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Synthesis and Characterization of a Novel Green Cobalt Corrinoid[1]

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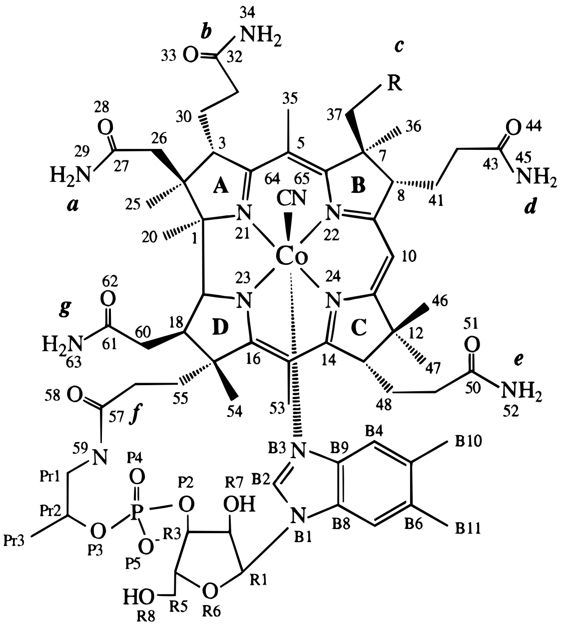
Cobalamins (Cbls[1]) with altered peripheral substituents are of considerable interest on several grounds. The six carboxamide corrin ring substituents provide polar hydrogen bond donating and accepting functionalities which are potential points of binding interactions with the various types of proteins that bind Cbls. Analogs with structurally altered peripheral substituents have consequently been used to study the structural basis of Cbl binding to vitamin B_{12} binding proteins,[3−5] vitamin B_{12} transport receptors,[6,7] and 5′-deoxyadenosylcobalamin-(AdoCbl[1]-) requiring enzymes.[8−11] In addition, recent work has suggested that steric interference with side chain thermal motions by the organic ligand of RCbls can provide significant entropic driving force for cleavage of the Co−C bonds in such complexes.[12] Analogs of CNCbl[1] (**1**) in which the *b*, *c*, *d*, or *e* amide side chain is hydrolyzed to a carboxylic acid are well-known and well-characterized,[12,13−19] as are the *N*-alkyl amides and alkyl esters produced from them.[8,9,12]

During a recent attempt to synthesize an analog of CNCbl in which the *c* acetamide side chain is truncated to a methyl group, we discovered that the *c* amino derivative, CNCbl-*c*-NH_2 (**3**), is readily converted in basic aqueous solution to a novel green cobalt corrinoid. The preparation, structure, and properties of this unique compound are the subject of this report.



1	$R = \overset{O}{\overset{\|\|}{C}}NH_2$	CNCbl
2	$R = COO^-$	CNCbl-*c*-COO^-
3	$R = NH_2$	CNCbl-*c*-NH_2
4	$R = NH\overset{O}{\overset{\|\|}{C}}CH_3$	CNCbl-*c*-$NHCOCH_3$
5	$R = NH\overset{O}{\overset{\|\|}{C}}OCH_3$	CNCbl-*c*-$NHCOOCH_3$

Experimental Section

Cyanocobalamin-*c*-lactone[14] was obtained by chloramine T oxidation of CNCbl as described previously[20] and converted to the *c*-monocarboxylate, CNCbl-*c*-COO^- (**2**), by reduction with Zn/NH_4Cl.[12] Dry CNCbl-*c*-COO^- (100 mg, 73.7 mmol) was dissolved in 1.0 mL of methanol, and 0.2 mL of diphenylphosphoryl azide and 0.1 mL of triethylamine were added. The reaction mixture was stirred at room temperature for 2 days, after which the methanol was removed by rotary evaporation. The residue was dissolved in 10 mL of 1.0 M KOH, and this solution was washed with three 10 mL portions of diethyl ether. Ether was removed from the aqueous solution by rotary evaporation, and the solution was applied to a column of Amberlite XAD-2 resin. After washing with water to desalt, elution with 10% CH_3CN/H_2O (v/v) removed a red band, leaving behind a green material which could be eluted with 50% CH_3CN/H_2O (v/v). CNCbl-*c*-NH_2 (**3**) was purified from the red band by semipreparative HPLC (yield 50 mg, 37.7 mmol, 51%). FAB MS, *m*/*z*: calculated for $M + H^+$ 1327.6, found 1327.6; calculated for $M + H^+ - CN$ 1301.6, found 1301.3. The ^{13}C NMR spectrum (available as Supporting Information) was tentatively assigned by analogy to that of CNCbl.[19,21] The acetamide derivative, **4**, was prepared by reaction of **3** with acetic anhydride in cold aqueous sodium acetate solution in essentially quantitative yield. FAB MS, *m*/*z*:

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(1) IUPAC−IUB nomenclature for the cobalt corrinoids[2] is used throughout. Abbreviations: Cbl, cobalamin; RCbl, alkylcobalamin; CNCbl, cyanocobalamin (vitamin B_{12}); AdoCbl, 5′-deoxyadenosylcobalamin (coenzyme B_{12}); CNCbl-*c*-COO^-, cyanocobalamin-*c*-monocarboxylate; Bzm, 5,6-dimethylbenzimidazole.

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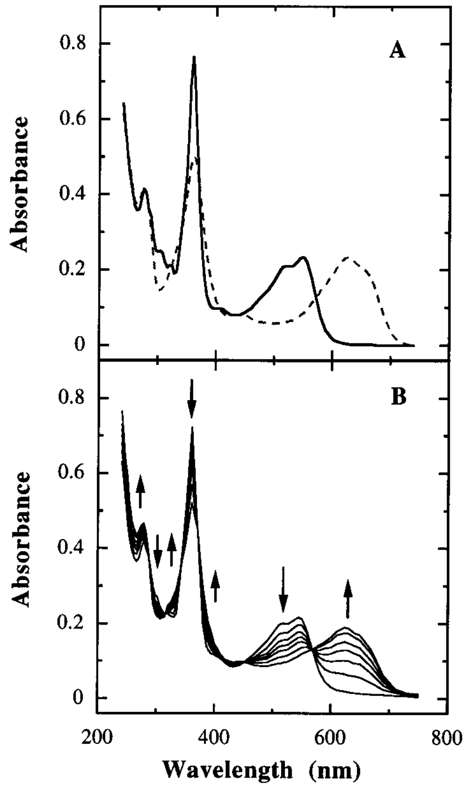

Figure 1. (A) UV−visible spectra of CNCbl, **1** (solid line), and the green corrinoid, **6** (dotted line), both at 2.75 × 10^{-5} M. (B) Spectral changes accompanying the conversion of CNCbl-*c*-NH_2, **3**, to the green corrinoid, **6**, at 50 °C, pH 10.0. The concentration is 2.75 × 10^{-5} M, and the spectra were taken at 0, 40, 80, 120, 160, 240, and 300 min after initiation of the reaction.

calculated for M + H^+ 1369.6, found 1369.9; calculated for M + H^+ − CN 1343.6, found 1343.3. The ^{13}C NMR spectrum and ^1H, ^{15}N HMQC spectrum (available as Supporting Information) were assigned by analogy to those of CNCbl.[19,21,22]

From the green band eluted from the XAD-2 column with 50% CH_3CN/H_2O, the green corrinoid, **6**, was isolated by semipreparative HPLC in yields which varied from ca. 20 to 40% depending on the length of time the reaction mixture remained in KOH (*vide infra*). FAB MS, *m/z*: calculated for M + H^+ (M = $C_{61}H_{83}CoN_{13}O_{13}P$) 1296.5, found 1296.5; calculated for M + H^+ − CN 1270.5, found 1270.7. UV−vis: λ_{max} (log ϵ): 277 (4.180), 362 (4.270), 446 (3.458), 624 (3.944), 658 s (3.874). The ^1H and ^{13}C NMR spectra were completely assigned by use of 2D homonuclear (COSY, HOHAHA, and ROESY) and heteronuclear (HMQC and HMBC) experiments at 600 MHz. ^1H and ^{13}C NMR assignments, an NMR correlation table, and the ^1H, ^{15}N HMQC spectrum for the green corrinoid are available as Supporting Information.

The green corrinoid could also be obtained directly from the amine, **3**, as follows. CNCbl-*c*-NH_2 (6.6 mg, 4.97 × 10^{-3} mmol) was dissolved in 50 mL of pH 10.0 CAPS buffer. The mixture was deoxygenated by purging with nitrogen for 30 min and then incubated at 50 °C overnight. The product was desalted on a column of XAD-2 and then eluted with 50% CH_3CN/H_2O (v/v). After purification by semipreparative HPLC, **6** was obtained in 95% yield (6.1 mg, 4.7 × 10^{-3} mmol).

Dark green crystals of **6** were grown by vapor phase diffusion of CH_3CN into an aqueous solution. A prismatic specimen, 0.8 × 0.65 × 0.3 mm, was wedged into a 0.5 mm capillary in contact with CH_3CN and the capillary sealed with paraffin. The crystal was tetragonal, of space group $P4_12_12$, with cell constants $a = b = 31.00(2)$ Å, $c = 18.01(2)$ Å, and $V = 17307(25)$ Å^3. Intensity data were collected in shells to $\theta = 18.75°$ (Mo Kα radiation, $\lambda = 0.710\ 73$ Å), above which intensities did not exceed the background scattering. A total of 7336 data were collected over 117 h, of which 6692 were independent and 3792 were unique. No absorption correction was applied, and no decay correction was deemed necessary on the basis of periodic monitoring of 3 (after every 97) reflections. The data were corrected for coincidence, Lorentz, and polarization effects.

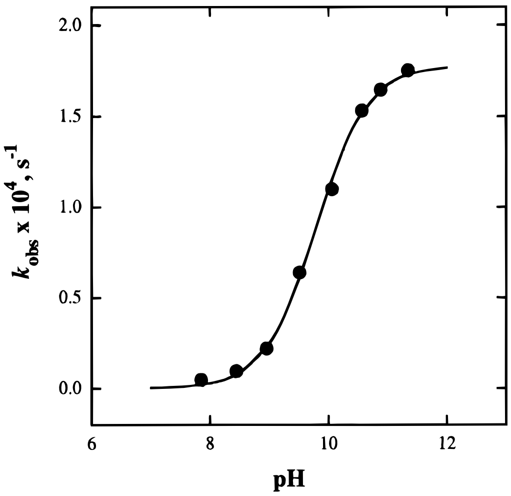

Figure 2. Dependence of the observed first-order rate constant, k_{obs}, for conversion of CNCbl-*c*-NH_2, **3**, to the green corrinoid, **6**, at 50 °C, ionic strength 1.0 M (KCl), on pH. The solid line was calculated using pK_a = 9.79 for the conjugate acid of **3** and a limiting rate constant at high pH of 1.78 × 10^{-4} s^{-1}.

Table 1. Crystal Data for the Green Corrinoid, **6**

empirical formula	$C_{61}H_{83}CoN_{13}O_{13}P\cdot{\sim}25H_2O$
formula weight	1706.57 (including 25 H_2O)
temperature (K)	295(2)
λ(Mo Kα) (Å)	0.710 73
space group	$P4_22_12$
$a = b$ (Å)	31.00(2)
c (Å)	18.01(2)
V (Å^3)	17307(25)
Z	8
crystal size (mm^3)	0.80 × 0.65 × 0.30
D (g cm^{-3})	1.31

The location of the cobalt atom was discovered by application of the Patterson function in SHELXS.[23] The model for the complex was assembled from difference Fourier calculations. The structure was refined by full-matrix least squares against F^2 with restraints on vibrational factors to allow them to slowly increase from the center to the periphery of the molecule. Eventually, all non-H atoms and their anisotropic vibrational factors were allowed to refine. Water oxygens, ultimately totaling 26 in number, were also included, some of which were partial-occupancy positions. The only significant disorder in the structure occurred in the *b* propionamide side chain where the two positions displayed *anti* and *gauche* conformations about the C30−C31 bond. H atom positions were calculated and allowed to contribute to the model except for the disordered *b* side chain and the waters. A small extinction correction was included (coefficient = 1.95(10) × 10^{-3}), and the absolute configuration was established by refinement of Flack's parameter[24] to +0.03(4). Water oxygens with partial occupancies less than 0.3 were not modeled. The model converged with $R_1 = \sum||F_o| - |F_c||/\sum|F_o| = 0.0556$ (on F for $I > 2\sigma(I)$), $R_{2w} = \{\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]\}^{1/2} = 0.1381$ (on F^2 for all 7336 data).

Results and Discussion

Synthesis of the Green Corrinoid. Treatment of CNCbl-*c*-COO^- with diphenylphosphoryl azide[25−28] readily affords a urethane intermediate, **5**, which in aqueous base produces the

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Table 2. Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters (Å^2 × 10^3) for the Green Corrinoid (**6**), Where *U*(eq) is Defined as One-Third of the Trace of the Orthogonalized $\mathbf{U}_{ij}$ Tensor

atom	*x*/*a*	*y*/*b*	*z*/*c*	*U*(eq)	atom	*x*/*a*	*y*/*b*	*z*/*c*	*U*(eq)
Co	8073(1)	9054(1)	7969(2)	67(1)	C20	7434(5)	9736(4)	6872(10)	97((7)
P	5646(2)	8243(2)	5442(4)	101(2)	N21	8062(5)	9627(4)	8664(7)	66(4)
OP2	6045(4)	8214(4)	6063(6)	94(4)	N22	8670(4)	9034(5)	7769(8)	66(4)
OP3	5286(5)	8399(5)	5986(10)	117(6)	N23	8036(5)	8464(4)	8328(7)	55(4)
OP4	5572(4)	7828(4)	5110(7)	111(5)	N24	7494(4)	9154(5)	8218(7)	58(4)
OP5	5714(4)	8603(5)	4968(7)	119(5)	C25	7387(5)	10630(5)	7269(9)	109(7)
NB1	7548(5)	8404(5)	6089(10)	75(5)	C26	7752(5)	10483(5)	8493(10)	99(6)
CB2	7612(6)	8530(6)	6854(13)	90(6)	C27	7844(9)	10970(8)	8522(16)	119(9)
NB3	7928(4)	8824(4)	6909(8)	63(4)	O28	8088(5)	11167(5)	8135(11)	186(9)
CB4	8368(6)	9229(6)	5905(12)	95(7)	N29	7748(6)	11115(5)	9203(12)	173(9)
CB5	8404(8)	9257(8)	5171(15)	100(8)	C30	8220(7)	10440(7)	6373(13)	133(8)
CB6	8183(7)	9003(8)	4688(15)	107(8)	C31A[a]	8292(10)	10988(10)	6500(20)	113(10)
CB7	7880(6)	8701(6)	4962(14)	101(7)	C32A[a]	8711(16)	11172(11)	6830(28)	151(14)
CB8	7825(7)	8666(7)	5709(12)	72(6)	O33A[a]	9103(11)	11119(9)	6434(24)	204(14)
CB9	8052(6)	8913(6)	6170(12)	58(5)	N34A[a]	8741(18)	11387(16)	7483(28)	258(23)
CB10	8750(6)	9547(5)	4915(10)	153(10)	C31B[b]	8075(16)	10795(14)	5962(28)	90(13)
CB11	8224(5)	9024(6)	3768(9)	142(8)	C32B[b]	8241(24)	10802(13)	5203(50)	163(18)
CR1	7189(6)	8161(6)	5858(10)	81(6)	O33B[b]	7848(20)	10937(17)	4849(26)	274(23)
CR2	6778(5)	8447(6)	5781(11)	86(6)	N34B[b]	8536(18)	10743(14)	4917(27)	192(24)
CR3	6439(6)	8081(6)	5818(11)	91(6)	C35	9109(4)	10168(4)	7381(11)	142(9)
CR4	6620(6)	7813(7)	6474(12)	126(7)	C36	9778(5)	9463(4)	7313(12)	160(10)
CR5	6500(8)	7261(9)	6457(13)	180(12)	C41	9763(5)	8507(5)	7859(10)	79(6)
OR6	7083(4)	7844(3)	6380(8)	99(4)	C42	9914(5)	8527(5)	8636(11)	87(6)
OR7	6757(4)	8760(4)	6270(7)	100(5)	C43	10248(8)	8198(8)	8807(15)	123(9)
OR8	6687(9)	7146(10)	5735(12)	406(21)	O44	10520(5)	8098(5)	8402(9)	173(8)
Pr1	5205(6)	8386(8)	7307(11)	170(10)	N45	10158(4)	7962(5)	9468(10)	140(7)
Pr2	5165(7)	8165(8)	6577(15)	138(9)	C46	8448(6)	7417(4)	8046(11)	165(9)
Pr3	4696(4)	7900(6)	6520(10)	144(9)	C47	8456(6)	7678(7)	9279(11)	238(15)
C1	7589(6)	9829(6)	7665(10)	75(6)	C48	7525(5)	7543(5)	8078(10)	90(6)
C2	7745(7)	10338(5)	7622(12)	88(6)	C49	7511(8)	7057(8)	8066(13)	200(11)
C3	8162(6)	10334(6)	7170(14)	110(7)	C50	7258(10)	6990(11)	8702(23)	186(13)
C4	8360(7)	9901(7)	7469(11)	106(7)	O51	7453(7)	6717(7)	9336(10)	255(11)
C5	8788(6)	9796(6)	7510(10)	74(6)	N52	6886(6)	7078(6)	8924(14)	203(12)
C6	8929(6)	9394(7)	7590(10)	79(6)	C53	6924(6)	8218(5)	9014(9)	118(7)
C7	9401(5)	9237(6)	7565(8)	53(5)	C54	6882(4)	9303(5)	9642(9)	112(7)
C8	9370(6)	8808(6)	7755(9)	71(5)	C55	6374(5)	8997(5)	8679(10)	83(6)
C9	8926(5)	8685(6)	7923(12)	76(5)	C56	6267(5)	8835(5)	7891(10)	90(6)
C10	8784(5)	8291(5)	8165(9)	61(5)	C57	5850(9)	8656(9)	7929(17)	156(9)
C11	8378(6)	8176(5)	8293(9)	58(5)	O58	5734(7)	8368(8)	8354(15)	402(19)
C12	8274(6)	7757(6)	8594(11)	73(5)	N59	5606(5)	8628(7)	7413(10)	152(8)
C13	7757(6)	7795(6)	8642(10)	70(5)	C60	6647(5)	9989(6)	8514(10)	97(6)
C14	7693(6)	8248(7)	8506(12)	77(6)	C61	6253(9)	10171(11)	8252(14)	176(11)
C15	7311(8)	8452(7)	8687(10)	74(6)	O62	6207(7)	9977(6)	7555(11)	241(10)
C16	7217(5)	8908(7)	8537(9)	56(5)	N63	6003(8)	10333(9)	8682(15)	516(25)
C17	6798(6)	9179(6)	8759(10)	82(6)	C64	8220(6)	9235(5)	8954(9)	65(6)
C18	6900(6)	9573(5)	8284(9)	74(5)	N65	8279(6)	9342(6)	9536(8)	124(7)
C19	7374(5)	9618(6)	8314(10)	61(5)					

[a] Site occupancy 0.60. [b] Site occupancy 0.40.

expected amine, **3**, in moderate yield. However, this product is always accompanied by a significant amount of a curious green corrinoid, the remarkable spectrum of which is shown in Figure 1A. Upon variation of synthetic conditions, the amount of the green corrinoid formed was found to vary as a function of the length of time the reaction mixture was allowed to stand in 1.0 N KOH to effect hydrolysis of the putative urethane intermediate, **5**. Subsequent experimentation with the amine showed that CNCbl-*c*-NH_2 is unstable in aqueous base, slowly decomposing to the green corrinoid (Figure 1B). In aerobic solution, the green corrinoid is itself unstable in base, decomposing to a mixture of unidentified products (by HPLC) in a reaction or reactions which are quite slow at pH 10 but become faster with increasing pH. However, in anaerobic aqueous base, the green corrinoid proved stable, and it could consequently be prepared from CNCbl-*c*-NH_2 essentially quantitatively under such conditions.

The kinetics of the formation of the green corrinoid from CNCbl-*c*-NH_2 at 50 °C could be readily monitored at 624 nm (Figure 1B). The reaction was first order in CNCbl-*c*-NH_2 and yielded the pH−rate profile shown in Figure 2. This behavior suggests that the protonated amine, CNCbl-*c*-NH_3^+, is in fact stable but that the free base spontaneously decomposes to the green corrinoid, although other interpretations are possible. From these data, the pK_a for the protonated amine can be estimated to be 9.79 ± 0.02 and the limiting rate constant to be $(1.78 \pm 0.04) \times 10^{-4}$ s^{-1} (50 °C, ionic strength 1.0 M (KCl)).

Structure of the Green Corrinoid. Because of the huge red shift of the α and *β* bands of the electronic spectrum of the green corrinoid (ca. 110−120 nm, Figure 1A), we suspected that the green corrinoid contained additional conjugation in the macrocycle. As a result, a single-crystal X-ray diffraction analysis was undertaken to determine the structure of this unique compound.

The compound crystallizes in the tetragonal system, space group $P4_12_12$, with 8 molecules in the unit cell. Details of the crystal data and structure refinement are given in Table 1, atomic coordinates are given in Table 2, and a stereoview of the

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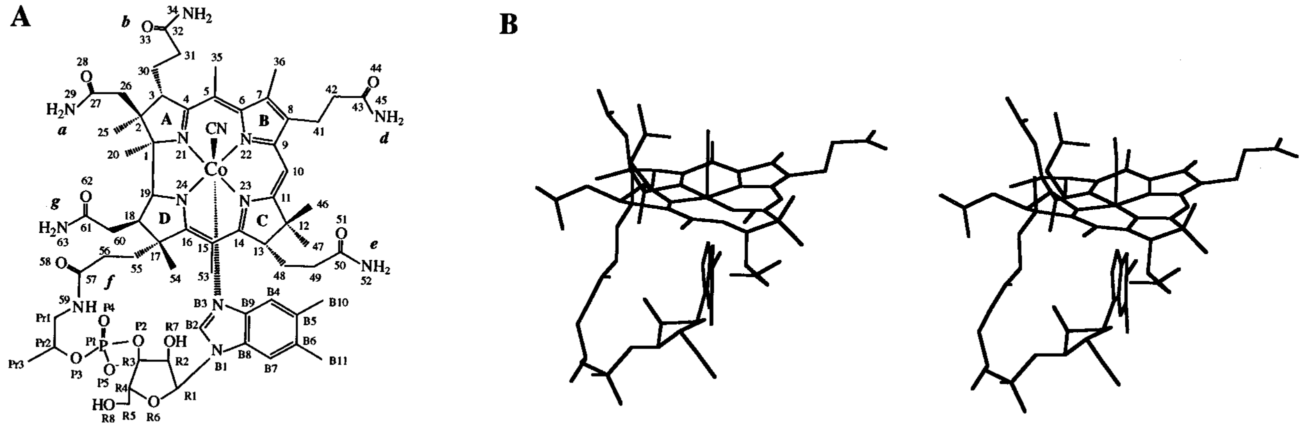

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Figure 3. Structural representation (A) and stereo line drawing (B) of the green corrinoid, **6**.

Table 3. Selected Bond Lengths and Bond Angles for the Green Corrinoid, **6**, and CNCbl

	6	CNCbl[a]		**6**	CNCbl[a]
		Bond Lengths (Å)			
C7−C8	1.38(2)	1.54(2)	Co−N22	1.888(11)	1.908(8)
Co−C64	1.90(2)	1.858(12)	Co−N23	1.943(12)	1.917(9)
Co−B3	2.085(14)	2.011(10)	Co−N24	1.872(12)	1.875(8)
Co−N21	1.859(13)	1.875(8)			
		Bond Angles (deg)			
Co−C64−N65	176(2)	179.0(11)	C64−Co−N24	87.7(7)	88.8(4)
C64−Co−B3	176.9(6)	176.4(4)	B3−Co−N21	93.0(6)	90.7(4)
Co−B3−B2	117(2)	123.3(8)	B3−Co−N22	91.4(6)	89.4(4)
Co−B3−B9	137.4(14)	133.0(7)	B3−Co−N23	88.3(5)	87.5(4)
N21−Co−N22	89.6(6)	90.3(4)	B3−Co−N24	94.0(5)	94.8(4)
N22−Co−N23	95.2(7)	96.8(4)	C6−C7−C36	129(2)	115.7(9)
N23−Co−N24	91.1(7)	89.3(4)	C36−C7−C8	127(2)	112.0(9)
N21−Co−N24	84.0(6)	83.8(4)	C6−C7−C8	103(2)	101.2(9)
C64−Co−N21	89.8(6)	91.7(4)	C7−C8−C41	124(2)	113.7(9)
C64−Co−N22	87(7)	87.9(4)	C7−C8−C9	112(2)	100.9(8)
C64−Co−N23	89.1(6)	90.5(4)			

[a] Reference 29.

complex is shown in Figure 3. A comparison of selected bond lengths and angles for the green corrinoid and CNCbl[29] is given in Table 3. The most striking attributes of the green corrinoid are the lack of a *c* side chain at C7 and the introduction of a C7−C8 double bond in the B pyrrole ring. These structural features are supported by the ^{1}H, ^{13}C, and ^{15}N NMR spectra (available as Supporting Information). The presence of the C7−C8 double bond is confirmed in the X-ray structure by the shortening of the C7−C8 bond from 1.54 Å in CNCbl to 1.38 Å in the green corrinoid and an increase in all of the bond angles to C7 and C8 (except for the C6−C7−C8 bond angle) averaging 12.3° (Table 3). In addition, C7, C8, and the heavy atoms attached to them (C6, C9, C36, and C41) are planar to within a mean deviation of 0.034 Å. This least squares plane is nearly as good as that for the Bzm[1] nucleotide (B1−B9, mean deviation 0.021 Å). We conclude that the B pyrrole ring has been aromatized by loss of the $-CH_2NH_2$ substituent from C7 and loss of the C8 hydrogen and that this aromatization, in conjunction with the extended double-bond system in the macrocycle, is responsible for the remarkable red shift of the α and *β* bands for the green corrinoid (Figure 1A). Figure 4 shows a superposition of the green corrinoid and CNCbl, in which the alteration of the geometry at C7 and C8 from tetrahedral to trigonal is quite clear.

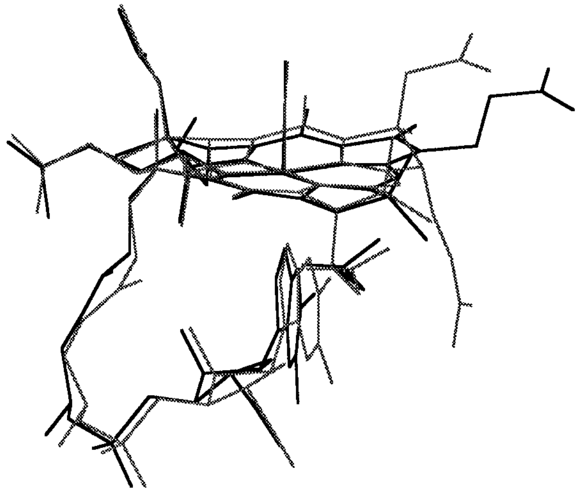

Figure 4. Superposition of the green corrinoid, **6** (dark lines), with CNCbl (light lines). The structures were superimposed at the four equatorial nitrogens.

The inner-sphere geometries of the green corrinoid and CNCbl are remarkably similar (Table 3), the only significant differences being a 0.07 Å increase in the axial $Co-N_{Bzm}$ bond length in the green corrinoid and a ca. 6° decrease in the Co−B3−B2 bond angle with a concomitant increase in the Co−B3−B9 bond angle. The latter reflects a slight tilt of the Bzm about its normal. Figure 4 shows that the Bzm in the green corrinoid is also tilted (ca. 10°) about an axis lying roughly normal to the equatorial plane and passing near B2, such that the six-membered ring is tilted toward the "western" hemisphere. Figure 4 also reveals that the aromatization of the B pyrrole apparently causes the macrocycle's upward "pucker" to flatten considerably. Glusker[30] has defined a corrin ring fold angle about the Co••C10 axis as the angle between the normals to a "northern" plane (N21−C4−C5−C6−N22−C9−C10) and a "southern" plane (N24−C16−C15−C14−N23−C11−C10). For CNCbl, this fold angle is 18.0°, but it is reduced in the green corrinoid to only 7.6°, among the lowest such fold angles found for cobalt corrinoids.[31]

Reduction of the Green Corrinoid. Treatment of the green corrinoid with $NaBH_4$ in neutral anaerobic solution produced a species whose spectrum (not shown) was typical of a normal reduced corrinoid and displayed no significant red shift. When such a solution was transferred by cannula to an anaerobic solution of HCl (to destroy the excess BH_4^-) and then exposed

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(29) Kräutler, B.; Konrat, R.; Stupperich, E.; Fäberm, G.; Gruber, K.; Kratky, C. *Inorg. Chem.* **1994**, *33*, 4128.

(30) Glusker, J. P. In *B*$_{12}$; Dolphin, D., Ed.; Wiley-Interscience: New York, 1982; Vol. 1, p 23.

(31) The mean deviations were 0.047 Å for the "northern" plane and 0.076 Å for the "southern" plane.

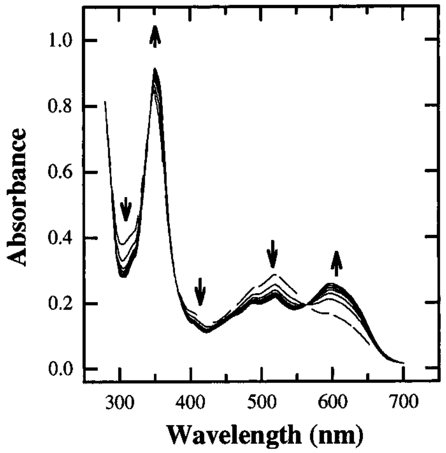

Figure 5. Spectrum of the green corrinoid, **6**, immediately after anaerobic reduction with $NaBH_4$, destruction of excess $NaBH_4$ with HCl, and admission of air (dashed line). The remaining spectra (solid lines) are subsequent scans of the same sample, 2, 4, 6, 8, and 10 min after admitting air.

to air, the metal center was immediately oxidized to produce the spectrum of a typical red corrinoid, as shown in Figure 5 (dashed line). This complex proved unstable in aerobic solution and readily oxidized to the green corrinoid, **6**, displaying a ca. 110 nm red shift of the α and *β* bands. Experiments such as the one shown in Figure 5 suggest that when **6** is treated with BH_4^-, both the metal center and the C7-C8 double bond in the B pyrrole ring are reduced. The introduction of air causes immediate oxidation of the metal center, producing a typical red cobalt corrinoid which, considering the spectra shown in Figure 1A, must have either the same macrocyclic ring conjugation as a normal cobalt corrinoid or at least the same number of conjugated double bonds. Somewhat more slowly, this species is oxidized in air to the green corrinoid, clearly containing one additional double bond. This suggests that, in the absence of quaternization at C7, the B pyrrole ring of the corrin is subject to facile autoxidation. This in turn suggests a possible rationale for the substitution of the C36 methyl group at C7 in the normal cobalamins—the stabilization of the corrin ring in its normal Cbl oxidation state in aerobic solution.

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Supporting Information Available: Listings of tentative ^{13}C NMR assignments for CNCbl-*c*-NH_2, **3**, and CNCbl-*c*-NHC(O)CH_3, **4**, amide ^1H and ^{15}N NMR assignments for CNCbl, **1**, CNCbl-*c*-NHC(O)CH_3, **4**, and **6**, and complete ^1H and ^{13}C NMR assignments for **6**, an NMR correlation table for **6**, text giving details of the data collection and solution and refinement of the crystal structure of **6**, tables of atomic coordinates for the water molecules in the crystal, calculated coordinates for hydrogen atoms, anisotropic thermal parameters, bond lengths, bond angles, and intermolecular contacts for **6**, and two ORTEP diagrams of **6** (24 pages). Ordering information is given on any current masthead page.

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