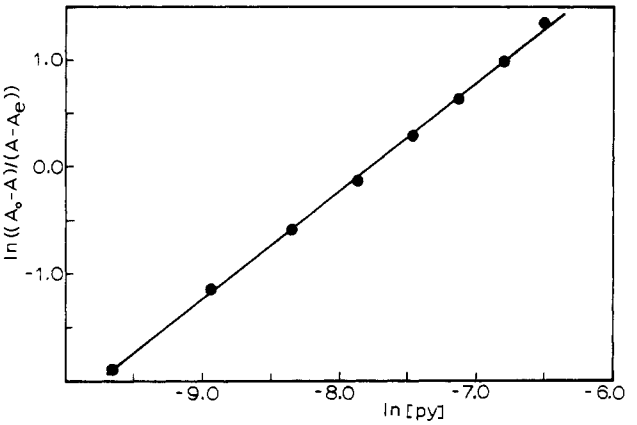


Figure 6. Plot of ln $((A_0-A)/(A-A_e))$ vs. ln [py] for reaction (1). Concentrations are similar to those indicated in Figure 5.

Table III. Equilibrium Constants for CoL^+–B Adduct Formation

system	q	$10^{-3}K_{eq}$, M^{-1}
$(CoL^1)^+$–MeIM	1.0	11 ± 3
$(CoL^1)^+$–py	1.0	2.3 ± 0.4
$(CoL^1)^+$–Br^-	1.0	0.23 ± 0.04
$(CoL^2)^+$–MeIm	0.98	33 ± 3
$(CoL^2)^+$–py	1.04	5.7 ± 0.3
$(CoL^2)^+$–lut	1.10	0.046 ± 0.002
$(CoL^5)^+$–MeIm	1.10	127 ± 5
$(CoL^5)^+$–py	1.01	4.5 ± 0.1
$(CoL^5)^+$–Br^-	1.04	1.8 ± 0.2
$(CoL^5)^+$–lut	1.22	0.089 ± 0.004

problems with oxygen were avoided.)

The equilibrium constants, K_{eq}, increase in the order lut < Br^- < py < MeIm for a given macrocyclic ligand L. This ordering is as expected based on the donor strengths of these species. For a given B, for example MeIm, the values increase in the order $L^1 < L^2 < L^5$. This ordering is understandable in terms of the withdrawing ability of the macrocyclic ligand substitutents. L^5, with phenyl groups on the imine carbons, should withdraw electron density from Co^I more effectively than should L^1, which has methyl substituents. The metal ion is therefore more acidic in $(CoL^5)^+$ than in $(CoL^1)^+$. The question remains, however, as to why the complexes are acidic at all. They are in fact potent Lewis acids, binding a variety of bases with equilibrium constants which are in all cases >50 M^{-1}. Electrochemical results show that the Co^I complexes are much more acidic than the corresponding Co^{II} complexes. This is unexpected, the higher charge of Co(II) normally making it a stronger acid. Further, preliminary experiments indicate that although the complex $(Ni^{II}L)^{2+}$ binds pyridine in the axial sites quite strongly, it is a weaker Lewis acid than $(Co^IL^1)^+$.[46] In this case, where the metals have the same configuration, it is truly remarkable that the stronger acid is the complex with smaller positive charge.

The relative acidities of CoL^+ and CoL^{2+} described above may be tentatively explained in at least two ways. The first explanation attributes the acidity of CoL^+ to the ability of the α-diimine macrocyclic ligands to function as a π-acceptors. Matchups of the metal d π donor orbitals with the π^* orbitals of the macrocycle is much better for Co^I than for Co^{II}, leading to extensive backbonding in CoL^+. It is conceivable that backbonding is so effective that the cobalt center may actually be *more positive* in CoL^+ than in CoL^{2+}. According to this explanation, CoL^+ should be a stronger acid than CoL^{2+} toward any Lewis base, regardless of the base characteristics.

A reviewer has suggested a second explanation based on the relative electrostatic and covalent characters of CoL^+ and CoL^{2+}. According to this explanation, CoL^{2+} is a primarily electrostatic acid and prefers electrostatic donors such as acetonitrile (with a large Drago E number[47]) to more covalent donors such as Py and MeIm (large Drago C number). Thus displacement of An solvent from the axial sites of CoL^{2+} is unfavorable. In contrast, CoL^+ is a primarily covalent acid and prefers covalent donors to electrostatic ones. Thus displacement of An solvent from the axial sites of CoL^+ is favorable. Experiments to differentiate between these two explanations are under way.

Registry No. $[CoL^1(An)_2](ClO_4)_3$, 63122-92-9; $[CoL^2(An)_2](ClO_4)_3$, 103093-30-7; $[CoL^5(An)_2](ClO_4)_3$, 103093-28-3; $CoL^1(An)_2(BPh_4)_2$, 73871-70-2; $CoL^2(An)_2(BPh_4)_2$, 111140-32-0; $CoL^5(An)_2(BPh_4)_2$, 111140-34-2; $[CoL^1](BPh_4)$, 111140-36-4; $[CoL^2](BPh_4)$, 111140-38-6; $[CoL^5](BPh_4)$, 111140-40-0; py, 110-86-1; MeIm, 616-47-7; Int, 108-48-5; DTBP, 585-48-8.

(46) Kildahl, N. K.; Antonopoulos, G. unpublished results.
(47) Porterfield, W. W. *Inorganic Chemistry: A Unified Approach*; Addison-Wesley: Reading, MA, 1984.

Contribution from the Department of Chemistry, Iowa State University, Ames, Iowa 50011

Molecular Orbital Study of Coenzyme B_{12}. Activation of the Cobalt–Carbon Bond by Angular Distortions

Longgen Zhu and Nenad M. Kostić*

Received June 19, 1987

A realistic model for coenzymes B_{12}, and the first one to contain the actual corrin and imidazole ligands, Co(corrin)Im$(CH_3)^+$, is examined with nonparametrized, iterative molecular orbital calculations by the Fenske–Hall method. Possible effects of the following four structural deformations on the Co–C bond strength are considered: tilt, θ, of the Co–C bond with respect to the corrin ring; distortion, ϕ, of configuration at the C atom; variation, d, of the Co–Im distance trans to the organic ligand; and rotation, ω, of the imidazole ligand. The first two deformations labilize the Co–C bond greatly; the third has a minor effect on its strength; and the fourth has no direct effect. The tilt of the organic ligand and the unusual configuration of the C atom, prominent structural features of coenzymes B_{12}, seem to be significant for their catalytic function. The theoretical findings contradict the notion that an agostic interaction exists between a C–H bond and the Co atom in B_{12} and corroborate the notion that the organic radical may perhaps be trapped by weak, reversible binding to the corrin macrocycle.

Introduction

Coenzyme B_{12} or 5′-deoxyadenosylcobalamin, designated AdB_{12}, together with some dozen enzymes catalyzes rearrangement reactions of various substrates. Methylcobalamin, designated MeB_{12}, with its enzymes catalyzes methylation reactions. The first organometallic compounds with a biological function, these and other cobalamins have been subjects of much research.[1-15] It is accepted

(1) Dolphin, D., Ed. B_{12}; Wiley-Interscience: New York, 1982; 2 vols.
(2) Halpern, J. *Science (Washington, D.C.)* **1985**, *227*, 869.

0020-1669/87/1326-4194$01.50/0

that the catalytic cycle begins by homolysis of the weak cobalt–carbon bond, whose energy is known.[2,7,16,17] The resulting organic radical then abstracts a H atom from the substrate, and skeletal rearrangement ensues. The important Co–C bond apparently is activated greatly by the coenzyme interaction with the apoenzyme, or by binding of the resulting holoenzyme to the substrate, or by both of these processes.

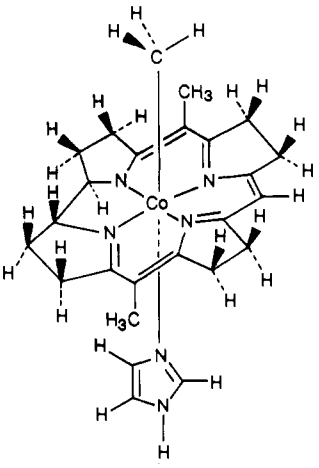
Why the Co–C bond in the holoenzyme B_{12} is labile remains largely unclear. Various steric and electronic interactions and their combinations have been proposed as possible causes of its labilization. Both size and basicity (i.e., σ-donation ability) of the α ligand L, which is trans to the β carbon ligand, affect the Co–C bond energy in the model cobaloxime complexes.[2,7] In coenzyme B_{12} the ligand L is a substituted benzimidazole, which is weakly bonded to the Co atom. The exceptionally long Co–N distance of 2.23 Å[18,19] and structural correlations among the model complexes were taken as indications that the cleavage of the Co–C bond may be triggered by the elongation of the Co–N bond trans to it.[3,20,21] Even a small rotation of the benzimidazole about the Co–N bond (probably because of the steric distortions that this motion would cause) was considered sufficient to labilize the Co–C bond.[3] Inherent instability of secondary and tertiary alkylcobalamins shows that the steric bulk of the alkyl ligand weakens its bond to the Co atom.[22–27]

The steric effects of the ligands within the coenzyme and of the apoenzyme upon the coenzyme perhaps are transmitted via the corrinoid ring; there is evidence both for[19,28] and against[29] the flexibility of this macrocycle. The probable cause of reactivity of AdB_{12} and of its model complexes with bulky organic groups is the steric cis interaction leading to the distortion of the corrin and of the organic ligand itself.[19,30–32]

Structures of AdB_{12}[18,19] and MeB_{12}[33] in the solid state are remarkably similar to each other and to the structures in solution.[34] Two features seem pertinent to the lability of the Co–C bond. First, it is tilted by ca. 5° away from perpendicularity to the mean CoN_4 plane in both coenzymes. Second, the configuration of the ligating C atom in AdB_{12} is strongly distorted from tetrahedral—the Co–C–$C_{adenosyl}$ angle is ca. 125°.[18,35] In MeB_{12}, in which all the substituents at the C atom are the light H atoms, such bond angles were not determined.

Although the activity of coenzymes B_{12} undoubtedly depends on their electronic structure and particularly on the Co–C bond—this notion underlies much of the structural and mechanistic research—quantum-chemical studies of bonding have been relatively few.[36–49] All of the calculations to date have dealt with cobalt complexes containing greatly simplified ligands. Most of the studies were aimed at assignment of the electronic transitions responsible for the absorption spectra of corrin and of its metal complexes. Only recently have molecular orbital calculations addressed expressly the problem of the Co–C bond activation.[45–47] Particularly informative was the study by Christianson and Lipscomb.[47] With an approximate ab inito method designated PRDDO, they examined the effects of various geometric distortions on the strength of the Co–C covalent bonding.

In the present study, a realistic model of B_{12}, shown in **1**, is treated with nonparametrized, iterative calculations. This is the



first model to include the actual corrin macrocycle as the equatorial

(3) Bresciani-Pahor, N.; Forcolin, M.; Marzilli, L. G.; Randaccio, L.; Summers, M. F.; Toscano, P. J. *Coord. Chem. Rev.* **1985**, *63*, 1.
(4) Finke, R. G.; Schiraldi, D. A.; Mayer, B. J. *Coord. Chem. Rev.* **1984**, *54*, 1.
(5) Toscano, P. J.; Marzilli, L. G. *Prog. Inorg. Chem.* **1984**, *31*, 105.
(6) Brown, K. L. *New Compr. Biochem.* **1984**, *6*, 433.
(7) Halpern, J. *Pure Appl. Chem.* **1983**, *55*, 1059.
(8) Lexa, D.; Saveant, J.-M. *Acc. Chem. Res.* **1983**, *16*, 235.
(9) Halpern, J. *Acc. Chem. Res.* **1982**, *15*, 238.
(10) Zagalak, B., Friedlich, W., Eds. *Vitam. B_{12}, Proc. Eur. Symp., 3rd* **1979**.
(11) Babior, B. M.; Krouwer, J. S. *CRC Crit. Rev. Biochem.* **1979**, *6*, 35.
(12) Golding, B. T. In *Inorganic Biochemistry*; Hill, H. A. O., Ed.; The Chemical Society: London, 1979; pp 75–87.
(13) Abeles, R. H.; Dolphin, D. *Acc. Chem. Res.* **1976**, *9*, 114.
(14) Babior, B. M. *Acc. Chem. Res.* **1975**, *8*, 376.
(15) For a summary of earlier studies, see: Pratt, J. M. *Inorganic Chemistry of Vitamin B_{12}*; Academic: New York, 1972.
(16) Halpern, J.; Kim, S.-H.; Leung, T. W. *J. Am. Chem. Soc.* **1984**, *106*, 8317.
(17) Finke, R. G.; Gay, B. P. *Inorg. Chem.* **1984**, *23*, 3041.
(18) Lenhert, P. G. *Proc. R. Soc. London, Ser. A* **1968**, *303*, 45.
(19) Glusker, J. P. In *B_{12}*; Dolphin, D., Ed.; Wiley-Interscience: New York, 1982; Vol. 1, Chapter 3.
(20) Summers, M. F.; Toscano, P. J.; Bresciani-Pahor, N.; Nardin, G.; Randaccio, L.; Marzilli, L. G. *J. Am. Chem. Soc.* **1983**, *105*, 6259.
(21) Summers, M. F.; Marzilli, L. G.; Bresciani-Pahor, N.; Randaccio, L. *J. Am. Chem. Soc.* **1984**, *106*, 4478.
(22) Grate, J. H.; Schrauzer, G. N. *J. Am. Chem. Soc.* **1979**, *101*, 4601.
(23) Chemaly, S. M.; Pratt, J. M. *J. Chem. Soc., Dalton Trans.* **1980**, 2259, 2267, 2274.
(24) Tsou, T.-T.; Loots, M.; Halpern, J. *J. Am. Chem. Soc.* **1982**, *104*, 623.
(25) Grate, J. H.; Grate, J. W.; Schrauzer, G. N. *J. Am. Chem. Soc.* **1982**, *104*, 1588.
(26) Finke, R. G.; Smith, B. L.; Mayer, B. J.; Molinero, A. A. *Inorg. Chem.* **1983**, *22*, 3677.
(27) Pratt, J. M. *Inorg. Chim. Acta* **1983**, *79*, 27.
(28) Geno, M. K.; Halpern, J. *J. Am. Chem. Soc.* **1987**, *109*, 1238.
(29) Bax, A.; Marzilli, L. G.; Summers, M. F. *J. Am. Chem. Soc.* **1987**, *109*, 566.
(30) Marzilli, L. G.; Toscano, P. J.; Randaccio, L.; Bresciani-Pahor, N.; Calligaris, M. *J. Am. Chem. Soc.* **1979**, *101*, 6754.
(31) Randaccio, L.; Bresciani-Pahor, N.; Toscano, P. J.; Marzilli, L. G. *J. Am. Chem. Soc.* **1980**, *102*, 7372.
(32) Randaccio, L.; Bresciani-Pahor, N.; Toscano, P. J.; Marzilli, L. G. *J. Am. Chem. Soc.* **1981**, *103*, 6347.
(33) Rossi, M.; Glusker, J. P.; Randaccio, L.; Summers, M. F.; Toscano, P. J.; Marzilli, L. G. *J. Am. Chem. Soc.* **1985**, *107*, 1729.
(34) Summers, M. F.; Marzilli, L. G.; Bax, A. *J. Am. Chem. Soc.* **1986**, *108*, 4285.
(35) Alcock, N. W.; Dixon, R. M.; Golding, B. T. *J. Chem. Soc., Chem. Commun.* **1985**, 603.
(36) Giannotti, C. In *B_{12}*; Dolphin D., Ed.; Wiley-Interscience: New York, 1982; Vol. 1, Chapter 11.
(37) Veillard, A.; Pullman, B. *J. Theor. Biol.* **1965**, *8*, 307.
(38) Offenhartz, B. H. *Proc. R. Soc. London, Ser. A* **1965**, *288*, 350.
(39) Kuhn, H.; Drexhage, K. H.; Martin, H. *Proc. R. Soc. London, Ser. A* **1965**, *288*, 348.
(40) Day, P. *Theor. Chim. Acta* **1967**, *7*, 328.
(41) Day, P. *Coord. Chem. Rev.* **1967**, *2*, 109.
(42) Ingraham, L. L.; Fox, J. P. *Ann. N.Y. Acad. Sci.* **1969**, *153*, 738.
(43) Schrauzer, G. N. *Naturwissenschaften* **1969**, *53*, 459.
(44) Offenhartz, P. O.; Offenhartz, B. H.; Fung, M. M. *J. Am. Chem. Soc.* **1970**, *92*, 2966.
(45) Schrauzer, G. N.; Lee, L. P.; Sibert, J. W. *J. Am. Chem. Soc.* **1970**, *92*, 2997.
(46) Salem, L.; Eisenstein, O.; Anh, N. T.; Burgi, H. B.; Devaquet, A.; Segal, G.; Veillard, A. *Nouv. J. Chim.* **1977**, *1*, 335.
(47) Christianson, D. W.; Lipscomb, W. N. *J. Am. Chem. Soc.* **1985**, *107*, 2682.
(48) Mealli, C.; Sabat, M.; Marzilli, L. G. *J. Am. Chem. Soc.* **1987**, *109*, 1593.
(49) Cuthbertson, A. F.; Glidewell, C.; Butler, A. R.; McIntosh, A. S. *Inorg. Chim. Acta* **1987**, *135*, 93.

ligand and imidazole (designed Im) as the α ligand. The side arm, the benzene ring fused to the imidazole, and the peripheral substituents at the corrin, structural elements undoubtedly essential to the biological function of the coenzyme,[50] had to be left out because they would have made the computations almost unfeasible without significantly improving their quality. The axial methyl group, which is the true β ligand in MeB_{12}, also serves as a model for the deoxyadenosyl ligand in AdB_{12}. This model for the coenzyme is unrealistic insofar as it excludes explicit interactions with the apoenzyme, but such limitations are inevitable in view of the computational requirements of any reasonably accurate molecular orbital method. Possible influences of the following four structural deformations, shown in **2**, on the strength of the Co–C bond are examined: (1) the tilt, θ, of this bond with respect to the corrin macrocycle; (2) the distortion, ϕ, of configuration at the C atom, explained in the next section; (3) elongation and compression, d, of the Co–Im bond trans to the C atom; and (4) rotation, ω, of the imidazole ligand. Factors 1[47] and 3,[47,48] the change of the Co–C distance,[47,48] and puckering of the corrin ring[47] were treated in previous quantum-chemical studies.

Details of the Calculations

An approximation to the Hartree–Fock–Roothaan technique, the Fenske–Hall method, has been described elsewhere.[51] Since this iterative SCF method is devoid of empirical or adjustable parameters, the results of calculations are determined solely by the molecular geometry[18] and basis functions.[52–54] In order to elucidate the electronic structure of the complex molecule and to examine the crucial Co–C bond in variously distorted structures, the complete molecule $Co(corrin)Im(CH_3)^+$ was constructed from the fragments CH_3^- and $Co(corrin)Im^{2+}$; the large fragment was built from subfragments Im and $Co(corrin)^{2+}$; the latter subfragment was made from Co^{3+} and $corrin^-$; ultimately, all the parts were composed from atoms. The required transformations of the basis sets and the partition of charges between the closed-shell fragments or subfragments facilitated the interpretation of the calculations without affecting their numerical results.

Total overlap population between the Co and C atoms, calculated according to Mulliken, can be taken as a measure of the strength of the Co–C covalent bonding. Since no single-configurational method, including the present one, is suited to the study of formation and cleavage of chemical bonds, only their relative strengths were followed in the course of structural distortions. Deformation ϕ amounts to the tilt of the H_3 plane with respect to the Co–C bond; the H–C–Co angles change while the H–C–H angles remain 109.5°. The four types of deformations, specified above, were not drastic; the bond lengths and angles were varied over reasonable intervals, consistent with the crystallographic findings on the coenzymes[18,33] and on the inorganic model complexes.[3] Numerous studies with the Fenske–Hall method have demonstrated its applicability to the semiquantitative optimization of bond angles. The method can also be trusted to show the change in relative energy of a covalent bond with moderate variation in the bond length.

Results and Discussion

Bonds of the cobalt atom to its six ligands in $Co(corrin)ImCH_3^+$ are essentially of σ type. The overlap populations corresponding to π interactions between the Co atom and the four equatorial N ligands are only 0.010 e; such interactions with the two axial ligands are even weaker. Indeed, the electrochemical[55] and spectroscopic[56] properties of cobalamins are explicable in terms of pure σ bonding. The LUMO in the five-coordinate $Co(corrin)Im^{2+}$ fragment is localized on the Co atom, axially oriented, and partly antibonding with respect to the Im ligand. The Co–Im bond is therefore much weakened by σ donation to the axial ligand in question from the CH_3^- ligand in the sixth (β) position. This bond weakening, consistent with the well-known trans influence of the methyl ligand,[57] is manifest in the decrease of the Co–Im overlap population from 0.202 e in the five-coordinate fragment $Co(corrin)Im^{2+}$ to 0.080 e in the six-coordinate complex designated **1**. These electronic effects, perhaps in conjunction with the steric bulk of the substituted benzimidazole, account for the unusually long Co–Im distance in B_{12}.[18,33]

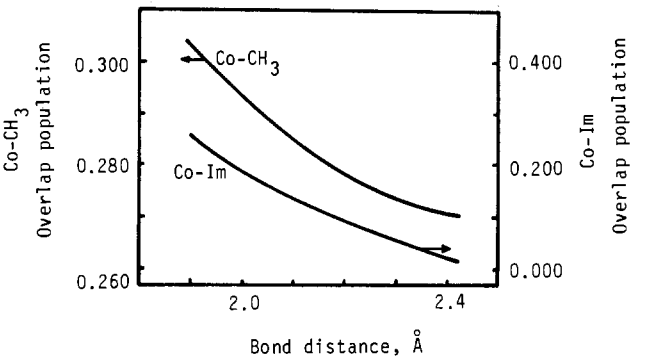


Figure 1. Dependence of axial bonding in $Co(corrin)ImCH_3^+$ on the Co–Im distance. Note the different scales on the two ordinates. The overlap populations are in electron units.

Table I. Effects of Angular Distortions in $Co(corrin)ImCH_3^+$ on the Strength of Four Covalent Bonds: Co–CH_3, Co–Corrin, Agostic Interaction between Co and H in CH_3, and CH_3–Corrin

		tot. overlap pop., e			
θ, deg	ϕ, deg	Co–C	Co–N_{eq}	Co–H^b	C–N_{eq}
90	109.5	0.277	0.269	−0.020	−0.002
	118	0.251	0.266	−0.060	0.003
	123	0.187	0.266	−0.116	0.003
	125	0.157	0.266	−0.136	0.003
100	109.5	0.272	0.259	−0.028	−0.001
	118	0.240	0.253	−0.070	0.006
	123	0.175	0.251	−0.115	0.009
	125	0.145	0.252	−0.134	0.009
110	109.5	0.251	0.240	−0.030	0.002
	118	0.213	0.227	−0.068	0.026
	123	0.142	0.222	−0.119	0.040
	125	0.110	0.221	−0.138	0.040
120	109.5	0.202	0.201	−0.030	0.035
	110	0.183	0.187	−0.050	0.075
	118	0.148	0.176	−0.080	0.111
	123	0.068	0.167	−0.129	0.156
	125	0.033	0.166	−0.149	0.169

In one series of calculations, the Co–C overlap population was monitored as the Co–Im distance was shortened and elongated moderately with respect to the actual value of 2.23 Å. The Figure 1 shows that the strength of the Co–C bond depends somewhat on the Co–Im distance, as expected on the basis of thermodynamic[2,7] and crystallographic[3,20] studies. This dependence, however, is too small to be taken as evidence that cleavage of the Co–C bond in B_{12} can be triggered by the elongation of the bond trans to it. Christianson and Lipscomb reached the same conclusion.[47] Since the alkyl ligand evidently has a pronounced trans influence and since the weakly coordinated benzimidazole is tethered to the corrin ring in B_{12}, a question of dissociation of the benzimidazole in the catalytic cycle of B_{12} may perhaps be considered.[27,58]

Since both CH_3 and Im are virtually pure σ ligands, the rotation of the latter is unlikely to affect bonding of the former with the Co atom. Indeed, the calculations show that both axial bonds remain unaltered upon rotation of the Im ring, i.e., that this motion has no direct electronic effect on the strength of the Co–C bond. In view of the crystal structures of coenzymes B_{12}, even an indirect steric effect of the rotation is unlikely: in both AdB_{12}[18] and MeB_{12}[33] the benzimidazole ligand has the same orientation, which apparently is controlled by several axially oriented atoms at the corrin periphery.[19,33]

(50) Toraya, T.; Krodel, E.; Mildvan, A. S.; Abeles, R. H. *Biochemistry* **1979**, *18*, 417.
(51) Hall, M. B.; Fenske, R. F. *Inorg. Chem.* **1972**, *11*, 768.
(52) Basch, H.; Gray, H. B. *Theor. Chim. Acta* **1966**, *4*, 367.
(53) Clementi, E. *J. Chem. Phys.* **1964**, *40*, 1944.
(54) Hehre, W. J.; Stewart, R. F.; Pople, J. A. *J. Chem. Phys.* **1969**, *51*, 2657.
(55) Rubinson, K. A.; Parekh, H. V.; Itabashi, E.; Mark, H. B., Jr. *Inorg. Chem.* **1983**, *22*, 458.
(56) Rubinson, K. A. *J. Am. Chem. Soc.* **1979**, *101*, 6105.
(57) Appleton, T. G.; Clark, H. C.; Manzer, L. E. *Coord. Chem. Rev.* **1973**, *10*, 335.
(58) Marzilli, L. G.; Summers, M. F.; Bresciani-Pahor, N.; Zangrando, E.; Charland, J.-P.; Randaccio, L. *J. Am. Chem. Soc.* **1985**, *107*, 6880.

Angular distortions, however, affect the Co–C bond strength markedly, as Table I shows. Since the total energy of such a large molecule cannot be calculated exactly, it is possible only to estimate the energetics of the distortions. The changes in the summed molecular orbital eigenvalues (for an isolated molecule, as in the gas phase) are approximately 50–200 kcal mol^{-1}, an amount of energy that probably can be compensated for by the interaction of the coenzyme with its apoenzyme in the actual catalytic process.

The weakening of the Co–C bond on account of its tilting, θ, with respect to the corrin plane (at the fixed Co–C distance) is a relatively straightforward consequence of one factor—the loss of σ overlap between the sp^3 hybrid on C and the σ-type hybrid of the Co and Im orbitals. As long as the configuration of the C atom is tetrahedral or nearly such, the bond weakening upon moderate tilting is appreciable but not great. For example, if ϕ is kept at 109.5°, the Co–C overlap population decreases by 27% as θ increases from 90 to 120°. Distortion ϕ (at the fixed tilt angle, θ) renders the C atom nontetrahedral and causes a greater weakening of the Co–C bond because two major factors are involved—rehybridization of the C atom, with the concomitant loss of the Co–C overlap and attraction, and the Co–H^b repulsion. For example, if θ is kept at 90°, the positive Co–C overlap population decreases by 43% and the negative Co–H^b overlap population increases nearly 7-fold as ϕ is varied from the tetrahedral value to the actual value of 125°. Finally, the concurrent tilt and distortion of the organic ligand labilize the coenzyme even more because all three of the aforementioned factors operate together. For example, the same distortion at the C atom (change in ϕ from 109.5 to 125°) weakens the Co–C bond by 43% when θ = 90°, but by 84% when θ = 120°.

Addition of the distortions ω and d to the angular deformations θ and ϕ does not produce significant further weakening of the Co–C bond. The motions of the Im ligand, which alone have little effect on the Co–C bond (see above), seem to have little effect even when combined with the angular deformations involving the organic β ligand.

In addition to the three major consequences of the angular distortions, there is a fourth one—a minor interaction that also depends on these bond angles. Distortion θ brings the C atom closer to the equatorial plane, and distortion ϕ renders this atom nontetrahedral. The σ orbital of the CH_3 group, previously aimed at the Co atom, now interacts partially with the p_σ orbital of an equatorial N atom as well. Already in the moderately distorted complex the CH_3 group seems to develop some bonding with a N atom in the corrin ring. This bonding increases as the Co–C and the affected Co–N bonding interactions decrease with the angular distortions.

These theoretical findings perhaps are informative about the early phase of the catalytic cycle involving B_{12}. The Co–C bond evidently is much weakened by the distortion of configuration at the C atom, especially when this distortion is accompanied by the tilt with respect to the equatorial plane. Both types of deformation are clearly evident in the coenzymes B_{12},[18,19,33] and they may well contribute to the activation of the Co–C bond.

The growing recognition of stabilizing agostic interactions between C–H bonds and metal atoms in organometallic complexes led to a proposal[59] that such an interaction occurs in B_{12}, too, i.e., that the ligating C atom has carbenoid character.[59,60] The data in Table I, however, contradict this notion. As ϕ changes from 109.5 to 125°, the Co–H^b distance decreases from 2.62 to 1.97 Å. The H^b atom actually seems to be repelled by the filled d_π orbitals of Co (corresponding to the t_{2g} level in an octahedral field) and would donate electron density into an antibonding sp hybrid of the Co atom. These two interactions, if they occurred, would be repulsive, between the Co and H^b atoms.

An observation that the cleavage and re-formation of the Co–C bond in a model complex containing the chiral C atom proceed with retention of its configuration led to the proposal that, in the catalytic cycle involving B_{12}, the alkyl group may be reversibly trapped by the equatorial ligand.[61] Although the present study does not address directly the question of trapping, the data in Table I do support this hypothesis. As angular distortions at both the Co and C atoms weaken the bond between Co and one of the N donors of the corrin ring, this N atom develops an attractive interaction with the CH_3 group; see Table I. Reversible transfer of alkyl groups to the N atom in metalloporphyrins was proposed[62] and actually observed[63,64] before. The weakness of this calculated interaction, especially when the distortions are small, is accordant with the reversibility of the presumed binding.

Conclusion

Molecular orbital calculations were used to examine a realistic model of coenzyme B_{12} and to assess relative contributions of four geometric factors to the labilization of the coenzyme and, particularly, to the activation of the Co–C bond. The tilt and angular distortion of the organic ligand, especially the latter motion, appear to weaken this bond greatly. The theoretical findings indicate that the structural deformations evident in the crystalline coenzymes may well be essential to their function under catalytic conditions. Two existing proposals concerning the catalytic mechanism are evaluated in light of the theoretical findings. This study, and prior such molecular orbital studies, show that methods of quantum chemistry, in conjunction with experimental ones, can profitably be applied to problems in bioinorganic and bioorganic chemistry.

Acknowledgment. This research was supported in part by the Computation Center at Iowa State University. L.Z. thanks Nanjing University, Nanjing, People's Republic of China, for a leave of absence. We thank David W. Christianson, Michael F. Summers, and Paul J. Toscano for their incisive comments on the manuscript.

Registry No. **1**, 111004-53-6; coenzyme B_{12}, 13870-90-1.

(59) Amir-Ebrahimi, V.; Hamilton, R.; Kulkarni, M. V.; Mcilgorm, W. A.; Mitchell, T. R. B.; Rooney, J. J. *J. Mol. Catal.* **1983**, *22*, 21.
(60) Rooney, J. J. *J. Chem. Res.* **1984**, 48.
(61) Le Hoang, M. D.; Robin, Y.; Devynck, J.; Bied-Charreton, C.; Gaudemer, A. *J. Organomet. Chem.* **1981**, *222*, 311.
(62) Lexa, D.; Saveant, J.-M.; Soufflet, J. P. *J. Electroanal. Chem.* **1979**, *100*, 159.
(63) Callot, H. J.; Schaeffer, E. *J. Organomet. Chem.* **1978**, *145*, 91.
(64) Dolphin, D.; Halko, D. J.; Johnson, E. *Inorg. Chem.* **1981**, *20*, 4348.