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Formation and structure of inclusion complexes involving α-cyclodextrin and alkyl(aqua)cobaloxime

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A series of inclusion complexes involving α-cyclodextrin (α-cd) and alkyl(aqua)cobaloximes has been synthesized for the first time and characterized by elemental analysis, one and two-dimensional ^{1}H NMR spectroscopy. Their formation constants K_a were determined by quantitative ^{1}H NMR methods. The crystal structures of α-cd–[Co(Hdmg)$_2$Pr^n(H$_2$O)] (H$_2$dmg = dimethylglyoxime) and its guest molecule [Co(Hdmg)$_2$Pr^n(H$_2$O)] were determined. According to both NMR and crystal structure data, 1:1 inclusion complexes of α-cd and alkylcobaloximes are formed, in which the alkyl groups of the guests are included into the cavity of α-cd. After formation of the inclusion complexes, variations in the bond lengths and angles around the cobalt atom, and conformation changes of the *n*-propyl(aqua)cobaloxime were observed. It is suggested that these changes in the guest molecule are probably due to the hydrophobic interaction between the alkyl groups and the α-cd cavities, and steric interaction between α-cd and Co(Hdmg)$_2$. It has also been established that the stability of the inclusion complexes in aqueous solution is related to the length and the size of the alkyl groups, the K_a values varying in the order n-C$_5$H$_{11}$ $\gg$ Bu^n > Pr^n > Bu^i.

Cyclodextrins (cds), a series of oligosaccharides consisting of six or more D-glucopyranose residues α-1,4-linked in a cyclic array, are one of the most fascinating naturally occurring molecular receptors.[1–3] The molecular geometry of cds is such that the interior surface of the cavity is hydrophobic and the external surface is hydrophilic. Previous investigations have revealed that they can form inclusion complexes with a variety of inorganic and organic molecules.[1–3] Since Harada and Takahashi[4] first reported the solid inclusion complexes involving cds and organometallic ferrocene in 1984, there has been a growing interest in the development of cds as host molecules for transition-metal complexes by including hydrophobic organic ligands in the cds cavity.[5–12] It has been found that after the formation of the inclusion complexes there are significant changes in the physical and chemical properties of the guest compounds, such as solubility, vapour pressure, ^{1}H and ^{13}C NMR chemical shifts, circular dichroism, optical absorption, conductivity, and fluorescence. However, until now, there has been no report on the structure and conformation changes of guest molecules revealed by X-ray diffraction methods.[2,3]

We have now synthesized a series of α-cd–[Co(Hdmg)$_2$R(H$_2$O)] inclusion complexes (R = Pr^n, Bu^i, Bu^n or n-C$_5$H$_{11}$; H$_2$dmg = dimethylglyoxime), where [Co(Hdmg)$_2$R(H$_2$O)] is a type of widely studied coenzyme B-12 model having a σ-type cobalt–carbon bond,[13] and characterized them by elemental analysis, one- and two-dimensional ^{1}H NMR spectroscopy and X-ray diffraction analysis. Organocobalt(III) complexes could function as intermediates in radical polymerization of alkenes, and organic substrate transformations.[14] Furthermore cyclodextrins have been proposed as artificial enzymes to demonstrate regiospecificity and stereospecificity during catalytic processes.[1,2] Therefore, we believe that our new inclusion complexes will show very promising properties in interesting potentially catalytic applications.

Experimental

All chemicals were A.R. or C.P. grade. α-Cyclodextrin (Sigma) was dried *in vacuo* at 80 °C before use.

Preparations

Alkylcobaloximes [Co(Hdmg)$_2$R(H$_2$O)]. The complexes [Co(Hdmg)$_2$R(py)] (py = pyridine) were prepared by reductive alkylation according to Schrauzer and Windgassen,[15] then eluted through a column of strongly acidic resin to obtain [Co(Hdmg)$_2$R(H$_2$O)]. The crude products were recrystallized from water–methanol solution. The product purity was confirmed by ^{1}H NMR spectroscopy and elemental analysis.

All manipulations in the preparations and measurements were performed in the dark or a dim red light.

Inclusion complexes α-cd–[Co(Hdmg)$_2$R(H$_2$O)]. The compounds [Co(Hdmg)$_2$R(H$_2$O)] and α-cd in 1:1 molar ratio were dissolved in water by constant stirring for 30 min at 50 °C. The resulting solution was filtered and the filtrate was stored at 25 °C in the dark. One week later, red-brown crystals precipitated. The product was filtered off and washed with water: R = Pr^n, yield 56% (Found: C, 41.95; H, 6.60; N, 4.35. Calc. for C$_{47}$H$_{85}$CoN$_4$O$_{36}$: C, 42.1; H, 6.40; N, 4.20%); R = Bu^i, yield 50% (Found: C, 42.4; H, 6.85, N, 4.20. Calc. for C$_{48}$H$_{87}$CoN$_4$O$_{36}$: C, 42.55; H, 6.45; N, 4.15%); R = Bu^n, yield 50% (Found: C, 42.6; H, 6.80; N, 4.35. Calc. for C$_{48}$H$_{87}$CoN$_4$O$_{36}$: C, 42.55; H, 6.45; N, 4.15%); R = n-C$_5$H$_{11}$, yield 52% (Found: C, 43.75; H, 6.95; N, 4.30. Calc. for C$_{49}$H$_{87}$CoN$_4$O$_{35}$: C, 43.55; H, 6.50; N, 4.15%).

^{1}H NMR spectroscopy

All ^{1}H NMR spectra were obtained at Bruker AM 500 MHz spectrometer. One-dimensional ^{1}H NMR spectra comprised 16 K data points and were zero-filled before Fourier transform. Chemical shifts were referenced in D$_2$O with respect to external sodium 4,4-dimethyl-4-silapentane-1-sulfonate. Two-dimensional nuclear Overhauser effect spectroscopy (NOESY) was performed by standard methods with a 5.8 μs, 90° pulse and 1 K × 256 time domain. The mixing time was 0.85 s.

Quantitative ^{1}H NMR spectroscopy[2,16]

Equimolar α-cd and $[Co(Hdmg)_2R(H_2O)]$ were dissolved in D_2O. A series of solutions of known concentrations (10^{-3}–10^{-4} mol dm^{-3}) were prepared by stepwise dilution. The HDO signal was preirradiated in the measuring process.

Formation constant (K_a) calculations[16]

Equation (1) describes the equilibrium of formation of 1 : 1 inclusion complexes; K_a is the formation constant and can be expressed by equation (2).

$$[Co(Hdmg)_2R(H_2O)] + \alpha\text{-cd} \overset{K_a}{\rightleftharpoons} \alpha\text{-cd–}[Co(Hdmg)_2R(H_2O)] \quad (1)$$

$$K_a = [\alpha\text{-cd–}Co(Hdmg)_2R(H_2O)]/[Co(Hdmg)_2R(H_2O)][\alpha\text{-cd}] \quad (2)$$

The chemical shifts observed for the inclusion complexes vary on changing the concentration of the 1 : 1 adduct. The relation between the chemical shift change and the concentration is given by equation (3),[16] where Δ is the difference between the

$$\Delta = \Delta_0 - (\Delta/X)^{\frac{1}{2}}(\Delta_0/K_a)^{\frac{1}{2}} \quad (3)$$

observed chemical shifts of the probe protons and those for the same protons in the free components; Δ_0 is the limiting chemical shifts, at which the 1 : 1 adducts are assumed to be fully formed, and X is the concentration of the 1 : 1 adduct. Therefore, the inclusion formation constants and the estimated associated errors could be calculated from quantitative ^{1}H NMR data by the application of linear least-squares programs to equation (3).

Crystallography

Raw intensities for $[Co(Hdmg)_2Pr^n(H_2O)]$ were collected in the variable ω-scan technique on a Rigaku AFC7R four-circle diffractometer using Mo-Kα (λ = 0.710 73 Å) radiation. An empirical absorption correction based on ω-scan data was applied. Raw intensities for the corresponding α-cd inclusion complex were collected on a Rigaku RAXIS-IIS imaging-plate system with a rotating-anode X-ray source (50 kV, 90 mA) and corrected for absorption using the DIFABS program.[17] For each complex all calculations were performed on a 486 personal computer with the SHELXTL-PC program package.[18] The Patterson method yielded the positions of the metal atoms and all non-hydrogen atoms were derived from subsequent Fourier-difference syntheses. The hydrogen atoms attached to the carbons of the ligands were placed in calculated positions (C–H 0.96 Å), assigned fixed isotropic thermal parameters, and allowed to ride on their respective parent atoms. Analytical expressions of atomic scattering factors were employed and anomalous dispersion corrections were incorporated. Refinement (on *F*) of the coordinates and anisotropic thermal parameters of the non-hydrogen atoms was carried by the full-matrix least-squares method.

Atomic coordinates, thermal parameters, and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1996, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 186/227.

Results and Discussion

NMR studies

One-dimensional ^{1}H NMR. The NMR method is a powerful technique to investigate the formation of inclusion complexes and interaction between cyclodextrins and substrates.[16,19–21] Previous studies have indicated that the formation of inclusion complexes usually causes significant chemical shift changes for H^3 and H^5, which are directed toward the interior of the cd cavity, whilst only marginal upfield shifts are observed for H^1, H^2 and H^4, which are located on the exterior of the α-cd torus, and H^6, which is at the narrow opening of the α-cd. On the other hand, some protons of guest molecules, inserted into the cd cavity, show obvious changes in chemical shifts. The magnitude of all the above chemical shift changes depends on the binding force between the substrate and cd. It is also related to the stability and concentrations of the inclusion complexes. Moreover, being due to the weak interaction between the host and guest, they are usually smaller than 0.1 ppm as described in the literature.[16,19–21] The chemical shifts of α-cd, $[Co(Hdmg)_2R(H_2O)]$ and α-cd–$[Co(dmg)_2R(H_2O)]$ (R = Pr^n, Bu^i, Bu^n or n-C_5H_{11}) are given in Table 1. Comparing the chemical shifts of the host, guest and inclusion complexes with each other, it can be concluded that: (*a*) after formation of inclusion complexes, upfield shifts of about 0.1 ppm are induced for H^3 and H^5; (*b*) upon inclusion, the asymmetry of the α-cd cavity causes the resonances of the symmetry-related α-protons, which are located on carbons directly connected to cobalt, to split into two signals; moreover, the resonances of the protons of the R ligands show downfield shifts to different extents, the most obvious (about 0.15 ppm) being found for one α-H; (*c*) the chemical shifts of methyl groups of the equatorial ligand move downfield by about 0.06 ppm and the singlet resonance splits into a doublet, which indicates that their chemical environments are not equivalent after formation of the adducts; (*d*) from the integrated signal areas, the molar ratios of α-cd to $[Co(Hdmg)_2R(H_2O)]$ are estimated to be 1 : 1.

The above experimental data suggest that 1 : 1 inclusion complexes involving α-cd and $[Co(Hdmg)_2R(H_2O)]$ in aqueous solution are formed.

Two-dimensional NOESY. Two-dimensional NOE spectroscopy,[22,23] which is normally employed to provide through-space connectivity between protons, can give structural information about molecules. In our experiment, we observed the connectivities between the alkyl groups R and α-cd in the inclusion complexes. With R = Pr^n, Bu^n and n-C_5H_{11} there are connectivity signals between the methyl groups of the alkyls and H^5 of α-cd. In addition, with R = n-C_5H_{11} there is a signal between the γ-methylene and H^5. However, with R = Bu^i, there was no signal. The above observations indicated that the R groups are included into the α-cd cavity, and longer carbon chains are inserted more deeply. Moreover, since the methyl groups at the end of alkyl chains and H^5 are near the narrow opening of α-cd, we suggest that the plane involving dmg and the cobalt atom is at the wide opening of α-cd. The absence of other NOE signals may be due to[23,24] (*i*) a large (> *ca.* 4 Å) interproton distance or (*ii*) short $T_{1\rho}$ values.

Formation constant (K_a). According to the above NMR results, the protons H^3 and H^5 of α-cd and some other protons of R or $Co(dmg)_2$ can be used as probes for quantitative measurement of the formation of α-cd–$[Co(Hdmg)_2R(H_2O)]$ inclusion complexes. In this study H^5 (of α-cd), CH_3 (of oxime) and α-H (at carbon connected directly to cobalt) were chosen as probe protons. The values of K_a and Δ_0 were calculated from equation (3) and are in acceptable agreement with each other for all α-cd–$[Co(dmg)_2R\text{-}(H_2O)]$ inclusion complexes according to the different probe protons (Table 2). Thus, K_a and $-\Delta G$ for five α-cd–alkylcobaloxime complexes are in the range 3.3×10^2–1×10^4 dm^3 mol^{-1} and 14.3–22.9 kJ mol^{-1}, respectively. The order of ease of formation is n-C_5H_{11} ≫ Bu^n > Pr^n > Bu^i. It is interesting that K_a of the n-C_5H_{11} complex is much higher than those of the other inclusion complexes. This indicates that the longer the alkyl chain the deeper is the inclusion of the R group into the α-cd cavity, as suggested by two-dimensional NOESY. Therefore, hydrophobic and van

Table 1 Chemical shift data (δ) for $[Co(Hdmg)_2R(H_2O)]$, α-cd and α-cd–$[Co(Hdmg)_2R(H_2O)]$

			R = Pr^n		R = Bu^i		R = Bu^n		R = n-C_5H_{11}	
			Guest	Complex	Guest	Complex	Guest	Complex	Guest	Complex
R	α-H		1.72	1.87	1.72	1.78	1.76	1.86	1.75	1.91
				1.73		1.73		1.77		1.77
	β-H		0.80	0.94	0.73	0.81	1.16	1.35	1.20	1.36
	γ-H		0.72	0.80	0.69	0.75	0.78	0.91	1.14	0.94
	δ-H						0.77	0.90	0.80	0.75
	ε-H								0.79	0.73
Hdmg	CH_3		2.23	2.29	2.24	2.26	2.23	2.29	2.23	2.30
				2.28		2.25		2.27		2.28
α-cd	H^1	5.04		5.04		5.04		5.04		5.04
	H^2	3.64		3.64		3.64		3.64		3.64
	H^3	3.98		3.87		3.95		3.89		3.86
	H^4	3.58		3.58		3.57		3.57		3.57
	H^5	3.83		3.78		3.80		3.77		3.76
	H^6	3.86		3.86		3.86		3.86		3.86

Concentrations of α-cd–$[Co(Hdmg)_2R(H_2O)]$ are about 3.6×10^{-3} mol dm^{-3}.

Table 2 Values of K_α, $-\Delta G^\circ$/kJ mol^{-1} and Δ_0/Hz for inclusion compound formation involving $H_2[Co(Hdmg)_2R(H_2O)]$ and α-cd

	H^5			CH_3			α-H		
R	K_a	$-\Delta G^\circ$	Δ_0	K_a	$-\Delta G^\circ$	Δ_0	K_a	$-\Delta G^\circ$	Δ_0
Pr^n	$(4.9 \pm 0.2) \times 10^2$	15.4 ± 0.1	46.6	$(7.6 \pm 0.3) \times 10^2$	16.4 ± 0.1	56.7	$(5.3 \pm 0.2) \times 10^2$	15.5 ± 0.1	154.1
Bu^i	$(3.7 \pm 0.3) \times 10^2$	14.7 ± 0.2	28.0	$(3.3 \pm 0.2) \times 10^2$	14.3 ± 0.2	30.8	$(3.6 \pm 0.2) \times 10^2$	14.6 ± 0.1	68.7
Bu^n	$(9.3 \pm 0.7) \times 10^2$	16.9 ± 0.2	44.2	$(1.1 \pm 0.1) \times 10^3$	17.3 ± 0.3	53.2	$(1.1 \pm 0.1) \times 10^3$	17.3 ± 0.3	89.2
n-C_5H_{11}	$(7.4 \pm 1.0) \times 10^3$	22.0 ± 0.4	43.4	$(9.2 \pm 1.0) \times 10^3$	22.6 ± 0.3	39.8	$(1.0 \pm 0.1) \times 10^4$	22.9 ± 0.3	87.3

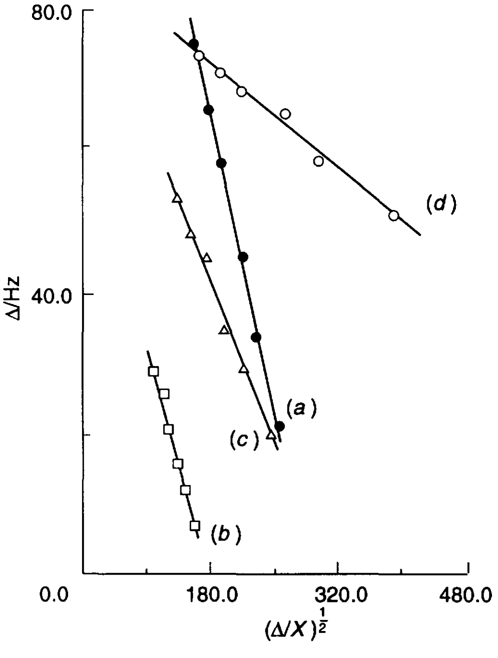

Fig. 1 Plots of Δ against $(\Delta/X)^{\frac{1}{2}}$ for α-H of dimethylglyoxime in $[Co(Hdmg)_2R(H_2O)]$ from quantitative ^1H NMR experiments: R = (*a*) Pr^n, (*b*) Bu^i, (*c*) Bu^n and (*d*) n-C_5H_{11}

der Waals interactions between them are enhanced. Our result is consistent with previous studies on cyclodextrin inclusion complexes involving alicyclic guests. In the latter a strong guest-size dependence is found for both the free-energy and enthalpy change for complex formation.[25] The smallest value of K_a for $[Co(Hdmg)_2Bu^i(H_2O)]$ may be due to the steric hindrance from the R group which cannot fit into the α-cd cavity (5 Å) properly and therefore a weak NOE is observed as mentioned above.

Crystal structures

Crystallographic data for $[Co(Hdmg)_2Pr^n(H_2O)]$ and its inclusion complex are given in Table 3.

$[Co(Hdmg)_2Pr^n(H_2O)]$. The atom numbering scheme of the crystallographically independent molecule is given in Fig. 2. Selected bond lengths and angles are in Table 4. The molecules lie across crystallographic mirror planes of symmetry which bisect the C(1)–C(1a) and C(2)–C(2a). Two hydrogen bonds between co-ordinated water and oxygens in other dimethylglyoximates were found [O(2b), 2.719; O(2c), 2.719 Å] as shown in Fig. 3.

The H_2O–Co–Pr fragment is characterized by a O–Co–C(1′) angle of 179.4° and Co–C(1′) and Co–O bond lengths of 2.000(8) and 2.063(4) Å respectively. The Co–CH_2–C_2H_5 angle is 129.3°. Atom C(1′) is slightly displaced from N(1) and N(1a), while O(1w) is slightly displaced from N(2) and N(2a); C(2′) and C(3′) are above the side of the equatorial ligands containing N(2) and N(2a). The $Co(Hdmg)_2$ unit appears to be relatively unaffected. The dihedral angle between the planes N(1), N(1a), O(1), O(1a), C(1), C(1a), C(3), C(3a), Co(1) (coplanar ± 0.014 Å) and N(2), N(2a), O(2), O(2a), C(2), C(2a), C(4), C(4a), Co(1) (coplanar ± 0.013 Å) is 1°; atom Co(1) is in the plane of N(1), N(1a), N(2), N(2a) (0.008 Å).

α-cd–$[Co(Hdmg)_2Pr^n(H_2O)]$. The structure of the molecule is depicted in Fig. 4. Selected bond lengths and angles are given in Table 5. The crystal is nearly isomorphous with crystals which have cage structure,[2] where the cyclindrical openings within the α-cd molecules are blocked at the open ends by continuous molecules (Fig. 5).

Inspection of Fig. 4 shows that the R group of $[Co(Hdmg)_2Pr^n(H_2O)]$ is included into the α-cd cavity from the secondary hydroxyl side. It also reveals that C(2′) and C(3′) are 0.57 and 2.05 Å respectively above the mean plane (plane 1) of the O atoms associated with the twelve secondary OH groups. Although C(1′) lies 0.28 Å below this plane, it clearly resides

Table 3 Crystallographic data for $[Co(Hdmg)_2Pr^n(H_2O)]$ and α-cd–$[Co(Hdmg)_2Pr^n(H_2O)]$*

Formula	$C_{11}H_{23}CoN_4O_5$	$C_{47}H_{83}CoN_4O_{30}\cdot 10H_2O$
M	350.3	1503.26
Crystal size/mm	0.24 × 0.31 × 0.40	0.24 × 0.22 × 0.32
D_c/g cm^{-3}	1.39	1.456
Space group	*Pnma*	$P2_12_12_1$
a/Å	14.587(3)	13.440(3)
b/Å	9.207(2)	17.593(4)
c/Å	12.475(2)	29.009(6)
U/Å^3	1675.4(2)	6859(3)
F(000)	736	3200
Unique data measured	2047	13 735
Observed data	1265	11 928
	$[\lvert F_o\rvert \geqslant 4\sigma(\lvert F_o\rvert)]$	$[\lvert F_o\rvert \geqslant 6\sigma(\lvert F_o\rvert)]$
hkl Ranges	0–18, 0–11, 0–16	−16 to 16, 0–22, −36 to 36
$2\theta_{max}$/°	50	
g In weighting scheme	0.0007	0
R_{int}	0.000	0.0653
R_F	0.059	0.0481
R′	0.085	0.0692
ρ_{max}, ρ_{min}/e Å^{-3}	+0.47, −0.64	+0.86, −0.53

* Details in common: orthorhombic, $Z = 4$, $\lambda = 0.710\,73$ Å, $w = \sigma^2(F_o) + gF_o^2$.

Table 4 Bond lengths (Å) and angles (°) for $[Co(Hdmg)_2Pr^n(H_2O)]$

Co(1)–O(1w)	2.063(4)	Co(1)–N(1)	1.896(4)
Co(1)–C(1′)	2.008(8)	Co(1)–N(2)	1.873(4)
O(1)–N(1)	1.364(6)	O(2)–N(2)	1.352(5)
N(1)–C(1)	1.288(7)	N(2)–C(2)	1.300(6)
C(1)–C(3)	1.474(8)	C(1)–C(1a)	1.465(11)
C(2)–C(4)	1.490(7)	C(2)–C(2a)	1.473(10)
C(1′)–C(2′)	1.237(12)	C(2′)–C(3′)	1.509(13)
O(1w)–Co(1)–N(1)	88.4(2)	O(1w)–Co(1)–N(2)	92.1(1)
N(1)–Co(1)–N(2)	98.9(2)	O(1w)–Co(1)–C(1′)	179.4(3)
N(1)–Co(1)–C(1′)	91.1(2)	N(2)–Co(1)–C(1′)	88.4(2)
N(1)–Co(1)–N(1a)	79.8(3)	C(1′)–Co(1)–N(1a)	91.1(2)
N(2)–Co(1)–N(2a)	82.3(2)	C(1′)–Co(1)–N(2a)	88.4(2)
N(1a)–Co(1)–N(2a)	98.9(2)	Co(1)–N(1)–O(1)	123.4(3)
Co(1)–N(1)–C(1)	118.0(4)	O(1)–N(1)–C(1)	118.6(4)
Co(1)–N(2)–O(2)	122.1(3)	Co(1)–N(2)–C(2)	116.4(3)
O(2)–N(2)–C(2)	121.4(4)	N(1)–C(1)–C(3)	123.8(5)
N(1)–C(1)–C(1a)	112.0(3)	C(3)–C(1)–C(1a)	124.1(3)
N(2)–C(2)–C(4)	123.5(5)	N(2)–C(2)–C(2a)	112.4(3)
C(4)–C(2)–C(2a)	124.1(3)	Co(1)–C(1′)–C(2′)	129.3(7)
C(1′)–C(2′)–C(3′)	126.0(9)		
O(1w) ··· O(2b)	2.719(4)	O(1w) ··· O(2c)	2.719(4)
Co(1) ··· O(1w) ··· O(2b)	118.6(5)		
O(2b) ··· O(1w) ··· O(2c)	97.0(5)		

above the rim defined by the H atoms of these OH groups. Atoms C(1′), C(2′), C(3′), Co(1) and O(1w) are 0.94, 0.17, 0.19, 0.77 and 0.72 Å respectively from the pseudo-C_6 axis. The plane (plane 2) comprising the four N atoms of the $Co(Hdmg)_2$ unit (coplanar ±0.003 Å) is nearly parallel to plane 1. The dihedral angle between planes 1 and 2 is 4°. The distances of N(1), N(1a), N(2), N(2a) from plane 1 are 2.33, 2.44, 2.30 and 2.20 Å respectively. In addition, there are three intra-adduct O ··· O contacts less than 3.3 Å between oxime and secondary OH groups: O(13) and O(2a) (2.84), O(33) and O(1) (2.65 Å), O(32) and O(2) (3.23 Å). Co-ordinated H_2O is involved in a hydrogen-bonding interaction with O(2w) (2.704 Å) and a secondary OH group [O(63)] in another cd molecule (2.833 Å). Part of the hydrogen-bonding interaction is indicated by dashed lines in Fig. 5.

The geometry of $[Co(Hdmg)_2Pr^n(H_2O)]$ is characterized by Co–C(1′) and Co–O bond lengths of 2.013(4) and 2.083(2) Å respectively with a C(1′)–Co–O angle of 175.9° and $Co–CH_2–C_2H_5$ angle of 124.0° respectively. The four N atoms of $Co(Hdmg)_2$ unit are coplanar within ±0.003 Å. The cobalt atom is displaced 0.038 Å from the mean plane towards the propyl. The bending angle of the $Co(Hdmg)_2$ unit is 10°.

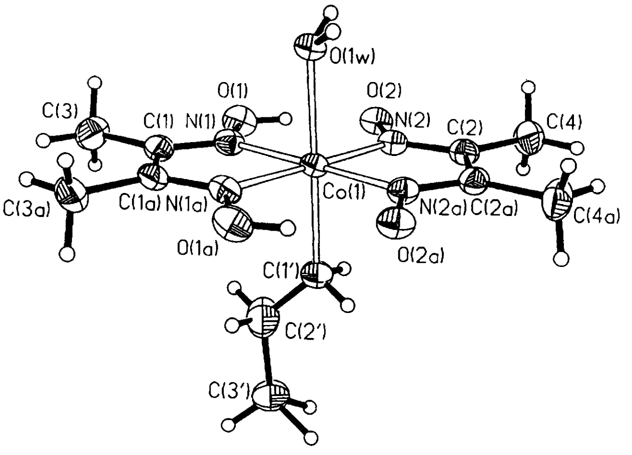

Fig. 2 Structure and numbering scheme of $[Co(Hdmg)_2Pr^n(H_2O)]$

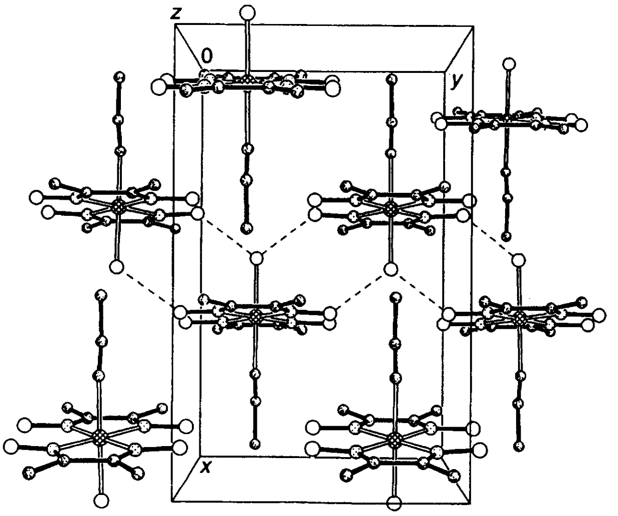

Fig. 3 Stereodrawing of the packing of $[Co(Hdmg)_2Pr^n(H_2O)]$ viewed down the *z* axis

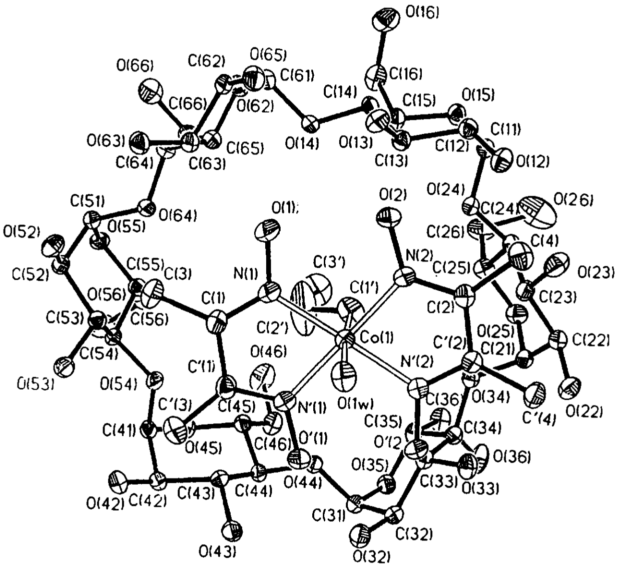

Fig. 4 Structure and numbering scheme of α-cd–$[Co(Hdmg)_2$-$Pr^n(H_2O)]$

Structure comparison. Our X-ray crystallographic investigation reveals that the α-cd molecule in the inclusion complex

Table 5 Bond lengths (Å) and angles (°) for [Co(Hdmg)$_2$Pr^n(H$_2$O)] in the inclusion complex

Co(1)–N(1)	1.901(3)	Co(1)–N(2)	1.898(3)
Co(1)–N′(1)	1.901(3)	Co(1)–N′(2)	1.885(3)
Co(1)–C(1′)	2.013(4)	Co(1)–O(1w)	2.083(2)
N(1)–O(1)	1.373(4)	N(2)–O(2)	1.353(3)
N(1)–C(1)	1.303(5)	N(2)–C(2)	1.313(4)
N′(1)–O′(1)	1.377(4)	N′(2)–O′(2)	1.374(3)
N′(1)–C′(1)	1.304(4)	N′(2)–C′(2)	1.305(4)
C(1)–C′(1)	1.465(5)	C(2)–C′(2)	1.473(5)
C(1)–C(3)	1.488(6)	C(2)–C(4)	1.501(5)
C′(1)–C′(3)	1.477(5)	C′(2)–C′(4)	1.484(5)
C(1′)–C(2′)	1.394(7)	C(2′)–C(3′)	1.500(7)
N′(2)–Co(1)–N(2)	82.4(1)	N(1)–Co(1)–N′(1)	80.5(1)
N′(2)–Co(1)–N(1)	177.4(1)	N(2)–Co(1)–N′(1)	177.5(1)
N(2)–Co(1)–N(1)	98.4(1)	N′(2)–Co(1)–N′(1)	98.7(1)
N(1)–Co(1)–C(1′)	92.6(1)	N(2)–Co(1)–C(1′)	90.8(1)
N′(1)–Co(1)–C(1′)	91.4(1)	N′(2)–Co(1)–C(1′)	89.9(1)
N(1)–Co(1)–O(1w)	91.5(1)	N(2)–Co(1)–O(1w)	89.1(1)
N′(1)–Co(1)–O(1w)	88.7(1)	N′(2)–Co(1)–O(1w)	86.0(1)
C(1′)–Co(1)–O(1w)	175.9(1)		
Co(1)–N(1)–O(1)	123.9(2)	Co(1)–N(2)–O(2)	124.0(2)
Co(1)–N(1)–C(1)	117.0(2)	Co(1)–N(2)–C(2)	115.2(2)
O(1)–N(1)–C(1)	118.8(3)	O(2)–N(2)–C(2)	120.5(3)
Co(1)–N′(1)–O′(1)	125.3(2)	Co(1)–N′(2)–O′(2)	122.7(2)
Co(1)–N′(1)–C′(1)	117.6(2)	Co(1)–N′(2)–C′(2)	116.3(2)
O′(1)–N′(1)–C′(1)	117.1(3)	O′(2)–N′(2)–C′(2)	120.7(2)
N(1)–C(1)–C′(1)	112.8(3)	N(2)–C(2)–C′(2)	113.1(3)
N(1)–C(1)–C(3)	123.7(4)	N(2)–C(2)–C(4)	124.1(3)
C′(1)–C(1)–C(3)	123.4(3)	C′(2)–C(2)–C(4)	122.7(3)
C′(1)–C′(1)–C(1)	111.8(3)	N′(2)–C′(2)–C(2)	112.7(3)
N′(1)–C′(1)–C′(3)	124.1(3)	N′(2)–C′(2)–C′(4)	124.1(3)
C(1)–C′(1)–C′(3)	124.1(3)	C(2)–C′(2)–C′(4)	123.1(3)
Co(1)–C(1′)–C(2′)	124.1(3)	C(1′)–C(2′)–C(3′)	117.1(4)

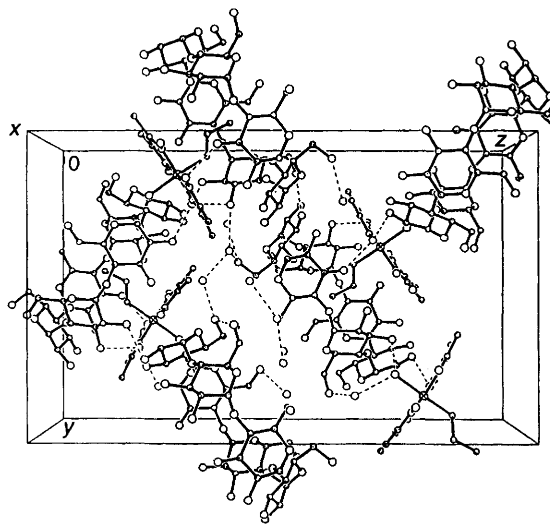

Fig. 5 Stereodrawing of the packing of α-cd–[Co(Hdmg)$_2$Pr^n(H$_2$O)] viewed down the *x* axis

assumes an unstrained, open, cyclic conformation common to all other inclusion complexes.[2] The C(1)–O(4)–C(4)–C(3) torsion angle appears to be confined to a narrow range 126 ± 10° and it is obviously different from native α-cd•2H$_2$O, where one of the angles is 170.4°.[26] In addition, a ring of hydrogen-bond distances between hydroxyl groups O(2)···O(3) in the inclusion complexes are in the normally accepted range of 2.8–3.10 Å. Therefore, compared to the native α-cd macrocycle,[26] that in the inclusion complex is rather cyclic and regular. On the other hand there are some obvious conformational changes in [Co(Hdmg)$_2$Pr^n(H$_2$O)] after insertion of the Pr^n group into the α-cd cavity: (*a*) the bending angle (α) of the Co(Hdmg)$_2$ unit becomes much more appreciable (from 1 to 10°), (*b*) the C(1′)–Co–N$_{eq}$ angles become larger by 1.5, 0.3, 2.4 and 1.5° respectively, (*c*) the Co–O length is increased by 0.02 Å, (*d*) the Co atom moves out of the plane of the four equatorial N atoms toward the propyl (0.038 Å), (*e*) the axial C(1′)–Co–O angle becomes smaller by 3.5°, and (*f*) C(1′)–C(2′) bond length at the axial R group is increased by 0.16 Å, whilst Co–C(1′)–C(2′) is decreased by 5°.

It is well known that the Co(Hdmg)$_2$ unit, like the corrin ring in cobalamins, is very flexible.[13,27] Convincing evidence has been presented that cobalt dimethylglyoximes often exhibit an upwardly bent conformation (butterfly conformation).[28,29] The extent of such a conformational distortion from planarity is measured by the bending angle (α) between the two Hdmg planes of the Co(Hdmg)$_2$ unit and displacement (*d*) of Co from the four-N equatorial plane. The bulk of the axial ligands (R and L) could influence the α and *d* values. It has been shown that on increasing the bulk of L in a cobaloxime α becomes much more negative, and the Co atom moves from the four-N equatorial plane to the base group. On the other hand, increasing the bulk of R makes the bending angle more positive and the cobalt atom moves from the four-N equatorial plane to the R group. In addition, the steric interaction of the R group with Co(Hdmg)$_2$ could induce (*a*) a widened L–Co–C angle, (*b*) C–Co–N$_{eq}$ angles that deviate from 90°, and (*c*) an increased Co–C(1)–C(2) angle and a shortened CH$_2$–R′ bond length. In addition, the Co–C bond has been demonstrated to be responsive to the conformational distortion of the Co(Hdmg)$_2$ unit. Slight, yet significant lengthening (0.1–0.2 Å) of the Co–C bond is found with increasing steric bulk of the R and L groups.[13] Moreover, kinetic studies on [Co(Hdmg)$_2$(CHMePh)(PR$_3$)] by Geno and Halpern[29] revealed that the Co–C bond-dissociation energy exhibits a marked inverse dependence on the size of L. The trend is consistent with results of structural studies. Further, X-ray crystallographic studies on alkylcobaloximes have revealed that the effect of the *trans* ligand on the Co–C bond length is steric and not electronic.[30] Solution Fourier-transform Raman results have provided clear evidence that there is no *trans* electronic effect on the Co–C stretching frequency.[31] This is consistent with an approximate *ab initio* study of angular distortion of the Co–C bond in a model of coenzyme B-12, which also shows that steric interaction is primarily responsible for the weakening of the Co–C bond.[32]

Therefore, with careful analysis the conformation changes of [Co(dmg)$_2$Pr^n(H$_2$O)] after the Pr^n group is included in the α-cd cavity, we propose that there is steric interaction between the α-cd and the equatorial ligands (Hdmg)$_2$ in α-cd–[Co(Hdmg)$_2$Pr^n(H$_2$O)], which indicates that the equatorial ligand bends away from Pr^n towards the axial H$_2$O and Co moves from the four-N equatorial plane towards n-propyl, so that the Co–O bond length is increased and all C–Co–N$_{eq}$ angles become larger. It seems likely that the capped cd behaves as a bulky R group above the Co(Hdmg)$_2$ equatorial unit. Concurrently, the steric strain between the R group and (Hdmg)$_2$ is released. As a result, there are some changes, *i.e.* the smaller angles for C(1′)–Co–O, Co–C(1′)–C(2′) and the longer C(1′)–C(2′) distance. However, the Co–C(1′) bond length has no observable variation, which otherwise should be shorter. In short, the observed conformation and structural changes in the guest molecule in the cd inclusion complex are probably due to the hydrophobic interaction between the n-propyl and the α-cd cavity and steric interaction between the α-cd and Co(Hdmg)$_2$ unit.

Extensive investigation of B-12 models, especially alkylcobaloximes, has clearly shown that interaction of the 5′-adenosyl with the enzyme could lead to a 'pulling' or 'bending' of the Co–C bond which would weaken it.[13] Recently, studies on an analogue of 2′,5′-dideoxyadenosylcobalamin, which is very similar both structurally and electronically though functionally different to coenzyme B-12, suggested that the 2′-hydroxyl group in coenzyme B-12 was involved in a hydrogen-bonding interaction at the active site which contributed to the steric enzyme-induced distortion of coenzyme B-12.[33] Thus, it seems likely that the interactions between alkylcobaloximes and α-cd are somewhat similar to that between 5′-deoxyadenosylcobalamin and the protein in the B-12-dependent enzyme system. We believe that much more work is needed for precise elucidation of the mechanisms and reactivities.

Conclusion

It has been established from elemental analysis, one- and two-dimensional ^{1}H NMR, and X-ray diffraction studies, that α-cd can form 1:1 inclusion complexes with [Co(Hdmg)$_2$R(H$_2$O)] (R = Pr^n, Bu^i, Bu^n or n-C$_5$H$_{11}$). The solution and crystal structures of the inclusion complexes revealed that the alkyl groups of the guest molecules are located in the α-cd cavities and the planes involving the dimethylglyoximes and cobalt atoms are near the wide opening of the α-cd cavities. Upon inclusion of the R groups there are steric interactions between α-cds and equatorial glyoximes, as well as hydrophobic interactions between α-cd and alkyls. These induce conformational changes of the RCo(Hdmg)$_2$ as well as bond length and angle variations around cobalt, as shown in the crystal structure of α-cd–propylcobaloxime. In addition, comparing the K_a for four α-cd–[Co(Hdmg)$_2$R(H$_2$O)] complexes, it is evident that the size and length of the alkyls may affect the stability of adduct formation.

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