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# Inorganic Chemistry

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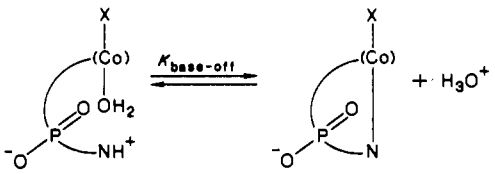
# Communications

## Heteronuclear NMR Studies of Cobalamins. 5. Proton-Coupled $^{31}P$ NMR[1]

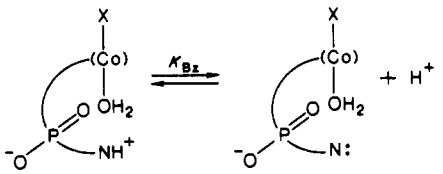
*Sir:*

Recently, we have shown[2] that while the $^{31}P$ NMR chemical shifts of all base-off cobalamins (eq 1) are identical, the $^{31}P$ chemical shifts of the base-on species of a series of 10 cobalamins whose $pK_{base\text{-}off}$ values (eq 1) range from 4.10 to −2.13 vary in a regular manner with the apparent strength of coordination of the axial benzimidazole ligand. The latter values have been estimated

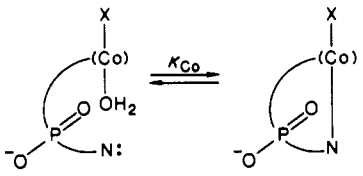



(1)

by considering the base-on–base-off equilibrium (eq 1) to be the sum of two consecutive equilibria (eq 2 and 3) allowing the




(2)




(3)

$$K_{base\text{-}off} = (1 + K_{Co})K_{Bz} \quad (4)$$

calculation of $\Delta G_{Co}$ (for eq 3) from eq 4 and the measured values of $pK_{base\text{-}off}$,[2,3] assuming that $pK_{Bz}$ (eq 2) is equivalent to the $pK_a$ of the conjugate acid of the detached axial nucleoside, α-ribazole ($pK_a$ = 5.56, at 25 °C, ionic strength 1.0 M[3]). Thus, the $^{31}P$ chemical shifts of the base-on cobalamins increase in an apparently linear fashion with the decrease in $\Delta G_{Co}$ throughout the series of compounds.

On the basis of the work of Gorenstein and co-workers,[4-6] who have shown that $^{31}P$ chemical shifts of phosphate esters and

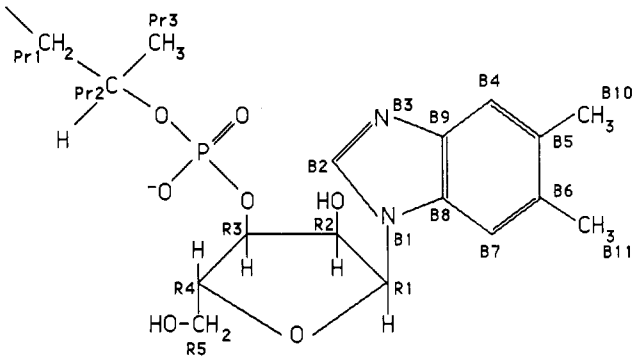



**Figure 1.** Structure and numbering scheme of the nucleotide loop of cobalamins.

phosphodiesters are largely, if not completely, controlled by O–P–O bond angles (i.e., phosphorus hybridization), we advanced a hypothesis for the dependence of the base-on $^{31}P$ chemical shifts upon $\Delta G_{Co}$ based on the idea of progressive increases in strain (and consequent RO–P–OR bond angle changes) in the nucleotide loop with the shortening of the axial Co–N bond (clearly seen in the X-ray crystal structures of base-on cobalamins[7-10]) as $\Delta G_{Co}$ (eq 3) becomes more negative. More recently, confirmation of this idea has come from a detailed study of the $^{13}C$ NMR of the nucleotide loop of base-on cobalamin,[11] which clearly showed that changes in the $^{31}P$ chemical shifts could not be due to changes in dipolar shielding by the metal atom and that regular changes in nucleotide loop conformation throughout the series of compounds could readily be detected as trends in the $^{13}C$ chemical shifts of the carbon atoms of the isopropanolamine moiety (Figure 1).

Further evidence of conformational effects in the nucleotide loop of base-on cobalamins should be obtainable from proton–phosphorus coupling constants since three-bond H–P coupling constants in phosphate compounds are well-known to be strongly dependent on POCH dihedral angles.[12,13] However, all of the $^{31}P$ NMR work on cobalamin so far published has found the $^{1}H$-coupled $^{31}P$ NMR resonances of cobalamins to be apparently symmetrical triplets with coupling constants of about 7–9 Hz[14-17]

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**Table I.** H–P Coupling Constants for Base-On and Base-Off Cobalamins, RCbl[a]

| R | $pK_{base\text{-}off}$[b] | $K_{Co}$[c] | $\Delta G_{Co}$,[d] kcal mol$^{-1}$ | $J_{H\text{-}P}^{base\text{-}on}$, Hz | pH[e] | $\alpha_{base\text{-}on}$[f] | $J_{H\text{-}P}^{obsd}$,[g] Hz | $J_{H\text{-}P}^{base\text{-}off}$,[h] Hz |
|---|---|---|---|---|---|---|---|---|
| $CH_3CH_2^-$ | 4.16[i] | $2.44 \times 10$ | −1.89 | 6.9 | 2.08 | $8.25 \times 10^{-3}$ | 7.2 | 7.2 |
| $CH_3(CH_2)_2^-$ | 4.10 | $2.80 \times 10$ | −1.97 | 6.8 | 2.00 | $7.88 \times 10^{-3}$ | 7.2 | 7.2 |
| $Ado^-$ | 3.67 | $7.66 \times 10$ | −2.57 | 7.2 | 1.50 | $6.72 \times 10^{-3}$ | 7.3 | 7.3 |
| $NC(CH_2)_3^-$ | 3.50 | $1.15 \times 10^2$ | −2.81 | 7.1 | 1.25 | $5.59 \times 10^{-3}$ | 7.3 | 7.3 |
| $CH_3^-$ | 2.89 | $4.67 \times 10^2$ | −3.64 | 7.3 | 1.00 | $1.27 \times 10^{-2}$ | 7.3 | 7.3 |
| $CF_3CH_2^-$ | 2.60 | $9.23 \times 10^2$ | −4.04 | 7.3 | 1.32 | $4.99 \times 10^{-2}$ | 7.3 | 7.3 |
| $CF_2H^-$ | 2.15 | $2.60 \times 10^3$ | −4.66 | 7.5 | 1.08 | $7.84 \times 10^{-2}$ | 7.3 | 7.3 |
| $NCCH_2^-$ | 1.82 | $6.40 \times 10^3$ | −5.19 | 7.6 | 0.91 | $1.10 \times 10^{-1}$ | 7.3 | 7.3 |
| $CF_3^-$ | 1.44 | $1.32 \times 10^4$ | −5.62 | 7.8 | 0.79 | $1.83 \times 10^{-1}$ | 7.4 | 7.4 |
| $CN^-$ | 0.10 | $2.88 \times 10^5$ | −7.44 | 8.3 | | | | 7.3[j] |
| $H_2O^-$ | −2.13 | $4.90 \times 10^7$ | −10.48 | 8.8 | | | | |

[a] Spectra obtained on a Nicolet NT-200 wide-bore superconducting spectrometer (4.7 T) operating at 80.988 MHz as previously described.[2] [b] Equation 1. Values at 25.0 °C, ionic strength 1.0 M (KCl) from ref 2, 3, and 17, except as noted. [c] Equation 3. [d] Calculated from eq 4 and the measured values of $pK_{base\text{-}off}$ assuming $pK_{Bz}$ (eq 2) is 5.56.[3] [e] pH at which the base-off $^1H$-coupled $^{31}P$ resonance was observed. [f] Fraction of base-on species present at observation pH, calculated from $pK_{base\text{-}off}$. [g] Observed coupling cnstant at the measurement pH. [h] Coupling constant of the base-off species, corrected for the presence of the base-on species via eq 5. [i] This work, determined as described in ref 3. [j] Value for base-off dicyanocobalamin ($(CN)_2Cbl$).

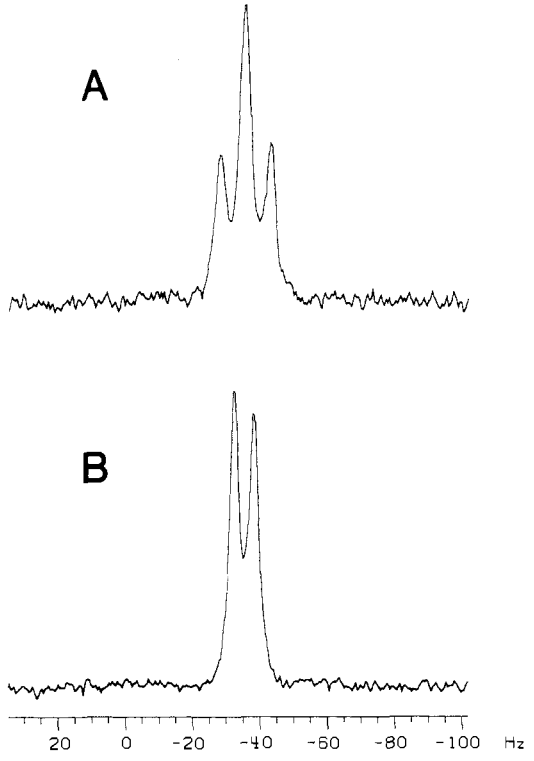


**Figure 2.** $^{31}P$ NMR spectra (80.988 MHz) of $NCCH_2Cbl$ (pH 0.89, $\alpha_{base\text{-}on}$ = 0.118): (A) $^1H$-coupled spectrum; (B) spectrum selectively decoupled at the frequency of the R3-H resonance of the zwitterion of the α-ribazole-3′-phosphate.

(Figure 2A) despite the fact that the nucleotide loop phosphorus atom would be expected to be strongly coupled to two structurally dissimilar and magnetically inequivalent hydrogens, i.e., the ribose R3 proton and the Pr2 proton (Figure 1). We have consequently considered the possibility that the H–P coupling constants for these two protons may be fortuitously identical or nearly identical so that the inner two members of the putative doublet of doublets coalesce to produce the apparently symmetrical triplets. As we have recently prepared the detached axial nucleotide, α-ribazole-3′-phosphate, from acid-catalyzed hydrolysis of cyanocobalamin and obtained its $^1H$ NMR spectra,[11] this hypothesis may now be tested.

The $^1H$ NMR spectrum of the zwitterion of α-ribazole-3′-phosphate shows a cleanly resolved multiplet at 4.842 ppm, assignable to the R3 proton by selective decoupling, which moves upfield only 0.13 ppm upon deprotonation of B3 (i.e., the dianion

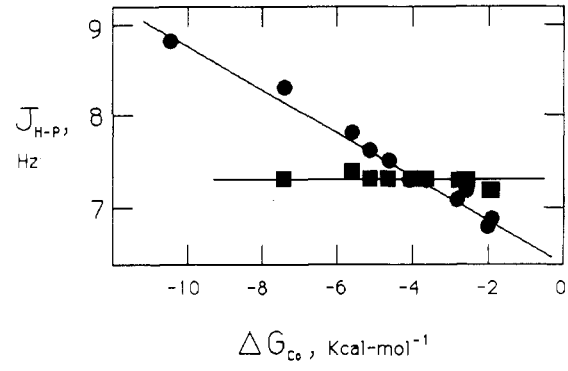


**Figure 3.** Plot of the proton–phosphorus coupling constants for the base-on (●) and base-off (■) species of the cobalamins listed in Table I. For the base-off values the solid line is the average value (7.3 ± 0.1 Hz). For the base-on values, the solid line is a least-squares fit, slope −0.230 ± 0.011 Hz kcal$^{-1}$ mol, intercept 6.46 ± 0.06, $r^2$ = 0.98.

species).[11,18] When solutions of cobalamins are irradiated with low-level, continuous-wave energy at the frequency of the R3 proton resonance of the α-ribazole-3′-phosphate zwitterion, the $^{31}P$ triplet is collapsed to a clean doublet (e.g., Figure 2B). This was the case for all of the cobalamins studied, in both the base-on and base-off forms. However, in virtually all cases, the apparent coupling constant obtained from the doublets was smaller (by 1.5–4.2 Hz) than that obtained from the fully coupled triplets. This is apparently due to the availability of some energy, even at the very low decoupling powers used, at the frequency of the Pr2 proton resonance, as evidenced by the fact that even as little as a 10% increase in decoupling power collapsed the doublet $^{31}P$ resonances to broad singlets. Futher evidence was obtained from two-dimensional proton–phosphorus correlated spectra of several representative base-on cobalamins, the experiment being optimized for couplings of about 7 Hz. In each case the phosphorus resonance was found to be strongly coupled to two proton resonances, one at about 4.72 ppm and one at about 4.32 ppm;[19] i.e., the average separation was only 0.4 ppm. We consequently assign the more downfield resonance to the R3 proton and the upfield resonance to the Pr2 proton and conclude that the multiplicity of the $^1H$-coupled $^{31}P$ resonances of cobalamins is due to fortuitous equivalence of the H–P coupling constants to the R3 and Pr2 protons.

Values for the coupling constants of the base-on and base-off cobalamins (obtained from $^1H$-coupled spectra) are listed in Table

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(18) The R3 proton resonance of α-ribazole, although occurring at higher field, shifts upfield on only 0.03 ppm upon deprotonation of the benzimidazole nitrogen.[11]

(19) The exact values were 4.682, 4.703, and 4.764 ppm for $CH_3(CH_2)_2Cbl$, CNCbl, and $H_2OCbl$, respectively, for the downfield resonance and 4.320, 4.272, and 4.365 ppm, respectively, for the upfield resonance.

I and shown graphically as a function of $\Delta G_{Co}$ in Figure 3. The absence of any significant broadening of the center member of the triplet phosphorus resonance throughout the series of compounds suggests that virtual equivalence of the two three-bond coupling constants is maintained throughout the series. In order to avoid extensive protonation of the phosphodiester moiety (p$K$ = –0.04[2]) and the possible attendant effects on H–P coupling constants, the base-off cobalamins were observed at pHs above about 0.8 and the observed coupling constants corrected for the presence of the base-on species by eq 5, where $J_{H-P}^{obsd}$ is the

$$J_{H-P}^{base\text{-}off} = (J_{H-P}^{obsd} - \alpha_{base\text{-}on} J_{H-P}^{base\text{-}on})/(1 - \alpha_{base\text{-}on}) \quad (5)$$

observed coupling constant at the measured pH and $\alpha_{base\text{-}on}$ is the fraction of base-on species present at that pH. This correction was not significant (to two significant figures) for any compound (Table I). The resulting values show that all of the base-off cobalamins have the same H–P coupling constant (7.3 ± 0.1 Hz), strongly supporting our contention[2] that the conformation of the phosphodiester is identical for all the base-off species. The base-on cobalamins, however, show a steady, and apparently linear increase in $J_{H-P}$ with increasing strength of coordination (Figure 3), although the range of values is quite small. This suggests a steady but small change in H–C–O–P dihedral angle as the axial Co–N bond length is changed, accompanying the small changes in CO–P–OC bond angles, which are responsible for the previously described $^{31}$P chemical shift trends.[2] Most interestingly, the coupling constants are identical for the base-on and base-off species of two of the cobalamins ($CH_3Cbl$ and $CF_3CH_2Cbl$), as was also the case for the $^{31}$P chemical shifts of the base-on and base-off species of these two compounds.[2] This supports our contention that when the axial benzimidazole is bound moderately weakly and the axial Co–N bond length is about 2.19 Å (as it is in base-on $CH_3Cbl$[10]), the nucleotide loop is not strained (relative to the base-off species) and the phosphodiester conformation is the same in both the base-on and base-off species. However, when the axial Co–N bond length is either increased (as in AdoCbl, 2.24 Å[9]) or decreased (as in "wet" CNCbl, 1.97 Å[8]), the nucleotide loop is strained and the phosphodiester conformation is changed, leading to the observed changes in phosphorus chemical shift and H–P coupling constants.

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## Synthesis and X-ray Crystal Structure of (Dicyanodihydroborato)bis(triphenylphosphine)copper(I): A New Linear Polymer

*Sir:*

There has been considerable interest in the various modes of coordination shown by the $BH_4^-$ and $BH_3CN^-$ groups,[1] and, following the recent synthesis of $BH_2(CN)_2^-$,[2] its role as a ligand is being explored. The first reported complexes of this species [$(Ph_2MeP)_3Cu(NC)_2BH_2$ and $P^3Cu(NC)_2BH_2$ ($P^3$ = 1,1,1-tris-((diphenylphosphino)methyl)ethane)][3] contain only one cyano group coordinated to Cu(I) in monomeric compounds. This communication reports that in the related compound of empirical formula $(PPh_3)_2Cu(NC)_2BH_2$, *both* CN groups are coordinated to *different* copper(I) atoms. The result is that the molecule exists as a linear polymer of an unprecedented type in cyanohydroborate complexes. The polymer is obtained from reactions between equimolar quantities of $Na(NC)_2BH_2$·0.65(dioxane) and either $(PPh_3)_3CuCl$ or $(PPh_3)_2CuCl$, with the colorless product being recrystallized from hot $CH_3CN$. Anal. Calcd: C, 69.89; H, 4.95; N, 4.29. Found: C, 69.59; H, 4.94; N, 4.35. The complex is insoluble in $CH_2Cl_2$, $CHCl_3$, $C_2H_5OH$, $CH_3OH$, $C_6H_6$, tetrahydrofuran, and dimethylformamide. Mp: 244–250 °C. Crystal data: $C_{38}H_{32}BCuN_2P_2$; $M_r$ = 652.98; triclinic; space group $P\bar{1}$; $a$ = 13.708 (3), $b$ = 20.179 (4), $c$ = 13.369 (3) Å; $\alpha$ = 105.81 (2), $\beta$ = 100.16 (2), $\gamma$ = 102.04 (2)°; $V$ = 3371 (1) Å$^3$; $Z$ = 4; $D_{calcd}$ = 1.29 g cm$^{-3}$; $\mu$(Mo K$\alpha$) = 0.798 mm$^{-1}$. Diffraction data obtained by using $\omega$ scan [$2\theta$ < 55°] techniques were collected at 24 °c on a Rigaku Automated four-circle diffractometer, Type AFC-5A, using graphite-monochromated molybdenum radiation (Mo K$\alpha$ (0.710 73 Å). Parallelepiped-shaped crystals were used of dimensions 0.40 × 0.35 × 0.20 mm$^3$. A total of 15 180 reflections ($\pm h,\pm k,+l$) were collected. The structure was solved by using the heavy-atom method with all hydrogen atom positions determined by difference Fourier synthesis. Scattering factors and anomalous scattering factors for non-hydrogen atoms[4,5] and scattering factors for hydrogen atoms[6] were taken from known references. A local version of the UNICS program system was used for analysis.[7] Final $R$ value was 0.047 for 8392 reflections with $|F_o| > 3\sigma(F_o)$. No estimate of agreement between equivalent reflections was made, nor were corrections made for absorption.

The crystal structure reveals the polymeric nature of the compound (Figure 1). The complex exists as a polymer parallel to the $c$ axis of the unit cell with the copper atoms bridged by $(NC)_2BH_2^-$. The chains are sufficiently far apart such that only interactions of the van der Waals type can occur between them. Although there are two crystallographically independent units in the polymer chain, their configurations are almost the same. Each copper atom is surrounded by two phosphorus and two nitrogen atoms in a slightly distorted tetrahedral arrangement.

The IR spectrum of the complex (Nujol mull) in the CN region contains two strong absorptions at 2223 and 2206 cm$^{-1}$, both higher than that of the free ligand (2203 cm$^{-1}$), indicating that both CN's are bound to the metal. (In the related $MePh_2P$ and $P^3$ complexes containing both free and coordinated CN groups, absorptions are observed at frequencies higher *and* lower than those of the free ligand.)[3] There are typical absorptions in the B–H region: 2418 (m–w), 2400 (s), 2385 (s), 2370 (m) cm$^{-1}$.

The $^{11}$B NMR spectrum consists of a 1:2:1 triplet, ($\delta$ = –42.3 referenced to $BF_3$·$OEt_2$, $J$ = 95.3 Hz), indicating that the boron signal is split by two equivalent hydrogens. The center of the multiplet is shifted only slightly from that of the free ligand (–42.1 ppm, $CH_3CN$) indicating little pertubation of the electron density on the boron nucleus upon coordination of the nitrogen to the metal.

Preliminary results indicate that this type of polymer may not be unique to $PPh_3$. Compounds of empirical formulas $(Ph_2PCH_2CH_2PPh_2)Cu(NC)_2BH_2$ and $(MePh_2P)_2Cu(NC)_2BH_2$ have also been obtained, although the latter is air-sensitive and reacts instantly with an excess of phosphine to produce the monomeric $(MePh_2P)_3Cu(NC)_2BH_2$. Studies are being carried out not only to examine the potentially interesting physical and

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