# Binding of the Lopsided 1,5,6-Trimethylbenzimidazole Ligand to Inorganic and Organometallic Cobaloxime $B_{12}$ Models

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The interaction of the lopsided dimethylbenzimidazole ligand with the corrin ligand in cobalamins (Cbls) may be one of the structural features involved in Co–C bond cleavage during $B_{12}$-dependent enzymic processes. Models of $B_{12}$ compounds usually contain alkyl ligands to mimic the coenzymes. However, the inductive effect of the Co on the benzimidazole ligand should be most pronounced when the trans influence of the other axial ligand is weak, e.g. Cl. In this report we describe the synthesis and three-dimensional structures of $Me_3BzmCo(DH)_2Cl$ (**I**) and several alkylcobaloximes, $Me_3BzmCo(DH)_2R$ (where $Me_3Bzm$ = 1,5,6-trimethylbenzimidazole, DH = the monoanion of dimethylglyoxime, and R = $CH_2NO_2$ (**II**), R = $CH_3$ (**III**), and $CH(CH_3)_2$ (**IV**)). The X-ray results suggest that this benzimidazole ligand does not have unusual bulk and closely resembles pyridine in steric effect. The geometry at the Co-coordinated N of $Me_3Bzm$ is characterized by large angular distortions. However, the distortions were not very dependent on the trans ligand. A two-term expression has been reported previously to explain the dependence of the $^{13}C$ NMR chemical shifts for the $\alpha$-ribazole (dimethylbenzimidazole-containing) moiety in Cbls on changes in the trans axial ligand. The first (through-bond) inductive term relates the inductive effect of the cobalt center to that of the proton. The second (through-space) anisotropic term relates the effects of changes in structure and cobalt anisotropy on chemical shift. We attempted to use an analogous expression to fit our structural and NMR data on $Me_3Bzm$ cobaloximes with trans ligands of greatly different trans influence. The proton inductive effects were not useful for explaining the cobalt inductive effects, since the $^{13}C$ NMR signal for B2 (the C between the two benzimidazole N's) moved downfield on coordination in our models but upfield on coordination in Cbls. Protonation causes the B2 signal to move upfield. Therefore, with our extensive data, we developed a new empirical inductive term which gave excellent fits of our data, expressed as coordination shifts. Coordination shifts are the differences in shift of the free and coordinated ligand. The possible significance of this new term is discussed in the light of the finding that it gave values consistent with the effects of other metal ions on the B2 coordination shifts and with other measures of the influence of axial ligands on the properties of the cobalt center. Furthermore, the upfield coordination shift of B2 in Cbls can now be confidently attributed to corrin ring anisotropy; the shift is only slightly modulated by cobalt inductive and anisotropic effects. Moreover, the small dependence of the B2 shift on the trans influence of the other axial ligand (the ligand-responsive shift) cannot be rationalized with the published two-term proton-based expression. With our new interpretation, a consistent description of ligand-responsive shifts emerges for both Cbls and $B_{12}$ models. Finally, our reinterpretation of factors influencing $^{13}C$ NMR shifts also accounts for some significant features of the $^1H$ NMR spectra of Cbls.

## Introduction

Lopsided heterocyclic ligands (imidazoles, purines, etc.) are widely distributed metal binding sites in proteins, nucleic acids, and metal cofactors; these ligands have a less bulky half and a more bulky half, e.g. 5,6-dimethylbenzimidazole (DMBz). Understanding the coordination properties and spectroscopic trends of lopsided ligands coordinated in simple compounds is essential in understanding such trends in complex biological systems.

For example, the ligand bulk and the response of the DMBz ligand to structural effects are of considerable interest because the structural interplay between the DMBz and the deoxyadenosyl axial ligands and the corrin equatorial ligand has been discussed frequently in terms of Co–C bond homolysis in coenzyme $B_{12}$ (5′-deoxyadenosylcobalamin, AdoCbl).[1–4] Because of the long-recognized relationship between Co–C bond cleavage and conformational changes in $B_{12}$-dependent holoenzymes,[3] considerable effort has been expended to gain structural information on $B_{12}$ and related compounds. The two most promising approaches are NMR spectroscopy and X-ray crystallography.[3–28] These studies have involved either cobalamins (Cbls)[4–12] or, more frequently, model organocobalt complexes.[13–28]

Since $^{13}C$ NMR shifts can be correlated with structural changes in $B_{12}$ compounds and models,[3,13,15] there is a need to understand the features influencing the dependence of the shift on the changes

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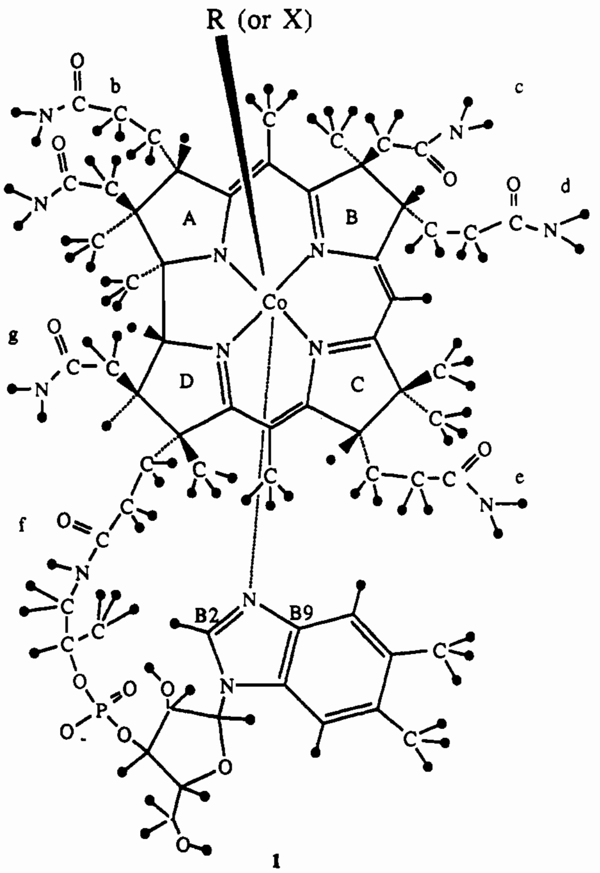
in the properties of the compounds. We call these shifts ligand-responsive shifts. In an attempt to interpret the $^{13}$C NMR spectra of a series of Cbls with various axial substituents (R) trans to the coordinated axial DMBz (see structure **1**), Brown and Hakimi (BH)[10] utilized the concept that the $^{13}$C NMR shifts in Cbls could be calculated with an essentially two-term equation:

$$^{13}\text{C shift} \propto \text{inductive through-bond term} + \text{anisotropic/geometric through-space term}$$

This general concept has been recognized for some time.[16,29] BH introduced the novel idea that the inductive term could be quantified by assuming that the inductive effect of the Co center was some fraction, $1 - \alpha$, of that of the proton. However, they felt that their treatment of the inductive term was probably inadequate and pointed out the need for further investigation.

**Chart I**



**1**

R (or X) = CN (vitamin $B_{12}$), $H_2O$ ($B_{12a}$), $CH_3$ ($MeB_{12}$), or adenosyl (coenzyme $B_{12}$)

In further assessing the BH two-term approach, we believe the study of 1,5,6-trimethylbenzimidazole ($Me_3Bzm$) models is useful for a number of reasons. First, model system results with non-benzimidazole axial ligands played an important role in interpretation of the through-space term by BH.[10] Second, protonation of N-heterocycles with aromatic rings leads to significant changes in bond lengths and angles within the ring, whereas such changes are not as significant for typical metal centers.[30] The structural changes in the DMBz rings of Cbls cannot be assessed as accurately as in models, and there are only five reported structures of alkyl Cbls.[4–7] Third, the inductive effect should be larger for models containing more electron-deficient metal centers. Since we had been engaged in synthesizing, structurally characterizing,[17] and examining the solution properties of $Me_3Bzm$ cobaloxime complexes of the type $Me_3BzmCo(DH)_2R$, where DH = the monoanion of dimethylglyoxime, we considered it worthwhile to use these models to evaluate the BH approach for relating the $^{13}$C NMR spectra to structure, particularly with a complex containing a weak trans-influence ligand. The electron deficiency of these compounds is evidenced by the well documented shorter axial Co–N bond lengths, slow rate of axial ligand dissociation, etc., compared to most other models and to Cbls.[3] Fourth, the complexity of Cbls could lead to other types of contributions (e.g., corrin-ring anisotropy, restricted rotation of the trans axial ligand, interactions with the amide side chains, etc.) not accounted for in the two-term equation. Equatorial ligand anisotropy has

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**Table I.** Crystallographic Data (Esd's in Parentheses) for Compounds I–IV

| | I | II | III | IV |
|---|---|---|---|---|
| formula | $C_{18}H_{26}CoClO_4N_6\cdot{}^3/_5CH_2Cl_2$ | $C_{19}H_{28}CoO_6N_7$ | $C_{19}H_{29}CoO_4N_6\cdot{}^1/_2CH_3OH$ | $C_{21}H_{33}CoO_4N_6\cdot{}^2/_5CH_3OH$ |
| fw | 535.8 | 509.5 | 479.5 | 505.4 |
| $a$, Å | 8.108(2) | 11.336(1) | 10.033(2) | 8.996(2) |
| $b$, Å | 14.828(2) | 9.939(2) | 11.581(2) | 11.374(2) |
| $c$, Å | 20.410(3) | 20.700(4) | 11.620(2) | 12.870(3) |
| $\alpha$, deg | | | 113.56(1) | 99.73(2) |
| $\beta$, deg | 94.49(3) | 90.52(2) | 96.52(1) | 96.14(2) |
| $\gamma$, deg | | | 92.25(1) | 108.98(2) |
| $D$(measd), g cm$^{-3}$ | 1.44 | 1.46 | 1.28 | 1.39 |
| $D$(calcd), g cm$^{-3}$ | 1.45 | 1.45 | 1.30 | 1.39 |
| $Z$ | 4 | 4 | 2 | 2 |
| syst abs | $h0l$ ($h + l$ odd)<br>$0k0$ ($k$ odd) | $h0l$ ($h + l$ odd)<br>$0k0$ ($k$ odd) | | |
| space group | $P2_1/n$ | $P2_1/n$ | $P\bar{1}$ | $P\bar{1}$ |
| $\mu$(Mo K$\alpha$), cm$^{-1}$ | 10.0 | 7.8 | 7.7 | 7.8 |
| cryst dimens, cm$^3$ | 0.04 × 0.03 × 0.06 | 0.05 × 0.04 × 0.08 | 0.08 × 0.06 × 0.08 | 0.05 × 0.07 × 0.08 |
| no. of reflcns measd | 6276 | 6073 | 6206 | 6053 |
| no. of indep reflcns ($I > 3\sigma(I)$) | 3677 | 2548 | 4389 | 4668 |
| $\theta_{max}$, deg | 28 | 28 | 28 | 28 |
| no. of varied params | 307 | 298 | 271 | 289 |
| $R$ | 0.053 | 0.048 | 0.053 | 0.046 |
| $R_w$ | 0.073 | 0.056 | 0.077 | 0.068 |

been demonstrated in recent comparisons of Costa-type $B_{12}$ models with a new lariat-type model.[13]

## Experimental Section

**Reagents.** 5,6-Dimethylbenzimidazole and dichloroacetonitrile were purchased from Sigma and Fairfield Chemicals, respectively. Chloroform-*d* (MSD Isotopes) and dimethyl sulfoxide-$d_6$ (Aldrich) were the solvents used for NMR studies. All other reagents were from Aldrich and were used without further purification.

**Instrumentation.** NMR spectra of 0.1 M solutions ($CDCl_3$ and DMSO-$d_6$) were recorded on Nicolet NB-360 (360 MHz, $^1H$) and Varian CFT-20 (20 MHz, $^{13}C$) spectrometers. $^1H$ and $^{13}C$ NMR chemical shifts are referenced to $Me_4Si$.

**Protonation and Metalation Studies.** $^1H$ and $^{13}C$ NMR spectra of 0.1 M solutions of $Me_3Bzm$ in DMSO-$d_6$ with increasing $H^+$/base or M(II)/base molar ratios were recorded on the spectrometers mentioned above. Required quantities of concentrated HCl, $HgCl_2$, $Zn(NO_3)_2$, or $Cd(NO_3)_2$ were added to the solutions in order to obtain the desired molar ratios.

**Preparations.** $Me_3Bzm$ was prepared by the literature method[31] except that an excess of KOH was added to ensure full deprotonation of 5,6-dimethylbenzimidazole. The crude $Me_3Bzm$ was recrystallized in a benzene/petroleum ether solution, and its purity was checked by $^1H$ NMR and elemental analysis. (Anal. Calcd for $C_{10}H_{12}N_2$: C, 74.97; H, 7.55; N, 17.48. Found: C, 74.84; H, 7.60; N, 17.39.) The $Me_3BzmCo(DH)_2R$ complexes were prepared by standard method[18] and recrystallized from methanol/water, acetone/water, or ethanol/dichloromethane solvent mixtures. The aquo complexes with R = $CH_2CN$, $CH_2NO_2$, and CH(CN)Cl were prepared from $PhNH_2Co(DH)_2CH_2CN$ ($PhNH_2$ = aniline), (1,2-dimethylimidazole)$Co(DH)_2CH_2NO_2$, and $PhNH_2Co(DH)_2CH(CN)Cl$, respectively, by treatment with strongly acidic ion exchange resin as described elsewhere.[19]

**Elemental Analyses.** C, H, and N analyses were performed by Atlantic Microlabs, Inc. (Atlanta, GA). The results were satisfactory and are given in the supplementary material.

**Crystal Data.** Compounds I (X = Cl) and II (R = $CH_2NO_2$) were crystallized from $CH_2Cl_2/CH_3OH$. Compounds III (R = $CH_3$) and IV (R = $CH(CH_3)_2$) were crystallized from $CH_3OH/H_2O$. Cell dimensions were determined from Weissenberg and precession photographs and refined on a CAD4 automated single crystal diffractometer. The crystal data are given in Table I. Crystals of compound III are unstable in air, so the crystal used for data collection was completely covered with glue. The intensity data were collected by the $\omega$–$2\theta$ scan technique using graphite-monochromatized Mo K$\alpha$ radiation ($\lambda$ = 0.7107 Å). Three standard reflections, measured every 50 min, showed no systematic variation throughout the data collection except for compound III, where a loss of about 30% in intensity was observed. A linear decay correction was then applied to intensity data of III. Reflections with $I > 3\sigma(I)$ were corrected for Lorentz and polarization factors and anomalous dispersion, but not for extinction. No absorption correction was applied because of the small size of the crystals employed and the low value of $\mu$ (Table I).

**Solution and Refinement of the Structures.** All the structures were solved by conventional Patterson and Fourier methods and refined by full-matrix least-squares methods. For compounds I, III, and IV, the Fourier maps revealed the presence of additional peaks, interpreted as crystallization solvent: disordered $CH_2Cl_2$ with occupancy factor 0.6 in I; disordered $CH_3OH$ in III and IV with occupancy factors 0.5 and 0.4, respectively. The methanol of crystallization in the latter two compounds was not refined. The contribution of hydrogen atoms at calculated positions (except those of the solvent molecules), held constant at $B$ = 5 Å$^2$, was included in the last anisotropic refinement. Final $R$ and $R_w$ values are given in Table I. The weighting scheme $w = 1/(\sigma(F) + (pF)^2 + 1)$ ($p$ = 0.03 for I and IV and $p$ = 0.02 for II and III) was chosen so as to maintain $w(|F_o| - |F_c|)^2$ essentially constant over all ranges of $F_o$ and $(\sin\theta)/\lambda$. Atomic scattering factors were those given in ref 32. All calculations were done with SDP computer programs from Enraf-Nonius. Final positional parameters for non-hydrogen atoms are given in Tables II–V. Anisotropic thermal parameters, and hydrogen and unrefined atom fractional coordinates as well as a full list of bond lengths and angles have been deposited as supplementary material.

## Results and Discussion

In this section, we first present and discuss structural results. Next, we compare the effects of the proton and cobalt species on the $^{13}C$ shifts of benzimidazoles. From this comparison and from a further discussion of the BH treatment,[10] the case for a different approach for calculating the inductive term is made. We then present our method of statistical analysis of the data, which utilizes a least squares multiple regression method.[33] A new empirical approach for assessing the inductive term is presented and the results compared to those with other metal centers. Finally, the significance of the new approach and its application to Cbls is considered briefly.

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**Table II.** Positional Parameters and Their Estimated Standard Deviations for $Me_3BzmCo(DH)_2Cl$ (I)

| atom | *x* | *y* | *z* | *B*,[a] Å$^2$ | atom | *x* | *y* | *z* | *B*,[a] Å$^2$ |
|---|---|---|---|---|---|---|---|---|---|
| Co | 0.39586(6) | 0.16904(4) | 0.23014(3) | 2.310(9) | C6 | 0.6907(5) | 0.2481(3) | 0.2699(2) | 3.28(9) |
| Cl1 | 0.5000(1) | 0.12813(9) | 0.13585(5) | 3.73(2) | C7 | 0.7050(5) | 0.1551(3) | 0.2928(2) | 3.30(9) |
| O1 | 0.2839(4) | –0.0105(2) | 0.2425(2) | 3.47(6) | C8 | 0.8553(6) | 0.1160(4) | 0.3285(3) | 4.7(1) |
| O2 | 0.2307(4) | 0.3163(2) | 0.1632(2) | 4.11(7) | C9 | 0.2794(5) | 0.1652(3) | 0.3710(2) | 2.58(7) |
| O3 | 0.5166(4) | 0.3473(2) | 0.2128(2) | 3.74(7) | C10 | 0.2960(5) | 0.0749(3) | 0.3914(2) | 3.04(8) |
| O4 | 0.5711(4) | 0.0194(2) | 0.2900(2) | 3.66(6) | C11 | 0.2606(6) | 0.0530(3) | 0.4539(2) | 3.36(9) |
| N1 | 0.2441(4) | 0.0722(2) | 0.2209(2) | 2.71(6) | C12 | 0.2842(8) | –0.0444(4) | 0.4771(3) | 4.7(1) |
| N2 | 0.2213(4) | 0.2299(2) | 0.1816(2) | 2.85(7) | C13 | 0.1692(7) | 0.0928(4) | 0.5665(2) | 5.0(1) |
| N3 | 0.5510(4) | 0.2649(2) | 0.2382(2) | 2.83(7) | C14 | 0.2055(6) | 0.1185(3) | 0.4976(2) | 3.60(9) |
| N4 | 0.5748(4) | 0.1082(2) | 0.2765(2) | 2.81(7) | C15 | 0.1854(6) | 0.2067(3) | 0.4775(2) | 3.50(9) |
| N5 | 0.3078(4) | 0.2088(2) | 0.3120(2) | 2.48(6) | C16 | 0.2229(5) | 0.2294(3) | 0.4147(2) | 2.85(8) |
| N6 | 0.2178(5) | 0.3100(2) | 0.3809(2) | 3.04(7) | C17 | 0.1696(8) | 0.3969(4) | 0.4072(3) | 4.9(1) |
| C1 | –0.0302(6) | 0.0211(4) | 0.1746(3) | 4.7(1) | C18 | 0.2704(5) | 0.2947(3) | 0.3215(2) | 2.99(8) |
| C2 | 0.1020(5) | 0.0899(3) | 0.1889(2) | 3.17(8) | C19 | 0.244(2) | 0.185(1) | –0.0033(6) | 8.5(3) |
| C3 | 0.0907(5) | 0.1829(3) | 0.1663(2) | 3.26(9) | Cl2 | 0.1342(5) | 0.2409(3) | –0.0554(2) | 9.02(9) |
| C4 | –0.0585(6) | 0.2203(5) | 0.1274(3) | 5.1(1) | Cl31 | 0.2748(9) | 0.0691(4) | –0.0278(3) | 8.4(2) |
| C5 | 0.8217(6) | 0.3179(4) | 0.2821(3) | 5.2(1) | Cl32 | 0.113(1) | 0.0798(4) | 0.0058(3) | 8.7(2) |

[a] Values for anisotropically refined atoms are given in the form of the isotropic equivalent thermal parameter defined as: $(4/3)[a^2b(1,1) + b^2B(2,2) + c^2B(3,3) + ab(\cos\gamma)B(1,2) + ac(\cos\beta)B(1,3) + bc(\cos\alpha)B(2,3)]$.

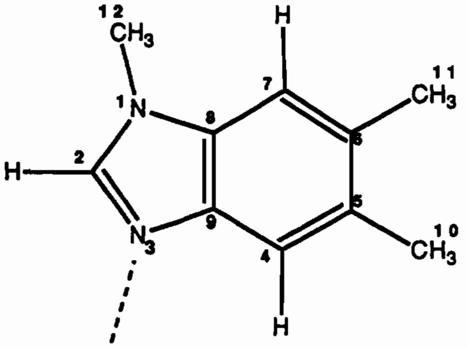
**Table III.** Positional Parameters and Their Estimated Standard Deviations for $Me_3BzmCo(DH)_2CH_2NO_2$ (II)

| atom | *x* | *y* | *z* | *B*,[a] Å$^2$ | atom | *x* | *y* | *z* | *B*,[a] Å$^2$ |
|---|---|---|---|---|---|---|---|---|---|
| Co | 0.46130(5) | 0.15523(7) | 0.19696(3) | 3.37(1) | C4 | 0.2889(6) | –0.0125(7) | 0.0388(3) | 6.5(2) |
| O1 | 0.2352(3) | 0.2373(4) | 0.2381(2) | 4.61(8) | C5 | 0.8022(6) | 0.1538(8) | 0.2712(4) | 7.9(2) |
| O2 | 0.5204(3) | –0.0009(4) | 0.0874(2) | 5.55(9) | C6 | 0.6756(5) | 0.1753(6) | 0.2559(3) | 5.1(1) |
| O3 | 0.6835(3) | 0.0477(4) | 0.1639(2) | 5.50(9) | C7 | 0.5943(5) | 0.2469(6) | 0.2970(3) | 4.9(1) |
| O4 | 0.4010(3) | 0.3074(4) | 0.3083(2) | 5.17(9) | C8 | 0.6290(6) | 0.3104(7) | 0.3594(3) | 7.0(2) |
| O5 | 0.5638(4) | –0.0614(5) | 0.3220(2) | 9.0(1) | C9 | 0.4400(5) | –0.0235(5) | 0.2384(3) | 4.5(1) |
| O6 | 0.3848(4) | 0.0013(5) | 0.3412(2) | 7.6(1) | C10 | 0.5692(4) | 0.3816(5) | 0.1098(2) | 3.16(9) |
| N1 | 0.2964(3) | 0.1741(4) | 0.1929(2) | 3.56(8) | C11 | 0.6737(4) | 0.3273(5) | 0.0880(2) | 3.9(1) |
| N2 | 0.4331(4) | 0.0606(4) | 0.1196(2) | 4.05(9) | C12 | 0.7462(4) | 0.4029(6) | 0.0494(2) | 4.2(1) |
| N3 | 0.6242(3) | 0.1246(4) | 0.2049(2) | 4.30(9) | C13 | 0.8627(5) | 0.3468(7) | 0.0277(3) | 5.6(1) |
| N4 | 0.4875(4) | 0.2459(4) | 0.2755(2) | 4.16(9) | C14 | 0.7912(5) | 0.6176(6) | –0.0124(3) | 5.6(1) |
| N5 | 0.4804(3) | 0.3310(4) | 0.1499(2) | 3.42(8) | C15 | 0.7130(4) | 0.5352(6) | 0.0305(2) | 4.2(1) |
| N6 | 0.4329(3) | 0.5397(4) | 0.1207(2) | 3.58(8) | C16 | 0.6081(4) | 0.5903(5) | 0.0514(2) | 3.9(1) |
| N7 | 0.4623(4) | –0.0283(5) | 0.3042(2) | 5.7(1) | C17 | 0.5382(4) | 0.5115(5) | 0.0914(2) | 3.22(9) |
| C1 | 0.1139(5) | 0.1292(6) | 0.1333(3) | 5.6(1) | C18 | 0.3670(5) | 0.6648(5) | 0.1157(3) | 4.5(1) |
| C2 | 0.2437(4) | 0.1229(5) | 0.1429(3) | 4.0(1) | C19 | 0.4031(4) | 0.4310(5) | 0.1550(2) | 3.6(1) |
| C3 | 0.3248(5) | 0.0554(5) | 0.0995(3) | 4.3(1) | | | | | |

[a] Values for anisotropically refined atoms are given in the form of the isotropic equivalent thermal parameter defined as: $(4/3)[a^2B(1,1) + b^2B(2,2) + c^2B(3,3) + ab(\cos\gamma)B(1,2) + ac(\cos\beta)B(1,3) + bc(\cos\alpha)B(2,3)]$.

## Structures

**Complex Geometry.** The ORTEP drawings for non-hydrogen atoms of the crystallographically independent molecules of I–IV are depicted in Figures 1–4 together with the atom numbering scheme. In all the structures, the cobalt atom has a distorted octahedral geometry. For the discussion of both the general features of these structures and for the NMR results, we will use B(number) and B(number)H and the following numbering scheme to designate $^{13}C$ and $^1H$ atoms of $Me_3Bzm$:



**Equatorial Ligand.** The two chemically equivalent DH moieties are nearly planar and their mean planes make the dihedral angles, $\alpha$, reported in Table VI. The hydroxyl group of the methanol of crystallization of **III** and **IV** makes a hydrogen bond with the O4 atom (2.73 Å) in **III** and with the O3 atom (2.78 Å) in **IV**.[3]

**Orientation of the $Me_3Bzm$ Plane.** In all the structures, the $Me_3Bzm$ is almost planar and its orientation with respect to the equatorial moiety may be defined by a torsion angle, $\varphi$, B2–BN3–Co–N*, where N* is the midpoint between the two equatorial N donors on the B2 side. This choice implies that $\varphi$ = 0° when the B2 carbon and N* are eclipsed and the $Me_3Bzm$ plane lies on the ideal symmetry mirror passing through the two oxime bridges. The negative sign of $\varphi$ indicates a clockwise rotation about the BN3-Co bond when the molecule is viewed from the benzimidazole side. The $\varphi$ values for some $Me_3Bzm$ derivatives are reported in Table VI, and the absolute values range from 0° to 23°.

We suggested that the orientation of planar ligands, such as $Me_3Bzm$ or pyridine (py), with respect to the equatorial ligand influences the Co–N(axial) distance.[20] This suggestion was supported by comparison of cobaloxime and Costa model analogues,[21] which have a propylene bridge in place of one of the O–H···O bridges in cobaloximes. It was found that orientations with $|\varphi| < 25°$ in cobaloximes correspond to Co–N distances shorter than those in Costa models with $|\varphi| = 90 \pm 30°$ orientations. The latter orientations are induced by the puckered propylene bridge of the equatorial ligand in Costa models. In some new lariat-type models, $[(R \text{ or } X)CoC_1py]^+$, where the pyridyl moiety is linked to the propylene bridge of the Costa-type equatorial ligand, the Co–N distances are shorter, as expected from this analysis.[13]

**Axial Fragment and $Me_3Bzm$ Coordination.** Table VI presents a comparison of the geometry of the axial fragment and that around N5 (BN3) for a series of $Me_3Bzm$ derivatives. The Co–N(axial) bond lengths increase with the increasing $\sigma$-donor

**Table IV.** Positional Parameters and Their Estimated Standard Deviations for $Me_3BzmCo(DH)_2CH_3$ (III)

| atom | *x* | *y* | *z* | *B*,[a] Å$^2$ | atom | *x* | *y* | *z* | *B*,[a] Å$^2$ |
|---|---|---|---|---|---|---|---|---|---|
| Co | 0.22881(4) | 0.17570(4) | 0.39733(4) | 2.554(8) | C5 | 0.4344(7) | 0.5037(6) | 0.6775(7) | 8.4(2) |
| O1 | 0.0325(3) | 0.1051(3) | 0.1771(3) | 5.41(8) | C6 | 0.3450(5) | 0.4052(4) | 0.5689(4) | 4.9(1) |
| O2 | 0.3412(3) | 0.0190(2) | 0.5096(2) | 4.78(6) | C7 | 0.2528(5) | 0.4311(3) | 0.4788(4) | 5.1(1) |
| O3 | 0.4213(3) | 0.2454(3) | 0.6195(3) | 5.50(8) | C8 | 0.2307(8) | 0.5624(5) | 0.4920(7) | 9.0(2) |
| O4 | 0.0939(3) | 0.3355(3) | 0.3021(3) | 5.45(7) | C9 | 0.0798(4) | 0.1923(4) | 0.5005(4) | 4.18(9) |
| N1 | 0.1111(3) | 0.0650(3) | 0.2552(3) | 3.64(7) | C10 | 0.4139(3) | 0.1817(3) | 0.1937(3) | 2.64(6) |
| N2 | 0.2578(3) | 0.0232(2) | 0.4137(3) | 3.35(6) | C11 | 0.3402(3) | 0.2419(3) | 0.1289(3) | 3.15(7) |
| N3 | 0.3418(3) | 0.2864(3) | 0.5436(3) | 3.71(7) | C12 | 0.3959(4) | 0.2642(3) | 0.0344(3) | 3.54(7) |
| N4 | 0.1885(3) | 0.3298(3) | 0.3895(3) | 3.76(6) | C13 | 0.3197(5) | 0.3361(4) | −0.0309(4) | 5.1(1) |
| N5 | 0.3881(3) | 0.1523(2) | 0.2952(2) | 2.70(5) | C14 | 0.5815(5) | 0.2448(4) | −0.1015(4) | 5.5(1) |
| N6 | 0.5902(3) | 0.0934(3) | 0.2448(3) | 3.14(6) | C15 | 0.5235(4) | 0.2231(3) | 0.0023(3) | 3.59(8) |
| C1 | 0.0193(6) | −0.1530(6) | 0.1236(7) | 8.6(2) | C16 | 0.5955(4) | 0.1630(3) | 0.0657(3) | 3.56(8) |
| C2 | 0.1064(4) | −0.0535(4) | 0.2330(4) | 4.6(1) | C17 | 0.5403(3) | 0.1447(3) | 0.1622(3) | 2.94(7) |
| C3 | 0.1922(4) | −0.0783(3) | 0.3278(4) | 4.16(8) | C18 | 0.7193(4) | 0.0424(4) | 0.2483(4) | 4.63(9) |
| C4 | 0.2047(5) | −0.2059(4) | 0.3273(5) | 6.6(1) | C19 | 0.4963(3) | 0.1008(3) | 0.3214(3) | 3.08(7) |

[a] Values for anisotropically refined atoms are given in the form of the isotropic equivalent thermal parameter defined as: $(4/3)[a^2B(1,1) + b^2B(2,2) + c^2B(3,3) + ab(\cos\gamma)B(1,2) + ac(\cos\beta)B(1,3) + bc(\cos\alpha)B(2,3)]$.

**Table V.** Positional Parameters and Their Estimated Standard Deviations for $Me_3BzmCo(DH)_2CH(CH_3)_2$ (IV)

| atom | *x* | *y* | *z* | *B*,[a] Å$^2$ | atom | *x* | *y* | *z* | *B*,[a] Å$^2$ |
|---|---|---|---|---|---|---|---|---|---|
| Co | 0.22395(3) | 0.32628(3) | 0.18920(2) | 2.066(6) | C6 | 0.3679(3) | 0.3143(2) | 0.3815(2) | 3.22(5) |
| O1 | 0.3507(2) | 0.4132(2) | 0.0114(2) | 3.36(4) | C7 | 0.4971(3) | 0.3629(2) | 0.3224(2) | 3.17(5) |
| O2 | −0.1057(2) | 0.2305(2) | 0.2116(2) | 3.74(4) | C8 | 0.6693(4) | 0.3948(3) | 0.3650(3) | 5.09(8) |
| O3 | 0.0952(2) | 0.2453(2) | 0.3681(2) | 3.95(5) | C9 | 0.2031(3) | 0.1434(3) | 0.1149(2) | 3.28(6) |
| O4 | 0.5495(2) | 0.4186(2) | 0.1642(2) | 3.41(4) | C10 | 0.1223(5) | 0.0429(3) | 0.1722(3) | 5.55(9) |
| N1 | 0.2191(2) | 0.3650(2) | 0.0526(2) | 2.48(4) | C11 | 0.3548(4) | 0.1318(3) | 0.0840(3) | 5.06(8) |
| N2 | 0.0008(2) | 0.2761(2) | 0.1475(2) | 2.63(4) | C12 | 0.3329(3) | 0.6329(2) | 0.2653(2) | 2.36(4) |
| N3 | 0.2286(3) | 0.2878(2) | 0.3254(2) | 2.80(4) | C13 | 0.4709(3) | 0.6791(2) | 0.2230(2) | 2.91(5) |
| N4 | 0.4458(2) | 0.3743(2) | 0.2286(2) | 2.58(4) | C14 | 0.5523(3) | 0.8095(3) | 0.2451(2) | 3.41(6) |
| N5 | 0.2299(2) | 0.5082(2) | 0.2604(2) | 2.42(4) | C15 | 0.7052(5) | 0.8599(4) | 0.2031(3) | 5.35(9) |
| N6 | 0.1437(3) | 0.6449(2) | 0.3595(2) | 3.11(5) | C16 | 0.5858(5) | 1.0372(3) | 0.3319(3) | 5.05(9) |
| C1 | 0.0555(4) | 0.3717(3) | −0.1108(3) | 4.34(7) | C17 | 0.4948(4) | 0.8944(3) | 0.3082(2) | 3.45(6) |
| C2 | 0.0801(3) | 0.3452(2) | −0.0012(2) | 2.90(5) | C18 | 0.3565(3) | 0.8490(3) | 0.3485(2) | 3.34(6) |
| C3 | −0.0499(3) | 0.2931(2) | 0.0556(2) | 2.93(5) | C19 | 0.2788(3) | 0.7183(2) | 0.3275(2) | 2.69(5) |
| C4 | −0.2218(4) | 0.2650(3) | 0.0125(3) | 4.57(8) | C20 | 0.0454(4) | 0.6908(3) | 0.4266(3) | 5.11(8) |
| C5 | 0.3960(5) | 0.3002(3) | 0.4945(3) | 5.10(8) | C21 | 0.1212(3) | 0.5223(3) | 0.3172(2) | 2.94(5) |

[a] Values for anisotropically refined atoms are given in the form of the isotropic equivalent thermal parameter defined as: $(4/3)[a^2B(1,1) + b^2B(2,2) + c^2B(3,3) + ab(\cos\gamma)B(1,2) + ac(\cos\beta)B(1,3) + bc(\cos\alpha)B(2,3)]$.

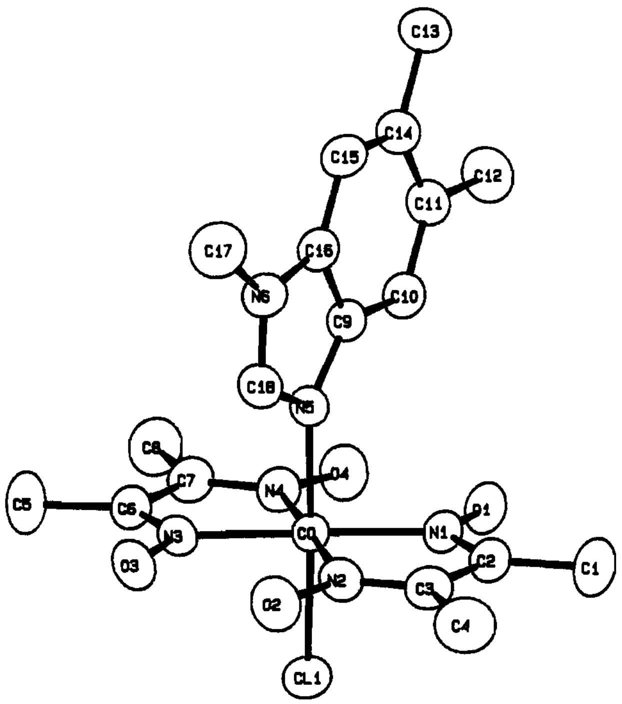


**Figure 1.** ORTEP drawing (thermal ellipsoid; 50% probability) and labeling scheme for non-hydrogen atoms of (I).

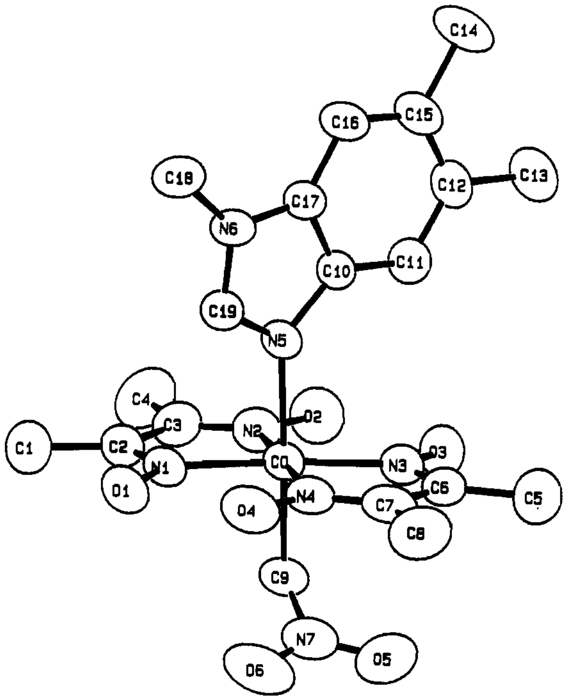


**Figure 2.** ORTEP drawing (thermal ellipsoid; 50% probability) and labeling scheme for non-hydrogen atoms of (II).

power of the trans ligand from 1.959(3) Å to 2.137(4) Å from the chloro to the adamantyl derivatives. In previous studies, we found that the Co–C bond length increases with the bulk of R; the Co–C bond lengths increase from 1.983(2) Å when R = $CHCl_2$ to 2.179(5) Å when R = adamantyl (Table VI). We suggest that, in contrast to organic compounds, the bond lengths indicate

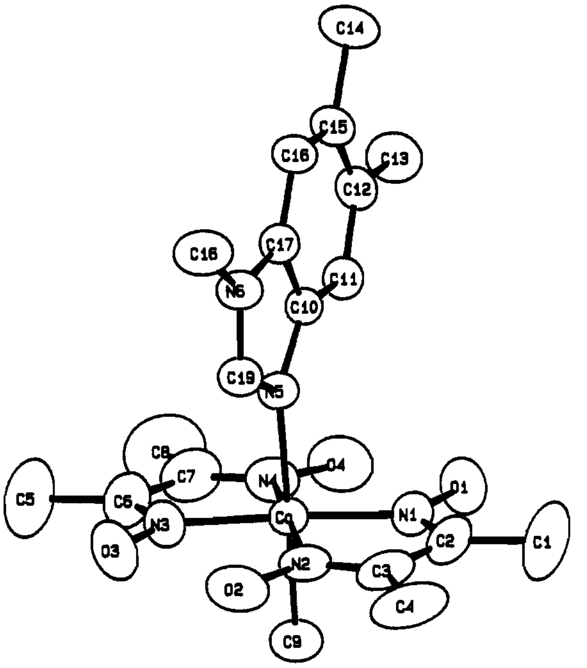


**Figure 3.** ORTEP drawing (thermal ellipsoid; 50% probability) and labeling scheme for non-hydrogen atoms of (III).

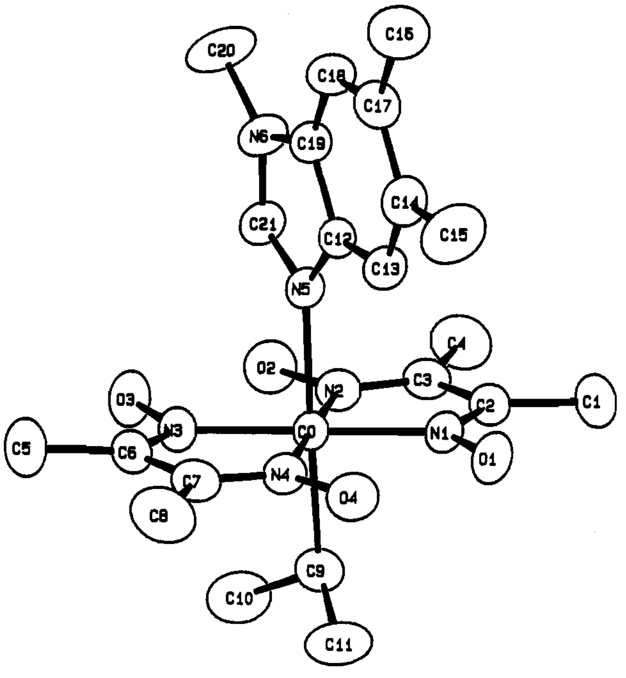


**Figure 4.** ORTEP drawing (thermal ellipsoid; 50% probability) and labeling scheme for non-hydrogen atoms of (IV).

that the effective bulk of $CHCl_2$ in its low-energy conformation in cobaloximes is comparable to that of methyl. The geometry around BN3 is characterized by a *narrow* Co–BN3–B2 angle ranging from 120.8 to 122.7° and a large Co–BN3–B9 angle ranging from 132.2 to 134.4°. The B2–BN3–B9 angle ranges from 104.7 to 105.3°. Therefore, the coordination of $Me_3Bzm$ to cobalt has essentially the same geometry in all the complexes, with the exception of the axial Co–N distance.

Furthermore, we have shown that the value of the C–N–C angle about the N bound to Co for planar ligands can be used to determine the steric effect of ligand bulk on the axial Co–N distance.[3,21] This angle of ~105° in imidazole derivatives allows distances shorter than those found in py analogues, where it is ~120°. However, when bulky side groups are attached to an $\alpha$-carbon atom of the neutral ligand, such as in $Me_3Bzm$, the interaction with the equatorial moiety provokes a lengthening of the Co–N axial bond as well as a marked nonequivalence of the two Co–N–C angles (Table VI). Consequently, this bond length has essentially the same value in py and $Me_3Bzm$ analogues when these planar ligands have similar orientations. Thus, in the series $LCo(DH)_2CH_3$ the axial Co–N distance is 2.019(3),[22] 2.068(3),[3] and 2.060(2) Å when L is imidazole, py, and $Me_3Bzm$, respectively, with $\varphi$ close to 0°. In contrast, for (1-methylimidazole)$Co(DH)_2CH_3$,[3] this distance is 2.058(5) Å and $\varphi$ is close to 90°. Furthermore, the following order of increasing Co–N distances for the same alkyl cobaloxime with different N-donor ligands is derived:[21] 1-methylimidazole < py ~ $Me_3Bzm$ < 1,2-dimethylimidazole < 2-$NH_2$py. Data on cobalamins[4–7] suggest that for this system the Co–N axial distance should lie at the 2-$NH_2$py end of this trend. Good linear relationships are found between the Co–N distances in the $Me_3Bzm$ and aniline series (Figure 5).

**Table VI.** Geometrical Parameters for $Me_3BzmCo(DH)_2R$ Complexes[a]

| R | Co–N5, Å | Co–C, Å | Co–N5–C, deg | C–N5–C, deg | $\alpha$, deg | $\varphi$, deg |
|---|---|---|---|---|---|---|
| Cl[b] | 1.959(3) | | 133.6(2)<br>121.1(2) | 105.2(3) | 1.1 | –0.7 |
| CH(CN)Cl[c] | 2.010(3) | 2.000(5) | 132.4(2)<br>122.7(2) | 104.7(3) | 1.9 | 1.3 |
| $CH_2NO_2$[b] | 2.013(3) | 1.988(5) | 132.7(3)<br>122.4(3) | 104.9(3) | 4.8 | –18.7 |
| CH(CN)-$CH_2CN$[d] | 2.031(3) | 2.061(3) | 133.7(2)<br>121.1(3) | 105.3(3) | 3.1 | 3.7 |
| $CHCl_2$[e] | 2.043(2) | 1.983(2) | 133.2(1)<br>121.6(1) | 104.9(2) | 1.5 | –10.3 |
| $CH_3$[b] | 2.060(2) | 1.989(2) | 133.6(1)<br>121.5(2) | 104.9(2) | 4.7 | 13.9 |
| $CH(CH_3)_2$[b] | 2.097(2) | 2.076(2) | 134.4(1)<br>120.9(2) | 104.7(2) | 4.0 | 6.6 |
| c-$C_6H_{11}$[f] | 2.105(2) | 2.073(4) | 132.2(3)<br>122.3(2) | 104.9(3) | –10.8 | 23.4 |
| adamantyl[c] | 2.137(4) | 2.179(5) | 134.4(3)<br>120.8(4) | 104.8(4) | –6.1 | 22.6 |

[a] The positive sign of $\alpha$ indicates a bending toward the R group. For the sign of $\varphi$, see text. [b] This work. [c] Reference 14. [d] Charland, J. P.; Attia, W. M.; Randaccio, L.; Marzilli, L. G. *Organometallics* **1990**, *9*, 1367. [e] Chen, Q.; Marzilli, L. G.; Bresciani-Pahor, N.; Randaccio, L.; Zangrando, E. *Inorg. Chim. Acta* **1988**, *144*, 241. [f] Attia, W. M.; Zangrando, E.; Randaccio, L.; Antolini, L.; López, C.; Charland, J.-P. *Acta Crystallogr.* **1989**, *C45*, 1500.

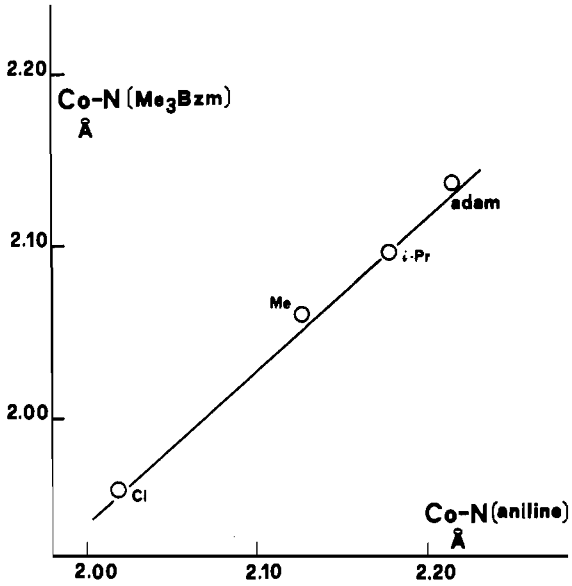


**Figure 5.** Plot of Co–N axial bond lengths (Å) in $Me_3Bzm$ cobaloximes *vs* Co–N axial bond lengths (Å) in $NH_2Ph$ analogues.

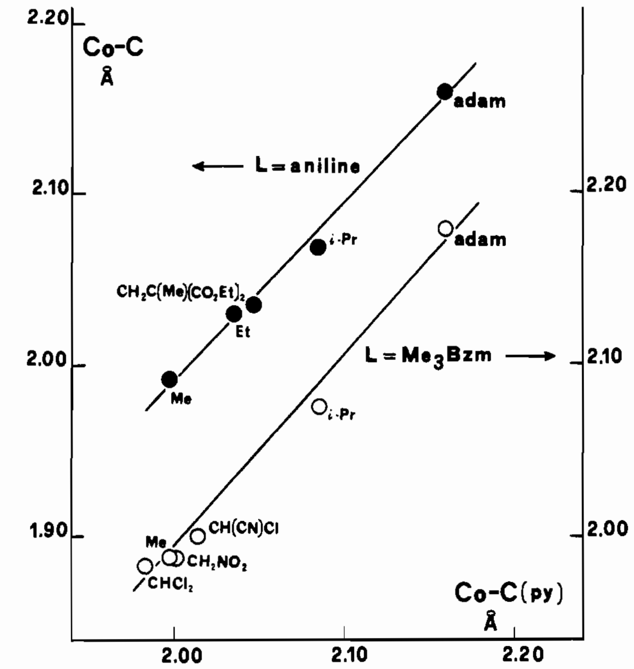


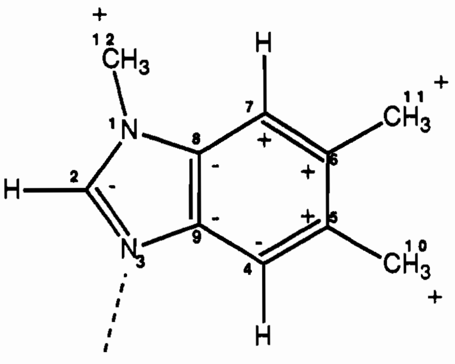
**Figure 6.** Plot of Co–C bond lengths (Å) in $NH_2Ph$ and $Me_3Bzm$ cobaloximes *vs* Co–C bond lengths (Å) in pyridine analogues.

**Effect of Bulk on Co–C Bond Lengths.** The Co–C bond lengths have the same trend in the series with different L ligands. The linear relationships are shown in Figure 6, where the Co–C distances in $Me_3Bzm$ and aniline are plotted against those in the corresponding py derivatives. The influence of the bulk of R on the Co–C distance is the same for all three ligands, so that this bond lengthens when the bulk of R increases, because of the steric interaction of R with the rigid $(DH)_2$ moiety. In fact, in alkylrhodoximes, $pyRh(DH)_2R$, the increase of the Rh–C distance in the order R = $CH_3$ < Et < iPr is smaller by ~50% than that observed in the analogous cobaloximes, as expected from a relief of the steric interaction between R and the equatorial ligand due to the larger ionic radius of Rh(III) than of Co(III).[23] In addition to the large effect due to the bulk of R, an additional lengthening of the Co–R bond with the increase of the bulk of L is apparent, particularly for bulky R such as adamantyl. Thus, the Co–adam bond lengths are 2.154(5) Å for L = 1-methylimidazole and 2.217(7) Å for L = $PPh_2Et$.[34] The value of 2.179(5) Å for L = $Me_3Bzm$ indicates that $Me_3Bzm$ is not an unusually bulky ligand.

**NMR Shift Trends. Effects of Cobaloximes on $^{13}C$ Shifts of $Me_3Bzm$.** $^{13}C$ NMR data for 10 cobaloximes are presented in Table VII for DMSO-$d_6$ and in Table VIII for $CDCl_3$. The standard numbering scheme for the DMBz in Cbls will be used to discuss the NMR properties of $Me_3Bzm$. Assignments are based on 2D NMR studies.[9,25] The shifts of each of the signals across the series of compounds follow relatively smooth trends, maintaining the same order regardless of the signal being monitored.

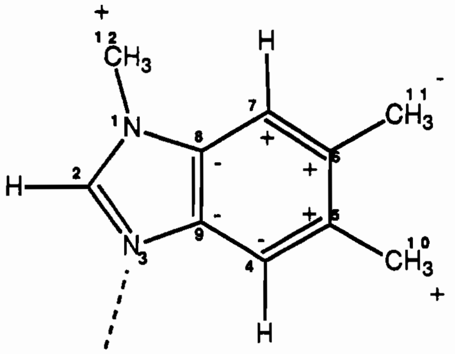
**Effects of Cbls on $^{13}C$ Shifts of 5,6-Dimethylbenzimidazoles.** The overall patterns of shift changes for aromatic ring carbons on coordination of the dimethylbenzimidazole-containing moiety ($\alpha$-ribazole) to Cbls are similar to those shown below for protonation (with a – sign indicating an upfield shift). Shift changes between the free and the coordinated ligands are called coordination shifts. The B2 signal exhibits an upfield coordination shift but not a significant ligand-responsive shift across a series of Cbls.[10]

**Effects of Protonation on $^{13}C$ Shifts of 5,6-Dimethylbenzimidazoles.** The maximum $H^+$-induced changes in shifts, $\Delta\delta_i^{H+}$ (Table IX) in $^{13}C$ NMR spectra of 0.1 M $Me_3Bzm$ DMSO-$d_6$ solutions occurred at $HCl/Me_3Bzm$ = 1. This pattern of $\Delta\delta_i^{H+}$, shown below, agrees with the results for $\alpha$-ribazole (Table IX):



**Effect of Labile Metal Species on $^{13}C$ Shifts of $Me_3Bzm$.** As stated above, because the very strongly electrophilic $H^+$ should cause measurable structural changes to benzimidazole rings, it is not a good model for the electrophilic characteristics of a metal center.[30] Therefore, we have examined the shifting effect of several metal salts ($HgCl_2$, $Cd(NO_3)_2$, and $Zn(NO_3)_2$). Since the salts were only 0.025 M (one-fourth of the ligand concentration), we believe that the metal is highly complexed in this crude experiment. We multiplied times four the changes in shifts, which were similar for the three salts, to approximate fully complexed ligand; we then averaged the shifts. This method gives a rough approximation of the generic effect of simple metal species. The average coordination shifts ($\Delta\delta_i^M$), crudely estimated for a fully formed $M(Me_3Bzm)$ compound, are given in Table IX.

**Comparison of Effects of Electrophiles on $^{13}C$ Shifts.** The overall pattern of coordination shifts in DMSO-$d_6$ observed for cobaloximes (Table VII) is



The pattern is essentially the same in $CDCl_3$ (Table VIII) as in DMSO-$d_6$. This pattern is the same as for Cbls except for B2. For both Cbls and cobaloximes, B2 shifts show little dependence on the trans axial ligand (Tables VII and VIII). Thus, B2 shifts are not very ligand-responsive. However, B2 coordination shifts are upfield by ~1 ppm for all Cbls and slightly downfield (<0.4 ppm) for cobaloximes, *except* for X = Cl and R = neopentyl in DMSO-$d_6$.

Except for B2, the $\Delta\delta_i^M$ values are similar in sign, and usually, *relative* magnitude to $\Delta\delta_i^{H+}$ values (Table IX). Since the metal ions are weaker electrophiles compared to $H^+$, the 40–60% smaller effects of $MX_2$ are expected.[30] This pattern holds particularly well for $C_i$ remote from BN3, i.e., B5, B6, B7, and B8; it also holds well for B9. However, the *opposite* coordination shift effect of $MX_2$ (compared to $H^+$) on B2 is not expected since B2 has roughly the same geometric relationship to the metal center as B9. ***We wish to emphasize that these $MX_2$ results were not used in our development of the new inductive term described below.***

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(34) Geremia, S.; Randaccio, L.; Zangrando, E.; Antolini, L. *J. Organomet. Chem.* **1992**, *425*, 131.

**Table VII.** $^{13}C$ NMR Data for $Me_3BzmCo(DH)_2R$[a]

| R or X | B2 | B4 | B5 | B6 | B7 | B8 | B9 | B10 | B11 | B12 |
|---|---|---|---|---|---|---|---|---|---|---|
| (free) | 143.56 | 119.31 | 129.52 | 130.71 | 110.03 | 133.12 | 141.98 | 19.79 | 19.96 | 30.45 |
| Cl | 143.47 | 116.62 | 132.23 | 133.07 | 111.29 | 132.23 | 137.64 | 20.23 | 19.62 | 31.88 |
| CH(CN)Cl | 143.90 | 117.11 | 131.86 | 132.75 | 111.07 | 132.53 | 138.68 | 20.19 | 19.68 | 31.66 |
| $CH_2NO_2$ | 143.85 | 117.17 | 131.80 | 132.68 | 111.03 | 132.58 | 138.79 | 20.18 | 19.68 | 31.61 |
| $CH_2CN$ | 143.78 | 117.28 | 131.67 | 132.60 | 110.96 | 132.60 | 139.07 | 20.17 | 19.71 | 31.56 |
| $CH_2CF_3$ | 143.64 | 117.36 | 131.54 | 132.46 | 110.87 | 132.58 | 138.96 | 20.13 | 19.70 | 31.51 |
| $CH_2Cl$ | 143.90 | 117.62 | 131.43 | 132.36 | 110.82 | 132.69 | 139.45 | 20.16 | 19.74 | 31.45 |
| $CH_3$ | 143.75 | 117.88 | 131.17 | 132.14 | 110.69 | 132.75 | 139.73 | 20.12 | 19.79 | 31.34 |
| $CH_2CH_3$ | 143.79 | 117.94 | 131.09 | 132.08 | 110.62 | 132.79 | 139.83 | 20.12 | 19.77 | 31.32 |
| $CH_2C(CH_3)_3$ | 143.49 | 117.85 | 130.95 | 131.96 | 110.57 | 132.73 | 139.44 | 20.10 | 19.74 | 31.29 |
| $CH(CH_3)_2$ | 143.81 | 118.07 | 130.92 | 131.92 | 110.53 | 132.79 | 139.73 | 20.07 | 19.78 | 31.28 |

[a] 0.1 M solutions in DMSO-$d_6$; in ppm, relative to $Me_4Si$; $Me_3Bzm$ $^{13}C$ resonance shifts only, see Supplementary Material for full data.

**Table VIII.** $^{13}C$ NMR Data for $Me_3BzmCo(DH)_2R$[a]

| R or X | B2 | B4 | B5 | B6 | B7 | B8 | B9 | B10 | B11 | B12 |
|---|---|---|---|---|---|---|---|---|---|---|
| (free) | 142.80 | 120.29 | 130.84 | 132.05 | 109.51 | 133.21 | 142.50 | 20.20 | 20.53 | 30.87 |
| Cl | 143.03 | 118.11 | 133.90 | 134.34 | 110.17 | 132.25 | 138.67 | 20.62 | 20.34 | 32.22 |
| CH(CN)Cl | 143.48 | 118.44 | 133.40 | 133.90 | 110.03 | 132.69 | 139.67 | 20.56 | 20.38 | 32.00 |
| $CH_2NO_2$ | 143.52 | 118.51 | 133.31 | 133.79 | 109.93 | 132.69 | 139.77 | 20.56 | 20.35 | 31.95 |
| $CH_2CN$ | 143.44 | 118.62 | 133.19 | 133.68 | 109.92 | 132.75 | 140.05 | 20.56 | 20.40 | 31.89 |
| $CH_2CF_3$ | 143.45 | 118.73 | 132.99 | 133.50 | 109.84 | 132.78 | 139.93 | 20.53 | 20.33 | 31.82 |
| $CH_2Cl$ | 143.69 | 119.00 | 132.85 | 133.35 | 109.76 | 132.85 | 140.44 | 20.51 | 20.40 | 31.78 |
| $CH_3$ | 143.64 | 119.17 | 132.57 | 133.09 | 109.66 | 132.96 | 140.72 | 20.50 | 20.40 | 31.66 |
| $CH_2CH_3$ | 143.74 | 119.24 | 132.46 | 133.01 | 109.64 | 133.01 | 140.81 | 20.47 | 20.47 | 31.63 |
| $CH_2C(CH_3)_3$ | 143.47 | 119.21 | 132.35 | 132.85 | 109.54 | 132.96 | 140.44 | 20.43 | 20.43 | 31.62 |
| $CH(CH_3)_2$ | 143.80 | 119.38 | 132.29 | 132.85 | 109.54 | 133.01 | 140.76 | 20.42 | 20.42 | 31.60 |

[a] 0.1 M solutions in $CDCl_3$; in ppm, relative to $Me_4Si$; $Me_3Bzm$ $^{13}C$ resonance shifts only, see Supplementary Material for full data.

Thus, the Co center in cobaloximes and in metal salts (see below) has different effects on B2 than do the $H^+$ and, to a limited extent, Cbls. Can this difference between cobaloximes and Cbls be due (a) to greater similarity in electrophilicity of the Co center of Cbls to $H^+$; (b) to a much greater anisotropy for the Co center in Cbls; or (c) to some other effect(s), such as solvation and/or corrin ring anisotropy? Before considering these questions, we first turn to a discussion of the two-term approach.

**NMR Shift Trends—Interpretation. The Brown–Hakimi Two-Term Equation.** Brown and Hakimi[10] used the following equation to predict $^{13}C$ shifts of Cbls, based on the $^{13}C$ shifts of the cationic and neutral forms of $\alpha$-ribazole (RBz) and the anisotropic shielding term $\Delta\sigma_i$:

$$(\text{obsd Cbl } \delta)_i = \{[\delta(\text{RBz}) - \delta(\text{RBzH}^+)]_i\alpha + \delta(\text{RBzH}^+)_i\} - \Delta\sigma_i$$

In this equation, the "$i$" specifies a particular nucleus and $1 - \alpha$ has values such that when $\alpha = 0$ the Co center is as electrophilic as the proton. The term for the effect on a particular nucleus of the cobalt magnetic anisotropy shielding, $\Delta\sigma_i$, can be calculated using the equation[29] for the shielding resulting from an axially symmetric point dipole. The $\Delta\sigma_i$ term is related to the anisotropy of the magnetic susceptibilities of the dipole ($\Delta\chi$) and a geometric term ($GT_i$) involving the distance, $r_i$, between that nucleus and the dipole and the angle $\theta$ between the symmetry axis of the dipole and the distance vector $r_i$[29], as follows:

$$\Delta\sigma_i = \Delta\chi \text{GT}_i$$

$$\text{GT}_i = [1 - 3(\cos\theta)^2]/3r_i^3$$

Evaluation of the two-term equation was limited to $^{13}C$ shifts of three Cbls structurally characterized by X-ray diffraction. The range of calculated $\Delta\chi$ values using this approach compares well to a value previously estimated for $pyCo(DH)_2Cl$ from $^1H$ shifts.[16] The $\Delta\chi$ values become more negative as the trans axial ligand becomes a stronger electron donor group. This relationship implies that, as the R group increases electron donation, the magnetic susceptibility parallel to the dipole symmetry axis ($\chi_\parallel$) decreases relative to the perpendicular component. Also, the apparent "partial protonation", $(1 - \alpha)$, increases with decreasing trans influence of the alkyl group, as expected. Because of the limited opportunity to evaluate the approach, Brown and Hakimi cautioned that this approach was only approximate.

Although the anisotropic term should be small and well accounted for in our model compounds, we found the direct application of the above equation to our cobaloxime data to be *very inadequate*. As mentioned above, the B2 shifts strongly upfield on protonation (Table IX) and the anisotropic effect usually leads to an upfield shift. Yet the B2 coordination shift for cobaloximes usually is *downfield*. Therefore, the BH approach, unmodified, cannot explain our findings for $Me_3Bzm$ cobaloximes.

This inadequacy is expected since the inductive term is probably poorly modeled by the proton, and a better approach to allow for the inductive effect is necessary. There are three components to be considered: the two terms and the fitting procedure. We shall first consider the appropriateness of the second (anisotropic/geometric) term. Next, we shall discuss the fitting procedure, and finally, we shall consider the inductive term.

**Anisotropic/Geometric Term.** From accurate atomic coordinates determined by X-ray crystallography, one can easily calculate $GT_i$ by assuming that the dipole symmetry axis lies along the normal to the least-squares plane of the equatorial nitrogens and going through Co. The least-squares equation of the plane can be obtained using either unit weights or weights based on the standard deviations of the atomic positions of the equatorial nitrogen atoms. In both cases, the direction cosines were similar and the calculated $\theta$ angles for a given atom agreed within two degrees for cobaloximes. Such small angular differences resulted in nearly identical geometrical terms for both methods of calculation. Since for Cbls, the standard deviations of the atomic positions are not always available,[4] we decided to follow the BH precedent and perform the least-squares plane calculations for the cobaloxime structures using unit weights.

There are several other factors that must be considered: (a) the geometric term might be so sensitive to changes in geometry that X-ray data are not accurate enough to estimate it; (b) the benzimidazole ligand structure might be so sensitive to changes in the trans ligand that structural correlations will be difficult; (c) equatorial ligand anisotropy might be so large as to preclude

**Table IX.** Changes in $^{13}C$ Shifts ($\Delta\delta$) Induced by Electrophiles

| | $Me_3Bzm$ | | | | DMBz[d] |
|---|---|---|---|---|---|
| | $\Delta\delta_i^{H+}$ | $\Delta\delta_i^{M}$ | "$\Delta\delta_i$" | "$\Delta\delta_i$" | $\Delta\delta_i^{H+}$ |
| B2 | −3.17 | 1.47 | 0.32 | 1.10 | −4.91 |
| B4 | −5.27 | −1.80 | −2.60 | −2.05 | −4.79 |
| B5 | 6.35 | 3.28 | 2.80 | 3.10 | 5.73[d] |
| B6 | 4.78 | 2.92 | 2.45 | 2.10 | 4.68[d] |
| B7 | 2.54 | 1.47 | 1.20 | 0.40 | 1.43 |
| B8 | −2.96 | −1.35 | −0.70 | −0.65 | −4.81 |
| B9 | −13.09 | −5.17 | −4.00 | −3.35 | −11.50 |
| B10 | +0.09 | +0.01 | 0.49 | 0.49 | 0.15 |
| B11 | +0.09 | −0.04 | −0.33 | −0.15 | 0.23 |
| B12 | 2.37 | 1.36 | 1.52 | 1.40 | 1.27[c] |
| electrophile | $H^+$ | M[a] | Co in $(DH)_2$ | Co in $(DH)_2$ | $H^+$ [b] |
| solvent | DMSO-$d_6$ | DMSO-$d_6$ | DMSO-$d_6$ | $CDCl_3$ | $D_2O$ |

[a] Average shift values for $HgCl_2$, $Cd(NO_3)_2$ and $Zn(NO_3)_2$ at 0.025 M × 4. [b] Reference 10. For α-ribazole phosphate, values for α-ribazole were similar. [c] R1 of ribose ring. [d] Reassigned from ref 10; see ref 11.

**Table X.** Geometric Terms for Various Cobaloximes[a]

| | C1 | adamantyl | | C1 | adamantyl |
|---|---|---|---|---|---|
| B2 | −0.2034 | −0.1745 | B8 | −0.0882 | −0.0787 |
| B4 | −0.0541 | −0.0596 | B9 | −0.1952 | −0.1738 |
| B5 | −0.0240 | −0.0254 | B10 | −0.0048 | −0.0068 |
| B6 | −0.0253 | −0.0247 | B11 | −0.0122 | −0.0123 |
| B7 | −0.0384 | −0.0356 | B12 | −0.0326 | −0.0291 |

[a] In units of $10^{23}$ $cm^{-3}$ molecule.

the use of a cobalt-centered anisotropy; and (d) solvation differences between free and coordinated $Me_3Bzm$ may influence shifts.

As can be seen in Table X, $GT_i$ does not change very much from the compound with the smallest trans influence ligand, Cl, to the compound with the largest trans influence ligand, adamantyl. This is true regardless of the method of calculating the least-squares planes of the equatorial atoms. Thus, factor a is not a concern.

These X-ray structural data showed that the $Me_3Bzm$ moiety does not undergo significant structural changes throughout the series. The same conclusion is reached for the DMBz moiety by examination of the X-ray crystal structures of AdepropylCbl,[7] AdoCbl,[4] $CH_3Cbl$,[5] and CNCbl.[4] The geometrical changes found for $Me_3Bzm$ in cobaloxime X-ray structures are minor and involve BN3, the nitrogen bound to Co. We have noticed, as expected, that the Co–N(Bzm) bond lengthens but that there is no clear pattern in the difference between the Co–N(Bzm)–C angles with increasing trans effect and trans influence of the alkyl group. Therefore, factor b is of no concern.

Another important consideration is that the equatorial ligand anisotropy could dominate the shielding term. However, the $(DH)_2$ equatorial ligands are not as electron-rich or delocalized as other $B_{12}$ model ligands (e.g., the Schiff base "saloph" ligand[14] or the Costa-type ligands[13,15,21]) or the corrin itself. Also, the X-ray results reveal that $\varphi$ is always small for $Me_3Bzm$ compounds, Table VI. The plane of the ligand is thus preferentially away from the anisotropic C═N bonds. It is reasonable to assume that the magnetic anisotropy of the equatorial ligand is a relatively smaller contributor to the dipolar shielding effect in cobaloximes than it is in Cbls. Thus, factor c is not of concern.

Finally, the $Me_3Bzm$ ligand should be solvated differently when coordinated, as compared to the free ligand. We have used two rather different solvents. Overall, the effects are similar, and at least for these two solvents, factor d is not a major concern.

For the $Me_3Bzm$ cobaloximes not structurally characterized by single-crystal X-ray work, the following approach was used to calculate the $GT_i$'s. For each $Me_3Bzm$ carbon atom, GT's derived from X-ray structures were plotted against the alkyl-related electronic parameters EP (see ref 26 and below for a description of the EP term). As reasonable "$GT_i$ *vs* EP" linear regressions with satisfactory correlation coefficients were found for all $Me_3Bzm$ $^{13}C$ resonances, interpolated $GT_i$'s were derived for compounds not structurally characterized by X-ray diffraction, using the appropriate EP parameter. In conclusion, the $GT_i$'s are easily calculated based on X-ray coordinates of $Me_3Bzm$ cobaloximes. Values for other cobaloximes, not characterized by X-ray methods, can be confidently estimated since, in any case, $GT_i$'s are not very sensitive to the trans axial ligand (Table X).

**The Fitting Procedure.** We tested the application of the BH equation to cobaloximes but using an equivalent expression:

$$\text{obsd cobaloxime } \Delta\delta_i = [\epsilon\Delta\delta_i^{H^+}(Me_3Bzm)] - \Delta\sigma_i$$

In the above two-term expression, the $^{13}C$ shifts of neutral, protonated and complexed $Me_3Bzm$ in DMSO-$d_6$ were used instead of RBz, $RBzH^+$ and CBls as follows:

$$\text{obsd cobaloxime } \Delta\delta_i = \delta_i(\text{cobaloxime}) - \delta_i(Me_3Bzm)$$

$$\Delta\delta_i^{H^+}(Me_3Bzm) = \delta_i(Me_3BzmH^+) - \delta_i(Me_3Bzm)$$

We use $\epsilon$, which is equivalent to $1 - \alpha$ of the Brown/Hakimi expression, and we use *differences* between shifts and try to fit these *differences*. Since the changes in shift typically observed are of the order of <10 ppm and the absolute values of the shifts are often >100 ppm, it was more convenient for us to use differences (i.e. coordination shifts) to monitor our progress.

**A New Inductive Term.** We developed a new two-term approach using the cobaloxime system. This approach had two components. First, we introduced a new approach for calculating the inductive term. Second, we utilized the multiple linear regression method in an iterative manner.

For each $C_i$ the $\Delta\delta_i^{H+}$ for $Me_3Bzm$ were replaced by a new set of relative inductive shifts, "$\Delta\delta_i$". Our reformulated equation is

$$\text{obsd } \Delta\delta_i = \epsilon\text{“}\Delta\delta_i\text{”} - \Delta\chi(GT_i)$$

These new "$\Delta\delta_i$" shifts of the signals of a particular $C_i$ reflect the sign and the relative sensitivity across the series. The absolute values of the "$\Delta\delta_i$" are not crucial since the coefficient for the term, $\epsilon$, will compensate for any error in magnitude. We chose "$\Delta\delta_i$" values that were large enough for $\epsilon$ to be less than one. We shall discuss possible implications of "$\Delta\delta_i$" below. These "$\Delta\delta_i$" values were obtained by the following procedure. Two $Me_3Bzm$ cobaloximes were selected on the basis of the following criteria: (a) their R(X) groups should have minimum steric trans influence, and (b) one of them should be a relatively good electron donor, while the other should be a poor one (i.e., they will "bracket" roughly the R groups used in the $Me_3BzmCo(DH)_2R$ series). Hence, we have chosen the chloro and ethyl derivatives. The "$\Delta\delta_i$" values for each $Me_3Bzm$ carbon were chosen iteratively to maximize multiple correlation coefficients for the least-squares fit of the coefficients for both $\epsilon$ and $\Delta\chi$ for the two-parameter equations for these two $Me_3Bzm$ cobaloximes.[33] Initial estimates

**Table XI.** Electronic and Magnetic Terms Derived from the Two-Parameter Model for $Me_3BzmCo(DH)_2(R\text{ or }X)$ in $CDCl_3$ and DMSO at 25 °C and a Comparison to EP Values[a]

| | DMSO-$d_6$ | | | $CDCl_3$ | |
|---|---|---|---|---|---|
| X or R | EP | $\epsilon$ | $\Delta\chi$[b] | $\epsilon$ | $\Delta\chi$ |
| Cl | −1.56 | 0.99(1) | −1.9(2) | 1.00(3) | −3.1(7) |
| $CH(CN)CH_2CN$[c] | −1.07 | | | 0.85(3) | −1.4(5) |
| $CH(CN)Cl$ | −1.10 | 0.836(6) | +0.2(1) | 0.84(2) | −0.6(4) |
| $CH_2NO_2$ | −0.98 | 0.808(6) | +0.2(1) | 0.80(1) | −0.5(3) |
| $CH_2CN$ | −0.75 | 0.756(8) | +0.2(2) | 0.75(2) | −0.3(3) |
| $CHCl_2$ | −0.70 | 0.75(1) | −0.4(3) | 0.747(8) | −0.6(2) |
| $CH_2CF_3$ | −0.55 | 0.723(3) | −0.74(7) | 0.71(1) | −0.8(2) |
| $CH_2Cl$ | −0.35 | 0.662(8) | +0.6(2) | 0.644(9) | +0.7(2) |
| $CH_3$ | 0 | 0.572(6) | +0.2(1) | 0.55(1) | +0.8(3) |
| $CH_2CH_3$ | 0.12 | 0.550(7) | +0.3(1) | 0.53(2) | +1.1(4) |
| $CH_2C(CH_3)_3$ | 0.19 | 0.54(1) | −1.6(3) | 0.52(3) | −0.6(6) |
| $CH(CH_3)_2$ | 0.24 | 0.52(2) | −0.2(4) | 0.50(3) | 0.9(7) |
| adamantyl[e] | 0.48 | | | 0.39(5) | 1.4(1.2) |

[a] Standard deviation given in parentheses. [b] In units of $10^{-29}$ cm$^3$ molecule$^{-1}$. [c] See footnote *d* in Table VI. [d] Chen, Q.; Marzilli, L. G.; Bresciani-Pahor, N.; Randaccio, L.; Zangrando, E. *Inorg. Chim. Acta* **1988**, *241*, 144. [e] Reference 17.

for each "$\Delta\delta_i$" were based on the observed $\Delta\delta_i$ for the X = Cl derivative since $\epsilon$ was expected to be largest for this derivative. The same method was applied to the DMSO-$d_6$ and the $CDCl_3$ data sets. The optimized "$\Delta\delta_i$" are listed in Table IX along with the $Me_3Bzm$ protonation data.

Comparison of the DMSO-$d_6$ $^{13}C$ data indicates that the cobaloxime "$\Delta\delta_i$" values reflect closely the crudely and independently derived $\Delta\delta_i{}^M$ values with an average difference of 0.7 ppm for the ring carbons. This agreement between the "$\Delta\delta_i$" and the $\Delta\delta_i{}^M$ values is actually *better* than that reported for Cbls by BH. Thus, the resemblance of the "$\Delta\delta_i$" and the $\Delta\delta_i{}^M$ values supports our contention that the Co(III) centers in these $B_{12}$ model compounds and $MX_2$ are weaker electrophiles than $H^+$. In the past, we have shown that metal centers are simply not as good as $H^+$ at inductively shifting the $^{13}C$ signals of ligands.[30] The ideal or most electrophilic cobaloxime cobalt center would have a value of $\epsilon$ of 1, and the "$\Delta\delta_i$" would be the inductive shifts for this center. The cobalt center in the chloro derivative should be close to ideal. Thus, we suspect that the "$\Delta\delta_i$" values used in our calculations are close to the highest that would be found since Cl has a weak trans influence.

With these "$\Delta\delta_i$'s" and the observed $\Delta\delta_i$ data, we calculated $\epsilon$ and $\Delta\chi$ values for each $Me_3BzmCo(DH)_2R$ using the multiple linear regression approach. The $\epsilon$ and $\Delta\chi$ values obtained from DMSO-$d_6$ and $CDCl_3$ data are listed in Table XI. As can be seen from the small standard deviations, excellent fits are obtained throughout. The fits are clearly superior to any previously used approach and indicate that these "$\Delta\delta_i$" are applicable to all cobaloximes investigated, not just the Cl and $CH_2CH_3$ derivatives.

It is important to note that the $\epsilon$ and "$\Delta\delta_i$" values are relative. Thus, if we were to select "$\Delta\delta_i$" values which were twice as large, the $\epsilon$ calculated would be half as large, so that the contribution from the first term would be identical. This self-compensating relationship gives some credence to the small values of $\Delta\chi$ calculated with our model. In Table XII, we give the values for the methyl complex as an example. Compared with the very poor fits for cobaloximes with the protonation model, the average difference between the observed and calculated shifts is less than 0.03 ppm. For the Cbls, these average differences calculated from the fitting procedure of BH are ~1 ppm.[10] For AdoCbl, the reported differences in the $^{13}C$ shift of the $\alpha$-ribazole on coordination average only about 1.3 ppm,[10] thus the *error* in the reported fit for AdoCbl using the BH procedure[10] is almost as large as the *effect* of coordination to cobalt.

Of some interest, as can be seen from Table XII, only for B2 in cobaloximes with poor electron donors such as Cl does the $\Delta\sigma_i$ term contribute appreciably to the calculated shifts. Thus, although the inductive (first) term of our approach can be reasonably estimated because of the self-compensating feature just described, the contribution of the anisotropic term to $\Delta\delta_i$ is too small to lead to a meaningful value for $\Delta\chi$. However, our method does demonstrate that $\Delta\chi$ *must be relatively small* for alkylcobaloximes. In other words, for $^{13}C$ $\Delta\delta$, the inductive term dominates except for B2 in a few compounds.

Since the $\epsilon$"$\Delta\delta_i$" term is empirical, it is worth considering its meaning. First, we compare the $\epsilon$ and EP values for the different axial ligands. The EP values are derived from a scale of substituent constants "$\Delta Y(i)$" for all substituents $Y(i)$ on the $CY(1)Y(2)Y(3)$ alkyl group bound to Co based on the $^{13}C$ NMR shift for the py $\gamma$-carbon in $pyCo(DH)_2R$ compounds.[26] Specifically, it was found that the sum, $\sum_i\Delta(Y(i))$, for the substituents $Y(i)$ of the $CY(1)Y(2)Y(3)$ group gave good correlations with Co–N bond length, with log (rate constant for L dissociation), and with $^{13}C$ and $^{31}P$ NMR shifts. We concluded that the influence of $Y(i)$ on the properties evaluated was mainly inductive (electronic trans influence). For each alkyl group, an electronic parameter was derived from the relationship $EP = \sum_i\Delta(Y(i))$. Figure 7 shows a plot of EP against the $\epsilon$ values obtained for several alkyl groups. The correlation coefficient of 0.996 shows that the two independently derived scales are in good agreement and that solution $^{13}C$ NMR data in general are indicative primarily of the inductive trans influence of the alkyl groups for both $Me_3Bzm$ and py cobaloximes.

The "$\Delta\delta_i$" values we obtained are rather different from the $\Delta\delta_i{}^{H^+}$ values used in the BH approach. The clear advantage of the BH approach is that the proton cannot have an anisotropic effect. The "$\Delta\delta_i$" values are similar to the $\Delta\delta_i{}^M$ values, which were determined independently from the effects of three different metal salts ($HgCl_2$, $Cd(NO_3)_2$, and $Zn(NO_3)_2$) on the shifts of $Me_3Bzm$ in DMSO. Thus, the "$\Delta\delta_i$" values are chemically more reasonable estimates of the inductive effects *provided* the $\Delta\delta_i{}^M$ values are not significantly influenced by the anisotropic effects of the three metal ions, a provision we now consider.

**Table XII.** Electronic and Anisotropic Shielding Terms and Calculated and Observed $\Delta\delta_i$ for $Me_3Bzm$ Cobaloximes[a]

| | Cl ($\epsilon$ = 0.99(1); $\Delta\chi$ = −1.9(2) × $10^{-29}$ cm$^3$ molecule$^{-1}$; mult corrln coeff = 0.9997) | | | | $CH_3$ ($\epsilon$ = 0.572(6); $\Delta\chi$ = 0.2(1) × $10^{-29}$ cm$^3$ molecule$^{-1}$; mult corrln coeff = 0.9997) | | | | $CH_2CH_3$ ($\epsilon$ = 0.550(7); $\Delta\chi$ = 0.3(1) × $10^{-29}$ cm$^3$ molecule$^{-1}$; mult corrln coeff = 0.9995) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| atom | $\epsilon$ term | $\Delta\sigma$ | calcd $\Delta\delta_i$ | obsd $\Delta\delta_i$ | $\epsilon$ term | $\Delta\sigma$ | calcd $\Delta\delta_i$ | obsd $\Delta\delta_i$ | $\epsilon$ term | $\Delta\sigma$ | calcd $\Delta\delta_i$ | obsd $\Delta\delta_i$ |
| B2 | +0.31 | 0.39 | 0.08 | −0.09 | +0.19 | 0.03 | +0.22 | +0.19 | +0.18 | −0.06 | +0.24 | +0.23 |
| B4 | −2.58 | 0.10 | −2.68 | −2.69 | −1.48 | −0.01 | −1.47 | −1.43 | −1.43 | −0.02 | −1.41 | −1.37 |
| B5 | +2.78 | 0.05 | +2.73 | +2.71 | +1.60 | −0.01 | +1.61 | +1.65 | +1.54 | −0.01 | +1.55 | +1.57 |
| B6 | +2.44 | 0.06 | +2.38 | +2.36 | +1.40 | −0.01 | +1.40 | +1.43 | +1.34 | −0.01 | +1.35 | +1.37 |
| B7 | +1.19 | 0.07 | +1.12 | +1.26 | +0.69 | −0.01 | +0.70 | +0.66 | +0.66 | −0.01 | +0.67 | +0.59 |
| B8 | +0.69 | 0.17 | −0.86 | −0.89 | −0.40 | −0.02 | −0.38 | −0.37 | −0.39 | −0.03 | −0.36 | −0.33 |
| B9 | −3.98 | 0.37 | −4.35 | −4.34 | −2.29 | −0.04 | −2.25 | −2.25 | −2.19 | −0.06 | −2.13 | −2.15 |
| B10 | +0.49 | 0.01 | +0.48 | +0.44 | +0.28 | 0.00 | +0.28 | +0.33 | +0.28 | 0.00 | +0.28 | +0.33 |
| B11 | −0.33 | 0.02 | −0.35 | −0.34 | −0.19 | 0.00 | −0.19 | −0.17 | −0.18 | 0.00 | −0.18 | −0.19 |
| B12 | +1.50 | 0.06 | +1.44 | +1.43 | +0.88 | −0.01 | +0.89 | +0.89 | +0.83 | −0.01 | +0.84 | +0.87 |

[a] 0.1 M solutions in DMSO-$d_6$; all values for shifts in ppm.

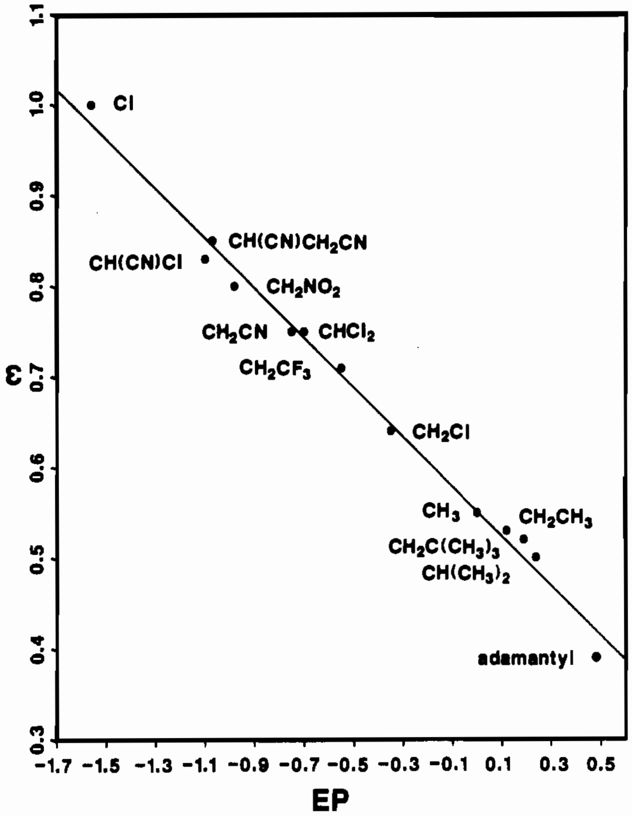

**Figure 7.** Plot of ε *vs* EP for the complexes in Table XI in $CDCl_3$.

If the three metal ions had inductive effects related to the proton (the BH approach), the inductive effect would shift *both* B2 and B9 upfield. If the $\Delta\chi$ were negative with the principal axis along M–BN3, *both* B2 and B9 have negative $GT_i$ values and would be shifted *upfield* because $-\Delta\sigma_i = -(\Delta\chi(GT_i))$. However, for all three cations, the B9 signal moved upfield, whereas the B2 signal moved *downfield.* The downfield B2 shifts can be understood only with a positive $\Delta\chi$, if the BH approach were correct. Furthermore, the following two points together demonstrate that the magnitude of the $-\Delta\sigma_i$ term for B2 must be significant (ca. +3 ppm). Point 1: Since the $\Delta\delta_i^M$ for B9 is upfield and quite large (−5.2 ppm), the contribution to $\Delta\delta_i^M$ of the B9 inductive term needs to be even larger (ca. −7 to −8 ppm, see below) to overcome the deshielding due to the positive $\Delta\chi$. Point 2: The effect of protonation on B2 is one-fourth that on B9. Therefore, the magnitude of the B2 inductive term is predicted to be ca. −1.7 to −2 ppm. Thus, $\Delta\chi$ must be large enough for the $-\Delta\sigma_i$ term to be ca. +3.2 to 3.5 ppm in order for the net deshielding $\Delta\delta_i^M$ for B2 to be 1.5 ppm.

We now assess the anisotropic contribution to $\Delta\delta_i^M$ for B9 and B2. From the relationship of $GT_i$'s for B2:B9:B2H of ~1:1:0.4, a +3 ppm $-\Delta\sigma_i$ term for B2 requires +3 and +1.2 ppm terms for B9 and B2H, respectively. The following lines of reasoning suggest the $-\Delta\sigma_i$ contribution to these $\Delta\delta_i^M$ is not large. For B2H, $\Delta\delta_i^M$ is only ca. +0.3 ppm. An inductive effect of −0.9 ppm is needed to overcome a $-\Delta\sigma_i$ contribution to $\Delta\delta_i^M$ of +1.2 ppm. However, the inductive effect of the proton on B2H is positive (ca. +1.3 ppm). Thus, $\Delta\chi$ cannot be positive, unless the inductive effect were negligible. For B9, $\Delta\delta_i^M$ is −5.2 ppm. Since the $-\Delta\sigma_i$ term would be +3 ppm, the inductive term for B9 (−8.2 ppm) is equivalent to {−8.2/−13.1} or ~0.6 of the proton. Such an inductive effect on the B2H signal is not negligible and would be ~0.8 ppm (0.6 × ca. +1.3 ppm). The combined terms of the BH approach predict a $\Delta\delta_i^M$ value of ca. +2 ppm for B2H, but $\Delta\delta_i^M$ is only +0.3 ppm. Thus, to explain the B2H shifts, $\Delta\chi$ must be negative.

From these lines of reasoning, we conclude that $\Delta\chi$ does not play a significant role in influencing shifts for the three metal ions investigated, since some shifts require positive $\Delta\chi$ (B2) and others negative $\Delta\chi$ (B2H). The principal factor is an inductive effect of the metal centers which causes B2 and B2H to shift downfield, but B9 to shift upfield. Therefore, the proton is not a good model for a metal center for explaining NMR shifts.

Further support for the above conclusions comes from a consideration of the cobalt species. Our approach suggests that the inductive effects of the Co in cobaloximes are similar to those of the three metal ions but that the anisotropic effects are different. In cobaloximes, the B2H observed $\Delta\delta_i$ is small, but it is upfield in DMSO (see supplementary material for $^1H$ shifts). Since the inductive effect causes downfield B2H shifts, the sign of the Co $\Delta\chi$ must be negative if the principal axis passes through BN3, or, alternatively, the upfield shift could be due to the equatorial ligand anisotropy. To assess these two possibilities, we consider the B4H shift. The B4H shift is rather sensitive to equatorial ligand anisotropy and insensitive to Co $\Delta\chi$ (the $GT_i$ term for B4H is close to zero). Protonation causes a very small downfield shift for B4H. For cobaloximes, the B4H observed $\Delta\delta_i$ is downfield, indicating little if any effect of equatorial ligand anisotropy as previously concluded for other cobaloximes.[16] Thus, the upfield observed $\Delta\delta_i$ of B2H (and B2 in $Me_3BzmCo(DH)_2Cl$) suggests that the sign of $\Delta\chi$ is negative. Model $B_{12}$ compounds, including cobaloximes, have been shown previously to have negative $\Delta\chi$.[16]

The Co–N bond lengths suggest that benzimidazole ligand binding is weaker in the Cbls than in cobaloximes,[3] yet the inductive upfield coordination shift of B2 calculated by the BH approach is large, up to ca. −2.1 ppm for CNCbl.[10] Given that the Co center is more electron deficient in cobaloximes than in the Cbls and $\Delta\chi$ is negative, very large upfield B2 shifts should have been observed for cobaloximes, if the BH explanation of the shifts is correct. Furthermore, the total B2 coordination shifts of −2.9 and −2.8 ppm for MeCbl and CNCbl estimated by BH greatly exceed those actually observed (−1.2 and −1.3 ppm).[10] Thus, the observed B2 coordination shifts in both cobaloximes and Cbls are downfield to values predicted by the BH approach.

Can our conclusion that Co anisotropic effects and inductive effects on B2 shifts are small, developed for cobaloximes, explain observed trends for Cbls? The B2 coordination shift for Cbls is upfield and fairly large (−1.5 ppm), but the ligand-responsive shift is *nearly zero* for a range of derivatives.[10] *This behavior cannot be explained by the BH approach.* However, it is expected from equatorial ligand anisotropy, which should not be very dependent on the R or X axial ligand. Again, to assess whether corrin ligand anisotropy can explain B2 coordination shifts, we turn to the examination of the B2H shifts. For Cbls, the B2H ligand-responsive shift varies little across a series of Cbls but the coordination shift is large, ca. −1.5 ppm.[7,9] This large coordination shift also suggests the corrin ring anisotropy is dominating. If so, there should be a large upfield coordination shift for B4H, as found.[7,9] Thus, the large upfield coordination shift of the B2 signal is consistent with a small downfield inductive effect counterbalanced by upfield shifting due to anisotropies of Co (small) and corrin (large). In this interpretation, the inductive effect of Co in Cbls will shift B2 downfield to a similar extent as found for the other metals studied here. The corrin equatorial ligand anisotropic effects are also consistent with the findings in Costa-type model compounds, where we find upfield shifts for B4H.[13,15]

A two-term approach is inadequate for the treatment of shifts for Cbls. The application of this approach by the BH method leads to incorrect estimates of the effects of inductive and Co anisotropic effects on the shifts. The justification used by BH to ignore equatorial ligand anisotropy was the absence of such effects in cobaloximes. However, B4H signals in other $B_{12}$ models exhibit significant upfield shifts attributable to anisotropy of equatorial ligands with less extensive π systems than corrins.[13,15]

## Conclusions

The $Me_3Bzm$ ligand, although it is larger than py, has an effective bulk similar to that of py. One side of the lopsided ligand is less bulky and the other side is more bulky than py.

An empirical approach to the inductive effect of Co on $^{13}C$ shifts in cobaloximes, when employed with the two-term expression, predicts inductive effects on shifts that more clearly reflect the shifts induced by simple metal ions than the shifts induced by the proton.

The coefficient ($\epsilon$) of the new inductive term is a measure of the ligand-responsive electronic properties of the metal center. This coefficient correlates with other measures of the electronic properties of the metal center and thus is chemically reasonable. In turn, the new empirical approach is reasonable.

In these and other simple $B_{12}$ models, the B2 coordination shifts are typically downfield, and this shift direction is also found for other metal ions. In contrast, the proton and the Cbl moiety shift this signal upfield. The proton should have the largest inductive effect, whereas the electron-rich cobalt center in Cbls should have the weakest effect; thus, the species at either inductive *extreme* appear to have the most similar effect on the B2 shift. These anomalies are easily rationalized by our model. The *cobalt center* in Cbls probably induces the same type of B2 coordination shifts as in the models, namely a small up- or downfield shift from inductive/anisotropic effects. The *corrin ring* in Cbls has significant anisotropy as evidenced by upfield coordination shifts of B2H and B4H signals.[7,9] This corrin ring anisotropy *dominates* over other effects leading to upfield B2 coordination shifts. The anisotropy of the corrin ring should be only slightly modulated by ligand-responsive changes in the cobalt center; thus, the small ligand-responsive trends for some signals (B2, B2H, B4H) relative to the large coordination shifts from the free $\alpha$-ribazole values for these signals are explained. Furthermore, our studies explain why the ligand-responsive shift for Cbls is negligible for B2 compared to B9.

The two-term quantitation in models has been performed with considerable success. A two-term approach is clearly inadequate for Cbls, but qualitatively the shift trends can be understood and rationalized with the known properties of Cbls.

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**Supplementary Material Available:** Tables of elemental analyses, $^1H$ and additional $^{13}C$ NMR shifts in $CDCl_3$ and DMSO-$d_6$, complete bond lengths and bond angles, hydrogen atom coordinates, and anisotropic thermal parameters (25 pages). Ordering information is given on any current masthead page.