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Isoamylcobalamin–acetone–water (1/0.385/12.650)

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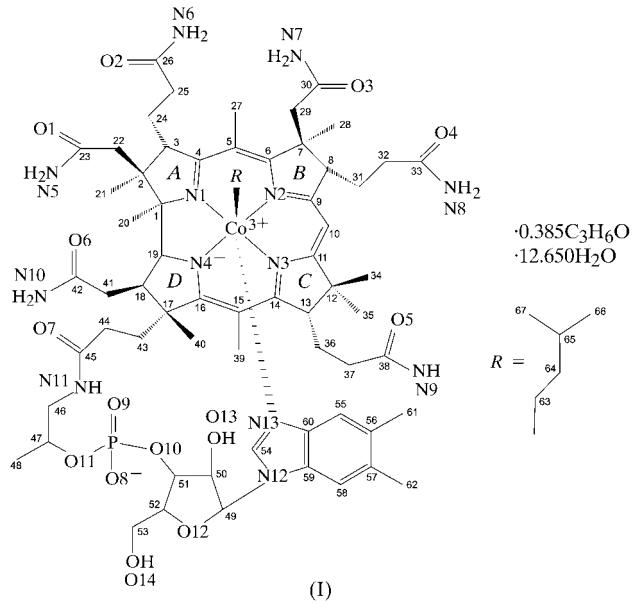
The title compound, $[Co(C_5H_{11})(C_{62}H_{88}N_{13}O_{14}P)]\cdot0.385C_3H_6O\cdot12.650H_2O$, contains the isoamyl (3-methylbutyl) anion bonded to the Co^{III} ion through a C atom. The compound is thus a structural analog of the two biologically important vitamin B_{12} coenzymes adenosylcobalamin and methylcobalamin. The lower axial Co—N bond length [2.277 (2) Å] is one of the longest ever reported for a cobalamin and reflects the strong σ-donor ability of the isoamyl group.

Comment

Cobalamins (derivatives of vitamin B_{12}) contain a six coordinate cobalt(III) ion coordinated equatorially by four pyrrole N atoms of a corrin ligand. The lower (α) axial ligand is 5,6-dimethylbenzimidazole-α-D-ribofuranose-3′-phosphate (DMB), while the upper (β) ligand, *R*, is variable ($R = CN^-$ in B_{12} itself). Adenosylcobalamin (AdoCbl; R = 5′-deoxyadenosyl) and methylcobalamin (MeCbl; $R = CH_3^-$) function as coenzymes in a number of biologically important 1,2-rearrangement and *trans*-methylation reactions, respectively (Ludwig *et al.*, 1999). The first step in the AdoCbl-dependent enzymes is homolytic cleavage of the Co—C bond to produce a Co^{II} ion and an Ado radical (Marsh, 1999). The means by which the enzyme activates the Co—C bond in AdoCbl for homolytic cleavage by a factor of 10^9–10^{12} (Hay & Finke, 1986; Brown & Li, 1998) remains unclear. The rate enhancement may be caused either by an upward conformational distortion of the corrin ring, induced by steric interactions with the large DMB base (Halpern, 1985; Hay & Finke, 1987; Pett *et al.*, 1987), or by the enzyme directly lengthening the Co—C bond or distorting the Co—C—C angle (Williams, 1995). Electronic effects of the *trans* ligand may also play a role in activating the Co—C bond for homolysis (Pratt, 1999). The *trans* influence refers to the effect that the β ligand has on the length of the Co—N13(DMB) bond.

We have determined the X-ray crystal structure of isoamylcobalamin (isoamylCbl), (I) (Fig. 1), a structural analogue of AdoCbl and MeCbl, in order to compare the ground-state *trans* influence of the $C_5H_{11}^-$ ligand to the β ligands in other cobalamin derivatives.



(I)

Compound (I) crystallizes in the orthorhombic space group $P2_12_12_1$ and is isomorphous with the other cobalamin derivatives belonging to packing type I (Gruber *et al.*, 1998). Selected bond lengths and angles involving the coordination sphere of the metal ion are listed in Table 1. The β alkyl ligand is disordered over two slightly different positions; in the first position [0.615 (4) occupancy], atom C65*A* points directly towards the *c* side chain, whereas in the second position [0.385 (4) occupancy], atom C65*B* points towards atom C10 when viewed from above the corrin ring. The β Co—C bond length [2.044 (3) Å] is longer than the corresponding bond length in MeCbl [average for two MeCbl structures =

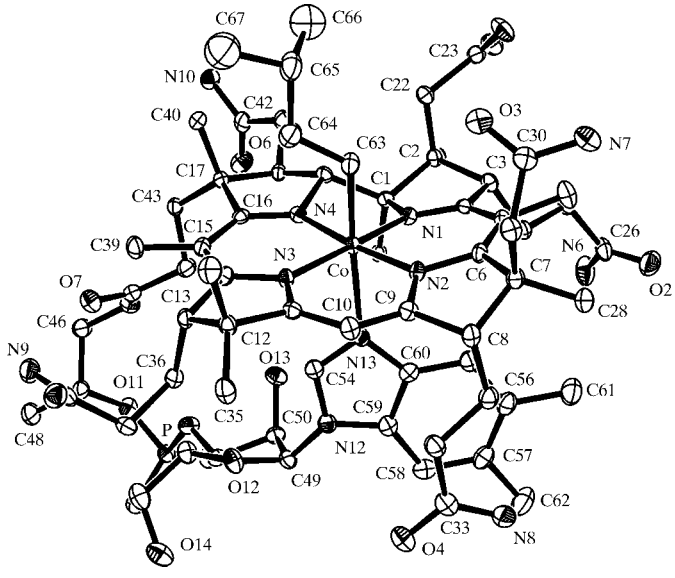


Figure 1
The molecular structure of (I). Displacement ellipsoids are drawn at the 50% probability level. H atoms, solvent atoms and disorder in the upper axial ligand have been omitted for clarity (for missing labels, see scheme).

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1.984 (7) Å; Rossi *et al.*, 1985; Randaccio *et al.*, 2000], and is also slightly longer than the corresponding bond length in AdoCbl [average for four AdoCbl structures = 2.01 (3) Å; Bouquiere *et al.*, 1993; Savage *et al.*, 1987]. The Co—N13 bond length [2.277 (2) Å] is substantially longer than that observed in MeCbl [mean for two structures = 2.18 (2) Å] and slightly longer than that in AdoCbl [average for four structures = 2.23 (2) Å], and is the second longest Co—N13 bond length reported for a cobalamin structure, the longest being for (*S*)-2,3-dihydroxypropylcobalamin (2.367 Å; Alcock *et al.*, 1985). The isoamyl group clearly is a strong σ-donor (comparable to the Ado group of AdoCbl) and markedly lengthens the *trans* Co—N13 bond. The Co—C—C angle [119.0 (3) or 116.0 (4)°] is slightly smaller than that observed for AdoCbl [mean for four structures = 122 (2)°], where there is steric pressure exerted on the adenine moiety by the C34 methyl group (Alcock *et al.*, 1985). The six amide side chains are extensively hydrogen bonded to either solvent water molecules or the side chains of symmetry-related molecules. This hydrogen-bonding scheme is similar to that of other cobalamin molecules belonging to packing type I.

The corrin fold angle, defined as the angle between the normals of the two least-squares planes passing through atoms N1, C4, C5, C6, N2, C9 and C10 (plane 1), and C10, C11, N3, C14, C15, C16 and N4 (plane 2), is calculated to be 10.57°. This angle is less than the fold angles for both MeCbl (14.72°) and AdoCbl [mean for four structures = 13.4 (6)°], and reflects the long Co—N13 bond.

Experimental

IsoamylCbl was prepared by a method similar to that used to prepare MeCbl (Brown *et al.*, 1997). CNCbl (50 mg) was dissolved in a methanol solution (40 ml) containing a 10% (*v*/*v*) acetic acid solution (10 ml). After purging the solution with argon for 40 min, zinc wool was added in excess. The reduction process was accompanied by a change in colour from red to brown and was monitored by high-pressure liquid chromatography (HPLC). Once the reduction process had been completed, a 100-fold excess of redistilled 1-bromo-3-methylbutane dissolved in deaerated methanol was transferred by canula into the reduced cobalamin solution in a darkroom, working only under dim red light. Formation of the product was again monitored by HPLC and, on completion of the reaction, the solution was transferred by canula into an empty vessel and exposed to air. The solution was then desalted on a 6 ml ISOLUTE SPE C18(EC) column and evaporated (303 K) to dryness on a rotary evaporator in the dark. The isoamylCbl solution was redissolved in the minimum amount of deionized water. Crystals were grown in H tubes in a refrigerator, by vapour diffusion of acetone into the aqueous solution. Crystals appeared after about two weeks.

Crystal data

$[Co(C_5H_{11})(C_{62}H_{88}N_{13}O_{14}P)]\cdot 0.385C_3H_6O\cdot 12.650H_2O$
M_r = 1650.69
Orthorhombic, $P2_12_12_1$
a = 15.959 (3) Å
b = 20.793 (4) Å
c = 24.403 (5) Å
V = 8098 (3) Å^3
Z = 4
D_x = 1.354 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 1015 reflections
θ = 3.0–26.5°
μ = 0.32 mm^{-1}
T = 123 (2) K
Rectangle, dark red
0.48 × 0.26 × 0.26 mm

Data collection

Bruker SMART CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.863, T_{max} = 0.922
45 443 measured reflections
16 502 independent reflections
14 388 reflections with $I > 2\sigma(I)$
R_{int} = 0.031
θ_{max} = 26.5°
$h = -20 \rightarrow 19$
$k = -17 \rightarrow 26$
$l = -30 \rightarrow 30$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.107
S = 1.05
16 502 reflections
1085 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.052P)^2 + 5.1666P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.002
$\Delta\rho_{max}$ = 0.59 e Å^{-3}
$\Delta\rho_{min}$ = −0.44 e Å^{-3}
Absolute stucture: Flack (1983), 7369 Friedel pairs
Flack parameter = 0.010 (10)

Table 1
Selected geometric parameters (Å, °).

C63—C64*A*	1.454 (10)	N2—Co	1.914 (2)
C63—C64*B*	1.506 (18)	N3—Co	1.915 (2)
C63—Co	2.044 (3)	N4—Co	1.889 (2)
N1—Co	1.869 (2)	N13—Co	2.277 (2)
C64*A*—C63—Co	119.0 (3)	C64*B*—C63—Co	116.0 (4)

H atoms were positioned geometrically and allowed to ride on their respective parent atoms, with C—H distances of 0.98–1.00 Å, N—H distances of 0.88 Å and O—H distances of 0.84–0.93 Å, and with U_{iso}(H) values equal to $1.2U_{eq}$(C) [$1.5U_{eq}$(C) for methyl groups]. The structure contains 11 ordered water molecules, one disordered water molecule and two water molecules that were assigned partial occupancy. In addition, a solvent acetone molecule was assigned partial occupancy (site occupancy = 0.385). No elemental analyses were performed, as these have been found to be unreliable with respect to the water content. The upper axial isoamyl group was found to be disordered and was refined over two positions, with the final occupancies being 0.615 (4) and 0.385 (4).

Data collection: *SMART* (Bruker, 1998); cell refinement: *SMART*; data reduction: *SAINT* (Bruker, 1999); program(s) used to solve structure: *SHELXTL* (Bruker, 1999); program(s) used to refine structure: *SHELXTL*; molecular graphics: *ORTEP*-3 (Farrugia, 1997); software used to prepare material for publication: *SHELXTL*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GD1306). Services for accessing these data are described at the back of the journal.

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