Reduction-Labile Organo-cob(III)alamins *via* Cob(II)alamin: Efficient Synthesis and Solution and Crystal Structures of [(Methoxycarbonyl)methyl]cob(III)alamin

by **Michael Puchberger**[1]), **Robert Konrat**[2]), and **Bernhard Kräutler***

Institut für Organische Chemie, Universität Innsbruck, Innrain 52a, A-6020 Innsbruck

and **Ulrike Wagner** and **Christoph Kratky***

Institut für Chemie, Universität Graz, Heinrichstrasse 28, A-8010 Graz

Dedicated to Professor *Jack D. Dunitz* on the occasion of his 80th birthday

An efficient synthesis of *Coβ*-[(methoxycarbonyl)methyl]cob(III)alamin (**6**) is reported as an example of a new method for the preparation of some easily reducible organo-cob(III)alamins *via* the alkylation of cob(II)alamin. The procedure represents a considerable improvement compared to earlier methods that were based on an alkylation of cob(I)alamin. Thus, aquacob(III)alamin chloride (**5**$^{+}\cdot$Cl) was reduced to cob(II)alamin (**4**), either by controlled potential electrolytic reduction or with an excess of sodium formate as reducing agent. The solution of **4** was then treated with an excess of methyl bromoacetate while being reductively poised potentiostatically or kept reduced by the formate, to give crystalline **6** in a yield of up to 91%. The structure of **6** in aqueous solution was mainly established by the completely assigned ^{1}H- and ^{13}C-NMR spectra (*Table 1*). The NOE data (*Table 2*) were best rationalized by the presence of a single main conformation of the (methoxycarbonyl)methyl ligand. Single crystals of **6** were obtained by crystallization from an aqueous solution, and the crystal structure was determined by X-ray analysis at cryotemperatures. The NMR and crystallographic data of **6** indicated similar structures in aqueous solution and in the crystal with the (methoxycarbonyl)methyl ligand preferring a 'southern' orientation in each case.

Introduction. – The standard method for the preparation of biologically important organo-cob(III)alamins, such as the adenosylcobamide coenzyme B_{12} (**1**, 5′-deoxy-5′-adenosylcob(III)alamin) and methylcob(III)alamin (**2**), is based on the rapid reaction of the highly nucleophilic cob(I)alamin (**3**$^{-}$; vitamin B_{12s}) with alkylation reagents, such as alkyl halides or alkyl tosylates [1–5]. The formation of **3**$^{-}$ requires strongly reducing conditions, with a rather negative half-wave potential of the critical redox couple cob(II)alamin (**4**; vitamin B_{12r})/cob(I)alamin (**3**$^{-}$) ($E_{1/2}$ (**4**/**3**$^{-}$) = −0.85 V *vs.* SCE (H_2O, pH 7) [6–8]. Indeed, the route *via* cob(I)alamin (**3**$^{-}$) in general provides a convenient way for the preparation of alkyl cob(III)alamins, as most *Coβ*-organo-cob(III)alamins are only reductively cleaved at potentials considerably more-negative than −0.85 V *vs.* SCE[3])

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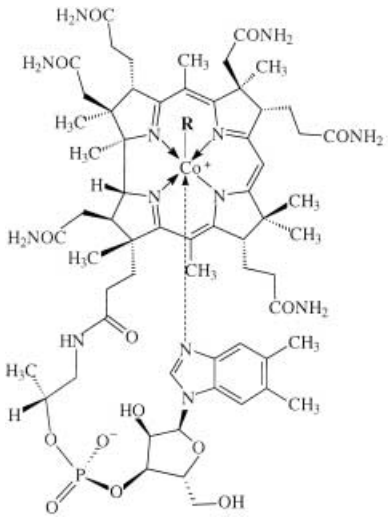
[1]) Current address: Institut für Materialchemie, Technische Universität Wien.

[2]) Current address: Institut für Theoretische Chemie und Molekulare Strukturbiologie, Universität Wien.

[3]) Methylcob(III)alamin (**2**): apparent half-wave potential of the reduction $Co^{III} \rightarrow Co^{II}$: −1.46 V *vs.* SCE (in DMF/propan-1-ol 1:1; −20°) [9].



1 **R** = 5′-deoxy-5′-adenosyl coenzyme B_{12} (Ado-Cbl)

2 **R** = Me methylcob(III)alamin (Me-Cbl)

6 **R** = $MeOC(=O)CH_2$ [(methoxycarbonyl)methyl] cob(III)alamin (Mcm-Cbl)

7 **R** = Br bromocob(III)alamin (Br-Cbl)

8 **R** = $NC–CH_2$ (cyanomethyl)cob(III)alamin (Cm-Cbl)

The redox potentials for the Co^{III}/Co^{II} couples of vitamin-B_{12} derivatives depend strongly on the nature of the axial substituents [6–10][1])[4]). As a consequence, under the strongly reducing conditions necessary for the formation of cob(I)alamin, the more easily reducible organo-cob(III)alamins can be reductively cleaved by direct electrochemical reduction [6] or by reduction with cob(I)alamin (**3**$^-$) [7].

For *Coβ*-[(methoxycarbonyl)methyl]-cob(III)alamin (**6**) in which an acceptor-substituted C-atom is directly bound to the Co-center, a peak potential of reduction of -0.90 V *vs.* SCE (in DMF, room temperature) was determined [10]. This value is close to that of the redox couple **3**$^-$/**4** [6][7]. Indeed, the difficulties encountered by *Scheffold* and co-workers [11], by *Abeles*, *Jencks*, and co-worker [12], and by *Brown* and co-workers [13] when preparing **6** *via* alkylation of cob(I)alamin (**3**$^-$) accordingly were explained by the reductively induced cleavage of the Co–C-bond of **6** [10][11][13]. Upon reduction, the organo-corrinoid **6** decomposed with formation of a (methoxycarbonyl)methyl radical (under conditions of low proton activity) or of methyl acetate (in presence of AcOH) [11].

We have become interested in exploring the alkylation of cob(II)alamin (**4**) as an alternative and mild method for the preparation of alkylcob(III)alamins and have used this method for the efficient preparation of methylcob(III)alamin (**2**) [14]. Obviously, such a method would promise to be specifically useful for the synthesis of *Coβ*-[(methoxycarbonyl)methyl]cob(III)alamin (**6**) and related organo-cob(III)alamins, which are easily reduced and which (presumably) are not stable in the presence of cob(I)alamin (**3**$^-$) [11].

Earlier, *Fukui* and co-workers reported that cob(II)alamin (**4**) and MeI in aqueous solution reacted with formation of methylcob(III)alamin (**2**) (*ca.* 50%) and aquacob(III)alamin (**5**$^+$) [15]. They suggested that **2** was generated by alkylation of the intermediate cob(I)alamin (**3**$^-$) with MeI. The nucleophilic **3**$^-$ was believed to arise

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[4]) Aquacob(III)alamin (**5**$^+$; vitamin B_{12a}): $E_{1/2}$ for the Co^{III}/Co^{II} redox couple **5**$^+$/**4**: $E_{1/2}$(**5**$^+$/**4**) = -0.04 V *vs.* SCE (in H_2O, pH 7) [6][8].

from a disproportionation of cob(II)alamin (**4**) to cob(I)alamin ($\mathbf{3}^-$) and aquacob(III)alamin ($\mathbf{5}^+$). This mechanism [15] was not supported by electrochemical investigations of *Lexa* and *Saveant*, who determined the relevant half-wave potentials $E_{1/2}$ ($\mathbf{5}^+/\mathbf{4}$) = −0.04 V and $E_{1/2}$ ($\mathbf{4}/\mathbf{3}^-$) = −0.85 V *vs.* SCE (in H_2O, pH 7) [6][8]. According to these electrochemical data, the left-hand side of the disproportionation equilibrium ($\mathbf{4} + \mathbf{4} \rightleftharpoons \mathbf{3}^- + \mathbf{5}^+$) is very much favored in the whole pH range. At equilibrium, the concentration of cob(I)alamin ($\mathbf{3}^-$) thus would not be high enough for the alkylation reaction to take place at the observed overall rate.

Blaser and *Halpern* [16] investigated the kinetics of the alkylation of vitamin B_{12r} (**4**) with various organic halides and determined the corresponding rate constants. They also concluded that the mechanism proposed by *Fukui* and co-workers [15] for the alkylation of **4** with MeI would not play an important role. Instead the reaction was suggested to take place directly *via* cob(II)alamin and radical intermediates[5]). *Scheme 1* shows the mechanism proposed by *Blaser* and *Halpern* [16] for the formation of *Coβ*-[(methoxycarbonyl)methyl]cob(III)alamin (**6**) by alkylation of **4** with methyl bromoacetate.

Scheme 1

$$B_{12r}\,(\mathbf{4}) + BrCH_2COOCH_3 \longrightarrow \text{Br-Cbl}\,(\mathbf{7}) + {}^{\cdot}CH_2COOCH_3$$

$$B_{12r}\,(\mathbf{4}) + {}^{\cdot}CH_2COOCH_3 \longrightarrow \text{Mcm-Cbl}\,(\mathbf{6})$$

$$\text{Br-Cbl}\,(\mathbf{7}) + H_2O \rightleftharpoons B_{12a}\,(\mathbf{5}^+) + Br^-$$

$$2\,B_{12r}\,(\mathbf{4}) + BrCH_2COOCH_3 + H_2O \longrightarrow \text{Mcm-Cbl}\,(\mathbf{6}) + B_{12a}(\mathbf{5}^+) + Br^-$$

We report here the efficient preparation of *Coβ*-[(methoxycarbonyl)methyl]-cob(III)alamin (**6**) from cob(II)alamin (**4**) by alkylation with methyl bromoacetate and on the analysis of the structure of **6** in solution and in the crystal.

Results. – The synthesis of *Coβ*-[(methoxycarbonyl)methyl]cob(III)alamin (**6**) starting with either electrochemical or formate reduction was investigated. All reactions were performed under inert gas in a glove box and with protection from light.

For the electrochemical reduction under potentiostatic conditions, aquacob(III)-alamin chloride ($\mathbf{5}^+ \cdot Cl^-$) was dissolved in 0.1M $Bu_4N(PF_6)$ in MeOH (see *Scheme 2*) and submitted to a controlled potential of −0.45 V (*vs.* 0.1N CE) to give the brown solution of cob(II)alamin (**4**). After the addition of an excess of methylbromoacetate, the solution was further kept at −0.45 V potentiostatically for another 32 h. Extraction of an aqueous solution of the reaction mixture with CH_2Cl_2 separated the H_2O-soluble alkylcob(III)alamin from the organic electrolyte salt. Further workup gave **6** as a microcrystalline powder (89% yield), and subsequent crystallization from cold H_2O provided red needles of **6** (75% yield).

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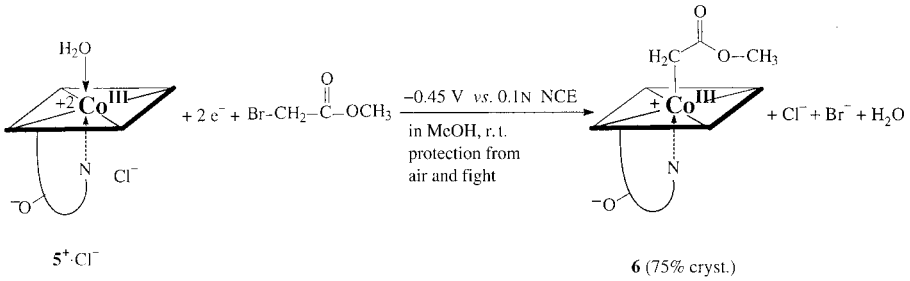
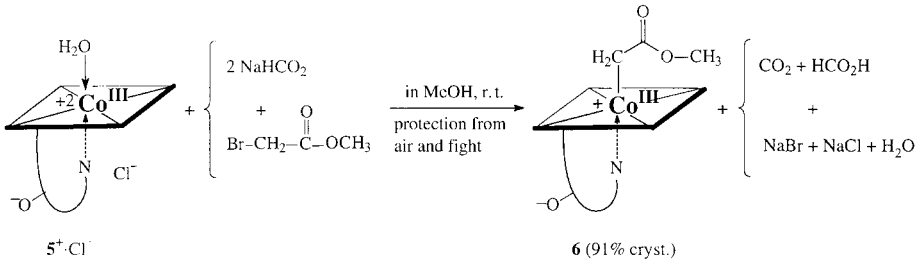
[5]) A radical mechanism was also proposed by *Schrauzer* and *Hashimoto* to account for the formation of unbranched-alkylcob(III)alamins or (ω-carboxyalkyl)cob(III)alamins under 'oxidizing-reducing' conditions in the presence of oxygen and V^{III}-salts [17].

Scheme 2



For the formate reduction (see *Scheme 3*), a deoxygenated solution of aquacob-(III)alamin chloride ($\mathbf{5}^{+}\cdot Cl^{-}$) in MeOH was treated with an aqueous solution of 3 equiv. of sodium formate. A UV/VIS spectrum showed the reduction to **4** to occur rapidly and to be complete within 5 min. After the addition of an excess of methyl bromoacetate, the O_2-free solution was stirred for 12 h in the dark and at room temperature. The workup was similar to that given above and furnished in high yield (91%) as red crystals with spectroscopic properties identical to those of the sample described above.

Scheme 3



A sample of **6** was crystallized twice, dried under high vacuum, and then identified by comparison of its UV/VIS spectrum (H_2O), IR spectrum, and FAB-MS with those of **6** reported previously by *Scheffold* and co-workers [11]. In addition, a CD spectrum of **6** in aqueous solution showed the characteristics of the spectra of *Coβ*-organocobalamins [18]. The structure of **6** in D_2O was examined by 1D and 2D NMR spectroscopy, and the assignment of the ^{1}H- and ^{13}C-NMR signals (see *Table 1* and *Fig. 1* for the atom numbering used [19]) was achieved with the help of 2D (gradient-enhanced) homo- and heteronuclear experiments, such as pulsed-field-gradient heteronuclear-single-quantum coherence (PFG-HSQC) [20] [21], and ^{1}H-detected multiple-bond heteronuclear-multiple-quantum coherence (PFG-HMBC) experiments [21][22], spin-locked NOE (ROESY) [23–25], and total correlation spectra (TOCSY) [26–28].

The ^{1}H-NMR signals of **6** could all be assigned unambiguously from these heteronuclear correlations, except for those of CH_2(21) and CH_2(71). The signals of these four protons were not resolved in their HSQC

Table 1. *Assigned Signals in the ^{1}H- and ^{13}C-NMR Spectra of* Coβ-*[(Methoxycarbonyl)methyl]cob(III)alamin* (**6**) *and Their Chemical Shifts*

	$\delta(^1H)$[a][b]	$\delta(^{13}C)$[c][d]		$\delta(^1H)$[a][b]	$\delta(^{13}C)$[c][d]
C(1)		88.7	Me(12A)	1.39	21.8
C(2)		47.6	Me(12B)	1.24	31.8
H–C(3)	4.10 (J = 9.3)	56.7	2 H–C(131)	2.06, 2.14	31.3
C(4)		178.7	2 H–C(132)	2.54	36.0
C(5)		106.5	C(133		[e])
C(6)		165.0	Me(151)	2.47	16.2
C(7)		51.0	Me(17B)	1.38	18.1
H–C(8)	3.38 (J = 10.6, 4.3)	55.7	2 H–C(171)	2.06, 2.14	33.1
C(9)		171.8	2 H–C(172)	2.54	33.7
H–C(10)	6.00	95.3	C(173)		[e])
C(11)		176.5	2 H–C(181)	2.61, 2.70	32.0
C(12)		47.4	C(182)		176.9
H–C(13)	3.21 ($J \approx$ 12.0)	54.0	2 H–C(175)	3.07 (J = 16.2, 8.5), 3.53 (J = 15.9)	45.1
C(14)		165.5	H–C(176)	4.31	73.7 (J = 6.1)
C(15)		104.5	Me(177)	1.19 (J = 6.3)	19.5
C(16)		178.0	H–C(1R)	6.25 (J = 3.1)	87.3
C(17)		59.0	H–C(2R)	4.22 (J = 3.6)	69.3
H–C(18)	2.74	40.4	H–C(3R)	4.71	73.8
H–C(19)	4.25 (J = 10.3)	73.9	H–C(4R)	4.05	82.7 (J = 7.6)
Me(1A)	0.47	20.9	2 H–C(5R)	3.72 (J = 12.8, 3.6), 3.87 (J = 12.8, 2.7)	61.3
Me(2A)	1.39	17.7	H–C(2N)	6.95	142.9
2 H–C(21)	2.40, 2.52	43.3	H–C(4N)	6.28	118.9
C(22)		[e])	C(5N)		132.6
2 H–C(31)	1.99, 2.10	27.0	C(6N)		135.3
2 H–C(32)	2.55	36.6	H–C(7N)	7.17	112.1
C(33)		[e])	C(8N)		131.0
Me(51)	2.47	16.2	C(9N)		138.6
Me(7A)	1.77	19.6	Me(10N)	2.20	19.7
2 H–C(71)	2.18, 2.51	43.3	Me(11N)	2.20	19.7
C(72)		[e])	2 H–C(1L)	0.69 (H_R), 1.30 (H_S) (J = 6.3)	12.8
2 H–C(81)	0.76, 1.82	26.5	C(2L)		185.0
2 H–C(82)	0.91, 1.77	32.1	Me(4L)	3.19	51.5
C(83)		[e])			

[a]) δ (HDO) 4.71, H_R and H_S specify $H_{pro\text{-}R}$ and $H_{pro\text{-}S}$, resp. [b]) J(H,H)-Coupling constants in Hz. [c]) δ (TSP)$_{ext}$ 0. [d]) J(C,P)-Coupling constants from the ^{13}C-NMR spectrum, in Hz. [e]) The six signals of the amide carbonyl groups at δ 175.7, 175.9, 176.5, 176.6, 177.8, and 178.7 were not individually assigned.

spectrum, because the corresponding signals of C(21) and C(71) overlapped completely at δ 43.3. These signals could be assigned, however, *via* the NOEs observed in the 2D-ROESY experiment (see *Tables 1* and *2*). The signals of the two diastereotopic protons of CH_2(1L) of the (methoxycarbonyl)methyl ligand were well separated and appeared at δ 0.69 and 1.30 (in contrast to the observation of a single broad signal at δ *ca.* 0.59 in DMSO [11]). The signal of the MeO group appeared at δ 3.19, but was overlapping with the *m* of H–C(13).

With the exception of the six carbonyl C-atoms (C(22), C(33), C(72), C(83), C(133), and C(173)), all ^{13}C-NMR signals were individually assigned. The signals of all three C-atoms of the (methoxycarbonyl)methyl ligand could now be observed (in contrast to the earlier report [11]) and appeared at δ 12.8 (CH_2(1L)), 185.0 (carbonyl C(2L)), and 51.5 (MeO). These chemical-shift values may be compared with those of the signals of methyl acetate [29], at δ 20.6 (Me), 171.3 (C=O), and 51.5 (MeO).

Table 2. *ROESY Intensities and Crystallographic Interproton Distances of* Coβ-*[(Methoxycarbonyl)methyl]cob-(III)alamin* (**6**)

H,H Pair[a])	ROESY[b])	X-Ray[c])	H,H Pair[a])	ROESY[b])	X-Ray[c])
H−C(19), Me(17B)	16.9	2.37	H_R−C(1L), H_S−C(1L)	100	1.76
H−C(19), H_a−C(21)	19.5	1.93	H_R−C(1L), H_a−C(71)	8.1	2.36
H−C(19), H_b−C(21)	17.7	2.14	H_R−C(1L), H_b−C(71)	2.3	3.62
H−C(10), Me(12B)	15.6	2.87	H_S−C(1L), H_b−C(21)	5.4	2.69
H−C(10), Me(12A)	45.2	2.01	H_S−C(1L), H_a−C(21)	–[d])	4.24
H−C(8), H−C(10)	37.0	2.52	H_S−C(1L), H−C(19)	10.6	3.20
			Me(4L), Me(17B)	–[d])	2.40

[a]) H_R and H_S specify $H_{pro\text{-}R}$ and $H_{pro\text{-}S}$, resp. [b]) Rel. intensities in %. [c]) Calculated H,H-distances in Å. [d]) Not determined (signal overlap).

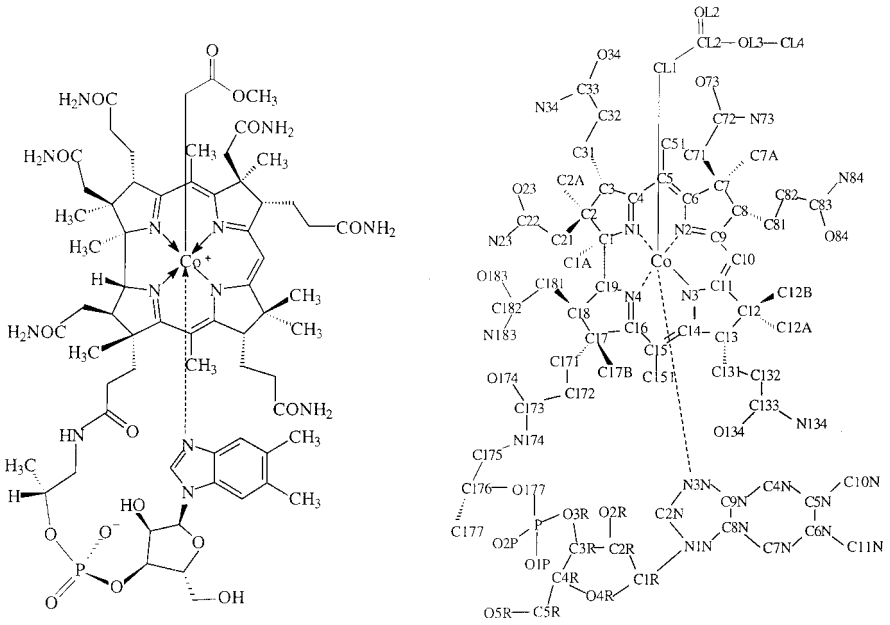


Fig. 1. *Atom numbering of* **6**

For the purpose of a conformational analysis of the structure of **6** in solution, and, specifically, of the (methoxycarbonyl)methyl ligand with respect to the corrin macrocycle, a 2D-ROESY experiment was performed. Two cross-peaks from ligand H-atoms to the corrin ring were found, both due to the two diastereotopic CH_2 protons of the (methoxycarbonyl)methyl group (see *Table 2*): the low-field proton ($H_{pro\text{-}S}$−C(1L) at $\delta = 1.30$) correlated with H−C(19) (at δ 4.25) and the high-field proton ($H_{pro\text{-}R}$−C(1L) at $\delta =$ 0.69) correlated with H_a−C(71) (at δ *ca.* 2.18). In addition, both of the two diastereotopic CH_2(1L) protons correlated with a signal(s) at δ 2.52 (where H_b−C(21) and H_b−C(71) overlapped). These NOE data confirmed the assignment of the low-field signal to $H_{pro\text{-}S}$−C(1L) and of the high-field signal to $H_{pro\text{-}R}$−C(1L) of the Co-bound CH_2 group. Furthermore, the overlapping signals of the MeO protons and of H−C(13) gave rise to cross-peaks to δ 1.24 (Me(12B)), 1.39 (Me(12A)), and 2.50 (CH_2(132) and Me(151)). Unfortunately, due to signal overlap, all three of these correlations may be from H−C(13), rather than from the protons of the Me group of the (methoxycarbonyl)methyl ligand, but significant further correlations were not seen in the spectrum.

The NOE data of **6** are consistent with an orientation of the (methoxycarbonyl)-methyl ligand in which the MeO substituent would be placed close to ring C of the corrin ligand, *i.e.*, similar to the conformation observed in the crystal (see below). However, the absence of significant NOE cross-peaks of the MeO group with Me(17B) as well as the NOEs between the corrin ligand and the protons of the Co-bound CH_2 C-atom would favor dominant conformations in which the (methoxycarbonyl)methyl moiety is oriented somewhat more counterclockwise than in the crystal structure.

To corroborate the NMR-based conformational assignments, an X-ray crystal-structure analysis of **6** was performed. Crystals were obtained by adding acetone to an aqueous solution of **6**, and crystallographic data were collected as described in the *Exper. Part*. The structural model refined to a reasonable R value ($R = 8.6\%$) taking into account that diffractometer data collected on a sealed-tube X-ray generator were used. Compound **6** crystallizes in the orthorhombic space group $P2_12_12_1$ with four cobalamin molecules and numerous solvent molecules (one acetone and *ca.* 18 H_2O molecules, some disordered, per cobalamin molecule) per unit cell. The packing of the cobalamin molecules in crystals of **6** conforms to one of the packing motifs observed in the majority of vitamin-B_{12} crystal structures [19][30]. Two views of the molecular structure as obtained from the crystal structure analysis are shown in *Fig. 2*.

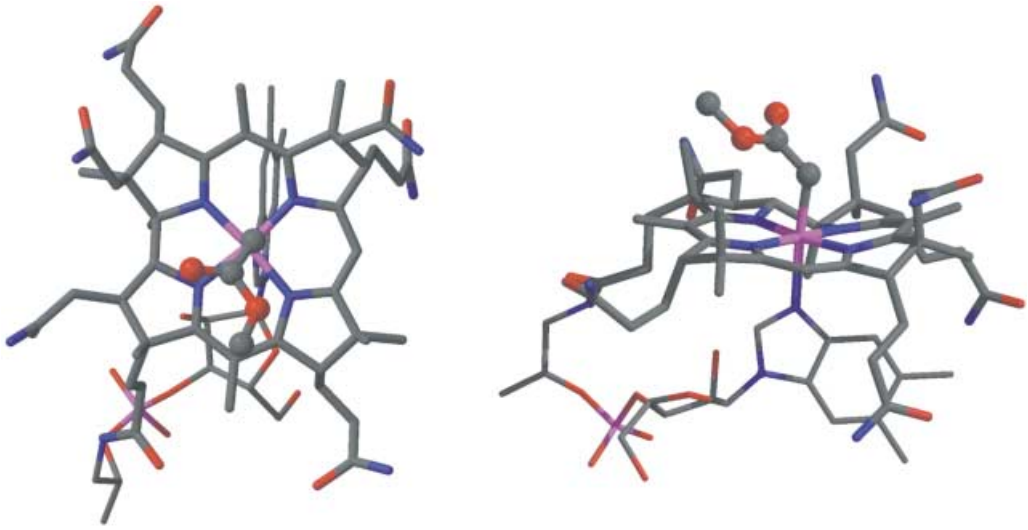


Fig. 2. *Two projections of the crystal structure of* Co*β*-*[(methoxycarbonyl)methyl]cob(III)alamin* (**6**). Stick model with hetero atoms color coded (Co magenta, O red, N blue, P pink) and featuring in 'ball-and-sticks' the (methoxycarbonyl)methyl ligand.

Discussion. – The easily reducible organo-cob(III)alamin *Co*β-[(methoxycarbonyl)methyl]cob(III)alamin (**6**) was prepared efficiently and in high yield by alkylation of cob(II)alamin (**4**). This method proved to be an excellent alternative to the well-established preparation of related organo-vitamin-B_{12} derivatives *via* alkylation of cob(I)alamin ($\mathbf{3}^-$) [1][3]. Under appropriate conditions, both methods are simple, and

high yields of the products may be achieved by either method [2][3]. The alkylation of cob(I)alamin ($\mathbf{3}^-$) may not give good yields of organo-cob(III)alamins, in case these are easily reduced by $\mathbf{3}^-$ [11][13]. The mechanism of the formation of **6** by alkylation of **4** was not investigated here in detail, but, clearly, it does not follow a nucleophilic substitution pathway. Instead, and according to the earlier proposal by *Blaser* and *Halpern*, radicals are likely to be involved (see above) [16]. Such a radical mechanism would indeed be in accord with the typical reactivity of vitamin B_{12r} (**4**) as a Co^{II} radicaloid [1][31] (*Scheme 1*).

The spectroscopic data indicate the structure of **6** in aqueous solution to be that of a base-on corrinoid in which the (methoxycarbonyl)methyl ligand is bound in an orientation with the MeO group close to ring C of the corrin ligand. A main difficulty for the characterization of **6** was caused by its low solubility in H_2O. *Scheffold* and co-workers used DMSO as a solvent for the characterization of **6** (but had difficulties in finding all of the major signals; see above) [11]. To simplify the comparison of various spectroscopic data of **6** with that from other vitamin-B_{12} derivatives, the spectroscopic work reported here was carried out mainly with H_2O as solvent. The ^1H- and ^{13}C-NMR chemical shifts of **6** were found to be rather similar to that of other *Coβ*-substituted vitamin-B_{12} derivatives, such as methylcob(III)alamin (**2**) [32–34], coenzyme B_{12} (**1**) [35][36], and similar 'complete' corrinoids in their base-on form [37][38]. From the NOE data, the (methoxycarbonyl)methyl ligand of **6** was characterized qualitatively in its conformation with respect of the corrin ligand (see *Table 2*) as being positioned towards the 'south' mainly, *i.e.*, close to ring C and the *γ-meso* position. A similar conformational preference of the *Coβ*-ligand is found in coenzyme B_{12} (**1**) and in most organo-cobalamins [19][30] and may arise from steric effects mainly.

The crystal-structure analysis (*Fig. 2*) shows molecules of **6** to occur in the crystal in a base-on form, in agreement with the available spectroscopic data of aqueous solutions of **6**. The (methoxycarbonyl)methyl moiety is observed in a conformation with the MeO group pointing 'southwards', *i.e.*, it is located roughly above the CH_2 group connecting rings C and D. While the accuracy of the crystal-structure analysis does not permit detailed discussion of the binding geometry, there is little indication for unusual bonding features. Specifically, the binding geometry of the axial Co ligands is similar to what was observed in methylcob(III)alamin (**2**) [32], *i.e.*, $d(Co-C_{ax}) = 2.03$ Å (*vs.* 1.98 Å in **2**), $d(Co-N_{ax}) = 2.16$ Å (*vs.* 2.16 Å). The observed upward-folding angle of the corrin ring is 16°, which fits reasonably into the correlation between fold angle and $Co-N_{ax}$ distance derived from a selection of accurate vitamin-B_{12} crystal structures [30]. The solution and the crystal structures of the vitamin-B_{12} derivative **6** are similar and show the features of a typical organo-cob(III)alamin in the base-on form.

In conclusion, the alkylation of 'complete' Co^{II}corrinoids [14][17] is presented here as a very useful method for the synthesis of reduction-labile Co^{III}organo-corrinoids. It is an alternative method to the more established synthetic procedures *via* Co^{I}corrinoids and is particularly efficient and practical for the preparation of easily reduced organo-corrinoids. As reported here, it allowed the efficient preparation of *Coβ*-[(methoxy-carbonyl)methyl]cob(III)alamin (**6**). In a further example of the same procedure, also crystalline *Coβ*-(cyanomethyl)cob(III)alamin (**7**) was prepared in high yield [39]. These procedures exploit the unique kinetic effect in radical reactions of Co^{II} corrinoids as persistent radicaloids (see, *e.g.*, [40]), and their high rates in bond-forming reactions

with radicals [16][41]. However, it may also be useful to consider a role for Co^{II} corrinoids in the formation of organo-vitamin-B_{12} derivatives in biological processes with organohalides. Vitamin-B_{12} derivatives play a crucial role in enzymatic (and other) reductive dehalogenation reactions [42][43], which often concern easily reducible organohalides and frequently produce rather easily reducible organo-corrinoids [44]. In some natural processes of this type, Co^{II}corrinoids may thus be rather relevant reactive intermediates in the formation of organo-vitamin-B_{12} derivatives.

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Experimental Part

1. *General.* Sample preparations were performed in a dark room. Chemicals and solvents: Aquacobalamin chloride (vitamin B_{12a}; pyrogen-free Fr. Ph. BP, 10.7% loss on drying, $<2\%$ cyanocobalamin) from *Roussel Uclaf*; methyl bromoacetate (*Fluka*, *purum*), distilled before use; (Bu_4NPF_6) (*Fluka*, *puriss.*), recrystallized 3 times from CH_2Cl_2/Et_2O; sodium formate (*Fluka*, *BioChemika*); Et_3N (*Fluka*, *puriss.*), distilled before use; MeOH (*Fluka*, *puriss.*), distilled from Mg; CH_2Cl_2 (*Fluka*, *puriss.*), filtered over basic aluminum oxide (*Woelm Pharma*, activity grade 1), acetone (*Fluka*, *puriss.*). UV/VIS Spectra: λ_{max} in nm, ε in $dm^3/mol \cdot cm$: *Uvikon 860* or *Perkin-Elmer PE-555*. CD Spectra: λ in nm, $\Delta\varepsilon$ in $dm^3/mol \cdot cm$, λ_0 in nm; *Jobin-Yvon Mark III*. IR Spectra: $\tilde{\nu}$ in cm^{-1}; *Perkin-Elmer 983*. ^{1}H-NMR Spectra: in $D_2O + 5\%$ CD_3OD; δ(HDO) 4.71, apparent coupling constants *J* in Hz; *Bruker WM-300*, *Bruker AMX-400*, or *Varian Unityplus 500*. ^{13}C-NMR spectra: in $D_2O + 5\%$ CD_3OD; δ in ppm rel. to external sodium 3-(trimethylsilyl)propane-1-sulfonate (DSS); *Bruker AMX-400* (100.62 MHz). Mass spectra: FAB, 3-nitrobenzyl alcohol; *m/z* (rel. % base peak); *VB-ZAB2-SEQ*, 8 kV acceleration voltage, Cs^+-ion gun.

2. *2D-NMR Experiments. Varian Unityplus 500*; 5-mm indirect-detection probe equipped with gradient facilities.

Pulsed-field-gradient-enhanced heteronuclear-single-quantum-coherence experiment (HSQC) [20][21]: Indirect detection of the low C(γ) nuclei was achieved by means of gradient-enhanced HSQC [20][21]. Two sets of spectra were recorded and processed according to the recipe of *States et al.* [45] to yield a pure absorption spectrum with quadrature in F_1. The one-bond ^{1}H, ^{13}C-shift-correlation spectrum resulted from a $2 \times 256 \times 1024$ data matrix size, with four scans per t_1 value and a delay time between scans of 0.6 s. The first gradient was applied with a strength of 19.75 G/cm and a duration of 2 ms, while the second gradient pulse of 19.48 G/cm was applied for 0.5 ms. Both gradients were rectangular and were applied along the *z* axis. Decoupling (during acquisition) was achieved with the GARP decoupling sequence [46], by using a 3.8-kHz radio frequency field. Shifted squared sine-bell window functions were used for both t_1 and t_2.

Pulsed-field-gradient-enhanced ^{1}H-detected multiple-bond heteronuclear-multiple-quantum-coherence experiments (PFG-HMBC) [21–23]: Magnitude-mode spectra were obtained by using the standard gradient-enhanced HMQC pulse sequence [21] with an additional low-pass filter as in the original HMBC experiment [22]. Values of δ_1 and δ_2 were 3.3 and 60 ms, respectively. The multiple-bond ^{1}H, ^{13}C-shift-correlation spectrum resulted from a 512×2048 data matrix size, with 128 scans per t_1 value and a delay time between scans of 1 s. The first two gradients were applied with strengths of 9.87 G/cm each, while the third gradient pulse had a strength of 4.98 G/cm. The durations of the three gradient pulses were 2 ms. All gradients were rectangular and were applied along the *z* axis. *Gaussian* line broadening was used prior to *Fourier* transformation for both t_1 and t_2.

Spin-locked NOE spectroscopy (ROESY) [24][25]: The ROESY resulted from a 512×1024 data matrix before and $1K \times 2K$ after zero-filling, with 32 scans per t_1 value. The predelay was 1.5 s, and the mixing time was 200 ms. A 1.8-kHz radio-frequency-field strength was used. A cosine bell squared filter and additional line broadening, to avoid truncation effects, were used in both t_1 and t_2 dimensions. Quadrature detection in F_1 was achieved by means of the recipe of *States et al.* [45].

Total correlation spectroscopy (TOCSY) [26–28] or homonuclear *Hartmann-Hahn* spectroscopy (HOHAHA) [35][47]: The HOHAHA spectrum resulted from a 512×1024 data matrix with 32 scans per t_1 value. A MLEV-17 mixing sequence [48] of 75 ms preceded by a 2.0 ms trim pulse was used. A 14.2-kHz radio-frequency-field strength (corresponding to 17.6 μs 90° ^{1}H pulse width) was used. A cosine bell squared filter and

additional line broadening, to avoid truncation effects, were used in both t_1 and t_2 dimensions. Quadrature detection in F_1 was achieved by means of the recipe of *States et al.* [45].

3. *Experimental Setup*. All prep. experiments were carried out in a glove box (*Mecaplex GB-80*) containing less than 3 ppm of O_2. The workup of the reactions was done outside of the glove box in a dark room under dim light. Electrolysis: *PAR* model *170*, two-compartment electrolysis cell, Hg-pool working electrode, Pt counter electrode, 0.1N calomel reference electrode (0.1N CE) (see [3] for a general discussion).

4. *Electrochemical Preparation of* Co*β-[(methoxycarbonyl)methyl]cob(III)alamin* (**6**). In the glove box, aquacobalamin chloride ($\mathbf{5}^+ \cdot Cl^-$; 100 mg, 79.5 μmol) was dissolved in 0.1M $Bu_4N(PF_6)$/MeOH (5 ml). This soln. was added into the cathode compartment of an electrochemical cell, containing a Hg pool as cathode material. The anode compartment and the solvent bridge of the electrolysis cell were each charged with 0.1M $Bu_4N(PF_6)$/MeOH (*ca.* 6 ml). The soln. was reduced under stirring at −0.45 V (*vs.* 0.1M CE) until the current had dropped from 0.6 mA to a level of 0.1 mA, and the color had changed from red to brown, indicating the reduction of cob(III)alamin to cob(II)alamin. Then the light was reduced, and methyl bromoacetate (110.4 μl, 1190 μmol) was added by syringe, whereupon the color of the soln. changed slowly from brown to red. The electrolysis at −0.45 V was continued under stirring for 32 h when a UV/VIS spectrum indicated the end of the reaction. The MeOH reaction soln. was poured into ice/H_2O (10 ml) and extracted with CH_2Cl_2 (3 × 20 ml). The aq. soln. contained $\mathbf{5}^+$ in its 'base-off' form according to its UV/VIS spectrum (λ_{max} *ca.* 470 nm) and was evaporated at r.t. The red residue was dissolved in H_2O (2 ml) containing 0.5% of Et_3N. This soln. was then added to acetone (30 ml) at 0°, leading to precipitation of the product. The precipitate was washed with acetone and dried to give 133.8 mg (88.8%) of a fine red powder. The powder was dissolved in MeOH, the soln. evaporated, the remaining residue again dissolved in a minimum of H_2O (6 ml), and the product crystallized in the refrigerator. Drying of the precipitate gave 112.9 mg (74.9%) of **6**. Red needles.

5. Co*β[(methoxycarbonyl)methyl]cob(III)alamin* (**6**) *by Formate Reduction*. In the glove box, sodium formate (13.2 mg, 194.1 μmol) was dissolved in H_2O (1 ml). This soln. was slowly added to a mixture of MeOH (4 ml) and aquacobalamin chloride ($\mathbf{5}^+ \cdot Cl^-$; 87.611 mg, 63.3 μmol). After 5 min, the color had changed from red to brown, indicating the reduction of $\mathbf{5}^+$ to cob(II)alamin (**4**). Then the light was reduced, and methyl bromoacetate (88 μl, 948 μmol) was added by syringe. After 12 h stirring in the dark, the alkylation was complete (UV/VIS) and the color of the soln. had changed from brown to red. The MeOH reaction soln. was poured in H_2O (10 ml) and extracted with CH_2Cl_2 (20 ml). The aq. soln. was evaporated at r.t. and the red residue was dissolved in H_2O (2 ml). The soln. was then added to acetone (30 ml), leading to precipitation of the compound. The precipitate was washed with acetone and dried, the powder dissolved in MeOH, the soln. again evaporated, the remaining residue dissolved in a minimum of H_2O (4 ml), and the product crystallized in the refrigerator. Drying of the precipitate gave 80.8 mg (91.1%) of **6**. Red crystals. UV/VIS ($c = 7.2 \cdot 10^{<M->5}$ M, H_2O): 260 (22230), 277 (sh., 18620), 287 (sh., 15960), 330 (12030), 347 (12190), 369 (11170), 421 (4680), 525 (7180), 545 (sh., 6460). CD ($c = 7.2 \cdot 10^{-5}$ M, H_2O): 259 (−6.10), 280 (−1.80), 288 (sh., −0.69), 302 (sh., 2.91), 325 (8.04), 358 (−10.30), 425 (−9.56), 473 (8.45), 520 (sh., 4.30), 564 (−1.39), 605 (0.28); λ_0 at 247, 292, 340, 384, 453, 548, 587. IR (KBr): 3400*s* (br.), 3190*s*, 2970*m* (sh.), 2940*m*, 2880*m* (sh.), 1667*s* (br.), 1625*s* (sh.), 1568*m*, 1545*w* (sh.), 1490*s*, 1480*m* (sh.), 1450*m*, 1435*m*, 1400*m*, 1350*m*, 1310*w*, 1230*m* (sh.), 1157*m*, 1100*m* (sh.), 1070*m*, 1020*m*, 996*m*, 925*w*, 900*w*, 865*w*, 848*w*. ^{1}H-NMR (500 MHz) and ^{13}C-NMR (125.15 MHz) in D_2O: see *Table 1*. MS: 1424.7 (31, $[M + Na]^+$), 1402.7 (49, $[M + H]^+$), 1351.8 (51, $[M + Na - C_3H_5O_2]^+$), 1329.8 (100, $[M^+ < M - > C_3H_5O_2]^+$), 1069.7 (16).

7. *X-Ray Analysis*. Red crystals of **6** were grown from H_2O/acetone. A specimen of the dimension 0.2 × 0.15 × 0.1 mm^3 was immersed into a drop of hydrocarbon oil, picked up with a glass fiber, and quickly cooled to cryotemperature in the cold gas stream of the cryostat. All diffraction experiments were carried out on a locally constructed 4-circle diffractometer (sealed-tube generator, MoK_α radiation, graphite monochromator, λ = 0.71069 Å) equipped with a gas-stream low-temp. device (temp. of gas stream 107(2) K). Crystals are orthorhombic, space group $P2_12_12_1$, $a = 15.995(20)$ Å, $b = 22.101(28)$ Å, $c = 26.102(35)$ Å, $V = 9227.2$ Å^3, $Z = 4$ for $(C_{65}H_{93}CoN_{13}O_{16}P) \cdot (C_3H_6O) \cdot (H_2O)_{14.5}$; M_r 1402.42, calc. density 1.239 mg/m^3, $F(000) = 3684$; 7375 reflections were collected for $4.11 \leq \theta \leq 24.00°$ ($0 \leq h \leq 17$, $0 \leq k \leq 25$, $0 \leq l \leq 29$), yielding 6963 independent reflections ($R_{int} = 0.1459$).

The structure of was solved by locating the Co-atom from a *Patterson* synthesis and then locating the lighter atoms in subsequent electron-density maps. It was refined by full-matrix least-squares on F^2, by using various versions of the program SHELX [49]. An empirical absorption correction (program DIFABS [50]) was applied to the data. Scattering factors including real and imaginary dispersion corrections were taken from the *International Tables of Crystallography*.

Table 3. *Atomic Coordinates* ($\times 10^4$) *and Equivalent Isotropic Displacement Parameters* ($Å^2 \times 10^3$) *for* Co*β-[(Methoxycarbonyl)methyl]cob(III)alamin* (**6**). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	*y*	*z*	*U*(eq)
Co	– 2378(1)	– 5949(1)	– 2456(1)	31(1)
C(1)	– 3543(7)	– 6814(5)	– 2917(5)	32(2)
C(2)	– 4523(7)	– 6959(5)	– 2831(5)	35(2)
C(3)	– 4909(7)	– 6304(5)	– 2819(4)	32(2)
C(4)	– 4196(7)	– 5923(5)	– 2607(5)	32(2)
C(5)	– 4306(7)	– 5322(5)	– 2368(5)	38(3)
C(6)	– 3624(8)	– 4953(5)	– 2276(5)	38(3)
C(7)	– 3634(7)	– 4319(5)	– 2053(4)	32(2)
C(8)	– 2727(7)	– 4068(5)	– 2232(4)	38(2)
C(9)	– 2271(7)	– 4661(5)	– 2261(5)	36(3)
C(10)	– 1400(7)	– 4711(6)	– 2167(5)	37(3)
C(11)	– 925(7)	– 5252(6)	– 2165(5)	39(3)
C(12)	– 38(7)	– 5276(5)	– 1972(5)	39(3)
C(13)	279(7)	– 5888(5)	– 2211(5)	35(2)
C(14)	– 585(7)	– 6228(5)	– 2274(5)	34(2)
C(15)	– 648(8)	– 6852(5)	– 2349(5)	40(3)
C(16)	– 1447(7)	– 7115(6)	– 2494(5)	40(3)
C(17)	– 1638(7)	– 7803(5)	– 2557(5)	36(2)
C(18)	– 2504(7)	– 7771(4)	– 2838(5)	36(2)
C(19)	– 2886(7)	– 7196(5)	– 2620(5)	33(2)
N(1)	– 3450(5)	– 6190(4)	– 2664(4)	31(2)
N(2)	– 2771(6)	– 5139(4)	– 2356(4)	36(2)
N(3)	– 1219(6)	– 5790(4)	– 2284(4)	37(2)
N(4)	– 2146(5)	– 6795(4)	– 2542(4)	33(2)
C(1A)	– 3287(8)	– 6780(6)	– 3492(5)	37(3)
C(2A)	– 4880(7)	– 7365(5)	– 3248(5)	37(3)
C(51)	– 5171(7)	– 5132(5)	– 2240(5)	37(3)
C(7A)	– 4336(8)	– 3880(5)	– 2208(5)	40(3)
C(12A)	481(8)	– 4724(6)	– 2103(7)	58(4)
C(12B)	– 60(9)	– 5339(7)	– 1381(6)	59(4)
C(151)	108(7)	– 7235(6)	– 2276(5)	42(3)
C(17B)	– 1702(8)	– 8107(6)	– 2023(5)	41(3)
C(21)	– 4653(6)	– 7256(6)	– 2298(4)	39(3)
C(22)	– 5537(7)	– 7377(5)	– 2120(5)	38(3)
O(23)	– 6166(5)	– 7190(4)	– 2368(4)	53(2)
N(23)	– 5628(6)	– 7720(5)	– 1713(4)	49(3)
C(31)	– 5209(7)	– 6001(6)	– 3325(4)	41(3)
C(32)	– 6149(7)	– 6150(6)	– 3470(4)	46(3)
C(33)	– 6390(7)	– 5793(6)	– 3951(5)	48(3)
O(34)	– 6707(6)	– 5282(4)	– 3916(4)	64(3)
N(34)	– 6259(7)	– 6066(5)	– 4394(4)	55(3)
C(71)	– 3615(8)	– 4397(5)	– 1451(4)	43(3)
C(72)	– 3569(7)	– 3815(6)	– 1163(4)	40(3)
O(73)	– 4260(5)	– 3551(5)	– 995(4)	72(3)
N(73)	– 2856(5)	– 3597(4)	– 1066(4)	35(2)
C(81)	– 2774(7)	– 3745(5)	– 2760(4)	44(3)
C(82)	– 1918(7)	– 3570(6)	– 2997(5)	50(3)
C(83)	– 1976(8)	– 3252(7)	– 3490(5)	62(3)
O(84)	– 2634(6)	– 2972(5)	– 3643(4)	72(3)
N(84)	– 1330(7)	– 3290(7)	– 3804(5)	90(5)

Table 3 (cont.)

	x	*y*	*z*	*U*(eq)
C(131)	687(6)	– 5874(6)	– 2756(5)	40(3)
C(132)	1622(6)	– 5664(6)	– 2760(5)	44(3)
C(133)	2162(7)	– 6006(5)	– 2392(5)	45(3)
O(134)	2255(7)	– 6588(4)	– 2425(5)	79(3)
N(134)	2518(6)	– 5711(4)	– 2028(4)	41(2)
C(181)	– 3080(7)	– 8339(4)	– 2765(4)	32(3)
C(182)	– 2787(7)	– 8920(5)	– 3020(5)	36(3)
O(183)	– 2556(5)	– 8921(4)	– 3482(3)	42(2)
N(183)	– 2838(6)	– 9418(4)	– 2749(4)	45(3)
C(171)	– 987(7)	– 8187(6)	– 2871(4)	41(3)
C(172)	– 712(7)	– 7919(5)	– 3397(4)	39(3)
C(173)	78(7)	– 8238(5)	– 3579(4)	40(3)
O(174)	756(5)	– 8199(4)	– 3347(3)	46(2)
N(174)	5(6)	– 8567(4)	– 4008(4)	39(2)
C(175)	713(8)	– 8867(5)	– 4260(5)	37(3)
C(176)	1085(7)	– 8479(6)	– 4698(5)	39(3)
C(177)	1707(8)	– 8839(6)	– 5012(5)	44(3)
P	215(2)	– 7664(2)	– 5233(1)	38(1)
O(1P)	– 564(6)	– 7679(4)	– 5549(4)	46(2)
O(2P)	980(5)	– 7407(4)	– 5489(3)	41(2)
O(177)	374(5)	– 8347(3)	– 5044(3)	39(2)
C(1R)	– 652(8)	– 5825(6)	– 4311(5)	41(2)
C(2R)	– 877(7)	– 6434(6)	– 4556(5)	34(2)
O(2R)	– 1270(5)	– 6800(4)	– 4164(3)	38(2)
C(3R)	1(7)	– 6653(5)	– 4691(5)	40(2)
O(3R)	65(5)	– 7312(4)	– 4689(3)	40(2)
C(4R)	574(7)	– 6387(6)	– 4287(5)	40(3)
O(4R)	130(5)	– 5889(4)	– 4057(3)	44(2)
C(5R)	1408(8)	– 6165(7)	– 4506(6)	51(3)
O(5R)	1280(7)	– 5688(4)	– 4880(4)	62(3)
N(1N)	– 1254(6)	– 5618(5)	– 3925(4)	39(2)
C(2N)	– 1353(7)	– 5863(5)	– 3447(5)	38(3)
N(3N)	– 2066(6)	– 5690(4)	– 3228(4)	32(2)
C(4N)	– 3250(8)	– 5018(5)	– 3579(5)	41(3)
C(5N)	– 3505(7)	– 4669(5)	– 4007(5)	37(3)
C(6N)	– 2951(8)	– 4613(6)	– 4442(5)	44(3)
C(7N)	– 2221(8)	– 4905(5)	– 4459(5)	41(3)
C(8N)	– 1976(8)	– 5261(5)	– 4033(5)	35(2)
C(9N)	– 2465(8)	– 5312(5)	– 3588(5)	36(2)
C(10N)	– 4344(8)	– 4343(6)	– 3999(5)	50(3)
C(11N)	– 3234(10)	– 4241(6)	– 4902(5)	58(4)
C(L1)	– 2654(8)	– 6043(5)	– 1701(4)	38(2)
C(L2)	– 2401(10)	– 6580(7)	– 1412(5)	52(3)
O(L2)	– 2828(7)	– 7059(5)	– 1359(4)	64(3)
O(L3)	– 1622(6)	– 6524(4)	– 1220(4)	58(2)
C(L4)	– 1273(10)	– 7019(7)	– 893(6)	67(4)
O(1Solv)	– 2663(6)	– 2379(4)	– 9657(3)	51(2)
O(2Solv)	– 1084(5)	– 1254(4)	– 9130(3)	49(2)
O(3Solv)	– 3323(6)	– 1206(4)	– 9441(4)	60(3)
O(4Solv)	– 1758(7)	– 2180(5)	– 1621(4)	73(3)
O(5Solv)	– 1138(10)	– 1843(6)	– 6168(6)	115(5)
O(6Solv)	– 2771(6)	– 2447(4)	– 728(4)	58(3)

Table 3 (cont.)

	x	*y*	*z*	*U*(eq)
O(7Solv)	– 1423(6)	– 721(5)	– 6722(4)	65(3)
O(8Solv)	– 3352(15)	– 2561(10)	– 4599(7)	183(9)
O(9Solv)	– 5017(39)	– 2994(29)	– 4433(24)	367(22)
O(10Solv)	– 2457(11)	– 219(7)	– 5191(7)	142(6)
O(11Solv)	– 2709(20)	– 1571(13)	– 5251(15)	288(16)
O(12Solv)	– 5020(76)	– 2788(52)	– 4657(36)	276(24)
O(13Solv)	– 5113(80)	– 2811(60)	– 4900(44)	351(27)
O(14Solv)	– 827(21)	– 4276(15)	– 5549(13)	129(11)
O(15Solv)	– 161(19)	– 3685(14)	– 5978(13)	124(10)
O(16Solv)	542(29)	– 4596(21)	– 5764(18)	189(17)
O(17Solv)	– 5904(20)	– 2887(15)	– 5451(12)	122(10)
O(18Solv)	– 5913(45)	– 3816(33)	– 5123(29)	532(36)
O(1Acet)	– 4904(9)	– 954(9)	– 6483(6)	128(5)
C(2Acet)	– 4472(13)	– 753(8)	– 6147(9)	92(5)
C(3Acet)	– 3637(12)	– 462(8)	– 6253(8)	93(5)
C(4Acet)	– 4722(12)	– 775(9)	– 5606(8)	95(5)

Anisotropic a.d.p.s were refined for all non-H-atoms of the cobalamin moiety, applying a 'rigid-bond' restraint [51] (effective standard deviation $= 0.01$ Å^2) for all 1,2- and 1,3-distances. H-Atom positions were calculated and refined as 'riding' on their respective non-H-atom. Methyl torsion angles were chosen to maximize the electron density at the three calculated H-atom positions and allowed to refine. An analogous procedure was applied to the two ribose OH groups. The (isotropic) a.d.p.s for the H-atoms were set to 1.5 times the equivalent isotropic a.d.p. of the adjacent non-H-atom. Chemically equivalent bond lengths and 1,3-distances of the amide side chains were restrained to be equal, the atoms of the amide groups and of the imidazole base were restrained to be coplanar.

The solvent electron density was modelled by including one molecule of acetone (anisotropic a.d.p.s) plus H_2O molecules on 18 sites, of which 11 were fully occupied (refined with anisotropic a.d.p.s) and 7 partially occupied (included in the refinement with half occupancy and isotropic a.d.p.).

Refinement of 1045 parameters against 6963 intensity data and 1762 restraints converged at the following values for the reliability indices: $R_1 = 0.1604$, $wR_2 = 0.2063$ (for all reflections) $R_1 = 0.0863$, $wR_2 = 0.2533$ (for data with $I > 2(I)$). Goodness-of-fit $= 0.921$. Features up to 0.688 e·Å^{-3} and down to -0.454 e·Å^{-3} were observed in a final difference electron density map. The absolute structure parameter [52] converged to 0.01(4) (a value of 0 indicating the correct and a value of 1 the opposite enantiomer).

Fractional coordinates of the non-H-atoms are given together with their equivalent isotropic a.d.p.s in *Table 3*.

REFERENCES

[1] J. M. Pratt, 'Inorganic Chemistry of Vitamin B_{12}', Academic Press, New York, London, 1972.
[2] K. L. Brown, in 'B_{12}', Vol. I, Ed. D. Dolphin, Wiley-Interscience, New York, 1982, p. 245.
[3] B. Kräutler, in 'Chemistry and Biochemistry of B_{12}', Ed. R. Banerjee, J. Wiley & Sons, New York, 1999, p. 315.
[4] E. L. Smith, L. Mervyn, A. W. Johnson, N. Shaw, *Nature (London)* **1962**, *194*, 1175.
[5] K. Bernhauer, O. Müller, G. Müller, *Biochem. Z.* **1962**, *336*, 102.
[6] D. Lexa, J. M. Savéant, *J. Am. Chem. Soc.* **1976**, *98*, 2652.
[7] D. Lexa, J. M. Savéant, *Acc. Chem. Res.* **1983**, *16*, 235.
[8] D. Lexa, J. M. Savéant, J. Zickler, *J. Am. Chem. Soc.* **1977**, *99*, 2786.
[9] D. Lexa, J. M. Savéant, *J. Am. Chem. Soc.* **1978**, *100*, 3220.
[10] D. L. Zhou, O. Tinembart, R. Scheffold, L. Walder, *Helv. Chim. Acta* **1990**, *73*, 2225.
[11] O. Tinembart, L. Walder, R. Scheffold, *Ber. Bunsenges. Phys. Chem.* **1988**, *92*, 1225.
[12] W. W. Reenstra, R. H. Abeles, W. P. Jencks, *J. Am. Chem. Soc.* **1982**, *104*, 1016.

[13] K. L. Brown, J. M. Hakimi, D. M. Nuss, Y. D. Montejano, D. W. Jacobsen, *Inorg. Chem.* **1984**, *23*, 1463.
[14] M. Tollinger, T. Dérer, R. Konrat, B. Kräutler, *J. Mol. Catal.* **1997**, *116*, 147.
[15] R. Yamada, S, Shimizu, S. Fukui, *Biochemistry* **1968**, *7*, 1713.
[16] H. U. Blaser, J. Halpern, *J. Am. Chem. Soc.* **1980**, *102*, 1684.
[17] G. N. Schrauzer, M. Hashimoto, *J. Am. Chem. Soc.* **1979**, *101*, 4593.
[18] M. Moskophidis, *Z. Naturforsch., C* **1981**, *36*, 497.
[19] C. Kratky, B. Kräutler, in 'Chemistry and Biochemistry of B_{12}', Ed. R. Banerjee, J. Wiley & Sons, New York, 1999, p. 9.
[20] A. L. Davis, J. Keeler, E. D. Laue, D. Moskau, *J. Magn. Reson.* **1992**, *98*, 207.
[21] R. E. Hurd, B. K. John, *J. Magn. Reson.* **1991**, *91*, 648.
[22] A. Bax, M. F. Summers, *J. Am. Chem. Soc.* **1986**, *108*, 2093.
[23] H. Kessler, M. Gehrke, C. Griesinger, *Angew. Chem.* **1988**, *100*, 507; *Angew. Chem., Int. Ed.* **1988**, *27*, 490.
[24] A. A. Bothner-By, R. L. Stephens, C. D. Warren, R. W. J. Jeanloz, *J. Am. Chem. Soc.* **1984**, *106*, 811.
[25] A. Bax, D. G. Davies, *J. Magn. Reson.* **1985**, *63*, 207.
[26] L. Braunschweiler, R. R. Ernst, *J. Magn. Reson.* **1983**, *53*, 521.
[27] A. Bax, D. G. Davies, *J. Magn. Reson.* **1985**, *65*, 355.
[28] D. G. Davies, A. Bax, *J. Am. Chem. Soc.* **1985**, *107*, 2820.
[29] E. Pretsch, T. Clerc, J. Seibl, W. Simon, 'Tabellen zur Strukturaufklärung organischer Verbindungen mit spektroskopischen Methoden', Springer Verlag, Berlin, Heidelberg, 1986.
[30] K. Gruber, G. Jogl, G. Klintschar, C. Kratky, in 'Vitamin B_{12} and B_{12}-Proteins', Eds. B. Kräutler, D. Arigoni, B. T. Golding, Wiley VCH, Weinheim 1998, p. 335.
[31] B. Kräutler, in 'The Biological Alkylation of Heavy Elements', Eds. P. J. Craig and F. Glockling, Royal Society of Chemistry, London 1988, p. 31.
[32] M. Rossi, J. P. Glusker, L. Randaccio, M. F. Summers, P. J. Toscano, L. G. Marzilli, *J. Am. Chem. Soc.* **1985**, *107*, 1729; L. Randaccio, M. Furlan, S. Geremia, M. Slouf, I. Srnova, D. Toffoli, *Inorg. Chem.* **2000**, *39*, 3403.
[33] M. Tollinger, R. Konrat, B. Kräutler, *Helv. Chim. Acta* **1999**, *82*, 1595.
[34] A. M. Calafat, L. G. Marzilli, *J. Am. Chem. Soc.* **1993**, *115*, 9182.
[35] A. Bax, M. F. Summers, *J. Am. Chem. Soc.* **1986**, *108*, 2093.
[36] M. F. Summers, L. G. Marzilli, A. Bax, *J. Am. Chem. Soc.* **1986**, *108*, 4285.
[37] R. Konrat, M. Tollinger, B. Kräutler, in 'Vitamin B_{12} and B_{12}-Proteins', Eds. B. Kräutler, D. Arigoni and B. T. Golding, Wiley VCH, Weinheim 1998, p. 349.
[38] K. L. Brown, in 'Chemistry and Biochemistry of B_{12}', Ed. R. Banerjee, J. Wiley & Sons, New York, 1999, p. 197.
[39] M. Puchberger, R. Konrat, C. Kratky, B. Kräutler, in preparation.
[40] H. Fischer, *J. Am. Chem. Soc.* **1986**, *108*, 3925.
[41] R. G. Finke, in 'Vitamin B_{12} and B_{12}-Proteins', Eds. B. Kräutler, D. Arigoni and B. T. Golding, Wiley VCH, Weinheim 1998, p. 383.
[42] G. Wohlfarth, G. Diekert, in 'Chemistry and Biochemistry of B_{12}', Ed. R. Banerjee, J. Wiley & Sons, New York, 1999, p. 871.
[43] C. Holliger, G. Wohlfarth, G. Diekert, *FEMS Microbiol. Rev.* **1999**, *22*, 383.
[44] J. Shey, W. A. van der Donk, *J. Am. Chem. Soc.* **2000**, *122*, 12403.
[45] D. I. States, R. A. Haberkorn, D. J. Ruben, *J. Magn. Reson.* **1982**, *48*, 286.
[46] A. J. Shaka, P. B. Barker, R. Freeman, *J. Magn. Reson.* **1985**, *64*, 547.
[47] A. Bax, D. G. Davis in 'Advanced Magnetic Resonance Techniques in Systems of High Molecular Complexity', Eds. N. Nicolai and G. Valensin, Birkhauser, Boston, 1986, p. 21; A. Bax, L. G. Marzilli, M. F. Summers, *J. Am. Chem. Soc.* **1987**, *109*, 566.
[48] M. H. Levitt, R. Freeman, *J. Magn. Reson.* **1981**, *43*, 502.
[49] G. M. Sheldrick, 'SHELXS86, Program for Crystal Structure Solution', University of Göttingen, Germany, 1986; G. M. Sheldrick, 'SHELXL97, Program for the Refinement of Crystal Structures from Diffraction Data', University of Göttingen, Germany, 1997; 'SHELXTL, Version 5', Siemens Analytical Instruments, Inc., 1994.
[50] N. Walker, D. Stuart, *Acta Crystallogr., Sect. A* **1983**, *39*, 158.
[51] F. L. Hirshfeld, *Acta Crystallogr., Sect. A* **1976**, *32*, 239.
[52] H. Flack, *Acta Crystallogr., Sect. A* **1976**, *39*, 876.

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