2OH group so that the Cβ-OH residue can hydrogen bond to the carbonyl oxygen of the *c*-acetamido group. The ribose ring in Ado-Cbl nestles in this channel since it has a chirality corresponding to that of the (*S*)-conformer. No hydrogen bonding occurs in the (*R*)-isomer. The larger Co–Cα–Cβ angle (Table 1) for (*R*) than for (*S*) has been attributed to the hydrogen bond and to less severe steric interactions in (*S*). On the other hand, the narrower Co–Cα–Cβ angle corresponds to a longer Co–C bond in the (*S*)-isomer. Although the experimental errors limit this comparison, it may be suggested that the response to the steric demands and to hydrogen bond formation takes place mainly through a lengthening of the Co–C bond in the (*S*)-isomer but through an opening of the Co–C–C angle in the (*R*)-isomer. Similar behaviour has been observed already in cobaloximes.[3]

The structure of a new crystalline form of CN-Cbl has been refined using diffractometer data.[25] Some geometrical parameters are reported in Table 1. The overall structure, although more accurate, does not differ significantly from those already reported.[22] The structure of a monocarboxylic acid derivative of CN-Cbl, in which an amide group (probably in chain *b*) is converted into a carboxylic

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group, has axial distances[26] very close to those of CN-Cbl, *i.e.* Co–C 1.91(1) Å and Co–N 2.01(1) Å.

High-resolution neutron and *X*-ray diffraction data for Ado-Cbl were collected[27] (Table 1) to obtain greater structural resolution than that of the early work.[22] The *c* side-chain of the corrin is disordered between two extreme positions. Six of the eleven methyl groups appear to be ordered while the remaining five either undergo an extensive thermal libration or are statistically disordered. The details of the solvent structure analysis have also been reported.[28] Comparison of the results reported in Table 1, although limited because of data accuracy, shows unequivocally that the Co–N(bzm) distance reflects the σ-donor power of the *trans*-ligand. An increase of 0.3 Å occurs in the order CN < Me < Ado < Dhp. The Co–C bond length is particularly short for CN-Cbl, as expected on the basis of the covalent radius of a C(*sp*) compared with that of a C(sp^3). On the other hand, the Co–Me bond length lies at the lower limit of the range found for the other alkylcobalamins of Table 1.

The structures of two Cbls having $P(O)(OMe)_2$ and P(O)F(OMe) as the axial ligand have been reported.[26] The accuracy of these results (Table 1) allows an evaluation of the *trans*-influence of the two axial groups. The relatively long Co–N(axial) bond in $P(O)(OMe)_2$-Cbl is in agreement with evidence in solution that $P(O)(OMe)_2$ is a strong *trans*-influencing group, similar to methyl, in both cobaloximes[3] and in Cbls.[21]

B. Kinetics and Co–C Bond Dissociation Energy.—Halpern[2] showed that a reasonable estimate of the Co–C bond dissociation energy (BDE) can be obtained from $\Delta H^{\neq}$ of the Co–C bond homolysis in solution of simple models. Since then, several determinations of Co–C BDE in Ado-Cbl and similar systems have appeared. In Ado-Cbl and related alkylcobalamins the Co–C bond homolysis can occur through both the base-on (a) and base-off (b) forms, which are in equilibrium (Scheme 1). A value of the base-on Co–C BDE of 26 ± 2 kcal mol^{-1} has been reported by Halpern,[6] which is lower than that of 30 ± 2 kcal mol^{-1} reported by Finke.[29] More recently, the latter authors have measured[5] the Co–C BDE in $AdoCbi^+$. An estimate of 34.5 ± 1.8 kcal mol^{-1} was suggested, so that the removal of the *trans*-axial base strengthens the Co–C bond by about 4 kcal mol^{-1}, while the coordination of the axial base to Co increases the rate of the Co–C bond homolysis by a factor of 10^2. As mentioned above, the Co–C(Ado) BDE in the complex natural cofactor Ado-Cbl is quite large and the precise value is the subject of controversy. Therefore, the factors influencing it and Cbl properties in general have been investigated extensively with model compounds such as those to be described next.

These elegant evaluations of Co–C BDEs require exhaustive and extensive

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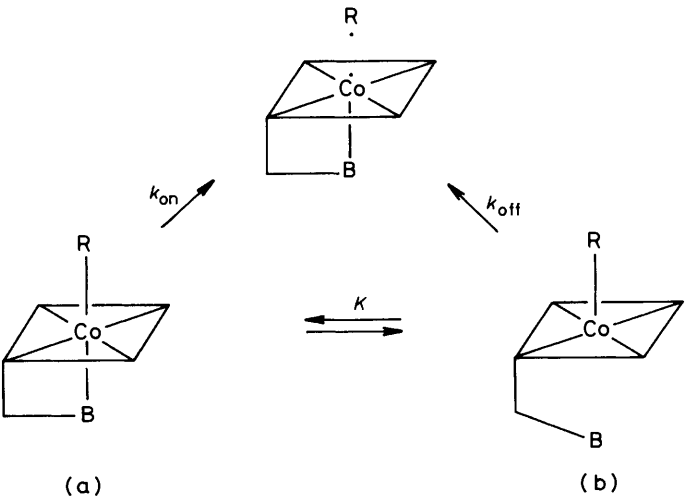


Scheme 1

experimental studies. The rates of decomposition of many alkyl Cbls have been evaluated in pioneering studies in Schrauzer's and Pratt's laboratories.[4] Although we note that the effects of steric factors in Co–C bond cleavage have been reviewed,[4] an abbreviated series relevant to our studies follows:

$$Me < 5'\text{-deoxyadenosyl} < Et < Pr^{i}, CH_2CMe_3$$

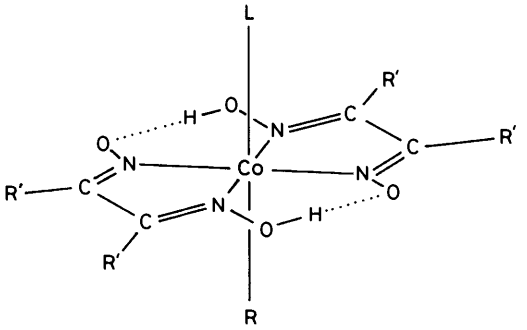
In this review, we shall consider the question: How does the series compare with precise structural information on models and the limited structural data on Cbls?

3 Dioximates

The most extensively studied model system, the cobaloximes containing the dioximate moiety, was reviewed in depth in 1985.[3] Since this review was published, many structural and solution data have appeared on dioximate cobalt complexes, most of them having bis(dimethylglyoximato), $(DH)_2$, as equatorial ligand (Figure 2). Some data have been reported for the bis(glyoximato), $(GH)_2$, and bis(diphenylglyoximato), $(PH)_2$, derivatives (Figure 2).

About 50 new structures of organometallic complexes have appeared in the past four years. Structural and solution results for these complexes will be reported in this section and discussed together with those reviewed previously.

A. Equatorial Moiety: *X*-Ray Results.—In our previous review[3] a statistical analysis of the geometry of $Co(DH)_2$ unit gave the bond length mean values for organocobaloximes reported, together with those of the dimethylglyoxime (DH_2) in Table 2. The corresponding structural results of the new series of organo-



R' = H $Co(GH)_2$
R' = Me $Co(DH)_2$
R' = Ph $Co(PH)_2$

Figure 2

Table 2 *Comparison of mean bond lengths* (Å) *of equatorial ligands* DH_2 *and* GH_2 *before and after ionization and coordination to cobalt*

	n^a	$Co(DH)_2$ [b]	DH_2 [b]	n^a	$Co(GH)_2$ [c]	GH_2 [b]
Co–N	306	1.8901(9)	—	20	1.884(9)	—
C–C	157	1.462(3)	1.474(3)	10	1.44(1)	1.453(1)
C–N	302	1.301(1)	1.288(3)	20	1.30(1)	1.2849(8)
N–O	306	1.3492(9)	1.410(3)	20	1.34(1)	1.3854(8)
C–Me	306	1.501(1)	1.487(2)	—	—	—
O···O	140	2.487(2)	—	10	2.49(1)	—

[a] Number of averaged measurements. [b] data from ref. 3. [c] Present work.

cobaloximes agree with these values within the experimental errors. The mean values for the $Co(GH)_2$ moiety, together with those of the free ligand GH_2, are reported in Table 2. Ionization and coordination to Co of the latter ligand provoke changes in the same direction observed in DH_2, with a significant decrease only in the N–O distance. Therefore, the delocalization in the $Co(GH)_2$ plane is small, as suggested for the $Co(DH)_2$ moiety.[3] The Co–N bond lengths, which are very close in the two systems, confirm this hypothesis.

B. Axial Ligands, *X*-Ray results.—The geometry of the L–Co–R fragment is reported in Table 3 together with the bending angle, α, between the two equatorial halves and the displacement, *d*, of the Co out of the four N-donor plane. Positive values for α and *d* indicate bending towards X or R and displacement towards L, respectively. The Co–L bond lengths reported in Table 3 confirm previous findings[3] that this bond lengthens with the σ-donor power of the *trans*-alkyl group (electronic *trans*-influence). For some series containing the same L ligand and different R groups, the electronic *trans*-

Table 3 *Structural parameters of the* L–Co–R *moiety and* d *and* α *values for cobaloximes having* GH *and* DH *as equatorial ligands*

L	R	Co–L (Å)	Co–C (Å)	L–Co–R (°)	Co–C–Y (°)	α (°)	*d* (Å)	*Ref.*
				GH				
py	Me	2.064(3)	2.005(4)	178.0(2)	—	5.6	0.05	*a*
	Et	2.067(6)	2.020(7)	178.4(3)	119.9(7)	1.1	0.04	*a*
	Pr^i	2.101(6)	2.084(9)	177.5(3)	116.2(8)	1.9	0.03	*a*
$P(OMe)_3$	Me	2.268(1)	2.041(4)	179.9(0)	—	4.0	0.08	*b*
PPh_3	Me	2.428(1)	2.033(3)	178.8(1)	—	6.0	0.11	*b*
				DH				
NH_2Ph	Me	2.129(1)	1.992(2)	178.19(7)	—	3.5	0.04	*c*
	Et	2.147(2)	2.030(3)	178.3(1)	117.8(3)	2.8	0.01	*d*
	$CH_2C(CO_2Et)_2Me$	2.143(2)	2.035(2)	170.86(8)	126.8(2)	−3.3	−0.01	*c*
	CH_2OMe	2.169(3)	2.013(4)	176.3(2)	119.4(4)	2.7	0.03	*d*
	Pr^i	2.177(2)	2.068(3)	178.3(1)	114.2(2)	−5.6	−0.02	*d*
	adamantyl	2.216(4)	2.158(4)	177.1(1)	110.2(4)	−10.8	−0.07	*e*
$(2\text{-}NH_2py)NH_2$	Et	2.156(3)	2.025(3)	174.1(1)	121.0(3)	4.0	0.01	*f*
$(R)\text{-}PhCH(Me)NH_2$	$(S)\text{-}CH(Me)CO_2Me$	2.074(5)	2.083(6)	174.5(2)	—	—	0.01	*g,h*
py	CH(CN)Cl	2.017(2)	2.015(3)	177.0(1)	117.0(2)Cl 112.9(2)CN	−7.0	−0.02	*i*
	CH_2CN	2.014(4)	2.024(6)	175.2(2)	115.1(5)	4.7	0.03	*j*
	$CHCl_2$	2.045(2)	1.995(2)	176.52(8)	115.7(1)	−7.6	−0.02	*k*
	CH_2CH_2CN	2.050(5)	2.002(7)	176.4(3)	123.6(6)	2.7	0.04	*i*
	CH_2CH_2CN	2.094(4)	2.005(5)	177.6(2)	—	—	—	*l,m*
	$(R)\text{-}CH(Me)CO_2Me$	2.049(5)	2.083(8)	176.6(2)	—	—	—	*n*
	CH_2Ph	2.056(3)	2.065(4)	177.1(1)	116.7(2)	5.0	0.04	*j*
4-CNpy	$(S)\text{-}CH(Me)CO_2Me$	2.076(6)	2.098(7)	176.4(3)	114.2(6)Me 108.7(5)CO_2Me	—	—	*o*
$4\text{-}Me_2NPy$	adamantyl	2.102(3)	2.160(4)	178.8(1)	111.0(3)	−10.5	−0.05	*e*
4-Mepy	$(R)\text{-}CH(CN)Me$	2.054(7)	2.05(1)	174.7(3)	—	—	—	*g*
$1,2\text{-}Me_2Im$	CCl_2CN	2.025(3)	2.047(4)	175.6(1)	114.1(2)Cl 112.6(3)CN	−8.5	−0.02	*p*
	CH_2NO_2	2.049(3)	1.999(3)	174.0(1)	114.5(1)	3.4	0.03	*p*

1,2-Me_2Im—*cont.*	CH_2CN	2.049(3)	2.018(4)	177.1(2)	116.5(3)	6.0	0.06	*p*
	$CH_2CH_2CH_2CN$	2.083(2)	2.023(3)	174.2(1)	119.4(2)	5.9	0.06	*p*
	Me	2.086(1)	2.001(2)	176.62(8)	—	3.4	0.06	*p*
	Pr^i	2.121(2)	2.096(3)	174.5(1)	114.4(2)	7.3	0.04	*p*
Me_3Bzm	CH(CN)Cl	2.010(3)	2.000(5)	177.1(2)	126.1(3)Cl 118.2(3)CN	1.9	0.01	*q*
	$CH(CN)CH_2CN$	2.031(3)	2.061(3)	175.3(1)	112.5(3)CN 116.5(3)CH_2CN	3.1	0.01	*r*
	CH_2NO_2	2.013(3)	1.988(5)	176.6(2)	115.7(4)	4.8	0.05	*s*
	$CHCl_2$	2.043(2)	1.983(2)	173.72(8)	116.2(1)	1.5	0.01	*k*
	Me	2.060(2)	1.989(2)	176.8(1)	—	4.7	0.06	*s*
	Pr^i	2.097(2)	2.076(2)	176.41(8)	114.2(2)	4.0	0.06	*s*
	adamantyl	2.137(4)	2.179(5)	178.0(2)	110.4(4)	−6.1	−0.03	*q*
Im	Me	2.019(3)	1.985(3)	177.2(1)	—	1.8	0.03	*t*
1-MeIm	CH_2CH_2CN	2.037(3)	1.989(5)	177.0(2)	127.9(5)	4.9	0.05	*p*
	adamantyl	2.065(4)	2.154(2)	179.2(2)	111.2(4)	−10.0	−0.06	*u*
pyrrolidine	CH_2Ph	2.114(8)	2.128(8)	173.1(4)	—	1.5	0.02	*v*
$P(OMe)_3$	adamantyl	2.313(1)	2.214(3)	178.91(8)	110.7(2)	−7.3	−0.02	*w*
$P(OPr^i)_3$	adamantyl	2.367(2)	2.199(6)	176.3(2)	111.2(5)	−7.5	−0.01	*w*
PBu_3	(*R*)-CH(CN)Me	2.316(2)	2.089(6)	176.5(2)	117.0(5)Me 111.9(5)CN	2.1	0.03	*x*
PEt_2Ph	(*R*)-CH(CN)Me	2.313(1)	2.074(4)	174.4(1)	—	1.8	0.01	*y*
$PEtPh_2$	(*R*)-CH(CN)Me	2.370(1)	2.098(3)	175.5(1)	—	5.1	0.05	*y*
PPh_3	(*R*)-CH(CN)Me	2.410(3)	2.08(1)	172.3(4)	116.4(9)Me 115.0(9)CN	11.6	0.08	*x*
CN	CN	1.911(7)	1.916(8)	178.8(2)	177.5(7)	—	—	*z*

[a] Ref. 34. [b] Ref. 33. [c] Unpublished results. [d] L. G. Marzilli, F. Bayo, M. F. Summers, L. B. Thomas, E. Zangrando, N. Bresciani Pahor, M. Mari, and L. Randaccio, *J. Am. Chem. Soc.*, 1987, **109**, 6045. [e] N. Bresciani Pahor, L. Randaccio, E. Zangrando, and P. A. Marzilli, *J. Chem. Soc., Dalton Trans.*, in press. [f] L. G. Marzilli, M. F. Summers, E. Zangrando, N. Bresciani Pahor, and L. Randaccio, *J. Am. Chem. Soc.*, 1986, **108**, 4830. [g] Ref. 40. [h] mean values for two crystalline forms. [i] E. Zangrando, N. Bresciani Pahor, L. Randaccio, J. P. Charland, and L. G. Marzilli, *Organometallics*, 1986, **5**, 1938. [j] N. Bresciani Pahor, L. Randaccio, E. Zangrando, and L. Antolini, *Acta Crystallogr., Sect. C*, 1988, **44**, 2052. [k] Ref. 35. [l] The equatorial ligand is bis[(*E,E*)-1-phenyl-1,2-propanedionedioximato-*N,N'*]. [m] A. Uchida, Y. Ohashi, Y. Sasada, and Y. Ohgo, *Acta Crystallogr., Sect. C*, 1985, **41**, 25. [n] Ref. 38. [o] T. Kurihara, A. Uchida, Y. Ohashi, Y. Sasada, and Y. Ohgo, *Acta Crystallogr., Sect. C*, 1984, **40**, 1557. [p] Ref. 30. [q] Ref. 36. [r] Unpublished results. [s] Ref. 31. [t] V. Pattabhi, M. Nethaji, E. J. Gabe, F. L. Lee, and Y. Le Page, *Acta Crystallogr., Sect. C*, 1984, **40**, 1155. [u] N. Bresciani, Pahor, L. G. Marzilli, L. Randaccio, P. J. Toscano, and E. Zangrando, *J. Chem. Soc., Chem. Commun.*, 1984, 1508. [v] S. K. Tyrlik, A. T. H. Lenstra, J. F. J. Van Look, H. J. Geise, and R. A. Dommisse, *Acta Crystallogr., Sect. C*, 1986, **42**, 553. [w] N. Bresciani Pahor, L. Randaccio, E. Zangrando, M. F. Summers, J. H. Ramsden, P. A. Marzilli, and L. G. Marzilli, *Organometallics*, 1985, **4**, 2086. [x] T. Kurihara, A. Uchida, Y. Ohashi, Y. Sasada, Y. Ohgo, and S. Baba, *Acta Crystallogr., Sect B*, 1983, **39**, 431. [y] Y. Tomotake, A. Uchida, Y. Ohashi, Y. Sasada, Y. Ohgo, and S. Baba, *Acta Crystallogr., Sect. C*, 1984, **40**, 1684. [z] C. Lopez, S. Alvarez, X. Solans, and M. Aguilo, *Inorg. Chim. Acta*, 1987, **133**, 101.

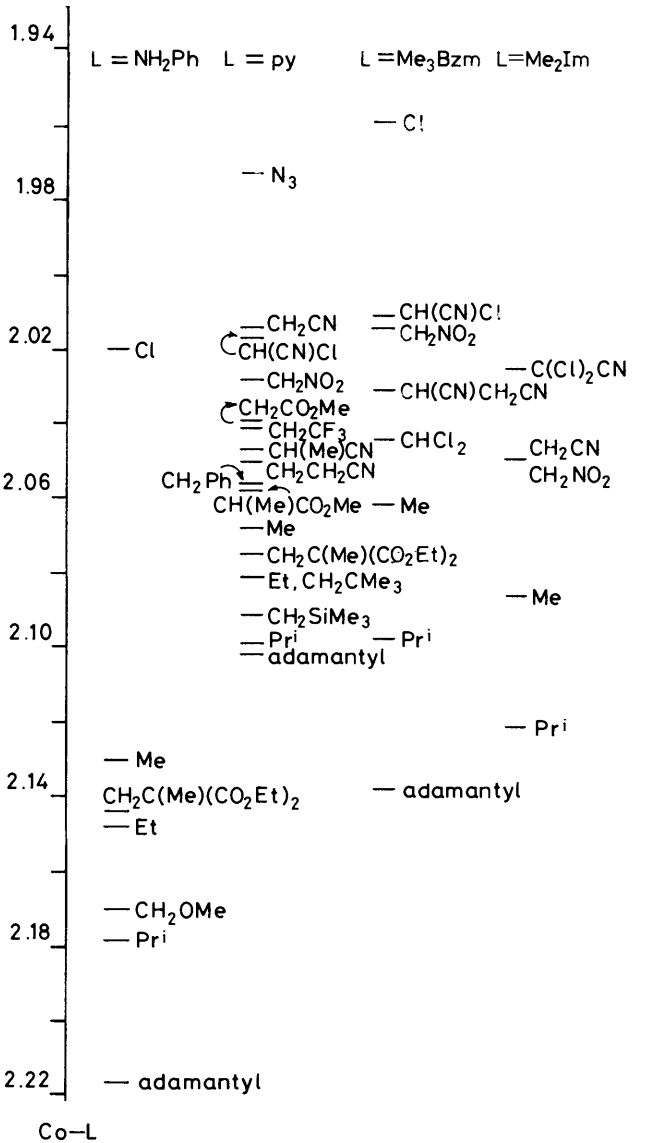


Figure 3 *Diagram showing the trend of the* Co-L distances (Å) *in cobaloximes for different alkyl groups* trans *to* L = NH_2Ph, py, Me_3Bzm, Me_2Im. *Available values for azido and chloro analogues are reported for comparison*

influence is clearly shown in Figure 3. For comparison, the Co–N distances *trans* to weak acido-donors are also given. An increase of about 0.2 Å in each series is

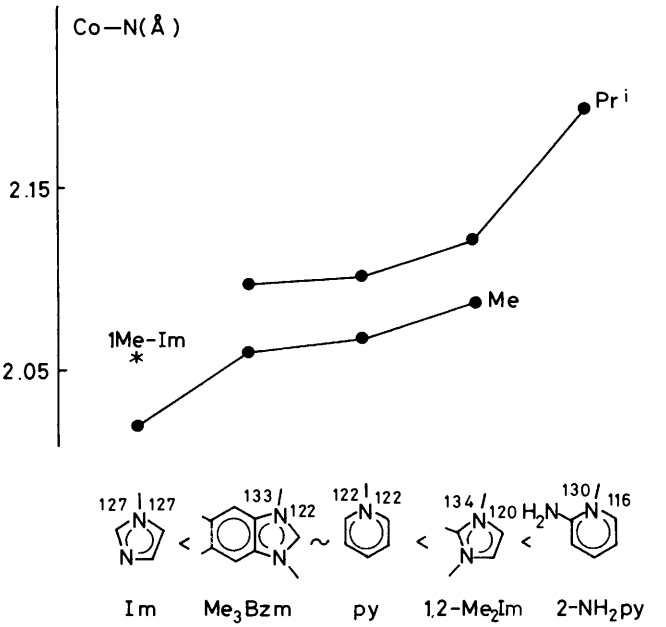


Figure 4 *Trend of* Co–N *distances for* $MeCo(DH)_2L$ *and* $Pr^iCo(DH)_2L$ *for different planar* L *ligands. The starred point corresponds to the* 1-methylimidazole *derivative, for which the orientation (b) in Figure* 5 *is found.* Im = *imidazole*

apparent. The Co–py distances and the Co–N(axial) distances in cobaloximes having different L ligands are linearly related.[30]

The Co–N(axial) distances are also influenced by the bulk of the L ligand (steric *cis*-influence). For the same alkyl group with different planar N-donor ligands, the order of increasing Co–N(axial) bond length is shown in Figure 4. This order is the same as that for the rate of dissociation of L (see below). The value of the C–N(axial)–C angle has been used[31] to determine the steric effect of the N-ligand bulk on the Co–N(axial) distance. This angle of *ca.* 105° in imidazole derivatives allows distances shorter than those found in py analogues, where it is about 120°. However, when bulky side-groups are attached to an α-carbon atom of L, such as in 1,5,6-trimethylbenzimidazole (Me_3Bzm) and 1,2-dimethylbenzimidazole ($1,2\text{-}Me_2Im$), the interaction with the equatorial moiety provokes a lengthening of the Co–N axial bond as well as a marked non-equivalence of the two Co–N(axial)–C angles (see Figure 4). Finally, another factor has been claimed[32] to influence the Co–N(axial) distance. In all the

[30] S. Geremia, Thesis, University of Trieste, 1988.
[31] J. P. Charland, E. Zangrando, N. Bresciani Pahor, L. Randaccio, and L. G. Marzilli, to be published.
[32] W. O. Parker, E. Zangrando, N. Bresciani Pahor, L. Randaccio, and L. G. Marzilli, *Inorg. Chem.*, 1988, **27**, 2170.

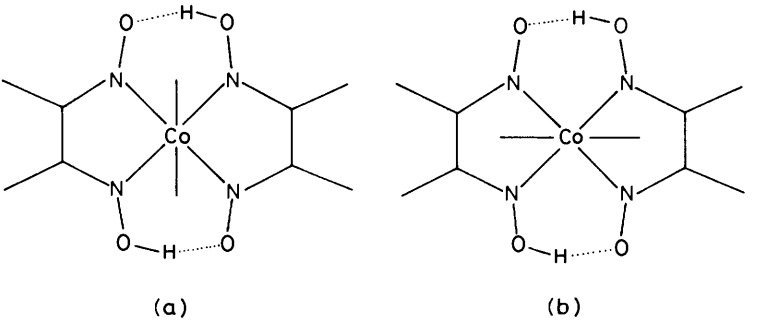


Figure 5

cobaloximes, planar L have almost the same orientation with respect to the equatorial moiety, as shown in Figure 5a. The only exceptions are 1-MeIm-$Co(DH)_2Me$ and 1-MeIm$Co(DH)_2CH_2CH_2CN$ (1-MeIm = 1-methylimidazole), where orientations close to the ideal sketched in Figure 5b are found. The (b) orientation, which is probably dictated by crystal packing forces, is compatible with the intramolecular steric requirements when L is a non-bulky ligand such as 1-MeIm. In Figure 4, the starred point represents the value of 2.058(5) Å in 1-MeIm$Co(DH)_2Me$. This value would be expected to be similar to that of 2.019(3) Å in the imidazole analogue, but steric clashes in orientation (b) lead to the longer Co–N bond.

It was already reported that in $PR_3Co(DH)_2X$ (X = Me, CH_2CN, Cl) the Co–P bond length is linearly related to the Tolman cone angle.[3] The Co–P distances relative to the phosphines reported in Table 3 show a similar trend when R = (*R*)-CH(CN)Me. Axial Co–P[33] and Co–N[34] distances, measured in $(GH)_2$ complexes for different R groups, are not significantly different from those reported for $(DH)_2$ analogues.[3] The Co–C distance is primarily influenced by the bulk of the alkyl group and increases for a given L by 0.2 Å going from Me to adamantyl derivatives, as shown in Figure 6. Data collected in Table 3 confirm also the previous findings[3] that the Co–C bond length is minimally affected by the nature of the N-donor ligand. Furthermore, for N-donor ligands, good linear relationships are found when Co–C distances in py complexes with different R groups are plotted against the analogous distances in 1,2-Me_2Im, Me_3Bzm, and NH_2Ph derivatives.[30,31] When L is a P-donor ligand, a slight but significant increase of the Co–C bond is observed compared to N-ligands (Figure 6). Since the extent of the increase depends also upon the bulk of the alkyl group (see Figure 6), this lengthening has been attributed[3] to the steric *trans*-influence exerted by L on the *trans* Co–R bond through the equatorial ligands. This influence is supported by the trend of the α values shown in Figure 6, which vary

[33] P. J. Toscano, T. F. Swider, L. G. Marzilli, N. Bresciani Pahor, and L. Randaccio, *Inorg. Chem.*, 1983, **22**, 3416.
[34] N. Bresciani Pahor, L. Randaccio, E. Zangrando, and P. J. Toscano, *Inorg. Chim. Acta*, 1985, **96**, 193.

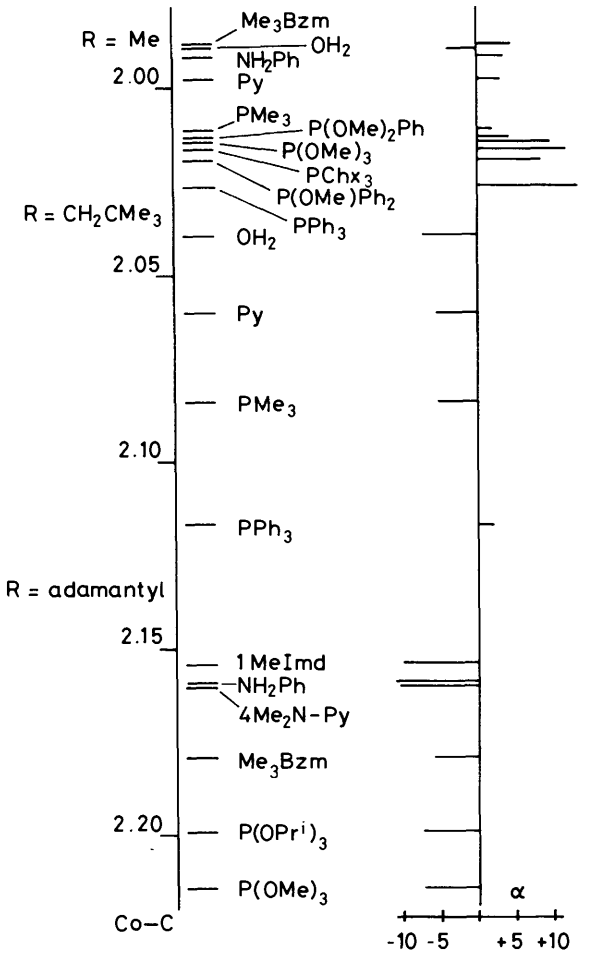


Figure 6 *Trend of the* Co–C *bond length* (Å) *and of the* α *angle* (°) *in cobaloximes having* R = Me, CH_2CMe_3, *and adamantyl and different* L *ligands*

with the bulk of both L and R, although crystal packing effects may also play a role.

We have assumed that the Co–C bond length is determined by the bulk of R and this appears evident from previous data[3] and from data of Table 3. However, since many other structures with potentially bulky electron-withdrawing groups have now been determined, we observe that the substitution of H by Cl at Cα does not provoke any lengthening of the Co–C bond. This could be ascribed to an 'effective' bulk of Cl very close to that of H, because the C–Cl distance (1.8 Å) is longer than the C–H distance (1 Å). However, it could also be

attributed to an electronic effect of the electron-withdrawing Cα substituents, such as Cl, which could shorten the Co–C bond.[35] Particularly short values of the Co–C bond lengths are also found for the CH_2CH_2CN group (2.00 Å), when compared to those of Et (2.04 Å). However, for other even stronger electron-withdrawing substituents, such as CN or COOMe, an increase of the Co–C distance with respect to Co–Me is observed, as for CH_2CN (Table 3) or CH_2COOMe.[3] Further investigation is needed to clarify this problem.

It was previously observed[3] that the steric interaction of bulky R with the $(DH)_2$ moiety also provokes severe distortions in the alkyl group geometry. For example, in CH_2CMe_3 derivatives the Co–CH_2–C angle has values up to 130°, very far from the ideal tetrahedral value. Also, in Et complexes the C–C bond length is shortened, whereas the Co–CH_2–CH_3 angle is opened up to 120°. It is also interesting to note that in adamantyl derivatives the lengthening of the C–C distances nearly parallel to the Co–Cα bond corresponds to the shortening of those involving Cα as well as those of the top six-membered ring of adamantyl.[36] These deformations may be interpreted in terms of the anomeric effect.[37]

Comparison of py$Co(DH)_2R$ (R = Me, Et, Pr^i) with $(GH)_2$ analogues does not show significant differences in Co–C bond lengths.[34]

C. Solid State Reactions.—Ohashi *et al.* have found[38] that the chiral –CH(Me)CN group in $LCo(DH)_2CH(Me)CN$ is both racemized and isomerized by *X*-ray exposure without degradation in crystallinity. Since the rate of isomerization is closely related to the packing of the R group in the crystal structure, these authors have defined a 'reaction cavity' for this group and have shown that the reactivity is correlated with the volume of this cavity.[39] On the other hand, the chiral $-CH(Me)CO_2Me$ derivatives with L = 4-Clpy and py were racemized only at high temperature. The single crystal *X*-ray structural analysis has shown that the 4-Clpy complex undergoes cooperative configurational and conformational changes at high temperature. In the methanol-solvated py analogue, a rapid desolvation at room temperature is accompanied by conformational change of the chiral group to fill the space voided by solvent loss and at 343 K random inversion occurs.[38,40] On the other hand, for L = 4-CNpy, (*R*)- and (*S*)-α-methylbenzylamine, no indication for such a reaction was obtained. Their crystal structures correlate with this inactivity.[41]

[35] Q. Chen, L. G. Marzilli, N. Bresciani Pahor, L. Randaccio, and E. Zangrando, *Inorg. Chim. Acta*, 1988, **144**, 241.
[36] N. Bresciani Pahor, W. M. Attia, L. Randaccio, C. Lopez, and J. P. Charland, *Acta Crystallogr., Sect. C*, 1987, **43**, 1484.
[37] A. J. Kirby, 'The Anomeric Effect and Related Stereoelectronic Effects at Oxygen', Springer Verlag, Berlin, 1983.
[38] T. Kurihara, A. Uchida, Y. Ohashi, Y. Sasada, and Y. Ohgo, *J. Am. Chem. Soc.*, 1984, **106**, 5718 and references therein.
[39] Y. Ohashi, A. Uchida, Y. Sasada, and Y. Ohgo, *Acta Crystallogr., Sect. B*, 1983, **39**, 54.
[40] T. Kurihara, A. Uchida, Y. Ohashi, and Y. Sasada, *Acta Crystallogr., Sect. B*, 1984, **40**, 478; A. Uchida, Y. Ohashi, Y. Sasada, and Y. Ohgo, *Acta Crystallogr., Sect. B*, 1984, **40**, 473.
[41] Y. Sasada and Y. Ohashi, *J. Mol. Struct.*, 1985, **126**, 477.

D. Kinetic Studies.—Rate and mechanistic studies on cobaloximes have been extensively reviewed[3] and we report here only the most recent results obtained for organocobaloximes.

It is now well established that for reaction 1:

$$LCo(DH)_2R + L' \longrightarrow L'Co(DH_2)R + L \quad (1)$$

the rate-determining step is the dissociative first step in the mechanism given in reactions 2 and 3:

$$LCo(DH)_2R \underset{k_{-1}}{\overset{k}{\rightleftharpoons}} Co(DH)_2\,R + L \quad (2)$$

$$Co(DH)_2R + L' \xrightarrow{k_1} L'Co(DH)_2R \quad (3)$$

and $k_{obs} = k$.

The values of log$k$ for $LCO(DH)_2R$ complexes, with different L and R groups, are given in Table 4. For a given L, log$k$, increases with the increase of the σ-donor power of R by several orders of magnitude, *e.g.* for L = 4-CNpy, the rate increases by 10^6 in going from $CH(CN)CH_2CN$ to $CH(Me)Pr^i$. Interestingly, the trend of log$k$, for different L ligands is very similar when R is varied. In fact, good linear relationships are found when log$k$ for 4-CNpy is plotted against log$k$ for the other neutral L ligands.[30] This similarity indicates that the changes in rate are not significantly affected by the nature of L when the R group is varied. On the other hand, for a given L, log$k$ increases with the increase of the σ-donor power of R and parallels the increase of the Co–L distance. Therefore, the kinetic *trans*-effect and the structural *trans*-influence have very similar trends. The values of log$k$ for complexes with the same alkyl group and different planar L reflect the bulk of L. The trend of log$k$ for the same R is 1-MeIm < $Me_3Bzm \approx$ py ⩽ 1,2-Me_2Im < 2-NH_2py and is very similar to that of the Co–N(axial) bond lengths (Figure 4). This suggests that the bulk of the L planar ligands affects both kinetics and ground state properties in a similar way. In addition, since log$k$ values for 1-MeIm do not show irregularity, it may be concluded that the 'anomalous' orientation and the Co–N(axial) bond lengths found in the structures of 1-MeImCo$(DH)_2$R, with R = Me and CH_2CH_2CN, are a consequence of the crystal packing, as suggested above.

The log$k$ values for $LCo(DH)_2R$ (R = $CHCl_2$, $CHBr_2$, and different L) reported in Table 4 provide some additional information.[35] First, substitution of H in methyl derivatives with Cl or Br provokes a significant decrease of k. The effect is greater in the Br derivatives, so that the donating ability of $CHBr_2$ is smaller than that of $CHCl_2$. Furthermore, the noticeably increased bulk of 2-NH_2py with respect to py is mainly responsible for the difference of about two orders of magnitude in the corresponding k value. Analogously, the larger dissociation rates for NH_2Ph than py analogues can be mainly attributed to the longer Co–NH_2Ph bond length.

Table 4 *Values of log* k *for* $LCo(DH)_2R$ *complexes*[a]

R/L	4-CNpy[b]	anisidine[c]	Me_3Bzm[d]	1-MeIm	DEA[e]	2-NH_2py	[f]H_2O[g])
CH(CN)Cl	−4.85*						
$CH(CN)CH_2CN$	−4.47*						
CH_2NO_2	−5.37*					−3.42	
$CHBr_2$	−3.28*[h]	(*h*)					
CH_2CN	−4.52	−3.77			−6.00		
$CHCl_2$	−3.08*[i]	−2.36[i]	−4.50		−4.40	−0.62[i]	
CH(CN)Me	−2.88*						
CH_2CF_3	−3.57	−2.96	−4.89		−4.84	−1.55	−0.04
CH_2CO_2Me	−3.57*	−2.62					
CH_2I	−2.79	−2.03					0.95
CH_2Br	−2.58	−1.76	−3.91	−5.19	−3.77	−0.82	1.02
CH_2COMe	−3.23*	−2.49					
CH_2Cl	−2.51	−1.46	−3.58				1.31
CH_2CH_2CN	−1.59*	−0.81					
$CH_2C(CO_2Et)_2Me$	−0.51	0.03[e]	−1.69	−3.24[e]	−1.62	1.43	
Me	−1.39	−0.33	−2.38	−3.60	−2.27	0.54	2.12
CH_2SiMe_3	−0.37	0.15		−2.96			
CH_2Ph	−0.48	0.45			−1.66		3.16
Et	−0.02	0.89	−0.95	−2.18	−0.81	1.76	3.31
Pr^n	0.08	0.93					
CH_2Pr^i	0.15	1.11		−2.00		2.00	
CH_2CMe_3	1.04	1.54	0.09	−1.28	0.00		
CH_2OMe	1.38*	2.18			0.71		
Pr^i	1.43		0.58	−0.80	0.45		
CH(Me)Et	1.60			−0.72			
c-C_6H_{11}	1.59		0.79				
$CH(Et)_2$	2.00						
$CH(Me)Pr^i$	1.92						
adamantyl			1.61				

[a] Values are from ref. 3 unless otherwise specified. The entering ligand is $P(OMe)_3$. [b] Starred data are from ref. *i* of Table 3. [c] Ref. *d* of Table 3. [d] Ref. 31. [e] Unpublished results from Emory University. [f] Ref. *f* of Table 3. [g] R. Dreos-Garlatti, G. Tauzher, and G. Costa, *Inorg. Chim. Acta*, 1984, **82**, 197, the entering ligand is thiourea in H_2O solvent. [h] For py log*k* = −4.8 and for NH_2Ph log*k* = −2.31, ref. 35. [i] For py log*k* = −4.34 and for NH_2Ph log*k* = −1.73, ref. 35.

E. Co–C Bond Dissociation Energy.—Co–C BDEs have usually been estimated by kinetic radical trapping procedures. However, for cobaloximes, two methods have been developed which do not require as many assumptions. This contrasts with the situation in other model systems. In 1979, Halpern[13] introduced the first non-kinetic method to determine cobalt–alkyl bond dissociation energies which was based on the measurement of the rates and activation enthalpies of reactions of the kind shown in equation 4.

$$LCo^{III}(DH)_2CHMePh \longrightarrow LCo^{II}(DH)_2 + PhCH{=}CH_2 + \tfrac{1}{2}H_2 \qquad (4)$$

Values of BDE, derived for cobaloximes with different P- and N-donor neutral ligands and R = CHMePh and CH_2Ph are given in Table 5. These data show that in cobaloximes containing N-donors the Co–C BDE increases systematically with basicity of the neutral ligand. A linear relationship is observed between BDE and pK_a of 4-Xpy having similar bulk. On the contrary, for cobaloximes containing P-donor ligands, for both CHMePh and CH_2Ph derivatives, the BDE decreases with the increasing size of the phosphine and linear relationships with the Tolman cone angle are found.[42] In the latter case the magnitude of this dependence is such as to mask the apparently much smaller influence of electronic effects. In fact, for the octaethylporphyrin (OEP) series, $LCo(OEP)CH_2Ph$, data reported in Table 5 reveal a linear dependence of BDE on the pK_a of the phosphine, similar to that found for 4-Xpy, but not on the variation in bulk of the phosphine.

More recently, Toscano and co-workers[43] have exploited the I_2 cleavage of Co–R bonds to give CoI + RI to measure the BDE by a calorimetric method. This has allowed the first determination of a Co–Me BDE, specifically in $pyCo(DH)_2Me$. This Co–C has a BDE of 34.6 ± 1.4 kcal mol^{-1}, in contrast to the Pr^i analogue which has a BDE of 21.3 ± 2.0 kcal mol^{-1}.

The BDE trends agree with the bond length results for cobaloximes. In fact, the increasing bulk of the neutral ligand *trans* to R weakens and lengthens the Co–C bond (steric *trans*-influence). However, no structural evidence of the influence of the neutral ligand basicity on the Co–C distance has been detected. This influence should be too small to be revealed by distance measurements, but large enough to be detected from BDE measurements. Furthermore, the bulkier the R group, *e.g.* Me *vs.* Pr^i, the weaker and longer the Co–C bond.

Comparison of BDE data for $(DH)_2$ and OEP series suggests that the porphyrin ligand is not sufficiently flexible to respond to the steric pressure of bulky neutral L ligands. Therefore, it cannot bend towards the alkyl group to weaken the Co–C bond, as occurs in cobaloximes. This effect (see above) is apparent in Co–C bond lengths only when large variation in the bulk of L occur, *i.e.* differences are detected when H_2O or py complexes are compared with PR_3 analogues. The lack of flexibility of the OEP equatorial ligand should represent a 'barrier', which almost cancels the steric *trans*-influence as measured from BDE.[42] The flexibility of the $Co(DH)_2$ system is supported by the range of α and d values reported in Table 3.

The solid-state thermolysis of a series of 24 $H_2OCo(DH)_2R$ and 19 $pyCo(DH)_2R$ complexes has been studied by differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA) techniques.[44] In the most favour-

[42] M. K. Geno and J. Halpern, *J. Am. Chem. Soc.*, 1987, **109**, 1238.
[43] P. J. Toscano, A. L. Seligson, M. T. Curran, A. T. Skrobutt, and D. C. Sonnenberger, *Inorg. Chem.*, 1989, **28**, 166.
[44] K. L. Brown, G. W. Young, R. Segal, and K. Rajeshwar, *Inorg. Chim. Acta*, 1987, **128**, 197.

Table 5 Co–C *BDE* (kcal mol^{-1}) *for* $LCo(DH)_2R$ *with different* L *ligands and* R = CHMePh *and* CH_2Ph. *Data relative to* $LCo(OEP)CH_2Ph$ *are also given*

L[a]	$LCo(DH)_2CHMePh$	L[b]	$LCo(DH)_2CHMePh$
4-NH_2py	21.2	PMe_2Ph	24
4-Mepy	20.1	$P(n\text{-}Bu)_3$	21
py	19.5	$P(CH_2CH_2CN)_3$	20
4-CNpy	17.9	$PEtPh_2$	19
Imidazole	20.8	PPh_3	17

L[c]	$LCo(DH)_2CH_2Ph$	$LCo(OEP)CH_2Ph$
PMe_2Ph	30.4	27.1
$P(Bu^n)_3$	28.9	29.3
$PEtPh_2$	26.8	26.1
PPh_3	25.8	23.8
$P(c\text{-}C_6H_{11})_3$	22.8	29.6

[a] Ref. 11. [b] Ref. 12. [c] Ref. 42.

able cases, three transitions ascribable to the loss of L, R, and decomposition of the $Co(DH)_2$ unit, are observed. The temperature of the first transition for aquoderivatives correlates well with: (i) the Taft constant σ^*; (ii) log*k* for the substitution reaction of H_2O by pyridine, as well as for the reverse reaction; (iii) the Co–N(axial) distances of pyridine analogues.

4 Cationic Organometallic Complexes having a Mixed Oxime-Schiff Base System as Equatorial Ligand

In 1969, Costa *et al.*[45] prepared new coenzyme B_{12} models, namely the organocobalt complexes having the tetradentate ligand $N^2,N^{2\prime}$- propanediyl-bis(2,3-butanedione-2-imine-3-oxime), [(DO)(DOH)pn], as equatorial ligand. These 'Costa' models differ from cobaloximes by having substituted one of the two oxime bridges with a propylene bridge (Figure 7). Thus, they are a mixed Schiff base–oxime system, with the equatorial ligand having the same -1 charge as the B_{12} corrin; they are typically ionic compounds with complex cations and PF_6^- or ClO_4^- anions. Until recently, only one relatively imprecise structure had been reported, namely $\{H_2O[Co(DO)(DOH)pn]Me\}ClO_4$.[46] A neutral di-organometallic complex Me[Co(DO)(DOH)pn]Me was reported[47] a few years later. More recently several $\{L[Co(DO)(DOH)pn]R\}PF_6$ complexes have been characterized by *X*-ray analysis in our laboratories.[31,48–53] We have also prepared and characterized several complexes containing a 2,2′-dimethyl-propylene bridge.[54]

A. Comparison with the Structure of Cobaloximes.—As already found in cobaloximes, the bond lengths and angles in the equatorial moiety of the

[45] G. Costa, G. Mestroni, and E. de Savorgnani, *Inorg. Chim. Acta*, 1969, **3**, 323.
[46] S. Bruckner, M. Calligaris, G. Nardin, and L. Randaccio, *Inorg. Chim. Acta*, 1969, **3**, 278.
[47] M. Calligaris, *J. Chem. Soc., Dalton Trans.*, 1974, 1628.

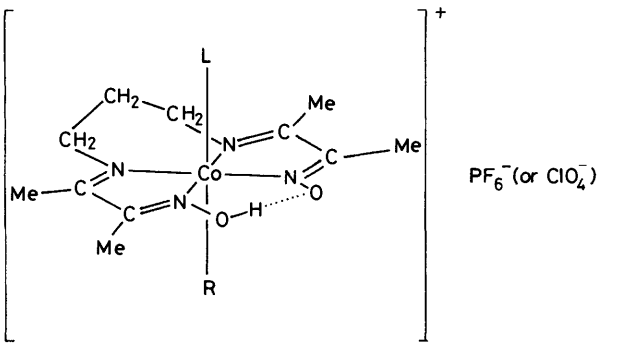


Figure 7

complex cations are not significantly influenced by the axial ligands. In contrast to cobaloximes, where the Co–N equatorial distances are essentially all equal [mean 1.8901(9) Å],[3] the mean distance of 1.912(8) Å involving the iminic nitrogen donor, *i.e.* on the propylene bridge side, is significantly longer than that of 1.880(9) Å involving the oxime N donor. Correspondingly, the N(1)–Co–N(2) angle becomes slightly narrower (mean 97.6°) and the N(3)–Co–N(4) angle slightly larger (mean 99.2°) than that found in cobaloximes (mean value 98.57(8)°). The other N–Co–N angles average to a value of 81.5(4)°, which does not differ significantly from that of 81.38(5)° reported for cobaloximes.[3] This small variation in the coordination parameters is in agreement with a slight, but significant, decrease of the O · · · · O distance in Costa models [mean 2.45(1) Å] as compared with the mean value for cobaloximes [2.487(2) Å]. The difference in O · · · · O distance should parallel the ease of the bridge deprotonation in the two types of complexes.[3] This suggestion is supported by the slower exchange of the proton in the oxime bridge of [(DO)(DOH)pn] complexes as compared to that of $(DH)_2$ complexes with similar axial ligands.[3,55] The mean values of the other bond lengths and angles agree with a structure having essentially double C=N and single (Me)C–C(Me) bonds (Figure 7), as are also found in cobaloximes.[3]

The six-membered chelate ring, involving the propylene chain, has the

[48] L. G. Marzilli, N. Bresciani Pahor, L. Randaccio, E. Zangrando, R. G. Finke, and S. A. Mayers, *Inorg. Chim. Acta*, 1985, **107**, 139.
[49] E. Zangrando, W. O. Parker, N. Bresciani Pahor, L. B. Thomas, L. G. Marzilli, and L. Randaccio, *Gazz. Chim. Ital.*, 1987, **117**, 307.
[50] W. O. Parker, N. Bresciani Pahor, E. Zangrando, L. Randaccio, and L. G. Marzilli, *Inorg. Chem.*, 1985, **24**, 3908.
[51] W. O. Parker, E. Zangrando, N. Bresciani Pahor, L. Randaccio, and L. Marzilli, *Inorg. Chem.*, 1986, **25**, 3489.
[52] E. Zangrando, W. O. Parker, and A. Mezzetti, *Acta Crystallogr., Sect. C*, 1987, **43**, 2277.
[53] W. O. Parker, N. Bresciani Pahor, E. Zangrando, L. Randaccio, and L. G. Marzilli, *Inorg. Chem.*, 1986, **25**, 1303.
[54] P. G. Yohannes, N. Bresciani Pahor, L. Randaccio, E. Zangrando, and L. G. Marzilli, *Inorg. Chem.*, 1988, **27**, 4738.
[55] R. J. Guschl and T. L. Brown, *Inorg. Chem.*, 1974, **13**, 959.

expected conformation with the central C atom out of the chelate plane, normally on the side of the less bulky axial ligand.

The deviation from planarity of the [Co(DO)(DOH)pn] unit may be described by the bending angle, α, between the two chemically equivalent moieties. The values reported in Table 6 appear related to the bulk of the axial ligands and are larger than those observed in cobaloximes[3] (Table 3) having the same axial ligands (see below).

The axial Co–C and Co–L bond lengths follow trends similar to those found in cobaloximes. A comparison is given in Table 6 for some L ligands. For example, in aqua-derivatives, the Co–C bond lengthens with the increasing bulk of the alkyl group. A small increase of the Co–C distance is also observed going from L = OH_2 to L = PR_3, *i.e.* approximately in the order of increasing bulk of L. Correspondingly, for alkyl groups with similar bulk, the α values range from negative values (bending towards L) in H_2O to large positive values (bending towards R) in Me_3Bzm derivatives. As already observed in cobaloximes[56] a lengthening of the Co–C bond is accompanied by increasing bending and cobalt displacement towards the L group, induced by the bulk of the *trans* neutral ligand (steric *trans*-influence).

As in cobaloximes, for the same L the Co–L bond lengths (Table 6) reflect the σ-donor power of the alkyl group. For planar N-ligands, the orientation of their plane with respect to the equatorial moiety in all the structures is close to the ideal one sketched in Figure 5b, *i.e.* the planar ligand almost crosses the two equatorial five-membered chelate rings. As we described above, the orientation of the planar L in cobaloximes, with the exception of two 1-MeIm derivatives, is that of Figure 5a. Comparison between cobaloximes and Costa models suggests that the orientation of the planar ligand is mainly dictated by the interaction of the axial ligand with the equatorial one. The orientation (a) in Figure 5 is the one most favoured in cobaloximes, but the substitution of one oxime bridge with a CH_2–CH_2–CH_2 chain increases the interaction with the axial ligand oriented as in (a), so that it is forced into orientation (b). This reorientation provokes a significant increase of both Co–N(axial) bond lengths and α bending angles in Costa models when compared with those in cobaloximes having the same axial ligands. Similar differences in Co–OH_2 bond lengths are observed in the comparison of H_2O derivatives, but no significant difference is detectable in PR_3 complexes.

As for cobaloximes, the geometry of the CH_2X group bonded to Co is significantly modified, with an opening of the Co–Cα–C angle up to 130° in CH_2CMe_3 and a shortening of the Cα–C bond length down to $\approx$1.40 Å in Et complexes. These two effects are more pronounced when L is bulky.[32]

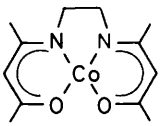
B. Kinetics.—In non-coordinating solvents, the L exchange in {L-Co[(DO)(DOH)pn]R}X complexes follows a first-order rate law, consistent with an S_N1 LIM mechanism, as for cobaloximes.[3] Results for complexes with L = py

[56] N. Bresciani Pahor, M. Calligaris, G. Nardin, and L. Randaccio, *J. Chem. Soc., Dalton Trans.*, 1982, 2549.

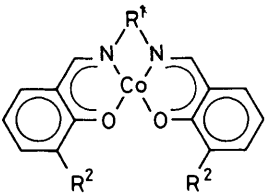
Table 6 *Comparison of* Co–C, Co–L, d *and* α *between* L[Co(DO)(DOH)pn]R *and* $LCo(DH)_2R$ *complexes. The first number in each entry refers to* (DO)(DOH)pn *derivatives, the second to cobaloximes. For the latter, data are from ref.* 3 *and from Table* 3

L	R	Co–C (Å)		Co–L (Å)		*d* (Å)		α (°)		*Ref.*
H_2O	Me	1.977(4)	1.990(5)	2.103(3)	2.058(3)	0.01	0.00	2.0	−4.0	*a*
	Et	2.020(3)	—	2.109(2)	—	−0.03	—	−9.3	—	*b*
	CH_2Ph	2.052(3)	—	2.099(1)	—	−0.02	—	−5.8	—	*b*
	Pr^i	2.073(2)	—	2.133(3)	—	−0.05	—	−6.6	—	*b*
1-MeIm	Me	2.001(3)	2.009(7)	2.042(2)	2.058(5)	0.05	0.05	4.8	4.4	*c*
py	Me	2.003(3)	1.998(5)	2.106(3)	2.068(3)	0.07	0.04	6.9	3.2	*d*
	CH_2Me_3	2.083(4)	2.060(6)	2.121(3)	2.081(4)	0.03	0.00	14.3	−5.2	*d*
Me_3Bzm	Me	2.011(3)	1.989(2)	2.100(3)	2.060(2)	0.09	0.06	13.8	4.7	*e*
	Et	2.041(4)	—	2.105(3)	—	0.10	—	16.7	—	*e*
1,2-Me_2Im	Me	2.003(5)	2.001(2)	2.100(4)	2.086(1)	0.10	0.06	19.7	3.4	*c*
NH_2Ph	Me	1.991(4)	1.992(2)	2.147(3)	2.129(1)	0.00	0.04	−11.3	3.5	*f*
	Et	2.030(4)	2.030(3)	2.174(3)	2.147(2)	0.01	0.01	−7.1	2.8	*g*
PPh_3	Me	2.018(5)	2.026(6)	2.405(1)	2.418(1)	0.10	0.11	8.2	14.0	*h*
$P(OMe)_3$	Me	2.021(5)	2.01(1)	2.265(1)	2.256(4)	0.05	0.10	3.3	10.0	*h*

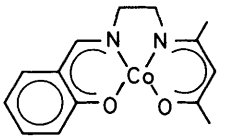
[a] Ref. 48. [b] Ref. 49. [c] Unpublished results. [d] Ref. 50. [e] Ref. 32. [f] Ref. 51. [g] Ref. 52. [h] Ref. 53.



Co(acacen)



$R^1 = -CH_2CH_2-$ $R^2 = H$ Co(salen)
$R^1 = -CH(Me)CH_2-$ $R^2 = H$ Co(salpn)
$R^1 = -CH_2CH_2-$ $R^2 = F$ Co(3F-salen)
$R^1 =$  $R^2 = H$ Co(saloph)



Co(acsalen)

Figure 8

and Me_3Bzm and different R groups show that the dissociation rate increases by 10^5 in both model complexes going from the weak electron-donor CH_2CO_2Me to the good electron-donating group Pr^i. Comparison of log*k* values with those of the analogous series of cobaloximes containing 4-CNpy and Me_3Bzm shows that there is a very good linear relationship in both cases, with slope close to 1. Furthermore, the reactivities of the Costa-type complexes are 10 times greater, on average, than those of the analogous cobaloximes.[32] This result is consistent with longer Co–N(axial) distances and larger α bending angles in the former complexes than those found in cobaloximes (see previous paragraph).

5 Schiff-base Complexes

The structural properties of cobalt complexes prepared with bis(salicylaldehydo)ethylendiimine ($salenH_2$) and bis(acetylacetone)ethylendiimine ($acacenH_2$) were reviewed in 1972.[57] Since then, the structure of the free ligands has been reported as well as many other structures of Co complexes having the tetradentate dianionic salen equatorial ligand or its derivatives (Figure 8).[58]

[57] M. Calligaris and G. Nardin, and L. Randaccio, *Coord. Chem. Rev.*, 1972, **7**, 385.
[58] M. Calligaris and L. Randaccio in 'Comprehensive Coordination Chemistry', ed. G. Wilkinson, R. Gillard, and J. McCleverty, Pergamon Press, Oxford, 1987, Vol. 2, p. 715.

Table 7 *Axial* Co–L *and* Co–C *bond lengths* (Å) *in octahedral cobalt*(III) *complexes of tetradentate Schiff bases*

	Co–L	Co–C	*Ref.*
$[MeCo(saloph)]_2$	2.435(4)	1.963(7)	*a*
$[EtCo(salen)]_2$	2.342(3)	1.990(7)	*b*
$py[Co(salpn)]CH(CN)_2$	2.060(9)	2.02(1)	*c*
$py[Co(saloph)]CH_2CN$	2.098(4)	2.000(5)	*d*
$py[Co(saloph)]CH_2CF_3$	2.126(9)	1.99(1)	*a*
$py[Co(salen)]CH{=}CH_2$	2.12(1)	1.93(2)	*b*
py[Co(saloph)]Et	2.214(4)	2.042(6)	*d*
$H_2O[Co(3\text{-}F\text{-}salen)]CH_2COMe$	2.13(1)	2.01(1)	*e*
$H_2O[Co(acsalen)]Et$	2.219(4)	1.996(6)	*f*
$MeOH[Co(salen)]CH_2COMe$	2.202(9)	2.02(1)	*b*
py[Co(acacen)]Me	2.16(1)	1.99(1)	*b*
$H_2O[Co(acacen)]CH{=}CH_2$	2.221(7)	1.89(1)	*b*

[a] Ref. 59. [b] Ref. 57. [c] N. A. Bailey, B. M. Higson, and E. D. Mckenzie, *J. Chem. Soc., Dalton Trans.*, 1975, 1105. [d] Ref. 63. [e] W. P. Schaefer, R. Waltzman, and B. T. Huie, *J. Am. Chem. Soc.*,1978, **100**, 5063. [f] M. H. Darbien, F. Dahan, J. P. Costes, J. P. Laurent, and G. Cros, *J. Chem. Soc., Dalton Trans.*, 1988, 129.

A. Structural Properties.—Organocobalt Schiff base complexes have been found as penta- and hexa-coordinated species. It should be noted that sometimes potentially pentacoordinate species XCo(chel) dimerize in the crystal as $[XCo(chel)]_2$ reaching six-coordination through a long bond from the cobalt of one Co(chel) unit to the oxygen of the other unit.[57] In Co^{III} pentacoordinate complexes the Co–C bond of 1.96(1) Å in the Me derivative is significantly shorter than that of 2.031(8) Å in the Pr^i analogue. This difference is strongly indicative of the greater bulk of the Pr^i group compared to that of the Me, a relationship already observed in hexacoordinate cobaloximes. Comparison with the corresponding hexacoordinated complexes reported in Table 7 indicates a slight but significant increase of the Co–C bond lengths in the latter.[59] This result appears to be in agreement with the lower BDE found in the base-on than in the base-off forms of B_{12} coenzyme, but the coordination number of the base-off species is not known.

Since the homolysis leads to Co^{II} species the structural features of Co^{II} compounds are of some interest. Although data for pentacoordinate Co^{II} complexes are limited, it appears that high-spin species, for which a significant increase of the basal coordination distances is found[60] with respect to the low-spin complexes, have shorter axial bonds. This feature may have implication in the mechanism of the Co–C bond cleavage in the coenzyme.

In hexacoordinate Co^{III} complexes (Table 7), more data are available for axial distances and the following relationships may be derived. The Co–C bond length (i) is not influenced significantly by the nature of the equatorial Schiff base, (ii)

[59] L. G. Marzilli, M. F. Summers, N. Bresciani Pahor, E. Zangrando, J. P. Charland, and L. Randaccio, *J. Am. Chem. Soc.*, 1985, **107**, 6880.

[60] M. Calligaris, G. Nardin, and L. Randaccio, *J. Chem. Soc., Dalton Trans.*, 1974, 1903; B. J. Kennedy, G. D. Fallon, B. M. K. C. Gatehouse, and K. Murray, *Inorg. Chem.*, 1984, **23**, 580.

increases with the increasing bulk of the R group, but (iii) depends strongly upon the hybridization of the carbon atom bonded to cobalt, as already observed in cobaloximes (see above). The Co–L distances are strongly dependent upon the nature of the *trans*-ligand. In fact, the Co–py bond length increases from 2.060(9) to 2.215(4) Å in the order of the *trans* ligands

$$CH(CN)_2 < CH_2CN < CH_2CF_3 \approx CH{=}CH_2 < Me < Et$$

irrespective of the Schiff base ligand. This trend follows the increasing σ-donor power of the R group, with the exception of the pyCo(salen)CH=CH_2 derivative. This exception could indicate that the nature of the equatorial Schiff base may influence Co–L distances, but this contrasts with the observation that the Co–OH_2 bond lengths in H_2OCo(acsalen)Et [2.219(4) Å] and H_2OCo(acacen)CH=CH_2 [2.221(7) Å] are very close, as expected on the basis of the σ-donor power of Et and CH=CH_2 groups. Nevertheless, it may be concluded that both electronic *trans*-influence and steric *cis*-influence, originated by the steric interaction of the axial ligand with the equatorial moiety, are reflected in bond length trends of Schiff base complexes in the same way as in those of cobaloximes. However, the Co–L distances in Schiff base complexes are significantly longer than those in other models having the same R group, so that the order of increasing Co–L distances is:

$$(DH)_2 < (DO)(DOH)pn < \text{Schiff base} < \text{corrin}$$

B. Solution Properties.—Since the general review of Costa *et al.*[61] and the recent review on synthesis and properties of similar B_{12} models,[62] relatively little work has been reported on organocobalt Schiff base complexes. Recently, Halpern *et al.*[14b] applied the kinetic method to estimate the BDE of the Co–C bond in the pyCo(saloph)R series. Values of 25, 22, 20, 18 kcal mol^{-1} were obtained for R = Pr^n, CH_2Ph, Pr^i, CH_2CMe_3, respectively. These data confirm that steric factors may play an important role in promoting the Co–C bond homolysis and show that the BDEs follow a trend similar to that found for Co–C bond lengths.

Dynamic NMR measurements of L dissociation rates of 3,5-lutidineCo(saloph)R compounds reveal rates 10^{10} times larger than those in the cobaloxime analogues. This enormous *cis*-effect is partly a ground-state effect, which follows the same trend of the *cis*-influence and partly arises from the higher stability of saloph pentacoordinate intermediate compared to that of cobaloximes.[63] The latter point is illustrated in the unusual example of both dimeric and monomeric molecules in the same crystal of the MeCo(saloph) compound. Furthermore, the rate constant increases in the order CH_2CN (2.25×10^4 s^{-1}) < CH_2CF_3

[61] A. Bigotto, G. Costa, G. Mestroni, G. Pellizer, E. Reisenhofer, L. Stefani, and G. Tauzher, *Inorg. Chim. Acta, Rev.*, 1970, **4**, 41.
[62] P. J. Toscano and L. G. Marzilli, *Progr. Inorg. Chem.*, 1984, **31**, 105.
[63] M. F. Summers, L. G. Marzilli, N. Bresciani Pahor, and L. Randaccio, *J. Am. Chem. Soc.*, 1984, **106**, 4478.

(2.76×10^5 s^{-1}) < Me (2.75×10^8 s^{-1}). This dependence on electron donation by R is greater than in other classes of B_{12} compounds (see above).[59] The quantitatively very different solution properties of organometallic Schiff base and cobaloxime complexes are in good agreement with trends expected on the basis of structural properties. The Schiff base complexes appear to have properties closer to Cbls than do cobaloximes, but unfortunately they are more difficult complexes to prepare and study. Probably, for both electronic (*i.e.* they are 'electron rich' systems closer to Cbls than 'electron poor' cobaloximes) and steric reasons [*i.e.* the equatorial ligand is more flexible than the $(DH)_2$ moiety] stable pentacoordinated organocobalt Schiff-base species can be characterized. Such species have been identified only as intermediates in cobaloximes. In base-off Cbls and in Cbi^+s, five-coordination is difficult to assess since these species are dissolved in H_2O, which may occupy the *trans*-axial position.

6 Conclusions

In this review, we have focused on a comparison of the most extensively studied model system for B_{12} coenzymes, namely cobaloximes. The structural properties of cobaloximes in the solid state have been very useful in interpreting solution data. The trend in structural data can be compared with Cbls on the one hand and Costa type and Schiff-base type models on the other hand. In general, these properties suggest the following trend:

$$Co(DH)_2 \approx Co(DO)(DOH)pn \ll Cbls \leqslant Co(Schiff\text{-}base)$$

The Co–C bond energies decrease for closely analogous species following this general trend, although the differences are not large. Indeed, relatively little difference is found in Co–C bond lengths for a given type of R-group. The more important structural factor is the length of the Co–C bond that reflects roughly the relative Co–C cleavage rates given in Section 2B above. A second important aspect of our findings is that distortions induced by L also lengthen and weaken the Co–C bond. These findings support the concept espoused by many groups (see reference 4) that the protein may distort the coenzyme and thereby labilize the Co–C bond. Interestingly, this suggestion was first made nearly two decades ago.[64] On the other hand, models have shown that the distortion of the Co–C–C angle[4] does not affect substantially the stability of the organometallic complex, since neopentylcobaloximes, where this angle is found to be 130°, are particularly stable.

In contrast to the similar Co–R bond lengths for a given R with different equatorial ligands, Co–N bond lengths are quite different and these as well as L dissociation rates indicate that Co–N bonding is weakest in the Schiff-base compounds. Equatorial ligand flexibility is more difficult to assess and does not necessarily strictly follow the trends in bond energies and bond lengths noted above. In this regard, the porphyrin analogues deserve greater scrutiny. The

[64] H. A. O. Hill, J. M. Pratt, and R. J. P. Williams, *Chem. Brit.*, 1969, **5**, 156.

solid-state information has laid a foundation of parameters that are likely to be important for interpreting NMR data and for developing methods of calculating conformations of Cbls. Indeed, new two-dimensional NMR methods for gaining insight into solution structure are usually most powerful when combined with molecular mechanics calculations. Therefore, despite their remoteness from Cbls in terms of physical properties, we expect cobaloximes to continue to play a central role in the development of methods for understanding B_{12} properties, especially the factors influencing the Co–C bond.

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